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LONDON
BAILLIÈRE, TINDALL AND COX
7 & 8, HENRIETTA STREET, COVENT GARDEN, W.C. 2
1929

Printed in Great Britain

EDUARDO PROVANO CATHCART,

M.D., D.SC., LL.D., F.R.S., C.B.E.,

PROFESSORI PHYSIOLOGIÆ APUD UNIVERSITATEM GLASGUENSEM

CUIUS INGENIO ET EXHORTATIONI

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PREFACE

THIS book was written primarily for the practitioner, with the object not only of indicating methods of treatment which he might employ in disorders of sleep, but of furnishing him, however provisionally, with a rational basis for the methods recommended. In addition, since no comprehensive treatise on the problems of sleep has appeared in English for some years, so far as I know, theoretical implications that may interest the researcher have not been disregarded. Hence the first chapter, to take an example, contains a brief account both of the normal physiological phenomena in sleep and of some of their pathological variants, experimental and clinical observations being as far as possible considered together. The position of the theoretical section at the end of the book is in accordance with the general plan; and it follows also the natural order, since even the most tentative theoretical conclusions can be satisfactorily based only upon a comprehensive survey of all the data, clinical and therapeutic as well as experimental.

The clinical material on which the writer's

own observations have been made, has been gathered in hospital and consulting practice, and especially at the Cassel Hospital, Guy's Hospital, the Phipps Psychiatric Clinic of the Johns Hopkins Hospital, and the Glasgow Royal Mental Hospital. Some of the matter of the following pages has already appeared in print in the *Guy's Gazette*.

I am indebted to the Assistant Librarians of the Royal Society of Medicine for help in finding the relevant literature.

R. D. G.

LONDON,
April, 1929.

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SLEEP

AND THE TREATMENT OF ITS DISORDERS

CHAPTER I

PHYSIOLOGY AND PATHOPHYSIOLOGY

"Of what nature are such sleeps as these? Are they remedial measures—trances in which the most galling memories, events that seem likely to cripple life for ever, are brushed with a dark wing which rubs their harshness off and gilds them over, the ugliest and basest, with a lustre, an incandescence? Has the finger of death to be laid on the tumult of life from time to time lest it rend us asunder? Are we so made that we have to take death in small doses daily, or we could not get on with the business of living?"—*Orlando*, by VIRGINIA WOOLF.

(*a*) General.

Depth of Sleep.—The depth of sleep can be measured by the amount of stimulus required to awaken the sleeper. In this way it is found that the threshold stimulus (*i.e.*, the least stimulus that will awaken) and therefore the depth of sleep, increases rapidly in the first hour of normal sleep, to fall at first rapidly and then more gradually towards the morning. Köhlschutter's experiments are classical. He used

noise as the awakening stimulus, a metal ball being allowed to fall upon a metal plate from various heights. The defect of this method was that the subject expected to be awakened. Michelson however, who used precautions to diminish the expectation of the subject, obtained similar results.

In a poor or light sleep, the apex of the curve representing the depth of sleep is reached more slowly than in sound sleep, and the curve runs for some time at a moderate height, instead of falling gradually towards morning. There is also some evidence that in a person going to bed after midnight, the maximum depth is reached more slowly than if he goes to bed before that time. There is considerable variation from one night to another in the same individual, but enough uniformity—*i.e.*, enough constancy of difference between the average sleep-curves of different individuals—to make the study of such curves profitable.

In children, there are two maxima of depth (Czerny), one being reached in the first or second hour, and the other, not so deep, in the seventh hour, deepening to the ninth hour. This is followed by a rapid diminution in the depth until the child awakens. In adults, in whom the second maximum is said not to occur, two types

of sleep-curve have been distinguished — an evening-type and a morning-type. In the evening-type, the maximum depth is rapidly attained, and is followed by a rapid diminution in depth. Persons of this type are fresh in the mornings The morning-type of sleep-curve approximates to what occurs in children, but with the difference that the first maximum is attained more slowly, in the third or fourth hour, and the second (morning) maximum is not so conspicuous as in children. Persons of this type are reputed to work best in the evenings.

It has however been asserted on the basis of experiment, that people in general work better in the evenings, than after waking in the mornings. In a number of healthy young men, it was found that the improvement in the evenings in the performance of a substitution test, in comparison with the early morning was as much as 6 per cent. Two explanations have been offered. The first is that " fatigue-toxins " which have hypothetically accumulated during the day, facilitate the evening's activity. The other and more likely explanation is that in the mornings the muscular relaxation which exists requires a preliminary " pulling in of the slack " before an efficient response occurs.

Other methods of estimating the depth of

sleep have been used to overcome the objections attached to Köhlschutter's and in a lesser degree to Michelson's method.

The tension of CO_2 in the blood and alveolar air has been utilised for this purpose. Another method is to record the movements of the patient during sleep, depth of sleep being assumed to be inversely proportionate to the amount of movement. A rubber-ball placed under the mattress and attached to a stout tube leading to a tambour, the pressure-changes in which are rendered on a kymograph, was the device used by Guttman. This method therefore examines sleep more from the motor aspect, while Köhlschutter's did so from the sensory side. The results obtained by Syzmansky and others by a similar method appeared to show that the depth of sleep varies considerably during the night. Deep sleep (" absolute rest ") is interrupted by periods of movement, which in the aggregate occupy a longer time than the period of absolute rest. There are not only considerable individual differences in the type of sleep, but variations in the same individual from day to day. In patients mentally ill (chiefly manic-depressives) there was an impressive similarity of the curves from day to day, with only brief periods that were free of movement. In psychoneurotic

patients, on the other hand, there was no constant curve, but a great variability from day to day. In them also there was a great susceptibility to hypnotics and to change of the hypnotic dosage, whereas in manic-depressive patients the curves were but little altered by hypnotics, even in large doses.

In children, the amount of movement during sleep is said to be increased by caffeine and atropine taken before bedtime, by study during the evening, by the presence of another child in the same room, and by suggestion (Karger).

Birth and Death.—The great frequency of births and deaths in the hours usually occupied by sleep is a popular belief which is statistically borne out. Of nearly 58,000 deaths in Berlin, Schneider found that a disproportionately large number occurred between 4 a.m. and 7 a.m. In Glasgow, Watson and Findlay found in a series of 14,000 deaths, a greater frequency between 5 a.m. and 6 a.m. than in any other hourly period of the twenty-four. It is usual to attribute these results to the lowered vitality of the night hours, which is assumed to be demonstrated by the physiological changes in respiration, circulation, and the like (*vide infra*). But a very similar distribution exists also in the case of births, which it would be odd to attribute to a lowered

vitality. Laignel-Lavastine, examining the birth statistics in a hospital in Paris over a period of 12 months, found these proportions:

Midnight to 6 *a.m.*	6 *a.m. to* 12 *Noon.*	12 *Noon to* 6 *p.m.*	6 *p.m. to* *Midnight.*
736	794	567	554

This does not completely substantiate the popular belief that births are specially frequent at night, but it does show the preponderance of births in the hours from 12 midnight to 12 noon, in comparison with the period 12 noon to 12 midnight.

(*b*) **Systematic.**

All experimental work on the physiology of sleep is rendered very difficult by the number of factors involved. It is wiser to speak of the physiological accompaniments of sleep, than of its physiology; for almost any one of the ordinary physiological changes that can usually be observed may be absent in a sleep normal in all other respects.

Nervous System.—The changes more directly dependent upon the state of the nervous system are the muscular flaccidity, which is generalised except in the orbicularis oculi, as Lhermitte points out, and in the sphincters of the iris, the bladder, and the rectum. The closure of the

orbicularis oculi is considered to be an active affair, since the eyes do not close completely from mere loss of tone in this muscle (*cf.* the half-open eyes as they are seen post-mortem). In many people also the masseters must retain their tone, since the mouth is kept closed. Infants not infrequently sleep with clenched fists, betokening an active contraction of the flexors of the fingers. The general diminution in muscle-tone is so great that in puppies, for example, the intestinal movements can be easily seen through the relaxed abdominal wall. The eyeballs are turned upwards and slightly outwards. The upward turning of the eyes results in protection against any illumination that might penetrate the closed eyelids. Piéron has noticed that on opening the eyes in a bright light, the eyeballs tend to turn upwards and avoid the light.

The outward divergence may betoken a reversion to a more primitive condition of independence of the movements of the two eyes. The pupils are narrow, but they react to light, although not rapidly. They will dilate however if a sufficient peripheral stimulus is applied to some other sense-organ. Any stimulus tends to bring the eyeballs back to the normal position, so that observation of their actual position during sleep is very difficult.

The possible reasons for the pupillary constriction are discussed in the chapter on Theories of Sleep (Chapter V.).

The condition of the reflexes, especially of the tendon reflexes, is not easy to examine during sleep. In some adults in deep sleep, but especially in infants, an extensor plantar response has been obtained. The basis of this reversal is uncertain. It may be that the flexor reflex is a phenomenon of " long-circuiting," and that where the cerebrum is functionally more or less isolated, as it is sometimes assumed to be in deep sleep, the extensor response appears as a manifestation of activity not higher than the medullary level. The extensor reflex then represents part of a massive defensive-reflex, the rest of which consists in flexion of the ankle, withdrawal of the leg, and so on: or it may be part of an automatic movement of progression as in walking (Pierre Marie and Foix), since the extension of the great toe and the withdrawal of the leg is frequently associated with extension of the other lower limb. Whatever the reflex-pattern involved, it is possible to regard it as a release phenomenon, of which the extension of the great toe is a part, and which is uncovered by the loss of cortical participation.

The cutaneous reflexes are first slightly in-

creased during sleep, but later they diminish progressively. In disease, these reflexes are diminished or lost when the pyramidal-tract connection with the brain is interfered with or severed. This furnishes further presumptive evidence that a functional disassociation of the brain from the spinal levels occurs in sleep. On the other hand, sleep raises the sensory threshold. Hurst has shown that some of the cutaneous reflexes at least disappear when the skin is anæsthetic (as in hysterical anæsthesia). Hence the diminution of skin-reflexes in sleep might be accounted for in whole or in part by the raising of the sensory threshold, rather than from functional interference with pyramidal conduction.

The knee-jerks gradually diminish (Piéron) till they are completely lost in deep sleep. Not much can be argued from this, since the briskness and amplitude of the knee-jerks, on which nearly all the investigations of tendon-reflexes in sleep appears to have been done, depends so much on muscular tone. But it has been shown that the diminution does not run parallel with the loss of muscular tone, so that presumably the diminution of the jerk and loss of muscle-tone are independent phenomena. In puppies, Kleitman showed that the knee-jerk was fully preserved in sleep.

The cough reflex from tracheal or laryngeal stimulation diminishes. This is obviously of clinical importance in respiratory diseases with much secretion.

It is usually said that the threshold for sensory stimulation is raised during sleep, sight being proportionately more dulled than touch and touch than hearing. The difficulty in verifying this statement lies in the difficulty of determining how the sensory acuity shall be measured. The stimulus may not be strong enough to excite full consciousness (*e.g.*, to awaken the sleeper), but it may be registered mentally, as in certain peripherally-determined dreams. One method of determining the sensory threshold in sleep consists in observing at what grade of stimulation a muscular movement not being an elementary direct reflex is produced; but the difficulty here is the diminution of muscle-tone, so that contraction takes place less readily, from the necessity for a preliminary pulling in of the slack. A dilatation of the pupil or a change in the respiratory rhythm may signify the passing of a sensory impulse over to the motor side, where no other signs of the effectiveness of a sensory stimulus can be observed. Since such reflex effects can be produced and since some of these effects are " purposive " motor activities,

although consciousness is not involved, it is evident that in sleep, the different levels of the nervous system are functionally affected in different degrees. When we come to the consideration of pathological variants of sleep (Chapter III.), it will be seen that in sleep some levels may exhibit no functional interference at all, so that they are capable of normal activity, while the rest of the nervous system is in the state which we recognise as sleep. Furthermore, not only may there be a dissociation of functions of different level, but there may be dissociation within the same level of activity, as in somnambulism (*vide* Chapter III.).

Although organised, useful movements can occur during sleep, for example, in soldiers who have marched while sleeping, these movements are of the automatised kind, in direct response to the stimulus of the moment. Intelligent activity—*i.e.*, activity varying in response to changing and complicated stimuli and with a remoter purpose, does not occur in normal sleep; nor does it occur in pathological variants of sleep, except in "somnambulists" of so highly organised a kind, that "sleep" in any ordinary sense comes to be a misnomer for their condition.

Circulatory System.—The circulatory changes in sleep are well known. The pulse slows, but

when conditions are properly controlled, the slowing that can be specifically attributed to sleep itself is very slight, and it has been asserted that the relation and absolute duration of the phase of the cardiac cycle is not different in sleepless rest and in normal sleep (Kanner). On the other hand, sleep with an increased pulse-rate exhibits a proportionately increased duration of systole and therefore increases the work of the heart, in comparison with normal sleep or sleepless rest. For example, a 16-year-old boy who in the daytime had a pulse-rate of 83 and a time of action (systolic time) occupying 40·72 per cent. of the total cardiac cycle, showed in sleep as the results of an exciting dream a pulse-rate of 104 and a time of action of 49·71 per cent.

The blood-pressure (measured in the brachial or other limb-artery), a change in which is now properly regarded as a secondary concomitant and not as an essential determinant of sleep, usually falls.

Commonly the systolic pressure falls from 15 to 30 mm. of mercury within the first two hours (Muller) and rises gradually in the later part of the night. It has been said that the fall is greater in women (Blumer). Campbell and Blankenhorn recorded an average fall from 110 to 101 mm. in 28 normal young men during sleep,

the fall being greatest at the end of the fourth hour. Muller's experience that the minimum is reached at the end of the second hour may be the result of the small dose of veronal he used to induce sleep. Landis, using the Erlanger sphygmomanometer for continuous registration obtained a fall of blood-pressure from 110/74 to 94/68 as his subject went to sleep. Awakening to sudden stimuli was accompanied by a steep rise in blood-pressure, while in natural awakening the rise was more gradual. The change in blood-pressure was but little influenced by the position of the body; whether the subject fell asleep while inclining or in a semi-erect position, the changes in blood-pressure were very similar. The fall in pressure is probably partly due to the diminution in pulse-rate, and partly to peripheral vaso-relaxation.

Normally there is a slight rise in pressure before waking and an abrupt one afterwards (Blankenhorn *et al.*).

Patients with an abnormally high blood-pressure seldom show a return to a normal level of pressure during sleep; and the higher the pressure while awake, the less according to some observers does it fall during sleep (Campbell and Blankenhorn). But Brookes and Carroll found that in 39 subjects with a high blood-pressure

(the systolic pressure averaging 204 mm.) an average fall of 44 mm. occurred after two hours' sleep.

The real fall in cerebral blood-pressure in sleep must be considerably less than the apparent fall, since the cerebral pressure would actually be higher in the recumbent position of sleep than in the erect position of the daytime, if the aortic pressure did not fall considerably. Recently it has in fact been shown that the retinal distolic pressure rises in changing from the erect to the prone position (Berens *et al.*).

There is also some clinical evidence which suggests that the blood-pressure within the cranium is frequently higher in the recumbent position at night than in the sitting position. One of the commonest complaints and characteristic signs of cerebral contusion (after the acute stage is passed) is the increase in headache when the patient lies down, and the difficulty in sleeping unless propped up by pillows. The effect of the recumbent position is evidently to congest further the already œdematous area of the contusion.

In face of the usual rule, that blood-pressure falls and the circulation is in general quieter during sleep, it is a curious fact that sudden hæmorrhages, whether cerebral, pulmonary, or

gastro-intestinal, as well as anginal pains which awaken the patient, and sudden deaths, for example from ventricular fibrillation, should be comparatively so frequent during the period of sleep. Sir Samuel Wilks long ago raised this question, and MacWilliam has recently answered it. In one of his subjects, the systolic pressure during the day in the recumbent position was 110 mm. On walking twenty steps upstairs it rose to 140 mm., but immediately after awakening after a disturbed night, it reached 182 mm., and 15 minutes later the pressure was still 145 mm. In another subject, a dream was accompanied by a rise of systolic pressure from 130 to over 200 mm. MacWilliam stated that during another dream, his subject's radial artery was large and tense and difficult to obliterate, and that the range of pressure-variation at each beat was palpably large (*cf.* Kanner's observation, *supra*, on the duration of systole during a disturbing dream).

Stimulation of the cardiac sympathetic, such as may occur from the emotional disturbances of dreams, especially when associated with a high blood-pressure, favours ventricular fibrillation. " Death," says MacWilliam, " may come like a thief in the night to a susceptible person living with circulatory conditions that approach

the danger-line, although the conditions may in favourable circumstances, and barring fresh developments, be compatible with many years of comparatively active life."

That the circulation through the brain diminishes during sleep might be expected to follow from the general falling-off in circulatory activity, since the cerebral circulation is closely although not entirely dependent on the latter (although the hydrostatic factor works in the contrary sense, as has been pointed out). The depression of the fontanelle in sleeping infants, and observations made through trephine or other gaps in the skull of adults, have substantiated this deduction, although some observers have seen no alteration in the vascular appearance of the brain surface during sleep (Kleitman). Occasionally an actual increase of the cerebral circulation has been observed. It has also been held that an increase in the volume of the limbs shown plethymographically during sleep, implies a decrease in the cerebral circulation by a kind of hour-glass arrangement; but experiment has shown that the other segment of the hour-glass complementary to the limb-volume is not so much the cerebral as the abdominal reservoir. On all the evidence, the diminution of the cerebral circulation on which Mosso at first placed

emphasis, is not invariable. Weber, after analysing the available results in the literature, concluded that in sleep there is usually an increase in the quantity of blood in the limbs and brain, and a diminution in the abdominal organs.

The swelling of the eyelids and face, and the pruritus often associated with sleep, are presumably related to the peripheral vaso-dilatation that usually accompanies sleep.

Respiration.—Breathing is usually slower in quiet sleep than on waking, but slowing is not invariable. It has been noted that the respiratory rate is frequently faster on passing from wakefulness to sound sleep, and that often there is no change in rate. Very slow rates are said to be always increased on going to sleep (Reed and Kleitman).

With the respiration as with the circulation, the change in the functional condition is probably not specifically related to sleep, but it can be largely accounted for as result of rest in the recumbent position (Piéron). It is usually stated that the breathing becomes thoracic, but this is not invariable. Some observers have not found it so at all (Reed and Kleitman). The relative length of the respiratory phase may be altered, inspiration being relatively longer, and even absolutely longer than expiration. This is prob-

ably the result of the general muscular relaxation. Snoring is another result of the loss of muscular tone, the soft palate partly obstructing the breathing and vibrating as the air passes.

The ventilation of the lungs diminishes. Binet and Dautreband found a diminution of nearly 25 per cent., the total ventilation falling from 53 litres in 6 minutes in the waking state to 42 litres in a similar period of sleep. The gaseous interchange also alters qualitatively. In comparison with the waking condition CO_2 is excreted less and more O_2 is absorbed; in other words, the respiratory quotient falls. But the alveolar CO_2 rises very rapidly during the first hour of sleep, to fall gradually towards morning. The hydrogen-ion concentration in the blood also rises. The respiratory centre must therefore be less sensitive than in the waking state. This may account for the occurrence of Cheyne-Stokes respiration, which is a phenomenon of diminished sensitiveness of the respiratory centre. To this diminished sensitiveness may in part be attributed the tendency for dyspnœic attacks (whether associated with cardiac or other organic disease) to occur during sleep, a greater degree of acidosis being reached before the centre is stimulated than would be permitted while the subject is awake. The acidosis

leads by direct stimulation of the centre to violent respiratory efforts, so rousing the patient. The diminished sensitivity of the respiratory centre has also a bearing on the employment of hypnotics of the morphine group, which further depress the centre in a way that would be dangerous in conditions such as chronic bronchitis with a failing heart, if bronchial secretions were in consequence allowed to accumulate. This is the more apt to occur since the cough reflex is also diminished, as we have seen. But it has been shown that the administration of morphine produces an increase in the hydrogen-ion concentration of the blood (a relative acidosis). If this is not simply a secondary effect of depressing the respiratory centre, then it will act in a contrary sense to the depressant action of morphine upon the latter. The question of the relation of the changes in the pH of the blood to sleep has recently been discussed by Wuth. He points out that although there is relatively an acidosis during sleep, yet in insomnia and in the drowsiness that follows prolonged insomnia there is no acidosis. Furthermore, some hypnotics like alcohol and morphine produce an acidosis with a fall in the alkali reserve of the blood lasting several hours, while others, especially of the barbituric-acid series, produce an

increase in the alkali reserve and a rise in the pH—*i.e.*, an alkalosis for several hours, followed by acidosis, reaching its highest point in 3 hours, and finally again by an alkalosis which may last 72 hours. It is therefore clear that the acidosis found in normal sleep is not a necessary determinant of sleep. The interesting question arises whether after sleeping with a hypnotic of the barbituric-acid series the lack of the feeling of refreshment which follows normal sleep may be related to the alkalosis that follows the administration of these hypnotics, as contrasted with the acidosis of the normal condition.

Basal Metabolic Rate.—The B.M.R. is probably about 15 per cent. less in sleep than in the waking resting state. Since the metabolic rate (waking) under basal conditions (*i.e.*, at complete rest) may only be about one-third of the metabolic rate per hour of an active working day, the actual consumption of energy while asleep although only 15 per cent. less than while awake and at rest, is very much less than the utilisation of energy in the ordinary daily activities. "Qui dort, dine" is therefore true enough; but it is true also that the sleepless patient uses but little more energy if he remains resting than he would do if he were asleep, the recumbent, compared with the sitting, position being very

economical of energy. The metabolism is 80 per cent. lower during sleep than when the subject is awake and sitting up (Benedict and Carpenter). In children, Benedict showed that a boy of six burned 36 calories per hour of sleep, but in waking activity might use 90 to 100 calories per hour; while a 15-year-old girl burned 50 calories per hour while asleep and 200 calories, or four times as much, during her active day. In both cases therefore the energy-consumption was four times as great in daily activity as it was in sleep. But in making inferences of this kind, it has to be remembered that even slight restlessness will greatly increase the energy requirement and more pronounced degrees of restlessness—*e.g.*, in crying—may increase the metabolism to more than three times the resting or sleeping rate (Aron). It is well known that the energy-requirements during the adolescent period of life is very great. Holt says that at this time a child may need 1,000 calories more in the 24 hours than an adult. It is sometimes difficult even with the best feeding to give them this, especially if they are overworking at school, and not getting enough sleep. It is often better to prescribe more sleep than more food for such children.

Alimentary System. — The gastro-intestinal movements are less active during sleep than in

the working hours, and the alimentary secretions are diminished. This diminution can be fully accounted for, according to Piéron, by the horizontal position of rest and by the abstinence from food. He quoted a case of duodenal fistula recorded by Friedenwald, in which some of the intestinal movements could be observed through the wound. In the night, peristalsis was absent, whether the patient was awake or asleep. As a corollary, it was observed that when sleep intervened after the midday meal, peristalsis proceeded as usual.

" Why do people sweat more during sleep ?" was one of the " problems " of Aristotle. Piéron answered it by declaring that it is principally a matter of insufficient ventilation of the body, from an overabundance of bed-clothes, and a stagnant bedroom atmosphere. The peripheral vaso-dilatation that accompanies sleep is also a factor. The experience of sanatoria for tuberculous patients, where by free ventilation night-sweats are abolished, supports Piéron's contention.

Urinary Secretion.—The total quantity of urine secreted in sleep is proportionately and absolutely diminished as a rule. In other words, there is a negative water-balance during the day, and a retention of water at night. But here also

there are other factors besides the sleeping state itself, such as the lack of ingestion of water, which act indirectly to produce the result. Sleep occurring during the daytime is not necessarily accompanied by a relative diminution of urinary secretion. The total output of urinary constituents is diminished as the result of the diminution in water-output, but not to the same extent, the night-urine being necessarily more concentrated than the day urine. The proportions of the constituents are altered—the concentration of chlorides and uric acid is diminished, while the concentration of urea is increased, in the night urine. In other words, the excretion of urea, creatinine, and total nitrogen follows the volume-curve more or less closely, while there is a retention of chlorides and uric acid (Simpson). But when total amounts are concerned, the excretion of all the constituents is diminished in sleep. It is an interesting fact that sleep in darkness diminishes the total output more than sleep in the light; hence darkness alone probably entails a saving in the internal wear and tear of the organism. The total excretion of phosphorus seems to be about the same during the night's sleep as during the day; this is reflected in the greater concentration of the phosphorus in night urine (Kleitman). The acidity of the urine

secreted during sleep is greater. This is to be correlated with the increased H-ion concentration of the blood, the diminished sensitivity of the respiratory centre, and the rise in the alveolar CO_2 tension.

Temperature.—It is well known that the body-temperature varies throughout the 24 hours, being highest in the late afternoon between 4 p.m. and 6 p.m., and lowest in the early morning, between 1 a.m. and 3 a.m. The maximum variation in health is about 1·5° F. In night-workers who sleep by day, a reversal of this order occurs. But what the relation of this rhythm of temperature is to sleep, is difficult to determine; a similar variation occurs in the absence of sleep. It may be that sleep accentuates the variation, probably not in any specific fashion but only in a secondary manner, as the result of more complete muscular rest (*vide* Chapter V.).

The surface-temperature, which would ordinarily rise as the result of the peripheral vaso-dilatation that usually accompanies sleep, readily falls, as the result of sweat-evaporation and of direct radiation from the body-surface exposed to the atmosphere. The resulting loss of heat is not easily restored in sleep, since muscular movement is wanting, and muscular tone is so much diminished. It is from these conditions

that the need arises for a greater covering than would readily be endured in a daytime rest.

The electrical resistance of the body is gauged by placing the body in a string-galvanometer circuit, the electrodes being placed on the skin of two parts widely distant from one another. Waller, Farmer and Thouless, and Richter have found that the apparent resistance of the body to a small current passed through it, rises with the onset of sleep, continues for a time to rise, and finally falls with waking. Richter concluded that the electrical resistance measured in this way is a very satisfactory measure of the depth of sleep. What is measured in all such experiments is not the resistance of the body but the skin-resistance, for if a needle-point be used as the terminal electrode and the skin pierced with it, the resistance disappears. Landis, using a slightly different method designed to avoid any polarisation of electrodes, found that the resistance of the skin during sleep held a low but constant level after a short period of adaptation. He concluded that the change in resistance that his predecessors had measured was in fact simply a polarisation phenomenon round an unsatisfactory electrode, capillary currents being set up at the surface of separation of salt solution and skin. If Richter's results rather than Landis's

are confirmed, they will form a useful confirmation of results from other sources having similar bearings on a theory of the physiology of sleep (*vide* Chapter V.). It is difficult to see how the criticism of Richter's results can be valid on the ground of polarisation, since Richter showed that in using the same electrodes a great rise in skin-resistance occurred only if the electrodes were placed on the palms and not if they were placed on the back of the hands. He suggested accordingly that the increased resistance was an inhibitory effect upon the sweat-glands, which are plentiful in the palm and absent on the dorsum. This seems to contradict the observation that the activity of the sweat-glands is often apparently not inhibited but increased during sleep (but see Piéron, *supra*).

Summary of the Principal Physiological Changes Accompanying Sleep.—There is as a rule a general diminution in the intensity of the various vital activities, as measured by the pulse-rate, respiratory exchange, and basal metabolic rate. The only indisputable deduction is of a saving process: of a restorative process involving the binding of a large amount of energy, or in other words, of the conversion of nutriment into potential energy, there is little evidence, since the oxygen-consumption reaches a lower level

in sleep than it does at complete rest in the waking condition. The urinary changes are slight, and do not furnish material for significant comment.

Any diminution that may occur in the cerebral circulation is the result principally of the slowing of the pulse-rate. It is likely that the blood-pressure within the cranium is often at a higher level in sleep than in the waking erect position.

There is a rise in the reflex threshold at all levels of the central nervous system. The change sometimes observed in the plantar response suggests a dissociation of certain central neural pathways. There is a rise also in the sensory threshold: but this rise is at least in part a matter of a rise in the threshold of sensory perception regarded as a cortical function, as there is evidence that stimuli not strong enough to arouse consciousness nevertheless produce reflex effects. The great diminution in muscle-tone is the result of the recumbent position (absence of proprioceptive stimuli), together with the rise in the threshold of reflex conduction and the absence of external stimuli (and probably also a fourth factor, namely inhibition, *vide* Chapter V.).

The nocturnal fall in temperature is an expression of the daily variation in the temperature-curve. Like the other vital activities mentioned,

this fall occurs whether sleep takes place or not, provided the subject remains at rest.

The only signs of increased physiological activity are found in the increased tonus of the sphincters (iris, bladder, and rectum), and in the perspiration. The cardiac slowing and the lessening of gastro-intestinal mobility may be positive phenomena—not mere reductions in activity—and in that event could be referred to the same cause that is responsible for the sphincteric tonus. These effects as a whole have been attributed to an increase of function during sleep of the bulbo-sacral autonomic system, which of course is largely composed of vagal fibres, and the ensemble has been called a "vagotonic state." The general function of the vagus is inhibitory. If these observations and inferences are correct, then there is usually in sleep a widespread inhibition of peripheral activity, mediated by the vagus and the sacral autonomic nerves.

CHAPTER II

THE EFFECTS OF SLEEPLESSNESS

THIS is a very important topic for several reasons. Patients commonly believe the effects of insomnia to be calamitous. Insanity is nearly always dreaded by the sleepless neurotic, and even death suggests itself to him as a possible outcome of long-continued loss of sleep. Moreover, patients are encouraged in this belief by misleading newspaper reports of "suicide following insomnia".

It is significant that it is very difficult to obtain authentic instances of *very prolonged total insomnia in man.* No one nowadays goes long with no sleep whatsoever. Such accounts of such a condition as are obtainable usually come suspiciously from newspapers, and obscure provincial American newspapers of the '60's or '90's at that. The following is an example from the local press of Anderson, Indiana (December 11, 1898):

"David Jones, of this city, who attracted the attention of the entire medical profession two years ago by a sleepless spell of 93 days and last

year by another spell which extended over 131 days, is beginning on another which he fears will be more serious than the preceding ones. He was put on the circuit jury three weeks ago, and counting today has not slept for 20 days and nights. He eats and talks as well as usual, and is full of keenness and activity. He does not experience any bad effects whatever from the spell, nor did he during his 131 days. During that spell he attended to all his farm business. He says now that he feels as though he will never sleep again. He does not seem to bother himself about the prospect of a long and tedious wake." The fear that he expressed looked ominous—not of a "long and tedious wake," but of an advertisement of a *tour de force*.

Compulsory deprivation of sleep was a form of torture used until recently (apparently) in China; and not so very long ago, in Scotland also. Forbes Winslow quotes the following account. Curiously enough, it is from a similarly suspect source as the previous instance.

"A Chinese merchant had been convicted of murdering his wife, and was sentenced to die by being deprived of sleep. This painful mode of death was carried into execution under the following circumstances. The condemned man was placed in prison under the care of three of

the police guard, who relieved each other every other hour, and who prevented the prisoner from falling asleep night or day. He thus lived nineteen days without enjoying any sleep. At the commencement of the eighth day his sufferings were so intense that he implored the authorities to grant him the blessed opportunity of being strangled, guillotined, burned to death, drowned, garotted, shot, quartered, blown up with gunpowder, or put to death in any conceivable way which their humanity or cruelty could invent" (*Semi-monthly Medical News*, Louisville, 1859)

Other instances have a more reputable origin. Boerhave is recorded not to have closed his eyes in sleep for a period of 6 weeks, in consequence of his brain being overwrought by intense thought on a profound subject of study. Forbes Winslow quotes a case (without mentioning the source) of a deranged person who was not known to have slept at all for a period of 3 months. He was in the habit of walking long distances, greatly excited during the day, and at night he never ceased talking to imaginary persons. No form or dose of opium had any effect upon him.

A Dr. Wigan, whom Forbes Winslow also mentions, had a patient under his care who is

said not to have slept for 15 days. He was in the habit of getting up at night and tiring three horses with galloping, in the vain hope that excessive muscular fatigue might induce a disposition to sleep.

Since the clinical data are so nebulous, let us turn hopefully to the results of experiment.

Experimental Evidence.

The Effects of Sleeplessness in Animals.— There is no doubt that complete deprivation of sleep in animals can be lethal. Young puppies 3 or 4 months old, when deprived of sleep for 4 or 5 days, died either at the end of that time or if then allowed to sleep, after a few more days. The younger the animal the quicker its death.

During long periods of enforced insomnia in animals, it has been observed that the red blood corpuscles diminish in number by as much as 25 per cent. (Kleitman), and a loss of weight occurs up to 15 per cent. of the original weight. There is a rise in pulse-rate followed by a sudden and pronounced fall. There is also a gradual fall in the rate of respiration; and before death, a sudden fall in temperature. Some puppies refused food and sometimes water after 3 or 4

days; others ate well and preserved their weight for as long as 7 days. Convulsions preceded death in some cases; but some puppies that had been convulsed, recovered if allowed to sleep.

Since in all the experiments from which these results are derived it was necessary to keep the animals moving to prevent their falling asleep, it is probable that many of these effects were the results, wholly or in part, not of sleeplessness as such but of neuro-muscular exhaustion.

Kleitman's description of the behaviour of puppies during a period of enforced insomnia is of considerable interest. At first, by allowing the experimental animal to play with a litter-mate (which was being used as a control), it was possible to banish the somnolence completely. But after 3 or 4 days of continued wakefulness, the puppy lost all interest in its surroundings, and from being friendly became vicious and unmanageable, biting the litter-mate that tried to play with it. Some of the animals developed a photophobia and made for dark corners. Almost to the very last however it was possible to bring about a change in the animal's behaviour by a brisk walk. The transformation of a sleepy apathetic creature into an alert and wide-awake one was very striking. Ultimately the animal would become too weak to walk, and no amount

of pushing and pulling could keep it awake. Disturbances in body-righting also appeared—if held in the air, back downward, the neck would be permitted to become dorsiflexed, the head consequently hanging downwards. This implies a loss of the labyrinthine righting-reflexes. The puppies would go to sleep in this position, if left undisturbed. This stage was never reached before the fourth day, but varied in its onset with different animals. It was at this stage that they were allowed to sleep, and all recovered, except two, who died on the following day in convulsions without awakening.

The behaviour just described of animals kept continuously awake, closely resembles the behaviour of human beings who voluntarily deprived themselves of sleep. Both animals and men remained awake with apparent ease while they were kept moving; both showed an inability to remain awake as soon as muscular relaxation was permitted, after the earliest part of the enforced sleeplessness, and both showed a change of attitude from friendliness to animosity.

Post-mortem examination of the brains of Kleitman's puppies that died at the end of a period of insomnia failed to reveal any change in the cortex. Manaceine had previously reported capillary hæmorrhages as well as micro-

scopic changes in the cells of many other organs. Crile, in 84 experiments, on rabbits which had "abundant food, sleep and rest," but were prevented from sleeping during certain periods up to 100 hours in length, found cellular alterations in the central nervous system, in the liver, and in the adrenals. In the brains of these rabbits it was the cortex that was specially affected; next in intensity came affections of the cerebellum; while changes in the cells of cord and medulla were comparatively slight or absent altogether. The changes described by Crile in the cortex consisted in swelling of the cell, displacement of the nucleus, loss of Nissl substance, vacuolation of the cytoplasm, and finally rupture of the cell-membrane and loss of differential staining. In the liver of animals dead after continuous insomnia, Crile observed enlargement and swelling of the cells, general disappearance of the cytoplasm, presence of vacuolated spaces, and displacement and occasional disappearance of cells. Similar changes were observed in the adrenals. In Crile's experiments, cellular alteration were slight in the medulla, but Bast and Bloemendal found definite changes in the cells of the medulla in rabbits that had been deprived of sleep. There was chromatolysis constantly in the reticular formation in the commissural

nucleus of the solitarius, and in the dorsal nucleus of the vagus. The alterations described by Bast and Bloemendal were not very pronounced, however; the nucleus of many cells stained less deeply, from diminution in chromatin, and there was some vacuolation of the cytoplasm; Nissl bodies persisted but were granular in appearance. These alterations were confined to the visceral motor cells, whereas the somatic motor cells (*i.e.*, those of the anterior horn and of the hypoglossal nucleus) were not affected.

How is the discrepancy between Kleitman's results, who found no cellular changes after insomnia, and the results to some degree contradicting each other, of Crile and of Bast and Bloemendal, to be explained ? Kleitman, whose animals were allowed something approximating more nearly to rest than those of the other experimenters, suggests that the changes described by others were really the result of muscular exhaustion, and not of insomnia, since to keep them awake the animals were kept continuously on the move in Bast and Lowenhart's experiments. This suggestion is supported by the observations of Bast, Sebacht, and Vanderkamp that in animals which had been left without sleep, but which had not been fatigued to the

point of collapse, it was practically impossible to detect any deviation from the normal in the cells of the spinal cord. Only in animals fatigued to the point of collapse were there definite nuclear changes and chromatolysis in a sufficient number of cells to permit the conclusion that the changes were the result of the special conditions of the experiment.

This objection—that the cellular alterations are the result not of deprivation of sleep but of muscular exhaustion—does not however hold directly for the changes described by Bast and Bloemendal in the viscero-motor cells of the medulla. But a continuous tax on the somatic muscles, which usually work intermittently, involves a continuous additional tax on the important visceral centres, since heart and respiration are involved in extra work to supply the working muscles; so that here also the apparent effect of sleeplessness in these experiments in producing cellular changes may simply be the indirect results of unremitting muscular exertion. Crile however claims that his experiments met these objections, his rabbits being kept awake by prodding, and not by keeping them continuously on the move.

It is nevertheless evident from the experiments described, that death can follow complete

and prolonged deprivation of sleep in animals. It is equally clear that many of the effects both clinical and histological observed in them are the result not of insomnia as such but of muscular exhaustion. In proportion as muscular exhaustion is avoided, the histological changes are slight. It is a little dangerous to argue from animals to man; dogs, for example, sleep proportionately longer but more lightly than humans. Moreover there are other important observations which were made by Crile. The first was that after prolonged continuous insomnia one period of sleep restored the brain-cells to a normal condition, except those in which the cell- and nuclear-membranes had ruptured. The second observation, which is not sufficiently known, was that the use of nitrous oxide for one hour out of every six during the period of insomnia, or the administration of opium, seemed to prevent or abolish the changes in the nerve cells, even when the sleep which would naturally have followed the giving of these agents was prevented from taking place. Crile does not mention whether the usual hypnotic drugs were tried in this way also, but presumably they would have a similar effect, since, like nitrous oxide, they depend for their narcotic action upon their lipoid-solubility.

Effects of Sleeplessness in Man.—These facts, especially the last two, are to be considered in their probable relation to the effects of insomnia in man. A number of persons have from time to time volunteered to deprive themselves of sleep for as long as possible. The record for voluntary deprivation appears to be held by Kleitman, who on one occasion deprived himself of sleep for 115 hours on end. There is however some evidence that he was not always widely awake during that time, and all of his fellow volunteers dozed a little at intervals. After his fourth sleepless night, Kleitman found that he performed simple tasks automatically while dreaming of something else.

The blood-sugar, alkaline reserve of the blood, hæmoglobin, red blood-corpuscles, white corpuscles, body weight, B.M.R., creatinin and total nitrogenous excretion, appetite, and the ability to perform simple mental tests, like naming letters and doing mental arithmetic, showed no alteration. The respiration-rate, pulse-rate, and blood-pressure showed a decrease, mainly or entirely due to the muscular relaxation of the recumbent-sleepy subject. The knee-jerk was unaltered; but steadiness in standing was very much impaired (Lee and Kleitman). On the other hand, other experimenters have found

that the bodily cost of work done after short sleep is high. Analysis of some subjects' exhaled air showed that after 10 minutes' multiplication, the caloric consumption was twice or three times as much when sleep was reduced as when it was normal in duration. This increase has been attributed to the greater effort of attention required after loss of sleep.

Patrick and Gilbert in their experiments found that at the end of 90 hours' continuous insomnia a very small extra amount of sleep beyond the normal caused complete restoration, all the "symptoms" of insomnia, including a fall in body temperature and a slight paradoxical rise in weight, disappearing. Tests of mental efficiency during prolonged voluntary sleeplessness showed no falling off from the normal (Robinson). But it is difficult to eliminate the effect of interest. McDougall and Smith found that voluntary partial deprivation of sleep, the subject sleeping only for 1 to $3\frac{1}{2}$ hours a night, actually increased the mental efficiency as shown by a decrease in errors in placing pencil dots in circles on a revolving tape (dotting machine). Sleep on the basis of these experiments appears more and more as a luxury. The improvement in mental performance noted by McDougall and Smith was however followed, although the subject

was now sleeping normally, by a period of diminished efficiency lasting 14 days.

Herz in a period of absolute sleeplessness lasting 80 hours observed in himself no physical change except a slight divergent squint. His reaction-time and his ability to repeat a series of figures were unaltered. Lee and Kleitman also found no impairment in the performance of mental tests, such as the tests of "naming opposites," cancellation, reaction-time, and naming colours, except where a very long series of colours was involved. The sensory threshold to electrical stimulation was unaltered.

Kleitman observed two facts relevant to a theory of sleep. It was fatal to the continuity of sleeplessness to allow the subject to lie down, the effect of muscular relaxation being to permit sleep to occur at once. Further, in the deep sleep following the conclusion of the experiment, the plantar response was extensor, which is what might be expected in profound inhibition of cortical function.

Conclusions.—It is clear from these experiments that by no known method has it been possible so far to demonstrate any but trifling physical or mental changes after prolonged insomnia in man. There is an obvious discrepancy however between the trifling nature of the

experimentally verifiable disturbances produced by insomnia and the intensity of the subjective discomforts. Also some of the less measurable objective disorders are remarkable. For example, in one group of experimenters (at George Washington University) when one member of a sleepless squad led the rest in singing, after a stanza or two he would break into a different song without realising that he had done so. Another member of the squad drove a motor-car into a ditch on the wrong side of the road during a sleepless period. The inference is that the experimental tests so far employed are not adequate to discover what changes in efficiency do occur as the result of prolonged sleeplessness (Johnson, Swan, and Weigand).

At present all that can be said is that the signs are almost entirely subjective, and that they can be abolished after as many as 115 hours of insomnia by a single period of sleep not greatly prolonged.

On experimental grounds therefore it can be said that while continuous insomnia in animals can lead ultimately to death, in man the discernible effects of such experimental insomnia as it has been possible to produce, are extraordinarily meagre. Clinically, it has not so far been my fortune, or rather misfortune, to observe

any effect of insomnia of a serious kind. I have yet to see a patient whose mental disorder could fairly be attributed to sleeplessness. And I have had under my observation patients who had reliably not slept more than 2 or 3 hours per night for several years. An important point arises here. When it is maintained that sleeplessness can produce mental illness, the cases that are instanced are usually cases of anxiety or of schizophrenia, or one of the other well-known " functional " syndromes. But if insomnia were the direct cause of a psychosis, it could act only by virtue of the physical—*i.e.*, nerve-cell—changes it is assumed to produce in man by analogy with the changes described in animals. A mental disorder thus arising would necessarily be of the organic type—delirium, followed perhaps by a permanent impairment of memory —and not of the " functional " variety at all. In point of fact, it is practically always the functional type of case that is adduced as evidence of the dangers of insomnia. Examples in the literature of acute organic reactions following insomnia are extraordinarily rare. Agostini records two cases of delirium with hallucinations following prolonged insomnia—one in a lady's-maid who became nurse to her mistress in the latter's illness and allowed herself no sleep

for 9 days, and another in a mechanic who did not have an opportunity of sleeping for six. The latter recovered completely after a sleep of 15 hours. Meynert records a similar case in a woman who had continuously looked after her child—which was ill with pneumonia—with almost no sleep for 14 days. Such delirious states are the only relevant types of reaction in this connection, and there are very few cases on record, whereas insomnia is one of the commonest of symptoms. To say, of course, that sleeplessness aggravates an existing "functional" mental illness is a different matter, and is often true.

Craig is a prominent advocate of this view, and also of the part played by insomnia in precipitating a mental disorder. He considers that insomnia weakens inhibition, and that weakening of inhibition leads to mental disorder of all kinds; but the question remains, what originally produces the insomnia in these patients in whom ultimately mental disorder appears? No matter what the answer is, whether it was toxæmia or a psychological upset that initiated the insomnia, the position of the latter is nearly always contributory, and very seldom primary.

Summary.—Recorded clinical examples of prolonged total or almost total insomnia in man are

very rare, and usually lack authority. In the few authentic instances of prolonged insomnia of this degree, where the insomnia was not a symptom of mental disease but was imposed from without, the end-result (where any distinctive mental result was reached) was a delirium, and this mental state was restored to normal as soon as a single period of sleep, lasting many hours, was permitted. There is no evidence that in the causation of other mental diseases loss of sleep has anything but a contributory rôle; in such instances the insomnia is principally symptomatic.

In sleeplessness in human beings experimentally induced no physiochemical alteration has so far been detected. The objectively measurable mental effects have been slight, and have consisted principally in a diminution in the power of sustaining attention; whereas subjectively the discomfort has been intense.

Experimental insomnia in animals if sufficiently prolonged ends in death; but as in human beings, a period of sleep after even very lengthy insomnia restores the animal completely. Histologically, loss of chromatin and actual degenerative changes have been described by some writers in various parts of the central nervous system and in one instance in some of the organs

(liver and adrenals). When allowance has been made for the more or less continuous motor activity imposed upon the experimental animals to keep them awake, the microscopic changes so far recorded have been slight; and like the clinical manifestation they are abolished by allowing sleep to occur, and with great rapidity.

CHAPTER III

PATHOLOGY OF SLEEP

THE types of disorder associated with sleep are conveniently divided into three classes:

1. Quantitative alterations in sleep itself, in the direction of decrease (insomnia) or increase (somnolence). It is an open question whether the profound quantitative alterations designated stupor and coma, involve a qualitative alteration in the fundamental physiological process of sleep as well.

2. Alterations in the incidence of sleep, including "attacks of sleep" (narcolepsy) and reversal of rhythm.

3. Interruptions of sleep by phenomena not normally associated with it:

(*a*) In the period of falling asleep or "predormitium" (Weir Mitchell)—hypnagogic states, such as hypnagogic hallucinations and sensory and motor shocks.

(*b*) In the period of sleep itself—night-terrors, nightmares, somnambulisms of varying degrees of complexity, "sleep-drunkenness," nocturnal epilepsy, nocturnal enuresis, and sleep-pains.

(*c*) In the period of awaking—sleep-paralysis, hallucinations, states of fear.

The varieties of insomnia are more conveniently discussed under treatment, since their variety is in their etiology rather than in the type of insomnia itself. It is sufficient to say that the diminution in sleep may be in depth or duration, but more usually both, and that the sleeplessness is in some patients habitually at the earlier part of the night, in others in the early morning; while in others it is a matter of frequent interruption of sleep.

Somnolence, or a state of sleepiness, may be more or less continuous, or it may be paroxysmal. When paroxysmal in its incidence, it is called "narcolepsy." Somnolence, whether continuous or paroxysmal, occurs both in the presence and in the absence of discoverable physical disease. When physical disease is the accountable cause, the disease may be general, as a toxæmia, or local, as organic disease of the brain. The use of the term "somnolence" implies a distinction from stupor and coma.

In somnolence the patient attends to the wants of Nature, and can be roused; when roused he talks coherently, and to the point; but he is kept awake with great difficulty. Although he remains correctly oriented for persons when fully

awakened, he loses appreciation of the passage of time. His dreams in the somnolent condition take the place of external reality, and in consequence he may confabulate during his waking conversation, talking of the dream-events as if they had actually happened. In somnolence, in addition to these distinctions from normal sleep, the only quality in a stimulus that makes it effective for rousing the patient is its intensity; whereas in normal sleep there is a selective factor. For example, Symonds quotes his experience during the war, when he could sleep soundly through the noise of an 18-pounder gun firing just behind his dug-out, while he awoke at once at the approach of an enemy shell.

Somnolence, occurring as a symptom of mental perturbation, is usually to be regarded as a refuge, a " flight into sleep." It is seen as such in patients with mild depression, who sometimes sleep long in the mornings, not because of any loss of sleep in the earlier part of the night, but because the contemplation of the daily round is so unpleasant. This practice is not confined to persons pathologically depressed. It would hardly be expected that people who worry continuously in the daytime should sleep soundly at night; but it is a remarkable fact that some patients with a pronounced psychoneurotic

anxiety-state involving continuous pre-occupation in the daytime, sleep extremely well.

Instances of prolonged continuous somnolence have been recorded following an emotional disturbance. For months at a time the patient has been awake only for very brief periods of a few minutes or a few hours (if he has been awake at all), and no organic or toxic basis has been found to exist. Some such instances of the catastrophic beginning of a somnolent period are included under "narcolepsy." A case of this kind was recorded by Müller in a young woman, who went to sleep for four years, following a sudden fright in her fourteenth year. Abrupt menstrual suppression occurred at the same time. In the first year she was awake for 1 minute to 6 hours per day. In the second and third year she averaged 4 hours wakefulness in 96. She took no nourishment spontaneously, and sometimes had no bowel movement for 16 days.

When prolonged episodes of somnolence follow an emotional upset, it is conventional to label these episodes hysterical. In a more rigid terminology, it would be more correct in many such instances to regard them as examples of emotional disturbance of a peculiar kind, similar to the paroxysmal narcoleptic and cataleptic episodes that follow emotion in some persons,

and to designate the somnolence hysterical only when other symptoms have existed of a hysterical sort, where a motive can be demonstrated, and where the condition proves modifiable by psychological treatment and by other factors of the same kind that ordinarily produce alterations in hysterical reactions.

There is less hesitation in designating as hysterical attacks of sleep (narcolepsy) which occur habitually in face of some embarrassing situation, as in the youth recorded by Ross, who went to sleep if he found himself in possession of an unsatisfactory hand at bridge.

The somnolence of organic brain-disease is most commonly associated with lesions of the floor of the third ventricle and with infiltrating growths of the hemispheres (gliomas), as well as with diffuse inflammatory processes like encephalitis and trypanosomiasis. In these instances it is an early symptom and may escape the physician's notice at first, since the patient is awakened by his friends for the doctor's visit. When somnolence is associated with brain-disease in other locations than the floor of the third ventricle it comes as a later sign, as the result of increased intracranial pressure or of actual œdema. It is possible that sometimes it may be the result of a toxæmia, since Speransky

has shown that the substance of some brain-tumours is toxic to a sound brain when injected into the latter.

The relation between somnolence and the site of the brain-tumour directly or indirectly causing it is shown by the following figures of Righetti, who out of 775 cases of verified cerebral tumour, collected 115 which were characterised clinically by somnolence.

Site of Tumour.	*Percentage of Cases showing Abnormal Sleep.*
Thalamus and third ventricle ..	34·7
Medullary	27·9
Hypophysis and vicinity	26·5
Corpora quadrigemina and epiphysis	28·6
Cerebellum	15·0
Central gyri	10·0
Frontal	6·0

No one histological type of tumour is more potent than another in producing somnolence (McKendree and Feinier). It is true that gliomas are the type most frequently found associated with somnolence, but they are also the most frequent of all cerebral neoplasms. Post-mortem, in a case where a neoplasm and somnolence have been associated, there may be no gross changes found in the ventricles. In

some cases, without ventricular distension, hyperplasia of the regions involved in the tumour has been observed. But somnolence was especially conspicuous in McKendree and Feinier's series, in cases where also there was found post-mortem considerable internal hydrocephalus; and on the other hand somnolence had usually been slight in cases in which ventricular distension was found to be slight or absent. The majority of the cases observed by McKendree and Feinier showed unmistakable signs of increased intracranial pressure, and they believe this to be the essential factor in producing somnolence, by interfering with the blood-flow. It has been shown that where the cerebro-spinal fluid pressure has been increased for some time before death, degenerative changes occur in the cells of the corpus callosum, the optic nerves, chiasma, and optic tracts, and in the ganglion cells of the cortex. Hassin attributes these changes to stasis, leading to the accumulation of catabolic products (chiefly basophil substances and lipoids).

It is however extremely important to recognise for diagnostic and also for theoretical purposes that two types of somnolence exist. One of these types is similar to, and, except in its incidence, identical with normal sleep. The appearance of the patient, the character of his

respiration, the circulatory quietude, and so on are indistinguishable from signs of normal sleep; moreover the patient can be awakened to full consciousness (Fulton and Bailey). The other type of somnolence varies from lethargy and torpor through all degrees of clouding of insomnia up to coma; and except in the mildest instances, when the patient is stimulated, there is a corresponding degree of dullness (clouding of consciousness or "confusion") at even the maximum degree of wakefulness to which the patient can be roused. Furthermore, the first type tends to be (but is not always) paroxysmal, while the second is continuous. The former is found in neoplasms, chronic inflammatory conditions and injuries of the base of the brain, especially of the floor of the third ventricle and the aqueduct, and it appears before the occurrence of increased intracranial pressure. The second type of somnolence is much more common, and is an accompaniment of increased intracranial pressure from whatever cause. It is to the second type that McKendree and Feinier's cases usually belonged.

Besides tumours in the subthalamic region, syphilitic meningitis of the base and tubercular meningitis in the interpeduncular spaces may provoke a syndrome of which somnolence is a prominent component. It has been stated that

continuous somnolence is always symptomatic, while narcolepsy (*q.v.*) may appear as an " idiopathic " disease (Freeman). But occasional cases of continuous somnolence lasting over years have been recorded in which no evidence of intracranial or other lesion presented itself. For example, somnolence lasted for years in a young girl described by Janet, and in an adult man in a hospital in Petrograd, mentioned by Pawlow. " In both cases the patients lay in a continuous sleep, entirely motionless, did not speak a word, and had to be fed artificially and kept clean." But during the night, Janet's patient was observed to eat and even to write. Of the Petrograd case, it was reported that sometimes during the night he got out of bed, and when " at the age of sixty, after twenty years of continuous sleep, he began to improve and could speak, he recounted that he often heard and saw everything occurring around him, but had no strength either to move or to speak." Pawlow suggests, on his theory of sleep as a cortical inhibition (which is discussed in Chapter V.), that both these cases presented an extreme weakness of the cortex, which led under the influence of strong stimuli to rapid fatigue, which in its turn led to a development of complete inhibition—*i.e.*, to sleep.

The somnolence of toxæmias of many kinds —whether the toxin is one of extrinsic origin, as alcohol and opium, or is a product of deranged metabolism, as in diabetes and uræmia—is very well known, and presents always the same general characters. Such differences as exist in the effects of various toxins on the brain, are found clinically rather in the mental phenomena that accompany the somnolence—the type of dreams in opium-poisoning, for example—than in the characteristics of the somnolence itself.

Sleep of Abnormal Incidence.

By **narcolepsy** is meant a condition of which the main or even the sole symptom is the occurrence in the daytime of paroxysmal attacks of a state closely resembling sleep. It has been customary to distinguish a symptomatic narcolepsy, in which the attacks occur in the course of some organic nervous disease, as, *e.g.*, epidemic encephalitis, from an idiopathic narcolepsy in which no organic lesion is desirable. An attempt has been made to restrict the term narcolepsy (first used by Gélineau) to cases in which the narcoleptic attacks, or attacks of sudden sleep, were associated with attacks of sudden loss of muscular tone following upon any transient

emotional disturbance such as anger, anxiety, or mirth. But Wilson prefers to use the term "narcolepsy" in a purely symptomatic sense, to "include all states of recurring diurnal sleep, whatever their etiology."

Brailovsky gives the following classification.

1. Functional narcolepsy. He quotes two examples, one of a peasant who married a woman he did not love, and finding himself impotent, developed narcoleptic attacks the following day. In another case, a peasant-woman married and found that her stepmother was exceedingly bad-tempered. Following this discovery, she entered a narcoleptic condition which lasted 10 years!

2. Narcolepsy associated with morbid physical conditions. Narcolepsy has been observed in a diabetic (Ballet), in a gouty subject, in whom an anti-fat cure cured also the narcolepsy (Robin), and in a woman during the first 8 months of pregnancy (Nevermann), and also in infantilism of hypophyseal type.

3. Narcolepsy in organic disease of the central nervous system, including tumours, especially of the subthalamic region, and chronic inflammatory processes in the same region. The factors are similar to those producing somnolence, which is not surprising, since narcolepsy in some of its forms is a paroxysmal somnolence.

4. Narcolepsy in toxic-infectious conditions of the central nervous system—*e.g.*, epidemic encephalitis. In this condition the narcoleptic attacks are associated with the chronic stage of the encephalitis, and the condition really falls in group (3).

5. " Genuine " or " idiopathic " narcolepsy.

Narcolepsy is a dramatic condition. The attack is sudden in its development, although frequently there is a warning, often of long duration.* In one of my cases the patient felt an increasing desire to sleep as the morning progressed, and finally succumbed to the desire as a rule just after midday. It is interesting that she could for a time postpone the onset by stimulation of the skin (*e.g.*, by pinching herself), in a way reminiscent of that in which epileptics can sometimes postpone their attacks. But sleep is sooner or later inevitable, and in some, and perhaps in most cases, it is irresistible from the beginning. The attack comes on independently of any state of fatigue, lasts a varying period from a few minutes up to some hours, and the patient awakes without after-effects. Some patients can be aroused by touching them or by

* C. P. Richter, *Arch. of Neur. and Psychiat.*, 1929, 21, 363, has in similar cases of his own observed a high and increasing electrical skin-resistance (*vide* p. 25).

shaking them; others can only emerge spontaneously. While direct observation shows no difference from the appearance of normal sleep (Kinnier Wilson), there is not always a loss of consciousness. The patient is aware of his surroundings, but is unable to move or speak. This is like a state which occurs in normal people in the mornings: " The subject is awake, because he is conscious and knows where he is, but for the moment he is incapable of innervating a single muscle. He lies in appearance still asleep, with eyes closed, yet within is engaged in an intense struggle for movement, with which is associated an acute mental anxiety; could he but manage to move a limb through a fraction of an inch, the spell would be instantaneously broken, and with a sigh of relief he would regain full power " (Kinnier Wilson). This is the " sleep paralysis " described by Weir Mitchell (*vide infra*). It is very similar indeed to the description of the cataplectic attacks that occur principally in patients who exhibit also narcolepsy. The cataplectic attack is provoked usually by some emotion, but may occur spontaneously, and consists in a loss of tone of all the limbs so that the patient sinks to the ground. The deep reflexes are abolished, while the plantar response in a case of Wilson's was extensor. In a patient

whom I observed in a cataplectic attack, the plantar response was absent, as well as the knee-jerks. Consciousness is often preserved in these attacks. My patient was able to tell all that I had said to him during the attack, although totally unable to reply at the time. Where such attacks occur spontaneously, without antecedent emotion, and last some minutes, the resemblance to some forms of trance-state or catalepsy is very close. But in catalepsy while the immobility may be sudden, there is not necessarily any loss of tone.

The relation between true narcoleptic attacks (attacks of loss of consciousness, with muscular flaccidity) and cataplectic attacks, and their variants, is obviously very close from the symptomatic aspect. Kinnier Wilson has shown from his cases that emotional disturbance may lead not to the cataplectic but to the narcoleptic state, that sleep may follow the cataplectic attack, that if sleep is prevented the cataplectic attack may ensue, and both the narcoleptic and the cataplectic states may develop spontaneously. For a theory of sleep these associations are of great interest; the phenomena of the cataplectic attack are so clearly dependent on an inhibition of muscular tone; and the so-called narcoleptic attack sometimes involves an inhibition of cortical activity and sometimes not. In the

latter case the narcoleptic seizure is indistinguishable from a cataplectic one. The obvious deduction suggests itself that the same process is at work in both types of attack—namely, a sudden inhibition, usually cortical and subcortical in the one case, subcortical only in the other. Furthermore, the resemblance of the narcoleptic attacks on the one hand to cataplectic attacks and on the other to the " sleep-paralysis " of normal persons, is so close as to approach identity; the only difference is in the circumstantial setting. The support that these clinical facts give to Pawlow's formulation of the essential physiological process in sleep as an inhibition which generalises itself is therefore strong. The fact that experimental reproduction of exactly similar states to cataplexy in animals has not yet been possible, is not a valid argument against adopting the conditioned-inhibition theory. The difference between normal sleep and these pathological states lies principally in the conditions of their occurrence, and not in the phenomena themselves, once they are established. Narcoleptic attacks are much more sudden than normal sleep usually is; they occur independently of the circumstances of quiet and repose and the like that favour normal sleep, and are entirely arbitrary and erratic in their

incidence. They are usually of only a few minutes' duration, and the normal night's sleep may not be affected in patients who suffer in the daytime from narcolepsy. (In one patient of mine, however, the night's sleep was much increased in duration from his previous habit while in health).

The treatment of "idiopathic narcolepsy" is in a very unsatisfactory condition. Naturally the first step is to ascertain whether the particular case really is "idiopathic." It may be very difficult to exclude psychological factors. Some such were discoverable in one of my cases, but psychotherapeutic treatment based on them had no lasting effect. Bromide, luminal, strychnine, caffeine, and hyoscine hydrobromide have all been tried. Gowers claimed a transitory effect from caffeine citrate. I have seen one case that seemed to benefit from it a little for a time, while in another case hyoscine seemed to lessen the number of attacks; but in both these instances, the hope derived from a new "remedy" was probably the potent factor; the results were very temporary.

Reversal of Sleep-Rhythm.

This is seen as a general phenomen on inpersons who have habituated themselves, usually as the

result of economic compulsion, to working at night and sleeping by day. In such cases, a general adjustment appears to occur, so that the body-temperature curve also becomes inverted.

In pathological states of continuous somnolence during the day, lasting over a period of years, it has been sometimes observed that the patient was capable of activity at night, when for example Janet's patient got up and wrote letters. Pawlow's explanation that the patient had a cortex that was easily fatigued, so that it passed readily into a state of inhibition when stimulated, has already been mentioned. On this hypothesis cortical activity would only be possible in the absence of any but slight external stimuli such as night-time offers. (It seems equally plausible, if such conditions are to be conceived in physiological terms, that a reversal of normal conditions had occurred in the cortex of such patients, in that the inhibitory process is more easily stimulated to occur than the excitatory one.)

The best-known example of sleep-reversal occurs in chronic epidemic encephalitis, and especially in children. The patient becomes more and more restless and excited as night-time approaches, and may even spend the night in a fury of activity—singing, shouting, and running

about—falling asleep only in the later hours of the morning, to remain asleep for a considerable part of the day.

Such a condition is hardly to be explained in terms of a readily fatiguable cortex. It suggests rather the autonomy of sleep as a function, which has attained a certain independence of environmental conditions; and it also suggests a lesion of a kind to cause a reversal of the neural process which follows the usually adequate stimuli to sleep, converting them into excitatory stimuli, and the usual waking stimuli into inhibitory ones.

It is necessary to avoid mistaking for such a primary reversal of sleep-rhythm, one that is secondary to some incidental discomfort. For example, a patient with headache following cerebral contusion usually finds the headache worse on lying down, and consequently may fail to sleep at night until he hits upon the expedient of propping his head upon numerous pillows; but in the meantime he may often fall asleep readily in the daytime sitting up in a chair.

I have seen one case however of head-trauma in which a reversal of sleep-rhythm had occurred as a direct result of the injury. The patient was a woman of 30, who a few minutes after a bus accident, in which she was dragged along the roadway clinging to the handrail, became

unconscious for about 15 minutes. Subsequently she suffered from severe pain radiating down the neck and over the right shoulder, which became worse on lying down, so that she soon found it more comfortable to prop herself on pillows at bedtime. She also experienced vertigo on stooping. When she looked upwards and to the right, a slight convergent strabismus became evident, and she had double vision in this position of the eyes only. There was also a slight ptosis of the right eyelid. These signs pointed to a mid-brain lesion. She slept well during the day, when she would fall asleep at odd moments even in the middle of a meal, but she slept almost not at all at night. Previous to the accident she had been healthy in every way.

Hypnagogic Conditions.

The sudden start of one or more limbs which occurs not infrequently in normal people as they are falling asleep, and which arouses them, is attributed by Gowers to an "insubordinate action of the lower centres, occurring during the gradual withdrawal of the higher control." It restores the connection with the higher centres, and awakes the sleeper (or more correctly the somnolescent, to use the term Gowers suggests),

probably by the sensory impression it produces. If the start is repeated again and again while the patient is endeavouring to go to sleep, and if the event is a nightly one, the hindrance to sleep becomes serious. Weir Mitchell mentions the case of a woman weighing 200 pounds, who spent her nights in a series of motor explosions so vigorous as at times to break the bed-slats. In aortic disease, "night-starts" are relatively frequent.

A similar disturbance may affect the sensory centres. This can occur in otherwise normal people, but Gowers records it also in a man with chronic aural vertigo, who also suffered from motor starts.

Weir Mitchell classified such sensory shocks in the following way:

1. In the sphere of general sensibility; the patient "feels as if struck, or as if he had a shock like that which a sudden arrest of motion causes; or it is a feeling of rending, or of a bolt being driven through the head."

2. Auditory; a loud noise, like a pistol shot, or a crash of broken glass.

3. Visual, as a flash of light.

4. Olfactory, as a sudden odour.

5. Emotional discharges, usually an "abrupt sensation of fear, sometimes preceding the sensory shock, and sometimes following it."

The sensations are often violent and alarming. There is sometimes an aura—*e.g.*, " an indescribable something "—passing slowly upwards from the feet to the head, or from the epigastrium. Mitchell emphasises that the sensations obtained in this way are of primary qualities, and are never " figured " sensations (*i.e.*, they are never hallucinations of definite forms). He also points out the close resemblance to epilepsy—both possess an aura of primary sensational quality, and sometimes sensory shocks lead to convulsions in women who are scared by the sensory experience, but the convulsions are then of the hysterical type.

Hypnagogic hallucinations are vivid sensory experiences, usually visual, occurring without external stimulus in the state between waking and sleeping. The similar experiences occurring in the process of awaking from sleep have been artificially distinguished as " hypnopompic." Such hallucinations consist usually in a series of more or less disconnected scenes passing apparently before the eyes. They are a normal occurrence, and are commonly concerned with events of the preceding day. In some persons however they occur more often and assume a grotesque form, sometimes of grimacing faces. Weir Mitchell says that children can see what

they will in this way, and "can control these visions," but asserts that he himself lost the power to do so as he grew older.

In rarer instances, there is more intrinsic connection, and less definite relation to the events of the day. Usually the person hallucinating in this way recognises his experiences as having no real existence. Sometimes he fails to do so, and may then base delusional beliefs upon them. Baillarger described a series of cases in which hallucinations of sight and hearing, fading when the eyes were opened, were at first rejected and finally accepted as part of a delusional system. Weir Mitchell quotes similar cases from his own experience. One of his examples was a woman of 40, who had a fall which injured her nose, the sequelæ being persistent headaches and anosmia. "Two years later she had, but only on going to sleep, a sense of horrible odours which were fæcal or animal and most intense. This lasted several months, and then were added sounds of voices, which were at first vague, but at last accusatory, and soon were heard in the day. The case ended in melancholia with delirium of persecution, during which the trouble as to smell passed away." But Weir Mitchell adds that in others of his cases hypnagogic hallucinations ultimately after

some years disappeared, leaving no evil consequences.

Hypnagogic hallucinations can be distinguished from the hallucinations of the waking life of persons mentally ill by their dream-like characteristics—the repeated sudden shifting of the scene, and the manner in which the details are forgotten, subsequent repetitions not tallying exactly with the first recounting of the hallucinatory incidents, just as the person who has dreamt forgets more and more the content of his dream. Furthermore, an inquiry into the circumstances will show that even when the subject was not in bed, yet the circumstances were favourable to sleep, and the feeling of relaxation afterwards suggests that the subject had been asleep (W. White).

States of persistent fear, without hallucinations and with no conscious cause, occur occasionally in the hypnagogic period. Similar states are so frequently associated with awakening from sleep as to be common knowledge as the aftermath of nightmares. In some instances however the state of fear that began with a dream persists for a long time after full wakefulness is attained, and causes the sufferer to be apprehensive of the smallest noise in a way which he realises, even at the time, to be absurd. Weir

Mitchell tells of a " scholarly, much overworked " man of 55, who was frequently troubled by terrifying dreams, from which he awoke with the realisation that it was a dream, but with a growing feeling of terror, so that he could not fall asleep again for some hours. On the night following such an experience, his recollection of his fear was so vivid that he could not retire to bed without alcohol till he was (intentionally) intoxicated, when he was able to bring his courage to the point of going to bed. These attacks were succeeded and replaced by a feeling of fear not so intense, confined to the period of going to sleep. The symptoms disappeared during a holiday, and did not return. It is interesting that an attack of the first type was preceded always by an " aura," consisting in a feeling of malaise on retiring, reminiscent of the foreboding of night-terrors described by Shackle (*vide infra*). Weir Mitchell's patient described his " aura " as a " difficulty in breathing, not being able to draw a full breath " (owing, as it seemed to him, to some obstruction in the lungs); " intense nervousness, and turning from side to side." It occasionally happens that the alarming dream itself not only persists in memory, but is for a time credited. I know of one elderly woman who awakes in terror, having dreamt that

she is to be transported to an asylum (although she is quite sane), and who cannot persuade herself that this is not so until she has been reassured by her husband.

Night-terrors are sleep disturbances with special characteristics, occurring in children, but seldom found in adults. In some instances they have persisted up to the age of 30 (Gowers). Their continuance after childhood is said to be more common in males, and sometimes there is a family tendency (Gowers). Soon after falling asleep the child starts up with a cry, and shows other signs of fear, although remaining imperfectly cognizant of his surroundings. The feeling of fear remains some time after he has become more completely awake. The child seems to have a vivid visual hallucination, but can afterwards give either no account of his experience at all or a very imperfect one. In describing his personal recollection of a night-terror, Shackle mentions a premonitory stage consisting in a feeling of malaise before sleeping. At the same time objects in the room illuminated by a night-light took on a " peculiar aspect," characterised by an exaggerated appearance of contrast in the blacks and whites of the wallpaper. More frequently however he slept soundly at first, and then frequently he became aware of a " fortifica-

tion figure." At the end of half an hour of this kind of aura, there followed the night-terror itself, in which all consciousness of surrounding objects was lost, and an image appeared which was peculiar to the night-terror. Vague ill-defined masses were seen, some enormously large, and others excessively small, conveying a general impression of prodigious contrast. The emotional accompaniment of this visual experience was a fear " of the most paralysing and dreadful kind, no fear experienced in nightmares or in real life bearing any relation to it whatsoever."

Night-terrors of this sort have to be distinguished from nightmares, which of course commonly occur also in adults, and in which the fear is an incident in the course of some dream, in which visual images are well developed, and which is usually recollected on waking. The cause of night-terrors has commonly been sought in constipation or in the partial asphyxia that may result from the presence of adenoids. Treatment of either of these conditions may be followed by cessation of the night-terrors, but this is certainly not always so. Night-terrors are common in " nervous " children, very often of the better-endowed type intellectually. A nervous heredity is said to be frequent in them; and the

rheumatic diathesis is stressed by Hutchison. Accordingly, excitement of any kind should be avoided so far as reasonably possible, without mollycoddling the child. He should not be expected to sleep alone or at least not out of earshot of parents or nurse, and if given a room to himself, a night-light should be provided and the door left ajar.

Cameron has suggested that night-terrors are the result of an acidosis, the consequences of a relative starvation which comes about in this way; the child uses comparatively more energy than the adult and requires an ample supply of carbohydrate. During the long foodless period of sleep the carbohydrate available for the tissues falls so far that fats have to be burned instead to provide the necessary energy. But as fats cannot be fully combusted in the absence of sufficient carbohydrate, fatty acids, the products of imperfect oxidation, are formed and an acid-intoxication results, which is assumed to produce the night-terror. The remedy indicated therefore is carbohydrate in as pure a form as possible just before bedtime. Barley-sugar, which is nearly free from admixture of fat, is recommended by Cameron for this purpose. Certainly the results are sometimes striking, the terrors ceasing at once and only recurring on nights when

the additional sugar is omitted. Night-terrors being commonest in bright, overactive children, who obviously use a great deal of energy, but often are indifferent eaters, the frequent incidence of night-terrors in them tends to support Cameron's theory of an acidosis.

Nightmares, which occur in adults as well as in children, are terrifying dream-experiences, in which there is a definite imagery. They are the nocturnal equivalent of the " anxiety-attacks " of the daytime, and in Freudian theory represent a partial failure of repression, the underlying emotional trend reaching such a pitch of intensity that the repressive devices employed in sleep (the symbolism of dream-imagery) are no longer sufficient to let the dreamer sleep on; the nightmare wakes the dreamer and the stronger repression of waking is brought into play. The disturbing trend, which threatened to come to consciousness in the relaxed vigilance of sleep, becomes then safely unconscious again.

In the interest aroused by Freudian theory, the meanings that were formerly attached to terrifying dreams have lately been lost sight of. But it has not infrequently been recorded that nightmares of a specially distressing kind have preceded an apoplexy in predisposed persons, and similar experiences occur as premonitory

symptoms in any acute brain affection whether structural or toxic. The fact that dreams, usually unpleasant, accompany all kinds of toxic states, especially the acute stage of fevers, is too well known to need emphasis. Some contemporary physicians—*e.g.*, Laignel-Lavastine—have even sought to base a system of rational diagnostic aids upon the study of dreams in bodily affections, by relating different types of dream-experiences to different types of disease.

Somnambulism is an occurrence which from its dramatic nature as well as from its frequent occurrence, especially in the young, is well known to the laity. The true somnambulist literally "walks in his sleep." Somnambulism is also of great clinical and theoretical interest, especially in its relation to hysterical manifestations and to epilepsy, and in its theoretical bearing on the nature of sleep. By simple somnambulism is here intended a condition occurring usually in children, and often only once or twice in the life of a child. The latter, after being asleep for a period, rises from his bed although apparently still asleep in other respects—*i.e.*, not conscious of the greater part of his surroundings—and goes somewhere, as to a window or to another room of the house. The walking may appear to have a definite object or it may not. One small boy,

for example, arrived always in his parents' bed, walking from his own bedroom. In other instances, the excursion is apparently haphazard, a different route being taken at different times. The somnambulist reacts to a part of his surroundings—he will avoid obstacles, but does not act in accordance with all the environmental stimuli. Thus obstacles may be avoided but no response to questions may be elicited; or sometimes a word or two may be obtained in reply without apparent relevance to the circumstances. Other neuro-muscular systems besides that of the lower limbs can come into action—*e.g.*, clothes may be picked up, or a window may be opened. The mental content, as judged by the reply to questions, if any reply is given, is extremely restricted—monoideational, in Janet's terminology. After waking, it is rare for the child somnambulist to be able to give any account of his activity. The whole picture in simple somnambulism suggests that sleep has continued except in certain neuromuscular systems, especially the lower limbs. It is as if most of the cortex were still in the state that exists in sleep, but that the motor cortex and some of the sensory cortex were in an active state. Somnambulism seems, in other words, to be a sleep of part of the organism coupled with a

waking state of the rest. It is the converse of the partial sleep which we experience when we are cognisant of ourselves and our surroundings, but cannot yet move our limbs, which is the condition described above in its exaggerated form as " sleep-paralysis." In the very interesting case which Gowers records of " half-waking somnambulism," there was a succession of these two states in the same person.

Gowers' "half-waking somnambulism" is more allied to the simple somnambulism than to the hysterical somnambulism to be hereafter described. He describes the case of a middle-aged medical practitioner, who as a boy of 15 had often gone partially to sleep. " Sitting by the fire, he would seem to go to sleep; he continued perfectly conscious of all that was going on around him, but could neither move nor speak, until he suddenly seemed to awake," and resumed his normal state. Gowers remarks that " there must have been a true sleep in part only of the brain, a condition comparable to trance and to a stage of partial waking," such as he described in connection with night-starts (*q.v.*). In the later years of the medical practitioner referred to, the condition was reversed, and now during complete sleep he " passed into a half-waking stage, in which he had full motor power but

imperfect perception." In this he acted under some impulse, which he could often remember afterwards. He often got up and went to a window and opened it, but never tried to get out. "Once he dragged his wife out of bed and then dragged her in again." Shortly before Gowers saw him he "had gone to sleep in a train and suddenly got up, opened the door and stood on the step, when the cold wind fully awakened him. He remembered the event afterwards dimly, as if he had half known what he was doing, but he could not recollect any motive for opening the door." Gowers designated this a "half-awake" proceeding and distinguished it from simple somnambulism, in which apparently he considered that there was no susceptibility to sensory impressions (a curious view, at variance with the experience of others). In the case recorded, bromide had the differential effect of preventing any recollection of preceding idea or motive, but not of stopping the sleep-activity.

Pawlow has demonstrated that a similar state, which he believes to be a partial sleep, can be produced experimentally in dogs. "The usual form of normal sleep . . . is evidenced by an absence of the normal function of the cortex, and a relaxation of the skeletal muscles." In another

form (" partial sleep ") the activity of the hemispheres is still absent, and "all conditioned stimuli remain without effect, different extraneous stimuli, unless exceptionally powerful, failing to evoke any reactions. Nevertheless the animal preserves an entirely alert posture; it stands with wide open immovable eyes, head up, extremities extended, not seeking support, remaining motionless sometimes for minutes and sometimes for hours." In other words, postural activity is present—the postural mechanism is " awake," but all the cortical functions in this case are in abeyance. In man, a condition in which not only the postural but the motor functions are in action during " sleep," which must on this view have been principally cortical, has been seen in soldiers who after great fatigue have marched while asleep. Here the great part of the cortical activities are in abeyance, but just enough of the sensorimotor part is left to enable walking to continue.

There is another type of somnambulism, differing from the simple type described above in certain characteristics. It occurs chiefly in adolescents and younger adults, and there is a definite mental content which bears a causal relation to the ambulatory activity. It is probable that the difference is of degree and not

of kind, the simple somnambulism of children having a narrower monoideistic mental content as compared with the polyideistic mental content of the type now under discussion. The relationship of this more complicated somnambulism to hysteria is very close; in fact, it is usual to regard it as a variety of hysterical manifestation, and to regard fugues (in which the patient, apparently fully conscious of his environment, but oblivious of the past, travels a considerable distance) simply as a more complicated type of activity of the same kind. Certainly it is difficult or impossible to distinguish fugues from somnambulism of this type, and the latter from the simple somnambulism of children, except by the extent and complexity of mental content, and correspondingly in the degree of reaction to environmental stimuli.

An instance of complex somnambulism, or fugue, was furnished by a patient of mine, a schoolboy of 16, who after falling asleep, would get up and leave the house (if permitted) although his eyes were half-closed, and he did not respond when spoken to. If an obstacle such as a chair were placed in his way, he avoided it. On several occasions he succeeded in leaving the school where he was a boarder, and travelled long distances on foot, with occasional " lifts " by

the usual methods of transport. Such a period of activity ended usually in an apparently normal sleep, from which he awoke with no recollection of what had happened. Sometimes while asleep he talked instead of walking. The gist of his talk was the same as what was obtained under hypnosis, when he was asked to recount the experiences he underwent during his somnambulisms or fugues—call them what you will. His tale was to the effect that 6 months before his somnambulism began, he had visited a travelling show, where his friends had " dared " him to submit himself to a professional hypnotist. He did so, in considerable apprehension, and was hypnotised. The hypnotist suggested to him while he was in the hypnotic state, that he would remain under the hypnotist's influence for 6 months, and that at the end of that time he must return to see him at the same place at the same hour of the day. The somnambulisms signalised the attempt to return. Such was his curious story and such was the content of his talk while asleep, and apparently also of his somnambulic state. How much of this tale was phantasy it did not prove possible to discover. It was said of the patient that he showed more capacity for arithmetic while in the somnambulism than he did while awake.

I was unable to get proof of this, but similar assertions have often been made.

Very complex actions are sometimes undertaken in somnambulisms. Tissot recorded an instance of a medical student who arose in the night, prepared his studies, and returned to bed without waking. Complicated activities of this scholastic kind were described also by the Archbishop of Bordeaux, in the case of a young priest who was in the habit of getting up during the night in a state of somnambulism, taking pen, ink, and paper, and composing and writing sermons. When he had finished a page he would read aloud what he had written, and would correct it. In order to ascertain whether the somnambulist made any use of his eyes, the Archbishop held a piece of cardboard under his chin to prevent his seeing the paper on which he was writing. He continued to write without being in the slightest degree incommoded. In this condition he also copied out pieces of music, and when it happened that the words were written in characters that were too large, and so did not stand over the corresponding notes, he perceived this error, blotted them out, and wrote them over again with great exactness.

It is probable that if the simpler somnambulisms of childhood were investigated, some

comparatively clear source of mental unrest motivating the somnambulism would be discovered.

A girl of 15, a domestic servant, frequently walked in her sleep. She had the reputation of being solitary in her habits, and given to day-dreaming. On investigation it was found that she felt neglected at home, where her father was kind enough, but had little time to show it, and where her stepmother took little interest in her. She had consoled herself for this state of affairs by fancying that she was the child of other parents, who were in her phantasy people of importance. In her somnambulisms she was endeavouring to find the parents of her phantasy.

Somnambulisms in the ordinary sense have to be distinguished carefully from **epileptic automatism** following a fit which has occurred during sleep. These are rare, but it seems likely that they are more dangerous than simple somnambulisms, and much more dangerous than the more complex somnambulisms just described, in proportion as the comprehension of the environment is interfered with and a motive related to conscious life is lacking. Where suicide or any dangerous enterprise or accident occurs, hysteria is an unlikely diagnosis. It is true that Montet records a suicidal attempt by

a woman somnambulist, but it was made in his presence, and other aspects of the case besides make it suspect of a dramatic origin. In what was presumably a post-epileptic automatism, I have known the patient to jump from a window and alight through the roof of a conservatory, cutting himself severely. The resemblance to post-epileptic automatism of the following homicidal act in a man of 27 is very close, especially in the light of the history of his earlier years. Once in boyhood he arose at night when asleep, dressed himself, took a pitcher, and went for milk to a neighbouring farm, as was his daily custom. At another time he worked in a yard in a rainstorm while asleep. Again, when about 21, he was seen in a mill-pond, wading about attempting to save his sister, who he imagined was drowning. The worst phases of his sleep-disturbances were the fears and terrible visions to which he was subjected. Sometimes he would imagine the house was on fire, and the walls about to fall upon him, or that a wild beast was attacking his wife and child; and he would fight, screaming shrilly the while. He would chase the imaginary beast about the room, and in fact had once grasped one of his companions, apparently believing he was in a struggle with a wild animal. He had often injured himself in

these struggles, and had attacked his father, his wife, sister, and fellow-lodgers, and while confined in jail he attacked one of his fellow-prisoners. His eyes were always wide open and staring on these occasions; he was always able to avoid pieces of furniture which were in his way, and he occasionally threw them at his visionary enemies. At the time of the murder for which he was tried he imagined he saw a wild beast rise up from the floor and fly at his child, a babe of 18 months. "He sprang at the beast and dashed it to the ground, and when he awoke, to his horror and overwhelming grief he found that he had killed his baby."

There is another form of motor activity interrupting the course of sleep, which takes the form of violence against some person or object in the environment, with evidence of imperfect comprehension, but with no other phenomena in the daytime or in the history to suggest epilepsy. In the cases recorded in the literature usually but one incident of the sort appears to have occurred. The essential factors seem to be two: first, a sudden partial awakening, in response to either an internal or an external stimulus which arouses at the same time considerable emotion, and second, imperfect comprehension of the environment in the half-awake

state. The condition has sometimes been described as "sleep-drunkenness." The patient continues after he is half-awake to act under the influence of the emotional state with which he awakened.

An example was quoted by Pagan in his "Medical Jurisprudence of Insanity" (1840). "Bernard Scheidmazig suddenly awoke at midnight; at the moment he saw a frightful phantom, or what his imagination represented to be a fearful spectre. He twice called out, 'Who is that?' and receiving no answer, and imagining that the phantom was advancing upon him, and having altogether lost his self-possession, he raised a hatchet which was beside him and attacked the spectre. It was found that he had murdered his wife, then lying by his side." Forbes Winslow relates how a pedlar who was in the habit of walking about the country with a sword-stick and sleeping by the roadside, being roughly awakened as a joke by a passer-by, drew his sword and killed the man. He was tried for manslaughter and found guilty, in spite of medical evidence to the effect that he could not have been conscious of his act in the half-waking state.

The medico-legal importance of recognising "sleep-drunkenness," nocturnal epileptic auto-

matism, and to a less extent somnambulisms, in the senses used here, is clear.

In a similar instance which has come to my notice attacks of "sleep-drunkenness" repeatedly occurred; they were apparently provoked by inner stimuli (of the emotional kind), and they ceased after some simple therapy. A young man several times became violent in the middle of the night, and to the great alarm of his wife smashed some of the bedroom furniture, without recollection in the morning and with no other symptoms, and with a previously clean bill of health. Adjustment of his marital relations was followed by a cessation of the attacks.

The differentiation of "sleep drunkenness" from epilepsy is obviously difficult. It must depend partly on the history of episodes of fits or of automatic activity at other times, and especially during the day. A basis for the sleep-actions in some strong emotion is in favour, but not indisputably so, of a "sleep-drunkenness" rather than epilepsy.

Simulation of somnambulism also occurs. For example, a very dramatic hysterical patient was asked whether she had ever walked in her sleep. She replied "No," in some surprise; but on the following night was found outside her bedroom door. When asked what she was doing there,

she replied coherently that she did not know. Next morning she denied all knowledge of the affair, the matter was made light of, and the " somnambulism " did not recur.

Treatment should depend on the results of an investigation of the factors involved. In the complex somnambulism of adults this may necessitate a mental analysis usually aided by hypnosis. In the simpler somnambulism of children, such an investigation has to be a guarded and limited one. The mere avoidance of stress, of overfatigue, and of excitement before going to bed may be enough. In the case of " sleep-drunkenness " an exploration of the circumstances of the patient's life, with the discovery of emotionally unsettling factors and their remedy, has been followed by a cessation of attacks as in the patient mentioned.

Where nocturnal epilepsy has been suspected, bromide in considerable doses, or luminal up to gr. ii. at bedtime, should be given.

Janet's discussion of somnambulism is of considerable theoretical interest. He regards somnambulism as the prototypic of hysterical manifestation. There is a progression in complexity from monoideistic somnambulism (simple somnambulism) through fugues to polyideic somnambulism, and to double personalities. Hys-

terical convulsions, hysterical fits of sleep, hysterical catalepsy, and hypnosis, which he regards as an artificial somnambulism, are all variants of the same general type. According to Janet, the characteristics of a somnambulic state are these: the perfection and intensity of its development, the perfect regularity with which it is repeated on each occasion, the absolute sensory indifference to any object not connected with the theme of the mental content of the somnambulism, the absence from the mental content of any recollection of the rest of the somnambulist's existence, and on recovery, amnesia for the events and content of the somnambulic state. The mental content has hallucinatory intensity—*i.e.*, is so vivid as to appear real. Fugues resemble somnambulisms in that a certain system of ideas is abnormally developed, and all other systems suppressed; but differ from monoideistic somnambulisms in the absence of hallucinations, and in the fact that the subject remains completely in rapport with his environment, so that the patient outwardly presents nothing abnormal in his fugues—*i.e.*, the mental content of the fugue does not exclude ordinary relationships with the environment, as the somnambulism does. Polyideic somnambulisms differ only in degree from monoideistic states and

from fugues, by having a more complicated mental content. Double personalities are prolonged and complicated " somnambulist " states of this polyideistic kind, according to Janet. A hysterical convulsive attack, by the same reasoning, is a somnambulism in which the motor activity is an ensemble of tics—there is an absence of the intelligible utterance and of the complex acts of somnambulisms ordinarily so-called, expressive movements alone being present. Hysterical sleep is a stage further in the series constituted by somnambulism, convulsive attack and hysterical sleep, even expressive movements being absent in the last, except perhaps minor ones of face, lips, and hands. Hysterical (hypnotic) sleep very closely resembles normal sleep, but movements connected with thoughts are more often seen, and it is possible to get into touch with these thoughts by speaking to the sleeper.

It is of considerable interest that by different routes, the one clinical and the other experimental, Janet and Pawlow have arrived at the same conclusion, which places catalepsy, somnambulisms, and sleep in the same category. Janet speaks of catalepsy as a variety of somnambulism, in which the patient neither speaks nor moves, but remains in an expressive attitude.

Pawlow observed of the dog already mentioned, in which partial sleep of the postural mechanism occurred, that in changing the position of a limb the latter retained the new position. This is closely similar to the "waxy flexibility," or *flexibilitas cerea*, which occurs also in the hysterical catalepsy of human beings.

Hypnotic Sleep.—The classical attempts at differentiation of hypnotic from normal sleep are futile (see Byron Bramwell's "Hypnotism" [London, 1921] for a summary of these). Since there are no infallible physiological accompaniments of normal sleep, there are none that can be used as reliable tests of its existence; and the outward spontaneous physical appearances of hypnotic sleep and normal sleep occurring in the daytime are, as everyone knows, indistinguishable. For a distinction to be made we have to fall back upon (*a*) the state of the subject's unconsciousness, and (*b*) his behaviour. Regarding (*a*) it is usually held that one of the fundamental marks of hypnotic sleep is that the subject remains in rapport with the hypnotist, which is held to mean, in part, that the subject can communicate with the hypnotist by speech and can be communicated with. But I have succeeded in establishing a similar relationship with a patient who was (I believe)

asleep in an ordinary way when I began the experiment. The difference from the usual hypnotic condition was, that his recollection of his experience on waking was of a dreamy mental state—the patient was aware of my presence, but was otherwise erroneously oriented. In the dream we were in another room, the time being vague. There is another point of similarity with hypnosis, for in normal sleep there is the often quoted selective adaptation to stimuli; for example, the mother's waking with unusual readiness at the cry of her child.

" Rapport " in the sense of a special affective relationship has been shown to be unnecessary for hypnosis. What is characteristic of the hypnotic as distinct from the dreaming consciousness, is that the former commonly consists of a revival of previous experience with thinking of the same order of logicality as waking life. It is as if a part of the subject remained awake, while the rest of him was asleep in a way indistinguishable from normal sleep. We are irresistibly reminded of the dissociation that occurs in some persons in the course of sleep. Janet has arranged normal sleep and its dissociative manifestations along with certain hysterical phenomena in a continuous series. The peculiarities of behaviour in hypnosis can be attributed

to dissociation—the subject is actually under the influence of that portion of his experience which remains "awake" (active). Very often the waking remnant is a singularly detailed recapitulation of some previous experience. Similar conditions can be produced by organic causes (head injury), as if some layer of experience had been irritated or released into activity by the trauma. Experimentally, Pawlow has claimed to produce states resembling hypnosis in dogs by methods precisely similar to those with which he induced sleep in the animals. The differences between certain hypnotic states in humans and in animals probably depend on differences in the "level" of the dissociated systems. In humans, the dissociation is often between a system of ideas and the psycho-motor system; in Pawlow's dogs, for example, it was between psycho-motor and postural systems.

Nocturnal Enuresis (Bed-Wetting). — The number of theories that have been advanced to account for a persistence of urinary incontinence during sleep after the age of about three, after which normally such incontinence does not occur, is evidence of our plentiful ignorance of its origin. Organic disease of the central nervous system is a possible, but in children a rare, cause; in idiots and imbeciles bed-wetting

is the result of an associated organic lesion involving the central nervous mechanism of micturition, or of the mental incapacity for education in sphincter control, or of both. In otherwise normal children, adenoids, urinary hyperacidity, endocrine deficiency, and local conditions such as phimosis or worms, have all been blamed; but in the majority no such condition can be found. What is commonly found however is a state of apprehension, shame, and self-consciousness about the symptom, together with a striking responsiveness to circumstances. An enuresis which is constantly present while the child is at boarding-school, frequently is absent while he is home on holiday. Also it has been observed that if the child be removed to hospital, the symptom usually disappears for the time. Cameron points out that the child removed to hospital because of enuresis is in a sense expected to wet the bed. Enuresis in these circumstances is no longer a crime but an everyday matter about which there is going to be no fuss. Consequently the child is no longer specially apprehensive about its happening, and it does not do so.

The influence of the attitude of the environment was very well seen in a boy of 11 in whom rectal incontinence occurred as well. He was

the youngest member of a large family, and his mother was dead. His appearance was extraordinarily cowed; he answered "Yes, sir," or "No, sir," in a weak voice to every question. It transpired that the "treatment" adopted to control his incontinence had been violently unkind, and had consisted of such measures as thrashing him and emptying buckets of cold water over him. After one conversation of encouragement and explanation and instructions to the parents, there was no further incontinence.

A further argument in favour of the origin of enuresis in faulty training, with consequent emotional perturbation in the form of anxious expectation, is the helpful influence of hypnotic suggestion, which is said to be frequently successful in curing the condition.

These considerations indicate that the success of treatment depends primarily on the installation of confidence, and the mitigation of feelings of shame. When attention to local conditions such as phimosis succeeds, it is probably chiefly because of the suggestive effect of the treatment, the child being assured in his own mind that the responsibility for the habit lies not in any mysterious weakness, but in a simple defect which has now been removed by operation. The

omission of fluids after 6 p.m., rousing the child to pass water after 2 or 3 hours' sleep, the avoidance of excitement in the evening, of fatigue, and of late hours, may jointly succeed, but more often they fail. It has also been recommended that the child should sleep on a hard mattress, with few bed-clothes, and that the foot of the bed be raised a little, with the motive of diminishing the pressure on the sensitive trigone.

More important than these measures is a helpful attitude of parents and school authorities. An absence of fuss, of an atmosphere of anxious expectation, is exceedingly important. At school, the avoidance of ridicule, such as is engendered by unwise schoolmasters, and of fines and punishments, which now fortunately are seldom heard of in this connection, is very necessary; although it is usually impossible to avoid the habit coming to a knowledge of schoolfellows. A kindly interest on the part of a housemaster may do much to set the boy's mind at rest and so to stop the enuresis.

Besides instruction on the above lines to parents, the child himself should have matters explained to him. He should be told that it is not a matter of weakness or disease, but of confidence and training; and he should be

assured that the condition always gets well. (Enuresis after the age of 20 is very rare.)

In young children of 4 or 5 years of age, where it is a question of prophylaxis rather than cure, the same remarks apply; and at this age a system of rewards is advisable. These rewards need not be material ones; the latter, if given at all, should be given only occasionally. But a calendar or diary can be kept in which a star is marked opposite every night of success, while the nights of failure are left blank. This can become a source of encouragement and emulation, if the thing is made an earnest but interesting business between child and parent or nurse. The atmosphere of fear and shame which has usually gathered is thus beneficially influenced.

There are some parents who are so apprehensive in their own natures that little success is to be hoped from their co-operation. If in such circumstances the methods described have failed, removal of the child for a time to an environment where they can be put more hopefully into practice becomes advisable.

Local treatment, such as circumcision for phimosis, have been mentioned already, and their rationale commented upon. The administration of belladonna is a favourite resource, based theoretically on the antispasmodic effect

of belladonna on involuntary muscle. The motto in its administration is to give large doses, the child being less susceptible to belladonna than the adult. The commencing dose is 10 minims of the tincture after each meal, for the first week. The dose is then increased to 15, 25, 30 minims, and finally even to a drachm, three times a day. Hutchison says that while the child may complain of slight dimness of vision from ciliary paralysis, or of dryness of the throat, he has not seen more than once or twice in children any general disturbance, such as a rash or a delirium. It is recommended that the full dose—*i.e.*, the dose at which enuresis ceases—should be continued for a month, and then gradually diminished till it is finally discontinued. Usually when enuresis has stopped during the administration of belladonna, it does not return with its discontinuance. It is customary to say that the habit has been broken. I am not impressed by the dynamic power of habit *per se*; it would be more accurate to say that the driving-forces behind the habit—namely, fear and the associated emotions of shame and the like—have been sufficiently curtailed.

When none of these measures have succeeded, hypnosis is worth trying. It is not recommended that it should be tried earlier, because of its

necessarily (to a child) rather mysteriously personal nature, and because of the fact that it is apt to enhance an already too great suggestibility, besides facilitating also in those subjects in whom hypnosis is readily possible, a tendency to dissociation which may in rare cases lead later to the appearance of hysterical phenomena.

Respiratory Failure in Sleep.—Where there is a partial paralysis of the muscles of respiration from peripheral neuritis, or in the paralytic stage of tabes, or in posterolateral sclerosis, respiration may be kept going at a sufficient pitch in the waking state only by the co-operation of considerable voluntary effort. When this voluntary effort is relaxed as in sleeping, suffocation may ensue, and the patient either wakes up and struggles for breath, or dies in his sleep.

Sleep-Pain is pain occurring in the lower extremities during sleep, and sufficiently severe to awaken the patient. The condition occurs in middle life, and is not associated with arterial or any other discoverable disease (Weir Mitchell). The " pain " is of the nature of an aching or distress. It is relieved by walking about. Mitchell advised morphine in an intractable case, no other remedy being of the slightest use.

Chorea.—Cases have been recorded in which choreiform movements occurred only during sleep and for an hour or two after waking.

Tonic spasm occurs sometimes in sleep, and continues after waking. In a patient of Weir Mitchell's it involved the lower limbs. The patient woke up with rigidity of the legs so extreme that he could not bend ankles or knees. The symptoms disappeared after a time, to relapse with a bout of alcoholism, and finally to disappear, to be followed by (apparently) locomotor ataxia. In another case of Mitchell's, there was no discoverable organic basis. The spasms were very painful, but finally disappeared. Mitchell saw a similar condition in hysterical women.

Sleep-Numbness: Nocturnal Paresis or Paralysis.—This condition appears to have been described first by Weir Mitchell in 1872. Day-numbness of the " functional " kind—" functional " in this sense is virtually synonymous with " transient " —whether it be hysterical, anæmic, gouty, or diabetic, is apt to repeat itself in sleep. But sleep-numbness may occur apart from any similar manifestation during the day, and may likewise be hysterical, gouty, anæmic, or diabetic in origin, or it may be the result of endarteritis in the vessels of the brain or cord. In the latter

case it may naturally end in paralysis; in diabetes, it may be a premonition of gangrene of the part. Weir Mitchell also considered the excessive use of tobacco to be a cause.

Sleep-paralysis, or sleep-numbness, occurs in various degrees, from a local transient slight feeling of numbness or tightening confined to one finger, or to a limb. There may even be transient hemiplegia with diminished sensibility to touch and pain. It may be repeated night after night, or at intervals for years. Pain is sometimes an accompaniment. The anæsthesia may give rise to a feeling akin to what follows amputation; the greater part of a limb is felt to be wanting, and the hands or feet feel as if brought close up to the trunk. Recovery of power occurs gradually after waking; in one case recorded by Weir Mitchell the process of recovery regularly took 3 hours to be complete. In Weir Mitchell's cases, the condition seems usually to have cleared up after some months of tonics.

Such transient paresis of a limb on waking is frequently complained of, especially by hysterical patients. When they are informed that the paresis is not of physical origin, they frequently counter with the remark that it cannot be of mental origin, else it could not be present before consciousness has fully returned. Such an objec-

tion depends on two fallacious conceptions: that hysterical paralysis is dependent only on fully conscious mental processes, and that sleep involves a total discontinuity in the mental life of the individual.

Sleep-ptosis occurs on waking. "The patient awakes with palsied lids; lifted, they fall." The recovery of voluntary movement may be slow, and even occupy as long as an hour. In one of Weir Mitchell's cases, the condition followed the death of the patient's husband, and disappeared on her re-marriage. In another case, a spasmodic contraction of the lids commenced during sleep, and the patient had to force her eyes open when she awoke.

Aural Vertigo during Sleep.—The suddenness of an attack of aural vertigo during sleep awakens the sleeper. Gowers records the case of a woman aged 33 in whom deafness and hissing tinnitus had existed for 18 months, and in whom also sudden vertigo, in which objects seemed to move anti-clockwise, had occurred at intervals for a year, with a feeling of motion both of herself and objects. During sleep she was awakened by a sudden grinding sensation in the head, and a feeling that she was sinking through the bed. (A similar sensation is not uncommon in neurotic subjects while lying in bed awake, and when no

sign of aural disease exists.) While in this condition Gowers' patient felt she dared not raise her head.

Gowers had himself a kindred experience on one occasion. As he fell asleep he had first of all the sensation of falling through space. This aroused him thoroughly and suddenly, and he caught the sound of a flutter in his ear which he interpreted as the result of contraction of a tympanic muscle, probably the stapedius. This would lessen the pressure in the labyrinth, and so would also lessen the pressure on the ampullæ which are at the lower ends of the canals. This effect, being normally that of sudden descent as in going down in an elevator, would produce the illusion of falling.

Gowers suggested that the occurrence of aural vertigo during sleep might be the result of a summation of stimuli upon the ampullæ, this summation being itself the result of the continuance of the recumbent position. The total effect of the stimulus at last overtops the threshold and a sensation breaks through into consciousness. This may be facilitated (he thought) by the functional disassociation of higher levels from lower ones that occurs during sleep.

General conclusions for a theory of sleep, from

a survey of the pathological conditions described above:—

Disturbances of sleep when they are dependent on discoverable physical causes, are immediately associated with brain-conditions, and are related to morbid conditions of other parts of the body only indirectly via the intermediation of the brain. A predominant rôle for the cerebrum in the physiology of sleep seems a legitimate inference. In the brain itself, lesions of the grey matter at the base, and especially of the region of the floor of the third ventricle and of the anterior end of the aqueduct, are more commonly associated with sleep-disturbance than any other region.

When no structural alteration in the nerve-tissues is discoverable, it is confirmatory of the above inferences to find that in certain morbid clinical syndromes disorders of sleep occur in conjunction with disturbance of other functions that are for other reasons presumed to have their physiological seat principally in the basal grey matter of the localities already mentioned. These syndromes are especially the narcoleptic-cataplectic series, in which disturbances of emotion, of muscle-tone, and of sleep are commonly associated.

That sleep as a function of the organism has

attained a certain degree of self-regulation is suggested by the reversal of its incidence in some lesions of the basal grey.

A dissociation of different parts of the central nervous system as regards sleep is shown by the phenomena of various types of somnambulism, and by sleep-paralysis, as well as by the variants of the narcolepsy and catalepsy group. An apparently legitimate inference is that the neurophysiological state which expresses itself clinically in sleep is one into which several functional elements or groups of elements may enter independently. Another conclusion on the same grounds, which seems probable, is that sleep is not determined by a general state of the blood and cerebro-spinal fluid, such as is implied by the hypothesis of a sleep-toxin.

CHAPTER IV

TREATMENT

Types of Sleeplessness.

For clinical purposes a very simple classification having reference to therapeutic methods is desirable.

1. Sleeplessness due to physical disease (*a*) of the central nervous system, (*b*) of other parts of the body. The insomnia so produced may be either a direct effect upon the brain cells, from toxæmia, anæmia, etc.; or an indirect effect via the mental route from discomfort or actual pain.

2. Sleeplessness from external irritation, such as climatic conditions.

3. Sleeplessness resulting from mental causes.

The diagnosis of the cause of sleeplessness of the first type is a problem in general medicine. It is wise to remember that insomnia may be one of the earlier symptoms of some bodily disease, and a complaint of sleeplessness should always lead to a careful **physical examination** before the case is included in the second or third groups. Moreover, the physical examination,

even if nothing is found, is of considerable importance in reassuring the patient. Nowhere is it more desirable to obtain his complete confidence than in the treatment of insomnia, and a painstaking examination goes a long way towards securing this. Where physical disease is found and is clearly the cause of the insomnia, the treatment is naturally that of the underlying disease and of its associated discomforts. For example, pain may be relieved by local applications, and cough by expectorants; but when these fail hypnotics are permissible.

The **general conditions** of the environment which should be secured are similar for all types of insomnia.

Burton's advice is good still, but perfect beyond the usual possibilities. "He that will intend to take his rest must go to bed . . . with a secure and composed minde, in a quiet place; . . . and if that will not serve, or may not be obtained, to seek then such means as are requisite. To lie in clean linen and sweet; before he goes to bed, or in bed to hear 'sweet musick' . . . or . . . to read some pleasant author till he be asleep, to have a bason of water still dripping by his bedside (Ovid), or to lie near that pleasant murmure 'leve sonantis aquæ' (of gently sounding water). Some flood-gates, arches, falls of

water, like London Bridge, or some continuate noyse—that may benum the senses; . . . as a gentle noyse to some procures sleep, so . . . a darke room, and the will itself, is most available to others " (" Anatomy of Melancholy ").

For insomnia of recent origin in the professional man who has definitely been overworked, there is nothing like a brief holiday of a few days, preferably at the week-end in some congenial spot, from which any communication with his working headquarters should as a rule be forbidden. He may be provided with a full dose of some rapid hypnotic on the first night, which can be left by his bedside, and which he is to take if not asleep by midnight. This breaks the habit and re-establishes some confidence, and in such circumstances it is usually found to be unnecessary to take the hypnotic on subsequent nights, although for a further night or two it may be left by the bedside in the same way.

Regular daily exercise in the fresh air, provided it is not taken with the object of producing fatigue, is valuable.

Excessive fatigue should be avoided; and when the nightly amount of sleep is much below the patient's average, a rest of an hour or two in the afternoon should be enjoined. If the patient should fall asleep during these afternoon rests,

so much the better. It is fallacious to suppose that an afternoon sleep will interfere with the night's sleep; on the contrary, the latter is facilitated.

The bedroom should be reasonably large and well-ventilated, away from special sources of noise, and in the winter it should be warmed to between 55° and 60° F. The blinds should be of dark material, so that even direct sunlight will not make much difference in the illumination of the room. The bed should be furnished with a spring mattress with a reasonable amount of "give" in it. Except in cases of acute illness requiring nursing attention, the patient should be left in the bedroom alone.

When the patient is sensitive to cold, it is better that he should wear a woollen vest underneath his pyjamas, than that extra bed-clothes should be added.

Lower altitudes and relaxing climates are to be preferred, when the question of a "change" arises in long-standing primary insomnia.

Insomnia from Physical Disease.

In **sleeplessness due to pain** opium is the mainstay, but the coal-tar preparations should usually be tried first, and may be combined with a hyp-

notic. Aspirin and phenacetin are of use only in the mildest cases. Pyramidon is more potent. Veramon, the molecule of which consists of one pyramidon linked to one barbitone molecule, has lately been introduced as an analgesic. In this compound, the hypnotic effect of the barbitone is neutralised by the physiological antagonism of the stimulant effect of pyramidon.

In **physical conditions other than pain,** causing sleeplessness, opium is commonly contra-indicated, especially in chronic bronchitis with profuse secretion, in the later stages of phthisis, in renal affections, and in all ailments of childhood and infancy. But the knowledge that morphine depresses the respiratory centre, and that its excretion is by the kidneys, has led to its being withheld in conditions where frequently it is of greatest benefit. For example, Osler strongly recommended morphine for the restlessness and delirium of uræmia; but Burney Yeo remarked that if it be used freely for this purpose, " the restlessness of uræmia may be relieved by the repose of death." But the cautious use of morphine in uræmia is not thereby invalidated. Similarly in pneumonia, to withhold morphine in the early stages before the fifth day is to deprive the patient of his most effective aid to sleep. Opium in the early stages of pneumonia

conserves strength, and diminishes the chance of delirium. Hutchison remarks that it is "wise to use it unhesitatingly at this period, so as to have some sleep in hand." After the fifth day, it is not safe, on account of the increasing respiratory embarrassment. Similarly, in bronchitis, caution should be tempered with courage in the exhibition of opium. Carr recently reported a case of acute general bronchitis in an elderly patient, whom morphine given orally (since by that route, although its action is slower, it is held to be equally effective and more safe) appeared to rescue from a hopeless condition of exhaustion and sleeplessness. In such a case it is wise to give atropine with the morphine, to diminish bronchitic secretion.

In **pneumonia,** after the fifth day, paraldehyde is the safest hypnotic. Like morphia, paraldehyde is apt to be given in doses that are too small. Since paraldehyde is non-toxic to the heart, it may safely be given in 2-drachm doses—and it is very often useless to give less. Chloral, combined with digitalis, has in the past been used as a routine treatment in pneumonia from the beginning of the illness. Its reputation as a cardiac depressant seems to be a good deal undeserved, and Hutchison has found it useful after the fifth day of pneumonia, when mor-

phine is no longer considered safe. Whisky in 2-drachm doses at intervals is not so much employed as formerly, but is useful when toxæmia is not severe. In bronchitis with much dyspnœa keeping the patient awake, when there is also much cyanosis, morphine is usually contra-indicated (*cf.* Carr's experience, *supra*), but opium by mouth, as Dover's powder, may be tried instead. In acute pulmonary conditions with dyspnœa, in general, oxygen is useful in aiding sleep if administered effectively—*i.e.*, by nasal tube, although the discomfort of the tube, on the other hand, may hinder sleep.

In **cardiac disease,** where sleeplessness may depend on one or more of several causes, especially dyspnœa, palpitation, cardiac pain, cough, and the like, the treatment must, as in all similar positions, vary to some extent with the particular cause. But where the latter has been dealt with as far as possible and insomnia persists, ammonium bromide (since the ammonium salt is less depressant), paraldehyde, or chloral may be tried. Chloral in 5 to 15 gr. doses repeated in 2 hours if necessary is said to be successful, especially in cases with a blood-pressure above normal (since it has a vaso-dilator effect).

It is probably wise however to avoid its use where extensive myocardial degeneration is sus-

pected. Where insomnia is the result of cardiac dyspnœa, morphine acts like a charm. The drug should be commenced in small doses, gr. $\frac{1}{6}$, the effects being carefully watched, and the dose gradually increased to gr. $\frac{1}{4}$ or more. When there is much bronchial secretion or pulmonary œdema, it is necessary to observe whether these are increased by the use of opium. In such cases, atropine should be given along with the morphine.

In **acute rheumatism,** when pain is interfering with sleep, a small dose of morphine can be given along with some of the doses of salicylate.

In **phthisis,** when the insomnia is due to cough, codeine is probably the most satisfactory measure. Heroin, dionin, and morphine may all be tried.

In **uræmia,** with dyspnœa causing sleeplessness, morphine is generally to be avoided, as already mentioned. Since the dyspnœa of this condition is the result of an acidosis, soda bicarbonate every 3 or 4 hours is theoretically indicated. When there is delirium and restlessness, hyoscine hydrobromide (gr. $\frac{1}{100}$ hypodermically) has sometimes had good results (Hutchison).

In the insomnia of **hypertonus,** it is worth while remembering that the diastolic pressure may be greater in the recumbent position, and

that a high pillow has therefore something to commend it in this condition.

Insomnia resulting from **organic disease of the brain** where the latter does not involve the increase of pressure that causes drowsiness, is often peculiarly resistant to the action of hypnotic drugs, partly because of the intimate relation of the lesion to the tissues in which sleep appears to have its principal seat, and partly because of the irritative and release phenomena which are often present. Difficulty in inducing sleep is especially evident in some cases of epidemic encephalitis, both acute and chronic. Even very large doses of hypnotics may fail. Fortunately the chronic encephalitic patient (at least) does not seem to feel the lack of sleep so much as normal persons do. Thus a Parkinson chronic encephalitic, who slept only 4 hours each night, felt as fresh as in former days when his average was seven. For the extreme restlessness of certain chronic encephalitics, especially children, a **warm wet pack** is sometimes very effective in producing sleep when everything else fails. Presumably it acts largely by immobilising the patient, the muscular relaxation inducing sleep. The bladder and lower bowel should first be emptied. All that is required is two blankets wrung out of water at a temperature of about

101° F. The patient is wrapped closely in them, the blankets being pinned lengthwise with stout safety pins, so that the patient looks rather like an Egyptian mummy. The packing is done sufficiently loosely to allow easy breathing, but tightly enough to prevent movements of arms and legs. For efficient packing more than one nurse is desirable if the patient is at all obstreperous.

For the usually less aggressive motor disturbances in adults following encephalitis, which may interfere seriously with sleep—clonic spasms of the limbs, for example—the **continuous tub** has been tried. In this the patient can remain for several hours if necessary with the water at a constant temperature, but this method has not met with much success in such conditions. It has lately been the fashion to instal continuous tub equipment in mental hospitals. Continuous tubs are undoubtedly useful, but in my experience —and others who have tried them have the same opinion—their application is much more limited than their advocates would have us believe. The patients for whom one would most like to use them—namely, the very excited patients—are precisely those who are too restless to be manageable in the bath without a struggle, which nullifies the effect intended. And in other

types of patient the effect in insomnia is often trifling. Nevertheless the effectiveness of continuous tubs, like everything else, depends largely on the manner in which they are used. A nurse or attendant experienced in this method of treatment is essential. The bath-room should be at some distance from the ward, or any other source of noise. There should be a mechanical means of assuring that the temperature of the tub shall be constant, somewhere between 92° and 97° F. The lighting of the room should of course be reduced. Shorter periods of 4 to 5 hours are more valuable than periods of 18 to 24 hours (Chapman).

Insomnia from External Irritation.

The methods of treatment for the second group of **insomnias resulting from external irritation** are obvious. But a caution is perhaps justified. A great many neurotic patients attribute their insomnia or much of it to noise. In hospital, or in a nursing home, they find themselves always in what they regard as a specially noisy part of the building. It is a safe rule, with few exceptions, to disregard the complaints of such patients to the extent of refusing to move them to another room or bed unless the dis-

turbance is very clear to others. "One hears only the noises one listens for," and the insomnia in these cases depends not on noise but on anxious expectancy of it. To change the room is only to admit that it is noise that is keeping the neurotic patient awake, and this is almost always an erroneous belief.

Insomnia from Mental Causes.

It should be realised that the mental causes of insomnia are in themselves various. Usually in descriptions of treatment what is emphasised is the different types of sleep disturbance that may occur. Some patients have difficulty in going to sleep, some awake too early in the morning, some suffer from broken sleep, some sleep lightly or unrefreshingly or both, and others hardly sleep at all (an hour or two per night). These distinctions have a limited use in determining to some extent whether, if hypnotic drugs become necessary, one shall use a rapidly acting drug like paraldehyde, or an agent with slower but more lasting action like sulphonal. But in practice such differences matter relatively little. What is more important is to discover if possible the kind of mental cause that is at work.

The particular mental causes are as numerous as the individuals concerned, but they fall into certain general types, which may be briefly described.

Insomnia originating in mental perturbation is apt to be complicated with physical effects; the psychological condition that produces the loss of sleep being capable of producing bodily effects such as palpitation and abdominal discomforts of various kinds, which may in themselves keep the patient awake. In some instances the psychological factors seem to work chiefly by this means, producing insomnia via the bodily route.

The most obvious and possibly the commonest psychological factor is overt worry or in more technical jargon **"anxious preoccupation."** The simplest example of this kind is furnished by the habit some people have of planning their next day's work after they have gone to bed, or of recapitulating the day's events, especially if the latter have gone wrong somewhere. This is a habit which can be voluntarily stopped with little effort when the patient's attention is drawn to its pernicious consequences.

Very often however, if after careful consideration you attribute a patient's sleeplessness to worry, he will indignantly deny that he worries at all at night. He will protest that he goes to bed

and " thinks of nothing " or only of indifferent topics. This is the kind of person who expects to be able to worry all day and yet to sleep at night simply because he changes the topics of his preoccupation. In point of fact, by thinking of " nothing," by which he means nothing unpleasant, he is making a tremendous effort at repression of his daytime perplexities, and it is the effort at repression that keeps him awake. The sound sleep that follows the *relief* of a prolonged anxiety is an illuminating contrast to the insomnia which results from such an effort of repression. It is clear that the only satisfactory method of treating insomnia of this kind consists in removing the daily habit of anxiety. The detailed treatment is that of the psychoneuroses in general.

In relation to anxious preoccupation as a cause of sleeplessness, it is well to emphasise the existence of a secondary topic of anxiety in nearly every sleepless neurotic patient. There are certain medical beliefs so widespread in the community that they rank almost as folk-lore; the belief in the profound and evil effects of insomnia is one of them. Insanity and even death are believed to be the inevitable sequel of prolonged deprivation of sleep, and few neurotic people are persistently sleepless in whom these apprehen-

sions do not loom large—not that they will necessarily mention their fears. To some patients the possibilities are so terrible that they dread confiding them to the doctor, lest the worst be confirmed. We are however in a position confidently to reassure them. The experimental data, as we have already seen, show that the effects of insomnia in man are of a trivial nature. Clinically, one can say also with confidence that loss of sleep has never been shown to be a dominant factor in the production of mental illness. Indeed, I have not personally seen a case in which it could be considered anything but a minor factor; the *causa causans* lies always behind the sleeplessness. It seems that if it were not for the almost universal belief in the catastrophic effect of insomnia, and if it were not also that patients complain so loudly when they do not sleep well—since insomnia occurs chiefly in just those people who make most moan of their discomforts of whatever kind—we should hear much less talk of the fundamental importance of combating sleeplessness and much less discussion of the dangers of hypnotic drugs. One thing emerges clearly however—that one of the important preliminaries in the treatment of almost any case of insomnia is the reassurance of the patient on these fears which, if not proffered,

should be warily sought for. Clumsiness in eliciting whether the patient is afraid of insanity may, of course, serve to increase his dread of it.

While most sleepless patients retire to bed in fear that they will not sleep, there are a few, curiously enough, who are afraid that they will. They lie awake because they are afraid to sleep. This is comparatively rare in ordinary practice, but during the war it was not uncommon in "shell-shocked" soldiers, whose dreams of war were so vivid and so distressing that they would willingly have lain awake in order to avoid them. Occasionally in civil practice a patient is encountered in whom there exists a fear of sleep itself. There is sometimes under the surface a fear of death, the patient as the result of certain events in his life or of certain mental impressions having come to identify sleep and death. Thus one patient, a woman, owed her fear of sleep partly to the fact that her father had died in his sleep, so that a misunderstanding of the association of sleep and death had persisted in her mind. Some neurotic persons fear equally the sleep of ether anæsthesia, again because of its identification with death. I remember a man who suffered severely from insomnia for 6 weeks before undergoing an operation of gastro-enterostomy, not because he feared the operation

itself, but because he feared the unconsciousness of anæsthesia—apparently, as it afterwards transpired, in relation to a feeling of guilt for sexual malpractices, for which he believed that he might be punished by illness or actual death.

Another anxious patient lived in dread of an apoplexy, and this fear produced feelings of " deadness " and numbness in his limbs, so that he had to keep moving them to reassure himself that they were not paralysed. In the evenings the paræsthesias reached a crisis, so that he felt that there was only a small fragment of himself left, and he was afraid to sleep lest that also should go. The real cause of his insomnia and of all these symptoms lay, of course, deeper—in a long-standing habit of anxiety about health, inculcated by his mother from early childhood, and in other factors.

It is clear that sleeplessness from the fear of sleep requires the same kind of psychological investigation and treatment as any other anxiety state.

There are cases in which insomnia begins in response to some cause of anxiety, and persists after the original cause of anxiety has disappeared, the patient having established an anxiety about sleep itself. In such instances however one finds that the individual is not ordinarily as stable as

he might be, and while reassurance along the lines already indicated may go far, some inquiry into the general attitude to health and other difficulties will often be rewarded by a greater general stability.

Another instance of disturbed sleep, arising from the presence of an anxiety-state, occurs in patients who fall asleep readily enough, but are distressed by awaking in a state of great fear, with palpitation, epigastric sensations, etc., an hour or two after they have gone to sleep. Apart from psychotherapy, and the use of sedative or hypnotic drugs if necessary, it is helpful if the patient knows that he can have a warm drink if he fails to fall asleep quickly again. A thermos flask with hot milk can be left by the bedside for this purpose.

As the result of the continual worry which anxious patients inflict upon themselves, they are unable to feel relaxed physically. Commonly they describe themselves as "all strung up." Muscular relaxation is an important precondition of sleep, as we have seen, and can be aided in various ways. The only radical method is of course the relief of the anxiety; and not much stress is to be laid on the methods about to be described. But the latter are useful as adjuvants, and besides helping towards muscular relaxation,

have some suggestive mental effect. The patient can be taught by precept and by means of passive movements to relax himself. It is not a bad plan also in people who can afford the time to do so to order them to take a complete rest in the recumbent position each day after lunch. A glass of beer or stout taken with lunch helps the desired effect of general relaxation. If some sleep follows so much the better. Many patients fear that if they sleep during the day they will not so readily sleep at night. Nothing could be more mistaken. The comparative peacefulness that often ensues after such a sleep, the relaxation produced, far beyond anything attainable while awake, and the confidence engendered go far towards helping the patient to sleep at night.

Other commonly used methods of inducing relaxation are the warm bath and gentle massage. Neither of them is uniformly helpful. Some people are made more uneasy by them than they were before. The bath should be kept warm—at 100° to 101° F.—and the patient should remain in it for 15 to 20 minutes. Massage, if it be used, should be of the gentle " effleurage " kind.

The other simpler methods for persuading sleep, such as reading in bed, have a narrow practical application. Some find them helpful.

It is a matter of individual peculiarity. Devices like "counting sheep," or anything involving evident mental effort of any kind, are to be vehemently discouraged. They are merely quasi-mechanical tricks for repressing unpleasant thoughts. Someone has remarked that the difficulty in inducing sleep is that by a voluntary act one tries to produce an involuntary condition. But there is no volition in going to sleep after one has placed oneself in the most favourable conditions that the environment of the moment may afford. One lies down, lets one's muscles relax and one's thoughts wander, and volition ceases. Sleep follows naturally in a short time. The normal person does not will himself to sleep. He allows himself to do so. His difficulty in ordinarily favourable conditions is not in going to sleep but in keeping awake. Everyone has noticed that in falling to sleep one's thoughts are cursory and disconnected. The sleepless person should imitate this, relaxing his thoughts as well as his limbs, thinking of anything provided it does not involve definite planning or vivid recapitulation of past events and the like. The essence of the matter is to avoid effort, letting one's thoughts be as disconnected as they please.

Another cause of insomnia, and especially of

difficulty in going to sleep, fortunately not nearly so common as those already discussed, arises in the obsessive-compulsive type of psychoneurotics. In a mild form the kind of anxious preoccupation involved occurs to all of us—as when we go to bed and become uneasy whether we have extinguished the gas or have closed the bedroom door properly. Sometimes we have reluctantly to get up again to make sure. A glance reassures us and we get into bed again with mingled relief and shame at our weakness. But the truly obsessive-compulsive patient has a much harder task to obtain relief. He usually has to go through an elaborate ritual before he can compose himself at all; and the ritual may have to be performed again and again in the course of the same night. For example, a certain patient had to place his shoes always at right angles to the wall, and had to get up several times to reassure himself that they were correctly placed in the perpendicular. If anyone passing along the corridor outside his bedroom accidentally disarranged his shoes, and the patient overhead the accident, he had to rise again to restore them to their original position. Similarly, he had to have his clothes arranged in a certain way on a chair, and nothing might be placed in his bedroom in such a position that it might by the

remotest chance fall during the night. Hence, his brushes, etc., were placed carefully away from the edge of the dressing-table. This outer rectitude was in part a compensation for an overwhelming sense of guilt, which itself disturbed his sleep also in a more direct fashion. Further, he could not compose himself to sleep until he had said his prayers exactly to his satisfaction—and this might involve repetitions lasting many hours, as he had to be word-perfect, and the wrong words would insist on cropping up. Such a condition is not very rare. The only sound method of tackling it is by psychological analysis, but this does not always succeed, and in such a case, or while psychotherapy is being proceeded with, other measures—including hypnotic drugs—may have to be resorted to.

It is very uncommon to meet with **deprivation of sleep as a malingering device**, but in the late war there were instances where men already in hospital with "shell shock," and knowing that insomnia was considered a bar to returning to the front, kept themselves awake for a considerable portion of the night by a voluntary effort.

Insomnia in the Psychoses.

In the **psychoses,** the insomnia which is so frequent is determined by several of a variety of factors. It may be part of a general excitement, and follows naturally from the mental over-activity and disregard of the need for rest and sleep. It occurs also as one of the outstanding symptoms of many depressions, partly the result of the unhealthy mode of life led by such patients —lack of exercise, discomfort arising from obstinate constipation, etc.—and partly the outcome of the incessant depressive or anxious preoccupation. The motor restlessness that accompanies so many psychotic conditions contributes to insomnia. The nature of the mental content —delusions and hallucinations—is frequently also a contributing or even the principal cause. It is important to bear in mind that the very weirdness of the psychotic's subjective experiences may be a sufficient cause of sleeplessness, and that auditory hallucinations especially, which many patients do not readily mention, may play an effective rôle in preventing sleep. A young man who had complained of inability to sleep, which had been attributed to " neurasthenia," was found on admission to hospital to be continually hearing voices which called him

opprobrious names. He had been considerably worried, having contracted a secret marriage. The hallucinations were the direct outcome of his feeling of guilty responsibility about this, and he did not confide their existence till specially questioned on the matter. The failure to inquire for such a cause of insomnia, especially in a case where the other symptoms arouse a suspicion of the existence, may cause an important point in diagnosis to be missed, and lead to faulty treatment. The patient mentioned recovered completely after he had confided the circumstances of his marriage, and had the union recognised and accepted by his parents.

Apprehensive delusional expectations can also serve to keep a psychotic patient awake—if he expects to be assaulted in the night, or to be poisoned or tortured or any other of the many gruesome possibilities which involutional melancholic, paranoid, and schizophrenic patients are especially likely to envisage. The psychotic forms an impressive contrast in many cases to psychoneurotics in that the amount of sleep he gets has to be recorded as far as possible by those attending him; for often, unlike the neurotic, he does not think of complaining even if his unaided sleep dwindles almost to nothing. It has been found helpful, both in calming restless-

ness and in favouring sleep, to nurse patients with prolonged psychotic illness as far as possible in the open air—verandahs being usually provided in mental hospitals for the purpose. Direct psychotherapeutic approach is not possible in acute psychotic conditions, and even where the patient's co-operation can be to some extent obtained, psychotherapy has a very limited application, at least as far as direct influence on symptoms is concerned. The aim of the physician in treating the insomnia of psychotics (or indeed in treating any kind of insomnia) should be to promote sleep by careful nursing and medical care, resorting to drugs only when these measures have failed to produce the minimum amount of sleep that seems desirable in the individual case. Elimination by the bowels is best obtained by salines given in laxative doses. Where the nutrition is impaired, and digestion is difficult from emotional or accidental causes, frequent feeding with a liquid diet is preferable, in order to place the least possible burden on the digestive system. In certain toxic-infectious psychoses in the acute stage, the administration of alkalis, in the form of sodium bicarbonate principally, is indicated because of the acidosis that has been ascertained to be present.

Hydrotherapeutic measures, especially sponging,

the warm wet pack, the cold wet pack, and the continuous tub are all worth trying before hypnotic drugs are resorted to. The **cold wet pack** should be reserved for patients in fairly robust physical health. It should be preceded by a hot foot-bath, with frequently renewed cold compresses to head and neck. While the patient is in the pack, cold compresses are left on the forehead. The pack itself consists of two sheets wrung out of cold water. The patient is swathed in these and then in a couple of blankets, which in the case of an excited patient can be pinned in front. If no reaction occurs in 30 minutes, the patient should be removed from the pack, hot-water bottles placed about him, and warm drinks given. If the pack fails to give a sedative effect, the patient should be removed from it as soon as restlessness begins or when he becomes overheated, as shown by flushing of the face (Chapman). The pack should be followed, if possible, by a neutral shower at 96° F. for a few seconds, and it is recommended that the patient should be dried with a sheet, without rubbing. The cold wet pack is specially useful in manic excitement in young, physically healthy patients.

In other conditions, such as the sleeplessness of **agitated depression,** the continuous tub is a more suitable form of hydrotherapy. It is also useful

in quieting manic excitement and inducing sleep in that condition. Medinal can be used as an adjuvant—at least, until the patient becomes accustomed to the tub. The details of continuous-tub treatment have been described under the treatment of insomnia in " organic disease of the brain." Several precautions must be observed. The pulse must be carefully watched while the patient is in the tub, especially in patients with cardiovascular lesions. The skin has to be looked after, as the continuous immersion not only leads to maceration of the skin, but is a ready vehicle for the spread of any skin infection that may be present—*e.g.*, a furunculosis. The conjunctivæ are specially susceptible to infection by this means. Chronic middle-ear conditions are said to have been aggravated by continuous-tub treatment.

Other Physical Methods.

In all excited patients, and in many of those that are simply restless, the provision of a **single room** with observation through a window in the door, is very helpful. Physical restraint, even to promote sleep, has gone out of fashion, but there are some who advocate a " rest-jacket," which is a sleeveless vest lacing up the back with

a loose fastening from a point about the small of the back of the vest to the head of the bed, and with sufficient play for free movements in the reclining position. This is said to be useful, for feeble patients, especially senile and arterio-sclerotic patients who are confused and resist nursing care. It is also applicable in some agitated depressions when the patient is threatening to exhaust himself by standing (Chapman).

Hypnotic Drugs in Psychotic Insomnia.

When drugs are resorted to, there is not the same necessity as in psychoneurotic patients for obtaining a sure sleep with the first dose for purposes of reassurance. The smallest likely dose may be given at first, and if this fails, increases may be tried till the quantity sufficient to produce at least 5 or 6 hours' sleep is found. A mixture of chloral and bromide, in the proportion of 20 gr. of the former to 30 gr. of the latter, or of 30 gr. of chloral and 40 gr. of bromide, is a prescription which can be continued for a considerable time without harm. It is useful in long-standing excitements, when the continuous restlessness interferes with sleep, and with the general nutrition. Medinal is a useful alternative which also can be continued for a

long time if necessary, without harm, if care is taken to avoid a cumulative action and its resultant toxic effects.

These are useful as routine hypnotics in patients where sleep has not proved controllable in other ways. Where a quick effect is desired, as in the sudden outbreak of excitement, or when the drugs just mentioned have failed, paraldehyde in doses of ii. or iii. drachms is often effective, and may in exceptional instances have to be repeated after an hour. When this fails to restrain the excitement, or when the patient refuses to swallow anything by mouth, hyoscine hydrobromide (gr. $\frac{1}{100}$) combined with morphine gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{200}$, is very useful, and has the advantage of being able to be given hypodermically. The dose may in some instances have to be repeated, but with very cautious consideration (*vide* p. 149).

Sulphonal, formerly much used for chronically excited patients in mental hospitals, has gone out of fashion, partly because of its reputation as a cumulative toxin, and partly because it is less certain and much less rapid in its action than the other hypnotic drugs. In doses of gr. 20 to 40, given at least an hour before sleep as is desired, it is usually effective enough. Another method, which produces a more con-

tinuously sedative effect, is to give it in divided doses, gr. 20 at 10 a.m., repeated, and at 8 p.m.

Hyoscyamus and cannabis indica can be combined in a mixture which has been used successfully in chronically excited patients, 20 to 30 gr. of the tincture of each being given with syrup of orange three times a day.

For the sleepless restlessness of **anxiety-depression,** medinal in divided doses throughout the day (gr. 2½ t.i.d.) with, if necessary, an additional 2½ or 5 grains at bedtime, may help considerably not only to produce sleep but to still the restlessness of the waking hours.

The treatment of sleeplessness in patients with **presenile** or **senile dementia** presents special difficulties. It is bound up with the treatment of the restlessness so frequent in them. For the motor unrest Kraepelin has recommended tincture of opium, beginning with 10 to 20 mm., and increasing to 20 or even 50 mm. three times a day, and then gradually reducing the dose. If this does not also help the insomnia, then one after another of the hypnotics already mentioned should be tried, until the most suitable one is found. For cases of presenile dementia (presbyophrenia and Alzheimer's disease) veronal or medinal (5 to 10 gr.) is suitable; but in patients with arteriosclerotic brain-disease and in senile

patients, either of these preparations is apt to produce a degree of drowsiness in the daytime which is undesirable, as this increases the mental confusion. This effect is partly due to the accumulation of the drug in the body, from the diminished excretory capacity of kidneys affected by arteriosclerosis, and partly to its greater effect on an already damaged cortex. For these reasons, the dosage of veronal or medinal should be small (2 to 5 gr.) and carefully watched, and other hypnotics, like chloral (except in the presence of grave myocardial signs) and paraldehyde are preferable. Ammonium bromide in 20 to 40 gr. doses may sometimes be sufficient; and in feeble old people, there may be nothing so effective as dilute whisky (grog) at bedtime. The importance of avoiding a heavy meal in the evening in these patients has to be remembered.

Delirium Tremens.—To obtain sufficient sleep for the patient is the primary necessity in the treatment of this condition. The other cardinal points are satisfactory elimination by the bowel, and a sufficiency of nourishment. It is usually possible to obtain sleep by medinal gr. xv., which may be repeated to the extent of gr. x. if the first dose has not been successful within an hour and a half. Paraldehyde gr. ii. or iii.,

also repeated if necessary, is a safe alternative, and it is to be preferred in elderly patients and in those with arteriosclerosis or kidney disease. Sometimes with hypnotic drugs alone, sleep does not come and a hallucinosis persists; in such cases it is wise, instead of proceeding at once to hyoscine hydrobromide hypodermically, to allow a little alcohol in the form of whisky ʒii. at intervals. This along with hypnotics frequently enables sleep to be obtained, and can be gradually withdrawn.

Sleeplessness in Children.

The restorative function of sleep is nowhere better seen than in children. There is no doubt that far too much has been made of the rôle of fatigue in the production of functional "nervous" symptoms in adults. In them fatigue plays a comparatively small part. But in children the case is different: there is little doubt that the functional nervous phenomena seen in children, especially morbid fears and muscular tics, are considerably accentuated by diminution in the usual allowance of sleep. It is of some theoretical interest that it is precisely those abnormal phenomena which imply a more direct failure of inhibition (obsessive fears and tics)

which appear to be most affected in children by insufficiency of sleep.

The point is well emphasised by a contemplation of the energy consumption in sleep, in comparison with that of the waking hours.

In Chapter I. it has been shown that the energy requirements in a child during the waking hours may be in ordinary circumstances four times as great as in sleep, and that even slight restlessness during sleep enormously increases the energy consumption.

No definite figures can be given for the quantity of sleep a child needs, except within wide limits. The amount depends not only on age, but also on weight, height, nutrition, liveliness, time of year, climate, and the like. Moreover there is a seasonal variation in energy requirements. F. Müller has calculated that the daily caloric requirements per square metre of body surface is 1,640 cals. in early spring and 1,430 cals. in summer. Also some children, even from an early age, appear to require less sleep than others. There are familial differences of this kind, as if there were a kind of inherited sleep-constitution. With these reservations, the following figures are given as representing the average time spent in sleep at different ages (O. Marburg):

First year	18 hours.
Second to fifth year	14 ,,
Fifth to sixth year..	12 ,,
Seventh to fourteenth year ..	10 ,,
Fifteenth to fiftieth year	8 ,,
Fiftieth to sixtieth year	5 to 6 hours.
Over sixty-five	3 to 4 ,,

The fact that the long allowance of sleep in the child of 2 up to the age of about 5 years is usually split into two periods, one at night and the other in the afternoon, may be related to the fact that sleep in children is deepest at the beginning, and that it is consequently more useful to divide the total sleep up into discrete periods, if it be assumed that the depth of sleep is proportional to its restorative capacity (Aron). Furthermore it has been claimed that, although the depth of sleep attained in the night following an afternoon sleep is at first less than it otherwise would be, its depth increases towards the morning, and the period of increased depth lasts longer (Czerny).

The treatment of sleeplessness in children naturally includes the same general principle as in adults—namely, that any relevant physical condition should be sought for and treated. Rickets, for example, is notorious for its accompanying sleep-disturbance.

It is of the first importance to study the temperamental constitution of the child.

The bright, excitable, often intellectually precocious youngster must be gradually conducted bedwards for an hour or two before the actual bedtime arrives, and without his realising that there is anything anticipatory in the arrangement. Quiet non-competitive games, picture-books, and stories of a placid sort, and in older children constructive games are to be preferred. An early, but not too early, bedtime (approximately in accordance with the table given above), and in younger children an afternoon sleep, will help to avoid physical over-fatigue. Cameron advocates securing the co-operation of the young child in making going to bed an interesting play. The aim is to overcome the natural reluctance to go to bed, not by force, but by making bedtime interesting. The child can be amused by helping (in his small way) to turn on the taps for his bath, to wave good-bye to his garments one by one as the nurse puts them away, and so on. But play of this sort is apt to be prolonged as an end in itself.

When it is not a case of simple over-stimulation leading to a difficulty in falling asleep, but where a habitual emotional disturbance enters, the matter is more difficult. Treatment then depends

partly on the age of the child, partly on the nature of the emotional disturbance, whether it be fear, anger at being put to bed (negativeness), or the petulant and motivated crying of the spoiled child. In a young infant which sleeps badly and cries a good deal when it should be sleeping, the crying is probably an expression of definite malaise, and is not to be treated by Spartan methods of turning a deaf ear. The matter is otherwise with older children, and even with a number of older infants. The crying of temper is not very difficult to distinguish from the other forms; and the avoidance of symptoms of negativism of this kind is a matter of tactful handling on the part of the parent or nurse—a matter which can hardly be conveyed in words. As far as the act of going to bed is concerned, resistance can be avoided on the same principle of making bedtime something of a game in which the child co-operates and which has already been described for over-excitable children.

Where fear is the hindrance to sleep, it is necessary to discover if possible why the child is afraid. Stories associating darkness or blackness with fearsome creatures are so commonly heard by children, that it is not surprising that so many of them are afraid of the dark. Further

sources of fear, especially when the child is left alone, have been described by Watson. In experimenting with conditioned reflexes in young infants, Watson found that one of the very few stimuli capable of directly arousing the emotion of fear in them is a sudden noise. If the emotion of fear be taken as the response, and the noise as the stimulus, then the reaction noise-fear is a native or inborn reflex, to be contrasted with the conditioned type of reflex, which is an acquired reaction. But all conditioned reflexes are built up from native reflexes by substitution or association; hence anything—*e.g.*, darkness—that is associated at any time with a sudden noise becomes of itself an arouser of fear. Watson therefore recommends that the doors and windows of the nursery and the adjacent rooms should be reasonably silenced.

When a child has for a long time exhibited fear after going to bed, a usual consequence is that the mother or nurse has felt obliged to stay with the child habitually until sleep comes, and even to sleep in the same room always. In such an event, the first step is of course to discover the cause if possible of the child's apprehension. For example, one older child thought she was liable to fainting attacks, and held herself rigid to avoid these. She trembled from a combina-

tion of fear and muscular tension, and so could not sleep. Explanation and reassurance to the child and her mother, and instructions to the latter on the necessity for concealing her anxiety, are the essentials of treatment in such a condition. When the cause has been discovered and explained, there comes the task of restraining the child so that he will go to bed without fear, and will be able to sleep alone. This should be done gradually. A night-light should be allowed, and the bedroom door at first be left ajar. After a time these can be gradually withdrawn. Visits of mother or nurse after the child has gone to bed are to be rapidly cut down, the child being taught at first to be comforted by the knowledge that some adult is at hand not far away.

The method is otherwise for the crying of the spoiled child, who wishes to tyrannise over his environment. "If he howls let him howl." The anxious mother usually finds it difficult to follow this maxim; but persistence in it for a few nights brings reward.

Over-excitement is often found to be coupled with anxiety in older children. For the school-child who is having too much work allotted to him, or who is anxious over examinations, and for the rare case of the boy or girl who has just

left school and has been plunged into work with long hours, sometimes including Saturday afternoons, the lines of rearrangement are obvious.

The essential in the treatment of all cases of sleeplessness in children is that a complete survey of the patient's daily life shall be made and a tactful investigation into the child's own ideas and mental attitudes undertaken, in order that the treatment may not be merely palliative.

So far what has been described is chiefly treatment by rearrangement of the child's routine, according to his age, his temperament, and the nature of concomitant disturbance that may be observed. When this is insufficient, means more directly calculated to induce sleep have to be employed.

In infants, the effect of a continuous hot bath, for 10 minutes or more, is well known for its soothing effects. Cameron recommends letting the infant lie in a soft towel swung like a hammock under the water. He also recommends that the restless infant should be carried not in arms but on a pillow, as this seems to enable the infant to relax more completely.

Of hypnotic drugs, chloral combined with bromide has met with most favour. Two grains of each and 10 minims of syrup of orange, at bedtime, will suffice for a child of 1 year and

twice that amount at 3 years, and three times at 6 years (Cameron). The hypnotic may of course be used in conjunction with a continuous bath for 10 minutes or a hot pack for 20 minutes. As in adults so in children, when a physical illness is responsible for the insomnia, opium is more effective than other hypnotics. It can be given as Dover's powder, together with antipyrin. The dose is 1 grain of each for each year up to three. For older children, the dosage of hypnotics has to be calculated on the basis of age in the usual way, and varied according to the special indications.

Nocturnal head-shaking has been described in children by Oppenheim and Tappert. It consists of a strong, rhythmic head-movement, continuous, with short pauses, during the entire night's sleep. Marburg calls this type of disturbance a sleep tic.

Spasmus nutans may appear during the night. Nystagmus (when the head is held fixed), blepharospasm, and strabismus may accompany these conditions.

Hypnotics.

General Rules in the Use of Hypnotic Drugs.—This is a very important topic, not only because of the undisputed efficiency of hypnotic drugs in producing sleep, but because of the divergence—

one might say the passionate divergence—of opinion on their effects and on the indications for employing them. Moreover, the general public has heard so much about them—and much more about their alleged harmfulness than about their benefits—and have received such confusing and contradicting instruction from medical men on the subject, that in prescribing a hypnotic the doctor at once raises doubts in the patient's mind—doubts which by their very existence tend to lessen the effect of the hypnotic upon him.

The indications for the administration of hypnotics in physical disease have already been described. The general treatment of insomnia due to mental conditions and of insomnia in specific mental syndromes has also been given. The following discussion is therefore confined principally to the indications for the use of hypnotic drugs in sleeplessness associated with mental disturbance of whatever kind; which is, after all, the commonest indication for their use.

In general these rules should be observed in prescribing hypnotic drugs.

1. Never use hypnotic drugs alone, but always in combination with other methods.

2. Use hypnotics only when the other methods tabulated above have failed in themselves to procure sleep.

3. When these methods are not answering do not hesitate to prescribe drugs till the patient is miserably uncomfortable and thoroughly frightened about his insomnia. A stitch in time may indeed save nine, although not in preventing insanity by means of hypnotics in any direct fashion as is sometimes alleged.

4. Always in prescribing a hypnotic inquire into the patient's attitude to hypnotic drugs—"dope" as he so often calls, and believes, them to be—and give explanatory reassurances about their effects and the question of possible addiction, since these are fears which are usually in the patient's mind when he takes a hypnotic drug. They will be discussed below.

The fourth rule is concerned with a specially important point at the present time. Just as the public who are our patients have been taught to dread the effects of sleeplessness, so they have learned to hold in horror the use of hypnotic drugs. It is true that it is well that they should be chary of using them, as they would be chary of using any medicine which may have to be employed repeatedly—for example, purgatives for constipation; and special self-restraint is necessary where a drug offers an easy, quick, and comfortable way of getting rid of a troublesome symptom. But this can be achieved

without dwelling on the supposed—and, as we shall see, doubtfully supposed—evil effects of hypnotic drugs. The dread of these effects has been fostered to an extent that tends to stultify in many patients the use of such remedies. The reasons for this general apprehension are best discussed in relation to the particular drugs employed.

Types of Hypnotic Medicaments.—The hypnotics most generally used are:

1. Chloral and its allies.

2. The sulphone group (sulphonal and methysulphonal or trional).

3. The barbitone group (medinal, veronal, luminal, etc.).

4. Paraldehyde.

5. Hyoscine.

6. Bromide salts are mild sedatives, rather than hypnotics. They are useful only in mild and recent cases, and then partly from the suggestion implied in giving them. Given in small divided doses, gr. v. throughout the day (t.i.d.), they are useful in the mild insomnia of over-working people, whose overwork depends not so much on necessity as on their anxious attitude to life.

I omit opium from this discussion as its use should be limited to conditions where physical

pain is the chief obstacle to sleep, and should seldom be given as a hypnotic only. Hyoscine is used rarely and only for patients not manageable by other means, and extremely restless and excited, so that they tend to wear themselves out or actually inflict physical damage on themselves. It has the advantage of being given hypodermically, and is therefore readily administered to an uncooperative or actively resisting patient. Its use is not unattended with danger, both from the patient's idiosyncrasy and from the difficulty in pharmacological standardisation of the dose. I have once seen alarming effects from gr. $\frac{1}{100}$ hypodermically, which is the usual dose. In this case collapse ensued, with a very slow pulse, respiration 6 per minute, and clonic jerkings of the limbs. But such sequelæ are rare. Hyoscine should never be used for the ordinary forms of insomnia, and it does not require discussion in this connection. Its special indications have already been mentioned.

Of the remaining four groups the barbitone group is at present the most popular for several reasons—the various preparations are not unpleasant to take, sleep is induced rapidly, toxic effects are uncommon with ordinary doses, although they do occasionally occur, and there are no unpleasant after-effects, except perhaps

some drowsiness and sluggishness in the morning. My impression is that they ought to be used only as occasional hypnotics in old people, or in people with kidney disease, as in these two classes of patient, on account of difficulty in excretion, they are apt to accumulate in the system and so give rise to toxic effects.

Since it is round the barbitone group that most of the controversy on hypnotics has recently been waged, and since the views expressed on one side of the controversy are typical of what the public are asked to believe, it is useful to review the discussion in this place.

It has been urged against the use of the barbitone group, and also of the sulphonal series of drugs, that (*a*) they are poisonous to man (inferentially in ordinary doses); (*b*) that they are habit-forming, *i.e.*, that persons who begin by using them end by abusing them, taking them constantly, in excess of what is medically indicated, probably in increasing doses, and in response to a craving which the drugs induce; and (*c*) that they are a frequent means of suicide. In support of this contention animal experiments have been adduced to show that medinal and its allies are toxic to the central nervous system, producing degenerative lesions therein. The question of **toxicity** can be dealt with at once. No one denies

that in large doses the barbitone-derivatives are poisonous or even lethal to man; but so is Easton's syrup. There are also a few persons who show an idiosyncratic reaction, developing especially cerebellar symptoms in response to moderate doses. Nystagmus, diplopia, vertigo, and ataxia have followed a daily dose of 10 grains for a week or two. But in a fairly numerous experience of the administration of barbitone compounds, I have seen these symptoms only twice, and then in elderly people. Rashes occasionally occur, but they are certainly very uncommon. As for the animal experiments mentioned, they are at once disposed of by the facts. The cats and rabbits utilised were given relatively high doses, some of them receiving in 6 weeks proportionately as much as would be taken, in doses of 5 grains a day, by a man in 40 years! Moreover, even after doses of this order of magnitude if the animals were allowed to recover instead of being autopsied, they recovered completely. Finally, it has been shown since the experiments were published, that the so-called degenerative changes that were described occur in apparently normal untreated animals of the same species. It can be concluded therefore that for practical purposes, except for persons with an idiosyncrasy, the toxic effect of ordinary

doses of the members of the barbitone group can be disregarded. There is one exception to this rule. There is evidence that the persistent use of luminal can produce harmful effects in the central nervous system. It has been noticed that in epileptics who have been treated with this drug over a long period, the convulsions may return in greater frequency and severity after the drug is withdrawn; but it is possible that this was due to the use of excessively large doses. Two grains of luminal in 24 hours is about the maximum that should be given over a long period.

As for **addiction,** it certainly does occur. It is, of course, impossible to determine even approximately the number of persons addicted to veronal, etc. By ransacking the literature of this and other countries for 25 years, only 400 recorded cases have been unearthed, which does not seem a great number over so long a time and over so wide an area as the civilised world. As far as clinical experience enables us to judge, the total number cannot be large. As there is no stimulating pleasurable effect from these drugs comparable to that obtainable from morphine and cocaine, it is extremely unlikely that the barbitone group will ever lead to anything like the same amount of addiction as in the case of

morphine. The best prophylactic of addiction is the careful prescription of the drug. Even with morphine it is found that a very considerable percentage of its addicts first began the habit when the drug was prescribed for the relief of some definite pain, and perhaps relatively more often when a doctor has begun by prescribing it for himself. Doctors are as a class proportionately the most frequent of drug addicts. Continuous drug users are recruited as a rule from among unstable psychopathic individuals —and by this is not meant the ordinary psychoneurotic, but the emotionally unstable, unreliable personality whose drug-taking is a symptom of his general deficiency of temperament and character. It is therefore clear that by exercising discretion in prescribing a hypnotic drug, especially in persons unstable in the sense described, and by insisting on general medical supervision in all cases while the indication for its use remains in any degree, the risk of addiction can be avoided. The medical supervision required in many cases may be nothing more than a regular weekly visit, or even much less often when the patient is well known to his doctor. It is useful when there is any doubt of the patient's discretion to entrust the custody of the supply and its administration to a trustworthy relative.

The third contention, that veronal and its allies are a ready means of suicide, has two aspects. In the first place, it is contended that the prescription of veronal leads to addiction, and that addiction leads finally to the taking of a lethal dose, the suicidal climax being held to be caused by the habit of taking the drug. The problem of addiction itself we have already briefly discussed. As to addiction being the cause of suicide, it can safely be said that suicide and addiction are alike the symptoms of an underlying defect of personality and that in no sense did the habit *cause* the suicide. Veronal in ordinary doses does not produce mental illness. The prevention of such suicides does not lie in merely withholding the drug but in dealing with the fundamental instability of the individual taking it.

The other part of the third contention is this, that the barbitone compounds being procurable by anyone who cares to enter a chemist's shop and ask for them, the means of suicide are made too easily accessible. It is probably true that most people seeking a means of suicide, unless they be very abnormal indeed, will seek a method that is both as comfortable to employ and as conveniently procured as may be. The hypnotic drugs fulfil the first of these conditions, and so long as they are not placed on the official list of

Dangerous Drugs—as I hope they will not be—they fulfil the second also. But so also does what is probably the most popular means of suicide of all—namely, coal gas—and if for the reasons stated hypnotic drugs are to be scheduled as dangerous drugs, what are we to do about coal gas? Has the latter to be rationed likewise and made obtainable only on medical prescription? The question is however what influence does the accessibility of hypnotic drugs exercise on the number of suicides per annum? There are those who point to the Registrar-General's statistics, which show that in 1924 the number of recorded suicides with veronal was 8, and in 1925 it rose suddenly to 25. (In 1914 it was 30, and in 1918, before the temporary restrictions on the sale of these drugs under the Emergency Regulations [Poisons Schedule] of the war, it was 12. Placing them on the schedule reduced the number of suicides by their means to 6 in 1919.) But in the same 2 years, 1924-25, the total number of suicides rose by 9 per 1,000,000 living—an absolute total of over 300. The increase in the number of suicides by coal gas alone accounted for more than half of the total increase. Therefore while the total number of suicides from overdoses of the barbituric acid group rose by 17, the number of persons employing for coal gas

the same purpose, and with success, rose by about 180. It can therefore hardly be claimed that the accessibility of these hypnotic drugs has increased the total suicide rate. People will continue to attempt suicide no matter what facilities are or are not available, but to lay the blame for the disaster at the door of the means employed is a curious reversal of causal reasoning. Even if it be shown in future years that the increase in the suicide rate is significantly related to the prescription or other accessibility of hypnotic drugs, it remains necessary to consider whether the many who can benefit from their use ought to be sacrificed to the few who abuse them. The problem of insomnia is a sufficiently difficult one without having a very useful therapeutic method branded as "dangerous." The vast majority of patients who suffer from sleeplessness are more or less anxious; to tell them that the means used to combat the malady are in themselves pernicious is not merely contrary to general experience; it is definitely harmful to the patient in question, and counteracts considerably the good that the methods employed are expected to achieve.

Pharmacology and Therapeutics of Hypnotics.

The general requirements for a satisfactory hypnotic are these (Dixon):

1. It shall produce sleep of sufficient depth without secondary action, especially in respiration and circulation. Hypnotics containing chlorine are more depressant on respiration and circulation.

2. Sleep shall be quickly induced—*i.e.*, within half an hour or so. This depends upon the ease with which they are dissolved and absorbed. Hence those soluble in water are preferable. For this reason, veronal is not so good as its sodium salt (medinal). Tabloids or tablets should always be crushed, or the hypnotic may be given as a powder in cachets.

3. The action should be of sufficient duration, lasting from 6 to 8 hours.

4. Rapid, but not too rapid and complete excretion or conversion into harmless products is necessary; otherwise cumulative effects arise.

The **action of hypnotic drugs** has been shown to be related to their solubility in lipoids (or fatty substances). If the hypnotics be arranged in a series according to their lipoid solubility it is found that the order of this series corresponds to the order of their hypnotic strength. If a

mixture of water and oil (or lipoid substance) be taken, and a substance be dissolved in the mixture, the proportion,

$$\frac{\text{solute dissolved in oily or lipoid phase,}}{\text{solute dissolved in watery phase}}$$

is called the "partition coefficient." The higher the partition coefficient the higher the relative solubility in oil. It is found that hypnotic strength is directly proportionate to the value of this coefficient (H. Meyer and Overton). The nervous system is rich in lipoids; consequently when a hypnotic is introduced into the body, it tends to accumulate in a high proportion in the nervous system. But the fatty tissues—*e.g.*, of the omentum—compete with the central nervous system for hypnotics; and it has been shown that some narcotics have a stronger action in emaciated animals. The brain of a starving animal absorbs almost twice as much of a given dose of chloral hydrate as that of a well-nourished one. The process is entirely reversible—when the concentration in the watery phase falls (in this case, the watery phase is the serum), the lipoid-soluble hypnotic tends to pass back into the serum, the partition coefficient remaining constant. Since the hypnotics in question have no direct chemical action on the cell constituents,

their effects must be primarily dependent on their physical properties. It has been suggested that their activity depends on their capacity for adsorption on surfaces, especially on the surfaces of the cell-lipoids. It has been surmised that by accumulating on the surface of the lipoid particles (which, since lipoids lower surface tension, tend to accumulate at the surface of cells, and so form a considerable proportion of the constituents of the cell-membrane) the hypnotic substances diminish the permeability of the cell-membrane by making its interstices smaller; and similarly they will separate the lipoid from the protein colloid particles and so interrupt the intracellular chemical processes. But it has been shown that their hypnotic activity is not proportionate to their adsorptive capacity. Probably they are first adsorbed on the surface of the lipoid particles, and then dissolved in them (Meyer and Gottlieb). More recently, Hirschfelder and Serles have shown that in an emulsion of oil in water, the hypnotic group of drugs converts the oil-in-water phase into a water-in-oil phase. This may be represented graphically. In an oil-in-water emulsion the oil-drops (the " discrete phase " of this emulsion) are separated from each other by the " dispersed " or " continuous " phase, formed

by the water which is everywhere continuous with itself.

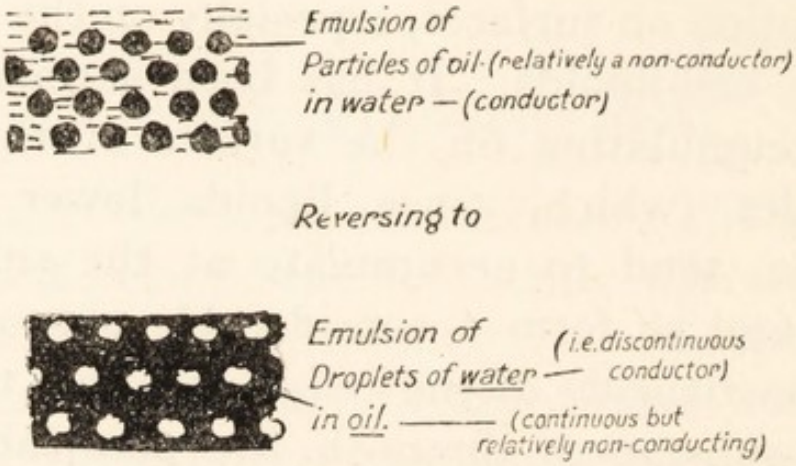


FIG. 1.

Since oil is now the continuous or dispersed phase, and the water is in drops separated from each other, and since oil is a very much less efficient conductor than water, the electrical conductivity of the emulsion is very much diminished, or, put in another way, its resistance is greatly increased.

In higher concentrations, narcotics make the lipoid constituents of the cell-membrane more fluid, and so punch the membrane full of holes, as it were, thus producing the opposite effect to that of small doses—namely, increased permeability to other substances besides electrolytes—*e.g.*, cell-ferments—which then escape from the cell. These are dangerous concentrations, because

one dose may go so far as to be irreversible, and the result is autolysis of cells and of entire organs which they compose, with consequent death.

The relation between the constitution and action of hypnotics is also dependent to some extent on the peculiar constitution and arrangement of molecules otherwise closely similar to one another. For example, the compounds of the alkyl group, which contain 4 or 5 carbon atoms linked together, are more effective as hypnotics than those containing their carbon linked with 1 or 2 other carbon atoms. Ethyl groups (C_2H_5) united to a carbon produce a more narcotic compound than if methyl (CH_3) groups occupy this position—*e.g.*, ethyl alcohol is more narcotic than methyl alcohol. This principle led in the laboratory to the synthesis of barbitone (veronal), and to the substitution of methylsulphonal for sulphonal. The potency of ethyl groups holds only for a certain arrangement of the molecule.

The introduction of halogen atoms (chlorine, bromine, and iodine) when directly united to a carbon, increases the narcotic action of such compounds as are already active (*e.g.*, adalin, which is bromodiethylacetylurea). Chlorine atoms change not only the degree but the

character of the action of the molecule in which they are incorporated. They can produce toxic effects on the heart and bloodvessels, and large enough doses of the hypnotics of which they are constituents, lead to convulsions.

Typical Methods of Administration. — The methods of giving the barbituric acid compounds may be taken as an example, since they are nowadays the most frequently used; and of these medinal, which is the sodium salt of veronal, is the typical and most generally useful hypnotic. Its chief advantage over veronal itself lies in its greater solubility in water. The dose of medinal that one should begin with in an ordinary case of sleeplessness where the use of hypnotics has been decided upon, is 10 gr. This is often more than is actually necessary, except in very distressed people or in long-continued insomnia, where other drugs have already been tried. But it is essential to gain the patient's confidence from the start, and it is therefore much wiser to make certain of sleep the first night the drug is tried than to begin with smaller doses of 5 or 7½ gr., which may fail. The failure of small doses shakes the patient's belief in the drug and in the doctor, and so entails a bigger dose than ever for success the following night. Hypnotics of the more potent

kind, like medinal, should be taken at or before going to bed. It is foolish for the patient to postpone taking them till 2 or 3 a.m. Where it is desired to give a hypnotic after midnight, as when the patient wakes up and cannot sleep again, one of the milder hypnotics with a rapid effect, but comparatively brief action, like adalin, should be prescribed. Sleep having been obtained for a night or two, it is usually possible in an ordinarily anxious patient to begin to reduce the dose first to $7\frac{1}{2}$ gr. and then to 5. This is best done without the patient's knowledge. A flavouring agent like syrup of orange should always be prescribed with the hypnotic. This serves two purposes: (*a*) it prevents the patient knowing exactly the drug he is getting, which is often useful—a blind faith is often stronger than a familiar one; (*b*) it also prevents his estimating from the intensity of the taste that his dose has been reduced. Dilution with water up to a constant volume is enjoined on the nurse, so that the patient may not have this means of recognising a reduction in strength. After a habit of sleep has been thus re-established—it may take only days or several weeks—the patient should be encouraged to exercise his own control. The draught may be left by his bedside with instructions that he may take it if he does not sleep

within an hour or so of going to bed. He should be instructed not to wait long before taking it, if he finds it necessary to do so, since to take a hypnotic in the small hours means inconvenient drowsiness when it is time to get up next morning. It can also be pointed out to the patient after a time that his dose has been reduced, and that therefore the sleep he obtains becomes increasingly an unaided one. This revelation should not be made too soon, otherwise the patient simply begins to fear that the reduced dose will not be efficacious. At the time of withdrawal, as patients are apt to be frightened by the idea of losing several nights' sleep in succession, they should be assured that they need never do so, and that if they sleep badly, say, for two nights in succession, sleep will be assured the following night by means of a hypnotic dose. A timely intervention, even for one night, will prevent a relapse by allaying anxiety, and the mere promise of such intervention may forestall the necessity for it.

An important factor in the success of hypnotic drugs is that their action helps the patient to get away from his excessive preoccupation with the problem, "Will I sleep tonight?" He knows that his sleep can always be assured, if it will not come spontaneously.

In the meantime, of course, every attempt must be made to build up the patient's interests in other directions—in work and recreation—and the importance of insomnia should be minimised. Concurrently should go the psychotherapeutic unravelling of the mental condition that produced the insomnia. In this connection however several disadvantages appear in the use of hypnotics. A patient made comfortable with a hypnotic is apt to feel less eager to solve the problems that were producing the mental discomfort that led to insomnia. It has also been remarked (T. A. Ross) that patients using hypnotics dream less than formerly, and so a source of psychological information that can be very valuable is lost.

Pharmacology and Therapeutics of Individual Hypnotics.

Bromide Salts.—Bromide salts exert their action on the central nervous system after being absorbed into the cells of the latter, where the bromide ions replace chloride ions, the excretion of chlorides being consequently increased after the administration of bromides. The excretion of bromides is slower than their absorption; hence repeated doses lead to an accumulation of

bromide in the central nervous system. All the cells of the latter, cortical, medullary, and spinal, appear to be affected about the same time, and the specific action of bromides on them has usually been considered to consist in a general depression of excitability. This is suggested by the results of electrical stimulation of the cortex in dogs who have had much bromide; in such circumstances it is impossible to produce convulsions even by continuous irritation. But Pawlow maintains that bromides act, not as direct sedatives diminishing sensibility, but by strengthening the activity of internal inhibition. He demonstrated this as follows. He selected a dog of excitable temperament, which responded very readily to environmental stimuli, and in which also inhibitions very easily developed—for example, sleep was readily induced during the course of an experiment. In this dog a conditioned reflex was built up to one stimulus, and the setting up of another conditioned reflex to a similar stimulus was then attempted. The attempt succeeded as long as the second stimulus was like, but not too like, the first. When the two stimuli closely approached identity, the whole demeanour of the animal changed abruptly. "The hitherto quiet dog began to squeal on its stand, kept wriggling about, tore off with its

teeth the apparatus for stimulation of the skin, and bit through the tubes connecting the animal's room with the observer—a behaviour which had never happened before." A similar condition which developed in response to similar circumstances in this type of dog lasted for some minutes, not improving even after the experiments were discontinued. The animal was then given 180 c.c. of a 2 per cent. solution of potassium bromide daily, as an enema. By the tenth day of the treatment all the reflexes which had been disarranged or desensitised returned to normal. Other reflexes, which had not been affected during the disturbed period, remained unaffected also after the administration of bromide.

It should be noted that in another dog, of a different temperament—the so-called "phlegmatic" type of dog—bromide had no effect in restoring normal responses, but spontaneous recovery occurred.

Excessive dosage leads to a degenerative change in the nerve-cells, which undergo chromatolysis. These changes, unless they are very far advanced, are reversible, the cells recovering their normal appearance after elimination of the accumulated bromide.

The effect of the cumulative activity of bromide

is seen clinically in a " bromide delirium," which does not in itself differ in any characteristic way from other deliria. But the patient is very drowsy, his tongue is usually furred, and saliva drools from his mouth. The gait is unsteady, from muscular weakness and general diminution in sensibility.

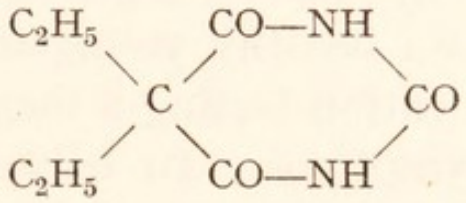
It has been asserted by Weir Mitchell that bromides may in some persons (and notably in the young) occasion " profound melancholic or maniacal tendencies, which on several occasions have been homicidal or at least madly destructive." Weir Mitchell did not say whether in such patients he had observed disorientation and other signs of an acute toxic (delirious) reaction; but it seems likely that the violent tendencies mentioned occurred in a setting of disorientation and probably actual delirium, the violence being a response to hallucinatory experiences. I have encountered patients in whom a similar response of excitement was said to have followed moderate doses of bromide, and in whom no disorientation or other signs of delirium were reported.

The effect of bromides on the skin in the form of acne is well known. For this reason, liquor arsenicalis ℥ii. or iii. is commonly prescribed along with bromides when the latter is given

over a long period of time. Some persons develop bromide acne when a comparatively small total amount has been digested.

Chemistry and Toxicology of the Veronal Group.

Veronal (barbitone, B.P., or barbital, U.S.P.) is a combination of two ethyl (C_2H_5) groups with a cylic compound built up from urea.



It is diethylmalonylurea, or diethylbarbituric acid. Medinal is its mono-sodium salt. Veronal is soluble to the extent of 1 part in 170 parts of water. Administered in warm milk, or as a powder or a cachet, it produces sleep in ½ to 1 hour, but there is great variation in different individuals. Medinal being more soluble produces sleep in about ½ hour as a rule. Veronal and medinal are excreted slowly unchanged. Of smaller doses of veronal given subcutaneously, 90 per cent. appears in the urine, but after larger doses the relative amount appearing in the urine within 24 hours falls off

to 40 or 50 per cent. only, and does not increase with continued administration. Hence toxic symptoms may occur from its accumulation.

Action.—While they may have the effect of producing a certain amount of vasodilatation, the hypnotic action of veronal and medinal depends principally on their affinity for brain-lipoids. They have no depressant effect on the circulation in ordinary doses.

Toxicology.—The fatal dose varies with the state of the organism; 75 gr. of veronal have been taken by a healthy young man, with only a sleepy intoxication lasting a long time without threatening symptoms. In other cases 60 gr. have been fatal; 150 gr. has been the average dose in suicidal attempts which have succeeded. To meet the possibility of a fatal result from an overdose, it has been suggested that along with each hypnotic dose of 5 or 10 gr. of veronal or medinal, pulvis ipecacuanhæ should be prescribed in 3 to 5 gr. doses, so that if a possibly lethal dose of veronal were taken, an emetic dose of ipecacuanha would be unwittingly taken at the same time.

Symptoms of Veronal and Medinal Poisoning.—Where small doses have accumulated to produce toxic effects, these are chiefly drowsiness, diplopia or actual strabismus, nystagmus and ataxia.

The symptoms have been mistaken for cerebellar disease. Erythematous rashes may appear. In large doses taken for the lethal effect, there is extreme drowsiness and actual coma, complete loss of the corneal reflex, sluggish reaction of the pupils to light, and in severe cases, high myosis with fixed pupils. There is relatively little interference with respiration and cardiac action. The heart is damaged only by concentrations which cannot be produced *in vivo*. In very large doses, the respiration becomes slow and shallow. There is a specific paralysis of the bloodvessels, partly from an action on the centre, and partly from a direct action on the vessel walls.

The cumulative effect of veronal is well shown by Guttman's method (*vide* Chapter I.) of registering the movements of a sleeping patient. There is a progressive diminution in the amount of restlessness recorded on the kymographic tracing on successive nights, although the dosage is kept constant. By the same method it was shown that a combination of opium and sodium-veronal (medinal) was disproportionately more effective in diminishing the restlessness than either alone.

In **Dial** the two ethyl groups present in veronal are replaced by two allyl (C_3H_5) groups, giving

diallylbarbituric acid. It is active in smaller doses (gr. 1½ to 4½) than veronal, but is more toxic. In large doses it is said to produce illusions and hallucinations (Marburg).

Luminal or phenolbarbitone differs from veronal in having one ethyl group replaced by a phenyl (C_6H_5) one. This change considerably increases the hypnotic action. Sleep occurs in the average case in ½ hour after a dose of 3 to 4½ gr., but doses up to 10 gr. have been used. The sodium-salt of luminal (containing 90 per cent. luminal) is much more easily soluble than luminal itself, and is weakly alkaline, so that it can be injected subcutaneously. It readily decomposes, and so must always be freshly prepared. Its equivalent dose is 10 per cent. greater than that of luminal itself. Solutions for hypodermic use should be freshly prepared from the powder with boiled and cooled distilled water. When given subcutaneously, curiously enough, the hypnotic effect develops more slowly, but is apt to be more prolonged. Intravenous injection is better, since luminal-sodium, given subcutaneously, has caused pain and necrosis. Luminal is excreted by the kidneys mainly unchanged.

Toxicology.—With large doses (5 gr. or more) drowsiness may persist on the following day, and vertigo, headache and nausea have been observed.

The continuous use of large amounts may produce ataxia, tremor, speech affections, and delirium. Skin eruptions (morbilliform and urticarial) may appear either in susceptible persons or after large amounts. A chronic mildly demented state has been recorded after the continuous use of large amounts, and it persists after the drug has been stopped. Luminal has to be used with great caution always, but especially in subjects with chronic nephritis or arteriosclerosis.

Ammonium bromide is incompatible with luminal-sodium (according to the B.P.C.).

Allonal is a compound of a hypnotic, allyl-isopropyl-barbituric acid, with an analgesic (amidopyrin), and is said to unite the properties of both. It is made up in tablets, each containing 1 gr. of the hypnotic element with 1⅔ gr. of the analgesic: and the dose recommended for hypnotic purposes is 2 tablets, but 4 tablets have been given. It is said to have been found especially useful in sleeplessness due to pain or to an irritant cough. Doses that were too large have produced drowsiness and vertigo, and in cases in which idiosyncrasy has in consequence been suspected, excitement and toxic rashes.

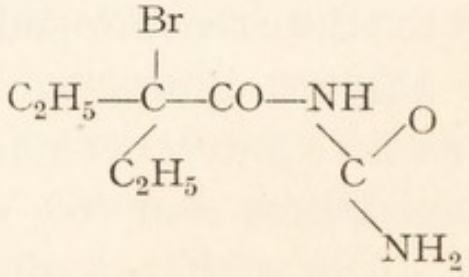
Somnacetin is medinal linked with phenacetin and codein. It is said to have the

advantage over medinal itself that it can be given without fear of cumulative toxic effects (in ordinary doses) in arteriosclerotic and senile patients.

Nirvanol (phenylethylhydantoin) is closely allied to the barbituric acid series. It is slightly soluble in water and tasteless. The dose is from 3 to 15 gr. Marburg uses it especially when sleep is disturbed by priapism.

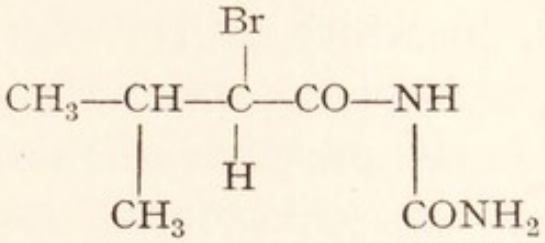
Adalin and Bromural are also compounds of urea, but they do not contain a carbon ring, and apparently for this reason are less potent and less toxic. They contain a bromide atom, which however is said to act as part of the molecule, and not independently, since it is not split off.

Adalin is bromodiethylacetylurea:



The dosage is 7 to 15 gr. It is not at all toxic. A dose of 180 gr. has been survived. Its solubility in water is almost nil. With average doses, the sleep lasts about 4 hours.

Bromural is bromisovalerianylurea:



The dose is 3 to 4½ gr., and sleep ensues within ½ hour. With such a dose the sleep lasts from 3 to 5 hours. The danger of poisoning with doses taken with suicidal intent is very small. In one case 135 gr. produced 36 hours' sleep without further consequences.

Amytal (isoamylethyl-barbituric acid) has the reputation of being a powerful hypnotic which causes relatively little depression. It has lately been used as a physiological antagonist to novocaine, combating the respiratory depression and convulsions which the latter in toxic doses tends to produce (Isemberger).

Noctal (β-bromopropenylisopropyl-barbituric acid) is said to be three times as active as veronal, and to be the most powerful hypnotic yet discovered.

Chloral hydrate, of which the hypnotic dose is 10 to 30 gr., is $CCl_3.CH(OH)_2$—the aldehyde of trichloracetic acid. It has an irritant effect, acting as a rubefacient when rubbed into the

skin. To prevent irritation of the stomach it should therefore always be given well diluted with water, in which it is very soluble. The theory that its hypnotic action was the result of its being split in the presence of the alkalies of the blood-serum into chloroform and formic acid ($CCl_3COH + KOH = CHCl_3 + HCOOK$) is no longer tenable. Chloral produces its effect as an entire molecule. It is excreted partly as trichlorethyl-glycuronic acid (urocholalic acid), and partly as nuchanged chloral hydrate. A small portion is retained in the organism a long time, undergoes gradual decomposition, and so causes an increased excretion of chlorides in the urine. Urocholalic acid is non-poisonous, and its formation is therefore a detoxicating process. It reduces cupric oxide in alkaline solution, but it does not ferment glucose, and it is lævorotatory.

In moderate doses (10 to 30 gr.) chloral produces sleep in about ½ hour, which lasts for 6 or 8 hours. The sleep is indistinguishable from normal sleep. Chloral depresses the vasomotor centre in the medulla and so causes a dilatation of the peripheral vessels, with sometimes a resulting skin eruption, which may be erythematous or urticarial. The systole of the heart-muscle is diminished by a direct action upon it, the auricles and then the ventricles being

successively affected. As the effect continues, the heart becomes overdistended with blood, and the systolic output is small. The blood-pressure falls as the result of the diminished systolic output and of the peripheral vaso-dilatation. But in chloral poisoning death is from respiratory failure, although dangerous cardiac depression simultaneously occurs. The action on the respiratory centre suggests the need for care, especially in children (Dixon). There is a fall in body temperature as the result of the increased loss of heat from the dilated skin vessels, and of the depressed action on the thermotoxic centre at the base of the brain. The total metabolic exchanges are diminished, less oxygen being used and less CO_2 given off, while the products of increased protein break-down are not completely oxidised. These changes have been attributed to the acidity of the tissues resulting from the presence of uro-cholalic acid, and can be prevented by giving an alkali along with chloral. With prolonged and excessive use, fatty degeneration may occur in the organs. Clinically, the toxic effects include exanthemata, gastric irritation, and (in a few patients with an idiosyncrasy) symptoms of excitement instead of a hypnotic effect. In view of the last point it has been recommended that

the first dose given to a patient new to the drug should not exceed 15 gr.

Chloral is a very satisfactory hypnotic in children, to whom relatively large doses can be given, although the effect on respiration must be watched. In them it is best given as an enema.

On account of its depressive action on the heart, chloral has usually been regarded as contra-indicated in cardiac diseases, bronchitis, and the later stages of exhausting fevers, and after influenza. But its effect on the heart has apparently been exaggerated, for it is often used without ill effects in chronic cardiac conditions. Whitla recommends its being given with 1 to 2 oz. of whisky, thus increasing its efficiency and diminishing the depressive action.

In acute poisoning there is coma, with a fall in body temperature, feeble pulse, insufficient respiration, and dilated pupils. As little as 60 gr. has been a fatal dose.

Chloralamide, or chloral formamide, CCl_3COH, $HCO.NH_2$ is not irritant and has only a slight taste, and in these respects has advantages over chloral. Its effect depends on a gradual setting free of chloral after absorption, and sleep is produced more slowly and with less certainty than with chloral.

Paraldehyde which is produced by the polymerisation of ordinary aldehyde (CH_3COH), consists of three of these molecules united in a ring. It is a volatile inflammable liquid, with a strong taste and odour, and for this reason has to be well diluted with water, flavoured with, *e.g.*, tincture of orange. The dosage is 1 to 2 drachms or even 3 drachms. It produces sleep rapidly in about 15 minutes as a rule. It has no deleterious effect on respiration, circulation, or metabolism, and is excreted unchanged largely by the lungs, the odour being readily perceived in the breath next day.

In spite of its not very pleasant taste and odour, paraldehyde habituation does occur; and some patients have claimed to swallow as many as 20 drachms in 24 hours as a regular routine.

Michelson showed that paraldehyde converts a midday sleep in normal persons (which give the type of curve characteristic of light sleep at night, as described by him and also by Kohlschutter) into a sleep approximating in its type of curve to that described by them for a normal deep night's sleep—*i.e.*, a steep rise in the first 2 hours, with a steady fall towards the hour of waking. Only three cases are said to be on record of death from paraldehyde poisoning. McFall recorded a patient who was a paralde-

hyde habitué and was believed to have swallowed 2½ or 3 oz. while in a state of semi-starvation. The only significant post-mortem findings were

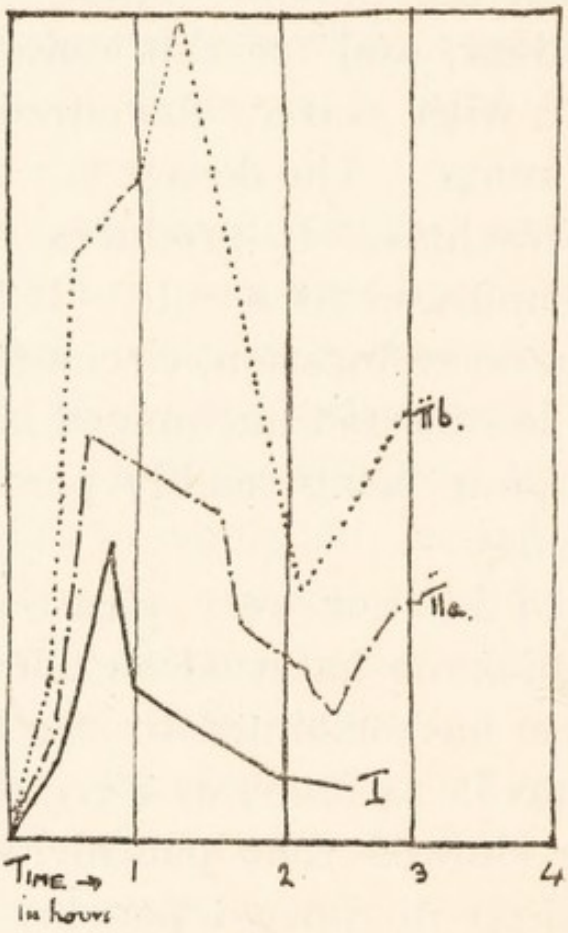


FIG. 2.

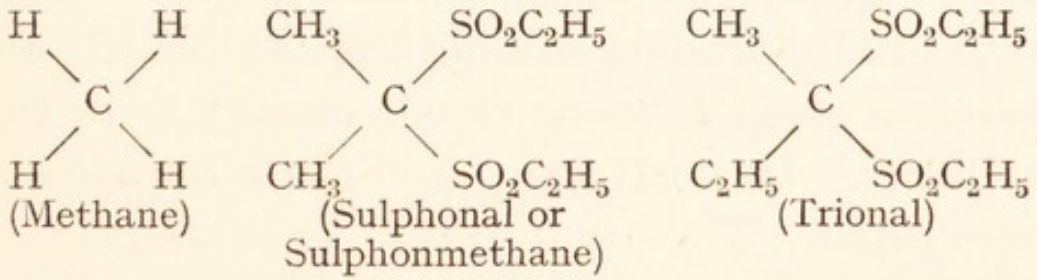
I. Depth of sleep during midday rest.
II*a*. Depth of sleep during midday rest after paraldehyde.
II*b*. Depth of sleep during midday rest after paraldehyde (larger dose).
The effect of paraldehyde is to cause a greater depth of sleep to be attained more quickly. (After Meyer and Gottlieb.)

hyperæmia of the mucous membrane of the stomach, and to a lesser degree of the duodenum, and congestion at the base of the lungs.

Amylene hydrate (dimethylethylcarbinol) is a colourless powder with a peppermint taste, soluble in water to the extent of 1 in 8. The dose is from 25 to 60 gr. Sleep ensues in about an hour. The lethal dose is placed by Marburg as high as 300 gr., but a fatal result of an overdose has not been recorded. It apparently does not have a cumulative action. Marburg mentions a patient who took amylene hydrate as a hypnotic for 20 years, without harm and without its losing its effect.

The Sulphone Group.

The members of this group can be regarded as chemically allied to methane, in which all the hydrogen atoms have been replaced by alkyl and alkyl-sulphonic radicles (Dixon).



(Methane) (Sulphonal or Sulphonmethane) (Trional)

Sulphonal is scarcely soluble in cold water (1 in 500). It should be administered as a powder in 20 to 40 gr. doses with a warm drink. Sleep occurs in 1 to 2 hours. Excretion is slow, and

the drug lingers in the urine for 3 or 4 days. There is apt to be drowsiness the following day. The result of the slow excretion is that with daily repeated doses a cumulative action may be obtained. The first sign of this action is the appearance in the urine of a peculiar porphyrin, resembling hæmatoporphyrin, but spectroscopically not exactly like it. The urine is discoloured to a cherry-red tinge. Skin eruptions, albuminuria and nephritis may appear. If this warning be neglected, there may occur general lethargy, depression, ataxia, vertigo, constipation, vomiting, drowsiness and actual confusion, sometimes with hallucinations. Very large single doses produced coma, stupor, paralysis of sphincters, anuria, a fall of temperature, and finally depression of respiration.

Methylsulphonal or trional, in which one of the methyl groups of sulphonal is replaced by an ethyl group, is more soluble than sulphonal and therefore sleep is more rapid, usually occurring in ½ hour. Its destruction and excretion are also more rapid. The usual dose is 15 to 25 gr.

Tetronal, in which both the methyl groups of sulphonal are replaced by ethyl groups, is said to be specially apt to be cumulative in its action.

Electricity in various forms of application has been recommended. It is a little difficult to

believe that it has any specific effect. More probably the action is in some forms that of a monotonous conditioned stimulus, and in all instances there is more than a trace of suggestion.

The constant current obtained from five cells of a Leclanché battery, with one electrode applied to the forehead and the other to the occiput, for 5 to 15 minutes, has been reputed useful. Successful results have been claimed for the application of an interrupted current to the spine, and for faradisation applied to the head. Whitla considered that static electricity is the most useful of the electrical methods. After insulation of the patient by having him sit on a glass stool, this body is brought into connection with the conductor of a Carré machine. A fine metal point is then held opposite several spots on the forehead and scalp, but not near enough to produce a spark. The sensation is as if a light wind or breeze were playing over the region.

Appendix.

The treatment of psychoses by prolonged sleep is not the same as the treatment of insomnia in the psychoses; hence it was considered desirable to place a discussion of this method of therapy in the position of an appendix.

It is not surprising that the induction of prolonged sleep should have been advocated for the treatment of psychoses, especially of those in which motor hyperactivity or sleeplessness, or both, are pronounced. To Wolff is assigned the credit of first suggesting this method in 1901. Trional was the drug he advocated. In 1922 Kläsi published his results by this method. He used "somnifen," which is the trade name for diethylaminediethyldipropenyl-barbituric acid, in doses of 4 c.c. (2 ampoules each of 2 c.c.) of the solution. The injection was made either deeply into the muscles or intravenously, as subcutaneous injection was found to produce sloughing. He preceded this first injection by one of morphine gr. $\frac{1}{4}$ and hyoscine gr. $\frac{1}{100}$, given $\frac{1}{2}$ hour before. The "twilight" sleep thus initiated had then to be maintained by doses of 1 ampoule of somnifen at intervals, usually of 6 or 8 hours, over a period of 5 days or even more. The treatment was carried out in a darkened quiet room. The patient was put on a liquid diet. The pulse, bladder and bowels were carefully watched. The depth of sleep was maintained at such a level that the patient could be roused temporarily, but fell asleep again if left unstimulated. Contra-indications to beginning the treatment are heart and kidney disease,

and extreme emaciation. Indications for interrupting the treatment were principally vomiting and cardiac failure, and the onset of menstruation. Müller subsequently collected fifteen instances of death directly attributable to somnifen treatment of this kind, representing a mortality of 5 per cent. Müller compiled a full bibliography up to 1925. The figures seemed to show that lasting improvement occurred in 8·5 per cent. of cases so treated. Oppler's figures were more favourable (39 per cent.). He recommended that other drugs should be tried, the drug chosen varying with the class of case and with the individual patient. For manic-depressive patients, he preferred dial. Wiethold advocated rectal injections of a mixture of paraldehyde and hyoscine (in very large doses), especially in deliria, acute excitements, whether catatonic, maniacal or hallucinatory, and in epileptic furor and status epilepticus. He believes that benefit results, especially in acute psychoses such as may follow influenza, where the removal of memories of delusional and hallucinatory experiences by this means may (in his opinion) prevent the development of a chronic delusional state with systematisation.

The pharmacological effect of somnifen consists in part in a lowering of both systolic and diastolic

blood-pressures, but with an increase in pulse-volume, and a peripheral vasodilatation with a consequently improved peripheral circulation (Hediger and Kläsi). In a series of 18 cases treated by somnifen, Dawson and Barkas obtained only transitory improvement and that only in some cases. In the 4 cases that showed improved contact with the environment, the improvement lasted only a few days. In many instances the pulse became rapid, weak and irregular. Only one case had retention of urine and cystitis.

Oppler has advocated anew the use of trional for the purpose of producing prolonged sleep in the psychoses. He claims that 40 per cent. of cases are lastingly better, and that schizophrenic agitated states are those which are most favourably influenced; while in manic excitements, trional is not in his opinion so good as somnifen and dial. Oppler maintains that the advantages of trional are that it produces quieter conditions in wards for acute cases, and enables the patients in whom it is used to be discharged earlier on the average from the institution than would otherwise have been the case. The dosage of trional he employed was 30 gr. twice a day, the dose being diminished on the third day at latest. The treatment is continued for from 4 to 10 days, and up to 330 gr. are given in all. The dangers

are from urinary retention and nephritis; and there is a possibility of hyperpyrexia. Oppler advocates paraldehyde and amylene hydrate to amplify the effect of trional. The advantage of somnifen and similar methods in the psychoses appears to be more administrative than therapeutic.

CHAPTER V

THEORIES OF THE NATURE OF SLEEP

" Non uno itinere potest pervenire ad grande secretum."

SYMMACHUS.

THE theories of sleep which have been propounded betray by their number the uncertainty that has beset, and still besets, the problem of its essential nature. Most of them have now only an historical significance. Howell suggested that sleep was the result of cerebral anæmia dependent upon a rhythmic activity of the medulla which in association with vasomotor fatigue at the end of the day brought about a dilatation of the skin-vessels. The splanchnic vasodilatation that follows a meal, having a similar reciprocal effect on the cerebral circulation, would tend to the same result. Circulatory theories of sleep are at least as old as the fifth century B.C. when Alcmeon, a contemporary of Pythagoras, declared that sleep depended on a " retreat of the blood into the veins." Blumenbach, in 1795, appears to have been the first to observe that in sleep the brain surface was usually paler than in the waking state. This observation

was later supported by an experiment of Mosso's, in which the experimental subject lay on a plank pivoted about its middle, and in which that end of the plank on which the subject's head lay rose when the subject fell asleep. This was thought to indicate a displacement of blood from the cranial cavity towards the abdominal reservoir. Mosso also made observations through trephine openings which confirmed Blumenbach's statement. But it has since been shown by Mosso himself among others that sleep can occur in the absence of relative cerebral anæmia and even when there is actually cerebral congestion. (The vascular state of the brain during sleep is discussed in Chapter I.)

Osmotic Theory.—It has been supposed by Rosenbaum that the nerve-cell as the result of its functional activity becomes saturated with water and that its excitability consequently diminishes. Devaux expanded this notion, and supposed that the osmotic pressure of the cell having increased as the result of its activity, caused water to enter from the surrounding lymph. The latter having lost fluid, increased in osmotic pressure, so that in turn water passed into the lymph from the blood, which in consequence became more viscous. Viscous blood flows more slowly, hence a slowing of the circulation through the brain,

and consequent sleep, from relative asphyxia resulting from deficient blood-supply. Against this complicated and entirely fanciful speculation, Piéron has pointed out that a hypertonic condition of the blood produces not somnolence but restlessness and even convulsions. Also in cases of fasting, or on a dry diet, the osmotic pressure of the blood rises without somnolence supervening. Piéron himself has shown that in insomnia the viscosity and specific gravity diminish, while the osmotic pressure remains practically unchanged. The brain of a dog killed after some days of sleeplessness shows no diminution in the water content, either of the grey or of the white matter of the cerebral hemispheres.

Dendritic Retraction.—An older hypothesis, now discarded, was propounded by Mathias Duval in 1895. Duval suggested that in sleep there occurred a retraction of the dendrites of the nerve cells of the central nervous system, so that contact was broken and presumably associative brain-processes were interfered with. There is no reliable histological evidence of this.

A corollary suggested itself, that the passage of a nerve-impulse produced a positive chemotropism of the processes of any two adjacent neuroses towards each other. An alternative

subsidiary hypothesis was that "nervi nervorum" existed to direct the appropriate neural processes towards each other. This supposition seems in principle to have no higher sanction than that "Greater fleas have lesser fleas upon their backs to bite 'em; and lesser fleas have lesser fleas, and so ad infinitum." A certain number of fleas may be good for a dog, but they are bad for a hypothesis.

Cajal suggested that a similar effect to that imagined by Duval might be produced by an amœboid movement of the glia, the processes of the latter interposing themselves between the points of contact of the neurones, and so producing a solution of continuity in nerve-paths and nerve-processes. Lugaro advocated a view precisely the opposite, when he suggested that the ordinary definite and limited relationships between the neurones no longer exist, but are rendered ineffective by the universal connections of the connecting paths which are supposed to develop during sleep. Again a basis of histological observation is lacking.

Toxic Theory.—One of the best known of all the theories of sleep has been the toxic theory, which owes most of its vitality to Piéron. On the basis of experiments with dogs, Piéron claimed that he had isolated from the blood and

spinal fluid of dogs who had gone without sleep for a prolonged period, a sleep toxin (" hypnotoxin "), which when injected into a normal dog produced somnolence in the latter. He found also that after prolonged insomnia in dogs, there were alterations of the cortical neurones (chromatolysis, eccentricity of nucleus and neucleolus, and vacuolisation) of the frontal region, in the layer of large pyramids, and in the polymorphous layer. Similar changes were found in the cells of the frontal cortex of normal dogs injected with the " hypnotoxin." According to Piéron, the frontal cortex is the centre for " sensori-motor tonus." He considers that the toxin is probably produced locally in the functioning cells and that later it diffuses itself into the C.S.F. and blood. Similar cell-alterations were described by Piéron in extreme instances of experimental insomnia in all parts of the cortex, in the spinal ganglia, and in the cerebellum, but never in the medulla and cord.

There are a number of strong objections to Piéron's hypothetical hypnotoxin. Everyday observation seems to contradict his deductions. Frequently we can sleep when we are not, to our knowledge, fatigued; and the only reliable indication of fatigue under ordinary circumstances at the present time is the subjective experience of

it. There are numbers of people who can take advantage of any period of freedom from the immediate necessity of working during the day to fall asleep. A certain distinguished physiologist can fall asleep at any time when his services are not immediately required during an experiment in which he is acting as subject. It would not do justice to the facts in such people to suggest that they are in a state of chronic intoxication. Furthermore, it is a common experience that if we are very tired, we cannot sleep; except the fatigue become so great that we are no longer able to stand or move unless stimulated, when such great fatigue can compel sleep if a moment's muscular relaxation be permitted (*vide* Kleitman's experiments, Chapter I.). The ability possessed by some people to awake more or less accurately at a prearranged hour speaks against the existence of a sleep-toxin. If even in spite of the facts of everyday experience, it were accepted that a hypnotoxin is steadily elaborated during the waking hours, its accumulation would not give a sufficient account of the occurrence of sleep. It would still be necessary to know whether the toxin acts directly on the brain-cells or on a special sleep-organ, or whether it leads to certain processes which result in sleep (Nachmansohn).

Piéron has felt this need and has presented the evidence, already alluded to, that the cells of the frontal cortex are altered by the supposed hypnotoxin, but although similar histological changes have been described by other observers, their production by a "hypnotoxin," and not simply by their own functional activity, remains unproven.

Another objection, directed against the supposed predominance of the frontal cortex in the sleep-process, is based on the observation that decorticated dogs continue to show an alternation of sleeping and waking, and on other facts which will be discussed in relation to sleep-centres (*vide infra*). It does not answer this objection to say, as Piéron does, that because a dog like Goltz's classical one, which lived for more than 18 months after the operation of decortication, showed perpetually two of the characteristics of sleep (namely, absence of spontaneous activity, and disappearance of elaborate reactions), therefore it was to be regarded as continuously asleep. This difference of opinion of course depends in part upon a disagreement on the very difficult question of the criteria of sleep.

The case of double monsters with a common circulation, of whom one may sleep while the

other remains awake, Piéron explains away on his theory by supposing that the toxin acts principally locally, where it is elaborated—*i.e.*, in the brain of one individual—and does not reach a sufficient concentration in the general circulation to affect the other.

To overcome the difficulty presented by the suddenness of falling asleep, and by the phenomena of narcolepsy, Piéron embraces a neurodynamic process of inhibition as a supplementary hypothesis. The hypnotoxin is supposed to set up a general inhibitory process affecting all the cerebro-spinal functions. Even in decerebrate animals, like Goltz's dog, a periodic inhibition might be assumed to occur. Drowsiness is then assumed to be the result of direct chemical action of the toxin on nerve-cells; while sudden deep sleep is supposed to involve the intermediate action of an inhibitory process.

It is all very like Burton, this combination of a hypothetical toxin, and the as yet physiologically mysterious function of inhibition. "Waking," says Burton (in his "Anatomy of Melancholy") "is the action and motion of the senses, which the spirits dispersed over all parts cause." In waking, according to Burton, who naturally followed the physiological beliefs of his time, the animal spirits coursed visibly along

the nerves. In sleep a binding or " ligation of the senses " proceeded from an inhibition of the spirits, " the way being stopped by which they should come." The stopping or inhibition was held to be caused by vapours arising out of the stomach, filling the nerves by which the spirits are conveyed. Terminology has altered somewhat; ideas not much.

In order to bring further facts of observation within his theory, Piéron supposes that conditions habitually associated with going to sleep may come to be in themselves sufficient to produce it. He feels obliged also to suppose that the mere rhythmic habit of alternating sleeping and waking may acquire an automaticity. In the end therefore not much is left of Piéron's toxic theory by its author. The hypnotoxin, unconfirmed by others, becomes in the end one of a number of conditions, the occurrence of some of which is better established than that of the hypnotoxin itself. In his own words, " Whilst the physiological data seem to imply . . . that the hypnotoxin developed by the intense activity of the nervous centres presiding over extremely complex nervous functions, arouses the inhibitory reflex, which then, by dint of frequent repetition, can be excited by its habitual accompaniment, and may even

supervene periodically in the absence of the original excitation; biological considerations, on the contrary, would lead us to consider as primary the calling into action of an inhibitory mechanism by external stimuli and its own regular rhythmic functioning, so that intoxication is avoided, thanks to the periodic inertia produced by the environmental circumstances, and in particular by the periodic succession of day and night." The presumed hypnotoxin, and the cellular alterations he describes, may nevertheless have a more plausible application to the problem of insomnia and its effects (*vide* Chapter II.).

Other toxic theories have involved in turn lactic acid, cholesterin, CO_2, "leucomaines" (unoxidised products obtained from muscle), "neurotoxins" (not further defined), and products of metabolism in general. These toxins were without exception supposed to be the result of waking activity, which were oxidised, eliminated, destroyed by antibodies, or otherwise dealt with during sleep. By some writers, an additional substance, accumulating during sleep and causing the organism to awake, has been postulated.

Endocrine Theories.—It would have been surprising had no one suggested that sleep might

be determined and regulated by an internal secretion of one or other of the endocrine glands. Salmon suggests that sleep is analogous to the secretory functions. It resembles urinary secretion, for example, in being a habit, excited psychically, executed reflexly, and preceded by specific sensations. There is an appetite for sleep as there is an appetite for food, or a desire to micturate. Its endocrine foundation is supported (Salmon considers) by the fact that sleep disturbances are among the characteristic disorders of endocrine disease—*e.g.*, in Graves' disease—and that our nightly sleep is similar to the hibernation-sleep of animals, and to the chrysalis state. The hibernal lethargy of animals coincides (he says) with the maximum development of a hibernal gland, and ceases when the latter loses its activity and cellular structure. Salmon concludes that sleep in man is a secretory function, presided over by an organ of internal secretion, and that the organ responsible is the hypophysis. Toxic elements resulting from the fatigue of the day are assumed to stimulate the gland to secrete a substance which in turn stimulates nerve-cell inhibition. He further assumes that the Nissl substance which accumulates in the cell is a colloid with almost no osmotic pressure, and so does not permit the

passage of an electric current. Its accumulation in the protoplasm causes a diminution of excitability. The nerve-cells deprived in sleep of their functional activity, and of their osmotic pressure, can no longer accumulate from the pericellular lymph the necessary substances of nutrition; they find themselves isolated, and so use up the Nissl bodies—hence conduction again becomes possible and waking occurs.

Such a theory is full of assumptions and contains very little fact. Not only does the latter part lack foundation, but it is actually contrary to the observed facts of accumulation of Nissl substance during rest and sleep, and its disappearance during the active waking hours. The disturbances of sleep in endocrine disease are dependent on so many factors and are so variable in type, that to refer them all to a purely hypothetical secretory function of the hypophysis, not experimentally supported, is entirely misleading. There is at present no experimental evidence that would substantiate an endocrinological regulation of sleep.

Theory of a Sleep-Centre.—The existence of clinical evidence in the neuraxis of a centre for governing sleep has long been advocated and is still a favourite hypothesis. Mauthner, while not the first to suggest such a centre, deserves

the credit of making the notion more precise. It had been observed by Gayet, Wernicke, Thomsen, and others that certain patients in whom a polioencephalitis superior had been found post-mortem, had exhibited somnolence, ptosis, and paralysis of the ocular muscles in frequent association. The polioencephalitic lesions were found in these cases in the central grey matter of the fourth ventricle, and of the floor of the third ventricle, and in the grey matter of the walls of the aqueduct of Sylvius. The associated somnolence was attributed by Mauthner to interruption of the centripetal and centrifugal cortico-spinal impulses, as the result of the lesions in the grey matter just described. Similarly, normal sleep was supposed to be the result of functional paralysis of the central grey matter, leading to functional interruption of the paths leading from periphery to cortex and *vice versa*. Hence sensory stimuli do not reach consciousness; and in dreams, although the motor centres may be intact, the impulses from them do not reach the periphery. The closing of the eyelids in sleep is considered in Mauthner's view to be a true ptosis. Since the syndrome, eye-muscle paralysis and sleep disturbance, is found in diseases of various etiology, such as epidemic encephalitis, Gerlier's disease, and Wernicke's

hæmorrhagic polioencephalitis superior, it must depend on the common anatomical site of the morbid process in these conditions. The fact that sleep-disturbance and ocular paralysis are not always found together (*e.g.*, in epidemic encephalitis), may be the result of their dependence on different centres placed close together. Intoxication processes can therefore be ruled out. There is additional ground for excluding a toxic origin of the sleep disturbances in such conditions, since the symptoms last so long after the acute process has ceased, and since clouding of consciousness is absent in epidemic encephalitis, where the sleep resembles normal sleep in that when the patient is roused he is at once clear mentally, as in normal sleep.

One of the principal arguments against the mechanical part of Mauthner's theory, although not absolutely against it, since the influence of a lesion in the central grey matter might be of some other kind than interruptions of impulse, is that in the pathological conditions cited there is no impairment of sensory conduction. Moreover the ptosis of the eyelids is held by some not to be an oculo-motor paralysis, but a release phenomenon (Wilbrand and Saenger). The high degree of pupillary narrowing that may occur in sleep is not the result of sympathetic paralysis,

but a phenomenon of increased tonus of the sphincter iridis like the tonus of the sphincters of the bladder and anus; and increased tonus of the sphincter iridis could hardly occur if there were a paralysis of the third nerve. (It has in fact been held that the CO_2 tension in the blood determines the size of the pupil in sleep.)

The success of the hypnotist's trick of getting the patient to try to fixate an object with his eyes within the near-point of vision and of emphasising the drooping of the subject's eyelids, has been held to support Mauthner's theory, the diplopia and ptosis being regarded as a hypnotic "aura." But hypnosis is possible in other ways, just as readily, in subjects not previously hypnotised by the method just mentioned.

Although Mauthner's hypotheses regarding the actual mechanism are poorly founded, there remain his observation and the observations of others, that lesions of the central grey matter, from whatever cause, are especially apt to be associated with disturbances of sleep. Others (including Tromner and Spiegel) have placed the hypothetical sleep-centre in the thalamus, sometimes on the basis of clinical cases which have exhibited sleep-disturbance in life and thalamic lesions post-mortem. In the cases adduced to support a thalamic hypothesis, the lesion has

usually either directly involved the central grey matter as well, or has caused it to be compressed. The manner in which the thalamus is supposed to function is similar to that advocated for the central grey matter; an interruption of impulses is supposed to occur. Thus Lucksch, on the basis of the case examined by him post-mortem, does not consider that the thalamus should be conceived as a " sleep-centre," but rather that a physiological dissociation of the thalamus from the cortex is the necessary precondition of normal sleep. Other writers however wish to attribute a certain autonomous co-ordinating function as well as a rhythmic inhibitory influence to the " sleep-centre," wherever it may be considered to be. Spiegel suggests that in normal waking life the centripetal impulses are " worked over " in the thalamus to a new form of impulses which form the groundwork of a primitive state of consciousness. These impulses go to the cortex and are the conditions underlying conscious processes. In sleep, the thalamic centre is assumed on this theory to be in a refractory phase.

Tromner's advocacy of a thalamic sleep-centre depends on general considerations—namely, that the thalamus is the sensory station nearest the cortex, and (less certainly) that it indirectly

influences the motor paths. He believes that a " sleep-organ " is necessary, since sleep is such a complex function, and requires a regulating centre, just as temperature regulation involves a " thermotoxic " one. The cortex cannot be causally concerned since (he says) in decorticated animals, such as Rothmann's dog, states identical with normal sleeping and waking regularly recur. The cortex he rules out also on the inadequate ground that insane patients with great intellectual disturbance may sleep well.

Against Tromner's theory of a thalamic centre it is urged by Nachmansohn that the thalamus is often only slightly affected in cases with profound sleep disturbance—*e.g.*, in epidemic encephalitis. Moreover bilateral lesions of the thalamus are not necessarily accompanied by sleep disorder. Dejerine and Roussy's thalamic syndrome does not include sleep disturbance of any kind. In the experimental instance of Rothmann's dog, the whole thalamus was degenerated, but there was no apparent disturbance of sleep. Such theories as these try to give sleep a locus, but not to explain its intimate mechanism. Some recent experimental work of Demole's not only suggests a locus, but hints at the possible physiochemical process as well.

Pharmacological Evidences for the Location of a

Sleep-Centre.—Pharmacology has recently furnished a contribution towards the elucidation both of sleep's preponderating locus and of its physical conditions. In pharmacological analysis of the brains of animals which had been given large doses of hypnotics before death, Kiesser recovered morphine from the diencephalon (thalamus and walls of the third ventricle) and from the cerebral hemispheres, but never from the mid brain, pons, medulla, or cerebellum. Barbituric acid derivatives he found principally concentrated in the thalamus, and to a lesser degree in the corpus striatum, but never in the hemispheres, medulla oblongata, pons, and cerebellum.

Experimental Evidence for a Sleep-Centre, and of the Physiochemical Processes involved.—It has been shown by Cloetta and Thomasen, and was confirmed by Demole, that in sleep the only detectable alteration in the blood is in its content of calcium and potassium ions. The concentration of ionic calcium in the blood was found to diminish during sleep. Demole, assuming that while calcium diminished in the blood it accumulated at the base of the brain, injected in a cat a solution of calcium chloride (0·03 to 0·08 c.c., containing 1 to 3 decimilligrammes of calcium) into the grey substance of the sub-

thalamic region in the neighbourhood of the tuber cinereum. He found that a sleep resulted which could be very deep (in direct proportion to the dose), and lasted some hours. The sleep had all the apparent characteristics of normal sleep—closing of eyes, myosis, slowing of pulse

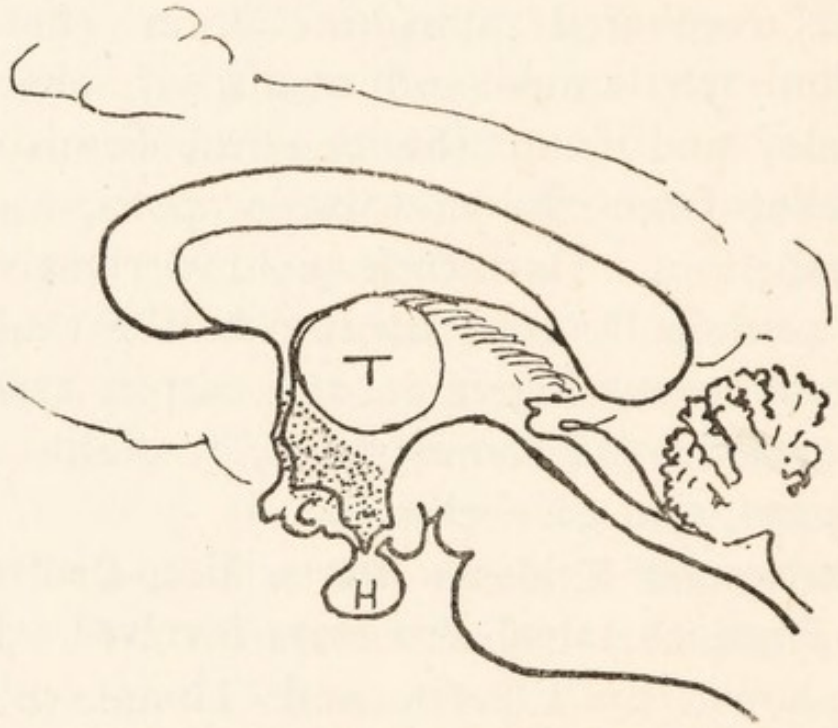


FIG. 3.—SAGITTAL SECTION THROUGH CAT'S BRAIN.
The dotted area indicates the site of the experimental injection of $CaCl_2$. (After Demole.)
T = Thalamus. C = Optic chiasma. H = Hypophysis.

and breathing, and muscular relaxation. The animal could be awakened, but if left alone would fall asleep again, and wake up naturally, waking being followed by a period of drowsiness. A state of well-being preceded and followed the sleep and was the most enduring phenomenon.

The injection of potassium chloride in the same place had a totally different effect—stupor, hypertonus, widening of the pupil, increase of pulse-rate and respiration, motor restlessness, delirium, and epileptiform convulsions constituted the response. Calcium diminishes but does not abolish this effect of potassium.

Demole's conclusion is that the characteristic experimental results are caused by the ionic condition of the vegetative centres in the floor of the third ventricle, comprising the supra-chiasmatic and parainfundibular grey matter, and the tuber cinereum.

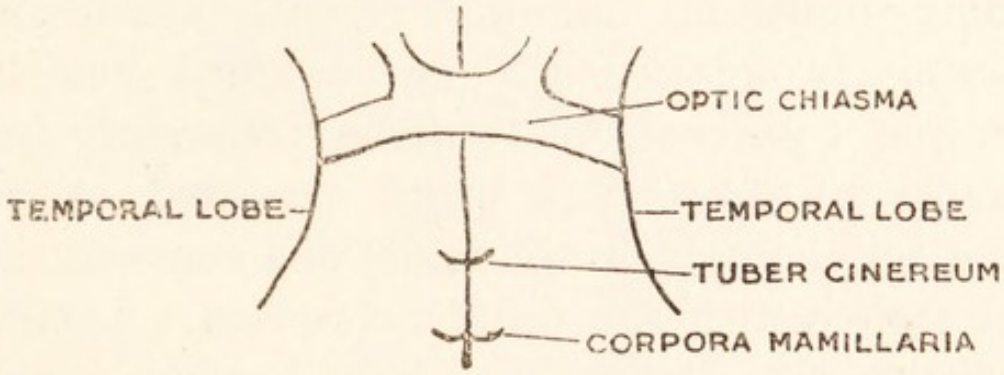


FIG. 4.

Demole generalises from this that sleep in man and animals is regulated by the functioning of this region of the brain. Lhermitte comments that anatomico-clinical facts show that all sleep-regulatory functions are not confined to this centre, but that the centre extends from the anterior end of the diencephalon to the mid brain.

It is of confirmatory value that experimental puncture of this region (*cf.* Claude Bernard's " diabetic puncture " of the fourth ventricle) has been followed by somnolence (Roussy). The **clinical evidence** in favour of the anatomical part of the hypothesis has already been alluded to in referring to the cases of Mauthner, Luschk, and others; but a much more impressively confirmatory instance has recently been recorded by Fulton and Bailey.

This patient was a married woman of 28, who for 6 years had suffered from amenorrhœa and polyuria (the latter practically disappearing just before admission), and more recently had become excessively adipose till she weighed 220 lbs. For 4 or 5 years she had suffered frequently from attacks of drowsiness which occurred at any time, for example, in the midst of a conversation, but from which she could be roused. Latterly however the somnolence had become almost continuous, although with a little effort she could always be awakened for meals.

There were also nausea and vomiting, increasing in severity and frequency, failure of vision, headaches, minor integumentary changes, and failure of memory, attention, and comprehension.

On examination there were primary atrophy of both discs and bi-temporal hemianopsia to rough

test. After operation (sub-temporal decompression) drowsiness and stupor increased, pyrexia appeared (104°), and she became comatose and died. Autopsy showed a normal pituitary and no ventricular distension, but a hard tumour occupying the space behind the optic chiasma. Its exact position is shown in the diagram (after Fulton and Bailey's article).

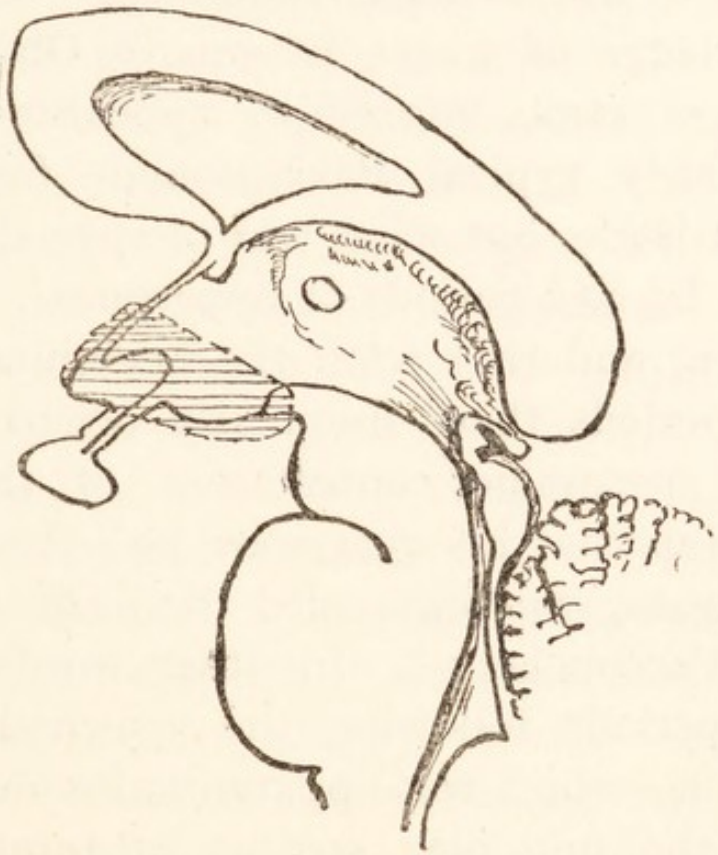


FIG. 5.—AFTER FULTON AND BAILEY'S SCHEMATIC DRAWING TO SHOW EXTENT AND RELATIONSHIP OF THE TUMOUR.

The close correspondence of the area occupied by the tumour with that stained by Demole's injection of calcium, is very suggestive.

Clinical Evidence for the Physiochemical Process involved in Sleep.—Clinical support for the physiochemical aspects of the theory may be precariously extracted from such instances as the following. The first case was that of a lad of 21, who had an attack of so-called influenza in January, 1926. Since then he had slept badly, but there had also been brief episodes when he " seemed to forget his surroundings " and " lost all knowledge of where he was." Objectively, there were some impressive appearances. He had a fairly typical Parkinsonian facies and bodily attitude, but what was of special interest was that he had periods of hyperpnœa, followed by apnœa, and that from the beginning of the apnœic periods there frequently occurred symmetrical spasmodic contractions of the facial muscles—so that his eyes were half-closed—and of his fingers, which assumed the position of the " main d'accoucheur." In other words, in the apnœic periods following the spasmodic overventilation—which was apparently involuntary—he had the muscular spasms of tetany, produced by the alkalosis resulting from the hyperventilation. Now, the alkalosis of hyperpnœa is associated with a diminution in the free ionic calcium. This chronic encephalitic patient therefore had a basal—presumably subthalamic—

lesion, with a nocturnal sleep disturbance, with brief episodes of unconsciousness, and with a paroxysmal respiratory disturbance leading to a periodic decrease in the calcium-ion concentration of the serum in the general blood-stream and to manifestations of tetany.

In another group of chronic encephalitics there are periodic losses of consciousness of longer duration. These episodes so closely resemble sleep that the condition has been labelled "narcolepsy." A typical case was that of a woman of 25 who had "influenza" three years before examination, and had ever since had a tendency to drowsiness. Sometimes she fell asleep in the middle of a conversation. Her drowsiness was worse after midday, when she had great difficulty in keeping awake at all. If she tried to resist the tendency it was notable that she "saw double." It is also noteworthy that the only method by which she could assure herself of keeping awake was by moving about continuously. She was a domestic servant and had lost numerous jobs from her habit of falling asleep while she was at work. Her illness distressed her greatly, and she was very desirous of being fit for work again. Caffeine in considerable doses—gr. 5 per day in divided doses—had some effect in diminishing the drowsiness. There

were no organic signs of disease. Now, it has been observed that in narcoleptic patients of this kind, in whom the history of epidemic encephalitis has been fairly clear, voluntary overbreathing readily induces an " attack " of sleep. It is said that even in normal persons a condition similar to sleep can be induced by sufficient hyper-ventilation. In chronic encephalitis therefore in which the preponderating lesion appears to be in the subthalamic structures, and which is notoriously accompanied by sleep disturbances, both in the direction of increase and in the direction of decrease of sleep, changes in the calcium-ion concentration in the blood are apt to occur, producing in some patients tetany and in others narcoleptic attacks.

The question next arises, How could the change in calcium concentration be supposed to act? We know that calcium has an important influence on cell-membranes. It is tempting to suppose that in sleep, which from the raising of the sensory threshold might be supposed to be associated with decrease in membrane-permeability, the latter might in some way be associated with the change in calcium concentration. Decrease in permeability of the cell-membrane means a decrease in electrical conductivity between each side of the membrane. Experi-

ments with a string-galvanometer have shown, according to Richter (*vide* Chapter I.), that there is an increase in the electrical resistance of the body generally during sleep. If these results be valid, then "sleep and his brother death" are less akin than the poets and people in general believe, for death is the opposite state of complete membrane-permeability (Lillie).

Pharmacological Evidence of the Nature of the Processes.—The action of hypnotics also suggests an influence on the permeability of membranes and therefore on the properties of the surfaces of cells. The action of changed physical conditions in the brain, for example increased pressure, in producing sleep-like conditions of stupor and coma, could also be partly explained on this basis, since a change in the general physical conditions within the cranial cavity, especially in the direction of increased pressure, presumably results in alterations in the physical condition of the cells. It is a frequently urged objection to the grouping together of somnolence from cerebral neoplasm and ordinary sleep as cognate phenomena, that in the somnolence of neoplasm the patient cannot be roused, or, if he is roused to some extent, proves to be mentally sluggish; but it is not absurd to suppose that in such a state the change in conditions on either side of

the cell-membrane, and therefore in its permeability, have reached an intensity that makes complete reversal impossible under the existing conditions. Remove these conditions (of increased pressure and its consequences on ionic concentration in the tissue-fluids) and reversibility is again complete and lasting, unless the osmotic changes resulting from pressure have gone so far as to cause partial disintegration of cell-membranes, a change which appears histologically as rupture of the cells.

Further Experimental Evidence.—In support of his thesis that sleep involves a change in permeability of cell-membranes, Crile has claimed on the basis of experiments with rabbits that after prolonged insomnia the electrical conductivity of the brain (removed rapidly from the animal after death) is decreased, in comparison with its conductivity after a period of rest following a period of insomnia, and that the decrease in conductivity varies inversely as the amount of rest that had been permitted to follow the insomnia. The differences he records were sometimes very small, and the total number of experiments was apparently few. Moreover when the conductivity was measured, the brains used were isolated from the animal's body and therefore dead. (Death however should change the con-

ductivity in the opposite direction—of increase—if the methods of experiment are valid.)

Crile's theory, based on the experiments mentioned and on other theoretical considerations, is that polarisation of cell-membranes occurs during work and depolarisation during sleep, just as in an electric battery, where the two processes alternate. "If a battery is made to work by keeping its current closed, polarisation of the plates will occur and the battery is said to be exhausted, which means that the difference of potential has diminished or disappeared. It would appear to be more than a mere analogy that such is the mechanism whereby prolonged consciousness unbroken by sleep tends to exhaustion and death" (Crile).

Summary of Evidences for a Sleep-Centre.—There are accordingly several lines of evidence that the grey matter of the diencephalon (thalamus, subthalamus, and grey matter of the aqueduct) is more intimately connected with sleep than other parts of the cerebral organisation. The clinical evidence shows that sleep is comparatively more frequently disturbed in one or other direction in the case of morbid conditions of this region, when there is no question of the results of increased intracranial pressure (McKendree and Feinier's results applying only

to cerebral tumours), than it is in lesions elsewhere, and pharmacological experiments on hypnotics and their concentration in various parts of the brain have pointed in the same direction. The experimental evidence just quoted tends to confirm this.

On the other hand, experiments on the effects of insomnia in animals have shown in the hands of various workers a curious diversity of results; some reporting lesions in various parts of the central nervous system (varying with each experimenter), others reporting none at all. But the interpretation of results of such experiments, even if they were uniformly in agreement, would be doubtful (*vide* Chapter II.). It is however no refutation of the clinical and experimental arguments, to say that no sensory interruption occurs in lesions of the subthalamic region and of the aqueduct. That argument is directed against a particular theory of how these regions work to produce or prevent sleep, and not against the association of lesions of them with disturbances of sleep. It has been suggested that since the control of the vegetative functions is centred in the subthalamic region, that the latter contains a co-ordinating mechanism from which emerges a sleep-controlling function. But the physiological changes normally observed in sleep, while they

tend to be associated with each other in a more or less uniform way, nevertheless, as we have seen (Chapter I.), are not essential conditions, individually or together, for the occurrence of sleep.

Moreover the physiological changes involved in the transition from waking to sleeping are quantitative only, and not, so far as we know, qualitative (von Economo however holds as a matter of opinion that the alterations are qualitative); nor does sleeplessness in man produce any apparent alteration in his physiological processes (so far as the limits of experimental sleeplessness in man can be pushed).

Sleep as a Function of Dissociable Parts of the Organism.—How then can such a centre be conceived to work? By a centre is meant a particular region of the brain from which the physiological process (whatever it is) that initiates, maintains and abolishes sleep is controlled. Before coming to tentative conclusions on the mode of functioning of the centre, it is necessary to consider the functioning of the cortex as a whole. We are very apt to identify sleep with loss of consciousness, and so to confuse the issue. It may be taken as very probable that consciousness in man is a function principally of the cortex. But loss of consciousness can occur in a form

which we do not recognise as sleep, and sleep, of part of the body, can occur without loss of consciousness (*vide* the numerous instances in Chapter III.). We may take it then, that parts of the body (including the nervous system) other than the brain-cortex, pass periodically and rhythmically into that condition which when it is generalised is described as " sleep." Decerebrate animals pass into states indistinguishable from sleep. The differential action of hypnotics is further evidence that sleep in its essential appearances is a function enjoyed by levels lower than the cortex. The bromides, paraldehyde, alcohol, and amylene hydrate are all more effective in the decerebrate animal. Chloral hydrate, barbital, and luminal, on the other hand, are said to lose their hypnotic effect on the decerebrate animal. No one who has suffered from insomnia will fail to agree that other parts of his body than his brain, and other functions of his organism than consciousness, are involved in sleep; the feelings of fatigue and of strain generally, which are certainly peripherally referred, but may of course originate centrally, seem to the subject convincing enough evidence of that. Crile described changes in the liver and adrenals, as well as in the brain-cortex, of his sleepless animals. But these latter two argu-

ments are of a different order from the preceding ones.

Loss of Consciousness not Essential to Sleep.— It is reasonable to infer on the basis of this accumulated evidence that sleep is not a function essentially of the cortex, but is equally a function of lower centres, and that incidentally loss of consciousness is not an essential mark of sleep. Normally cortex and lower centres participate; not all the lower centres necessarily, or at least not the centres below a certain level, since it has been shown that in a dog with the spinal cord so cut that the fore-legs remained connected with the brain while the hind-legs did not, the reflexes in the fore-legs were much diminished in sleep, whilst those of the hind-legs were unaltered. Presumably there is a process in sleep which is resident in the cortex and lower centres above a certain level, the spinal centres not being involved in the process, but being affected only indirectly.

Sleep at Different Levels has Different Marks.— The principal marks of the process in the cortical field are loss of spontaneous activity and loss of consciousness, and of the subthalamic and mesencephalic part of the process, loss of tone. This conception is illuminated to some extent and supported by the epileptic-narcoleptic series (Chapter III.), in which paroxysmal affections

of the cortex are manifested in loss of consciousness; while similar affections, probably of the mid brain, result in general muscular flaccidity and loss of ability to move spontaneously with preservation of consciousness, but muscular flaccidity and loss of power of voluntary movement do not run *pari passu* (as shown by the jerky movements of the head in a patient of mine as his head fell forward, from tonelessness of the neck muscles, in a cataleptic attack). What is this neural process, which seems to proceed sometimes, as in the decorticated animal, from the lower, and especially the subthalamic centres, and in the intact animal appears to depend largely on the state of the cerebral cortex, and which in its minute details, as we have seen, probably involves alteration in the permeability of the membranes of nerve cells ?

The Nature of the Neurophysiological Process in Sleep : Relation to Fatigue and Adaptation.—Goldscheider, assuming what it seems permissible to assume—namely, that in sleep there is a diminished activity of the cortical cells—points out that two main classes of condition lead to a diminution of cortical activity—namely, lack of stimuli, and fatigue. But fatigue is brought about by too persistent stimulation. Hence not only stimuli but the lack of them lead to sleep.

Both of these latter propositions are borne out by everyday experience; but they cannot be adopted at their face value. We sleep more readily if stimuli are lacking; whether we necessarily fall asleep in the absence of stimuli is a question that is difficult to answer. Pflüger's famous boy with but one eye and one ear available as a means of communication with the outside world, and having no common sensation, fell asleep as soon as these portals were closed. But another explanation—namely, hypnosis—has been advanced in this instance, and has even been preferred by Pflüger himself—assuming (what is arguable) that hypnosis is essentially different from sleep. There was also Ribot and Binet's case of a young woman with an anæsthesia that was general, except for one eye and ear, in whom closure of these is reported invariably to have induced sleep. But these are isolated instances susceptible of alternative explanations. It would be sounder to base our conclusions about the effect of the absence of stimuli on our everyday observation, and to say that lack of sensory stimulation is one of the conditions that favours sleep. This formulation would leave room for those instances in which sleep is hindered by the lack of stimuli. It is well known that persons accustomed to a certain

amount of noise may be unable to sleep when at first deprived of their habitual stimulation in this direction. There was the instance of the blacksmith's wife whose insomnia was remedied by having her bedroom moved back to its old position over her husband's forge where the noise of the hammer on the anvil could be constantly heard; and the other instance of the hospital patient who could not sleep till she had her loud-ticking clock brought from home and placed by her bedside. Conversely in the old days the miller was said to be awakened by the *stopping* of his mill-wheel; and the mother or nurse who wakes up at the cry of the infant and not at other sounds of like intensity, is constantly quoted. What is wanted is a concept that will cover all these circumstances, and that will include both the presence and the absence of stimuli among the conditions both of falling asleep and of waking up. As for Goldscheider's other generalisation, that fatigue of the centre results in sleep, it does not help greatly to explain one mystery in terms of another, for fatigue is still physiologically as intangible as sleep itself; and there are many observations that suggest that fatigue and sleep are not coterminous.

Inhibition is the Common Process.—It would be a philosophical advantage if the phenomenon

we call " sleep " could be subsumed as a special instance of a more general physiological state. Fatigue, whatever it is, is a phenomenon that is found with the same general marks at some stage or another of practically all physiological processes. But we have seen that for obvious reasons of commonplace observation it is impossible to regard sleep as a special case of fatigue. They are related but they are not identical. But there is another physiological phenomenon also generalised, to which fatigue is functionally closely related, but with which also it is not identical—namely, inhibition. It is true that, like fatigue, the intimate physiochemical nature of inhibition is still very much in doubt; but this term has a descriptive basis in that it covers a widespread physiological phenomenon having not merely the negative characteristic of absence of excitation, but the positive one of interference with activity. The simplest example is the knee-jerk, where contraction of the extensors is accompanied, not merely by absence of contraction of the flexors, but by an actual relaxation—relaxation being an active process, involving an electrical change similar to that of contraction, as well as a palpable diminution in muscular tone.

The theory of the conditioned reflex is now

well established physiologically. The actual fact of the conditioned reflex phenomenon in animals, and presumably also in man, is that any stimulus whatever can by training be linked up with any response. The classical and fundamental experiment was simple. In a similar way it was found that any stimulus could be substituted for the original one in the inborn stimulus-response relationship. Furthermore, it was found that not only excitatory responses (like the flow of saliva) could become linked to any stimulus, but that inhibitory responses (the capacity for which is possessed by the nervous system generally) could be similarly linked, so that, for example, while the dog might learn to respond to the sound of a bell with a flow of saliva, the sound of a metronome could by training be made to result in an arrest of salivary secretion (*i.e.*, instead of an excitatory process of secretion, an active inhibitory process was set up by the stimulus). Furthermore it was found that these two processes, of excitation and inhibition, could be mingled in such a way that the one followed the other after an interval. This was done by arranging that the conditioning stimulus was "reinforced" only after an interval of several minutes—*i.e.*, the dog was fed only after an interval of, say, 3 minutes had elapsed from the

application of the stimulus. In this way after some training the result was obtained that no secretion at all was produced during the first 3 minutes after the application of the stimulus (*i.e.*, inhibition persisted), and was at the end of that time followed by a copious flow of saliva. This is the so-called " delayed " reflex.

When an animal was trained in such a way that it responded to one stimulus with an excitatory response and to another closely similar stimulus with an inhibitory response, the process of establishment of such responses was called by Pawlow " differentiation " of a conditioned reflex, the " differentiation " referring to the closely akin stimuli.

Now it was also found that frequent repetition of the same conditioned stimulus, with the resulting excitatory response, led very quickly to a state in which no excitatory response occurred. " Under the influence of conditioned stimuli, the cortical elements enter sooner or later into an inhibitory state." There was a cessation of function, which Pawlow regarded as inhibitory in origin. Pawlow considered this to be an expression of the fact that " the cortical elements . . . are functionally exhausted with comparative ease." But he is far from identifying fatigue and inhibition. " The progressively

developing inhibition, which itself cannot be regarded as a functional exhaustion, but which is the result of exhaustion, assumes the rôle of protector of the cortical elements, preventing excessive fatigue of the cortical cells. During the period when the cells are in a state of inhibition, being free from activity, the cortical elements recover their normal state. This applies to all the cellular structures of the cortex equally, and therefore under conditions in which a great number of cortical points are repeatedly entering into a state of excitation, the whole of the cortex may be expected sooner or later to become subjected to inhibition." Such a state of widely-spread inhibition Pawlow identifies with sleep itself. In support of this he points to the fact that in the development of a differentiated reflex, sleep is very apt to supervene during the experiment; and similarly with the development of a long-delayed reflex. Both these reflexes, as has been pointed out above, involve inhibitory processes in a special degree. The identity of sleep and an inhibitory process is further suggested by the fact that the different external agencies in their rôle of conditioned stimuli fall into an identical order of classification as regards the rapidity with which they lead to internal inhibition and to sleep. Internal inhibition, on

this theory, is nothing but a scattered sleep, sleep of separate groups of cellular structures; and sleep itself is nothing but internal inhibition which is widely irradiated, extending over the whole hemispheres and involving the lower centres of the brain as well. Inhibition sets in much more rapidly in the cortex than in the spinal cord and medulla. "While in a normal dog an investigatory reflex to a definite sound (orientation of the appropriate receptive organ, in this case the ear, in the direction of the stimulus) quickly vanished, the same sound in a dog with extirpated cortex, under identical conditions, called forth an investigatory reflex in a stereotyped manner and for an unlimited number of times." Further points of resemblance between inhibition and sleep, according to Pawlow, are that both develop slowly; and both spread gradually, some parts of the brain being inhibited or asleep before others. Inhibition in Pawlow's experiments is reproduced with greater and greater ease upon practice and repetition, and by employing different forms of stimulus. It is an everyday experience that sleep is brought about in new surroundings (*i.e.*, among new stimuli) more and more readily as habituation to these surroundings proceeds.

According to this inhibitory theory, the day's

activity leads to an over-stimulation of a great number of different cortical points, which then become centres for the irradiation of inhibition; for it is one of the postulates of the theory that inhibition tends to spread over the cortex from a focus. The consequent widely distributed inhibitory state descends to affect some or all of the lower cerebral centres, and the result is sleep, which is a more or less complete cerebral inhibition. The normal alternation of sleep and wakefulness is thus, physiologically speaking, an alternation of more or less general inhibition, and of more or less generalised excitation, of the cortex and of the lower centres.

If sleep depends, then, on an irradiation of inhibition, the focus from which it radiates may be anywhere in the central nervous system that is prone to the development of inhibition. That the focus of origin should frequently be the cortex is not surprising from its position of dominance and its continued activity; and clinical experience, as we have seen, suggests that another frequent focus of origin is the sub-thalamic region. Von Economo has suggested that this centre, where are situated sympathetic, parasympathetic, and vegetative centres, presides over body-sleep, and the cortex over brain-sleep. On this supposition, the " sleep-centre "

for total sleep of the organism becomes a complicated cortico-subcortical interconnection of a physiological rather than an anatomical kind.

This conception of sleep as a physiological state of the entire organism characterised by a more or less universally reduced activity, and governed by a positive brain-process* which is itself a reaction to stimuli, external and internal, makes it possible to include numerous other facts of observation in a general biological scheme of sleep. The influence of external stimuli, of light and darkness, of habituation to surroundings, and of repetition of stimuli in general becomes understandable as so many conditioned

* Naturally, a theory of sleep which depends upon the supposed characteristics of an inhibitory process must take account of theories of the nature of inhibition itself. One of the theories of inhibition (not that utilised here) is McDougall's " drainage-theory." McDougall considers that in reciprocal inhibition, as in the knee-jerk, drainage of normal energy occurs towards the active neurons from the neural supplying the antagonistic muscles. Dr. L. H. Richardson, F.R.S., has constructed an ingenious model which shows many analogies with the phenomena of reciprocal inhibition, and at least one analogy with normal sleep—namely, that in an already drowsy subject while easy mental tasks may be accomplished, an attempt at a more difficult one may send the subject completely to sleep. Dr. Richardson's model depends for its characteristic properties on the peculiarities of the behaviour of two neon lamps (personal communication).

stimuli of a sort peculiarly apt to initiate inhibitory processes. The relation between sleep and fatigue becomes clearer; one is not the direct consequence of the other, but fatigue is one of the numerous kinds of stimuli that may set going an inhibitory process, which may then generalise itself as sleep. The absence of stimuli, like the presence of the habitual conditioned stimuli, is comprehensible on this view also as a precondition of sleep; for the absence of excitatory processes in the cortex is a peculiarly favourable state for the spreading of inhibition over it. Even Claperède's theory that sleep is an instinct, that we sleep not because we are exhausted but in order that we should not become tired, is seen to have a physiological basis, although the teleological formulation may still be dubious. Sleep becomes comprehensible as an adaptive function, which can be fully understood only in reference to the environment, and not by the consideration of neural changes alone.

Biological Function of Sleep in the Evolution of Complex Organisms.—It is remarkable how few of those who speculated on the nature of sleep have emphasised its occurrence at night. Darkness deprives the organism of a large field of stimulation, not only of visual stimulation

but of all other kind, since most forms of life are less active at night. Hence in primitive times less vigilance was exercised in general at night than in the daytime. It is therefore likely that from very early times there occurred a rhythmic reduction of activity, especially of adaptive behaviour, which is essentially neural. Perhaps what accounts for the absence of convincing evidence of sleep in fishes is that the alternation of darkness and light does not occur to any extent with them. One can see also that the organism would be enabled to work at a higher potential during the day by reason of the opportunity for restoration at night. It is surely a significant fact that the lowest organisms show no alternation of activity and rest. The ciliary movements of lowly organisms like vorticella show no interruption of activity. Among some insects —the orthoptera—Piéron failed to discover periods of diminished excitability. But, as the animal scale is ascended, sleep becomes a more and more obtrusive occurrence. A higher rung on the animal scale means, as a rule, an increased complexity of neural organisation.

Complex neural organisations, as is well known, are more easily disorganised than simple ones. It seems likely that the nervous system of man could not have been evolved to its present level

of intricate complexity unless a periodic restoration of energy-reserve and of other cellular conditions had been possible. This does not mean that sleep is determined simply by the recurrence of fatigue. The stimulus of fatigue *may* originally have been the adequate stimulus to sleep, but that is at least doubtful. It is more likely that sleep and fatigue are independent phenomena, which became associated in a secondary manner partly as a biological result of the conditions above indicated, and partly through the intermediary of rest; for fatigue is the adequate stimulus to rest, and rest, in favourable conditions, and even apart from fatigue, leads, as everyone knows, to sleep. That complete rest, such as is only attainable in the recumbent position, with its resulting muscular relaxation, is an adequate stimulus to sleep is shown not only by the nightly practice of all of us, but by the more novel experience of certain experimenters. Kleitman, for example, in the course of his work with subjects who had volunteered to deprive themselves of sleep for as much as 90 hours, found that it was fatal to the experiment to allow the subjects to lie down—if permitted to do so they fell asleep at once.

Furthermore, we can sleep when we are not tired, and cannot sleep if we are very tired. The

latter is a commonplace observation, which was confirmed by Piéron in his experiments in over-fatigued dogs. We have therefore two processes evolving together, fatigue and sleep, both calculated to bring about a restoration of the organism, the one by inducing to rest, the other following upon rest—sleep might be described as the completest state of rest—so complete that conscious, neural, and muscular activity are alike abolished. But there is not a direct continuity from rest to sleep. The onset of sleep is accompanied by an entirely characteristic rise in the sensory threshold, quite foreign to the state of mere rest, and by a degree of muscular relaxation only attained otherwise in such conditions as deep narcosis. Sleep is in fact a positive process, with characteristics of its own, discontinuous with those of mere rest, and these characteristics, according to Pawlow, are those of cortical inhibition.

Psychological Aspects of Sleep.—A purely psychological formulation of sleep must necessarily be incomplete. Sleep is a psychophysical phenomenon, in the sense that it involves changes both in the psychological and physiological conditions of the organism. The psychological condition *par excellence* is an alteration of consciousness. This alteration may be a dulling or a complete

abolition. Where the diminution in psychological activity has reached only the stage of more or less dulling, hypnagogic hallucinations, and in a further stage dreams, present themselves. The essential of all these types of alteration is a withdrawal of interest—not only from the outside world (which would produce the psychogenic stupor of schizophrenia or dementia præcox), but from all stimuli whatever, external or internal. The psychoanalytic school sees in this an analogy with the prenatal intra-uterine condition, to which sleep is conceived to be a symbolic return or regression. The analogy has struck others before them. Meredith says, "Designing slumberers are such infants. When they have awakened and stretched themselves flat, it seems that they have really gone back to their mother's breasts, and they fret at whatsoever does not smack of nature, or custom."

In many patients sleep consciously or unconsciously symbolises death.

In sleep, attention relaxes, and association processes are interfered with, and in deeper sleep abolished. Where they persist, although changed, and dreaming results, the determinants of the trend of the dream-associations have been shown by Freud to be largely different from those that regulate the associations of waking

life. Directed thinking—*i.e.*, logical thinking, or thinking with a goal in view—is absent; the associations are "free," but only in the sense that they are directed by emotional trends and complexes in the individual's mind, rather than by the laws of orderly thought. The "freedom" and apparent haphazardness of the sleep associations are in this view spurious. The Freudian interpretation of dreams depends upon this hypothesis, and upon the associated postulate of a process of repression.

Another characteristic of mental processes during sleep is the predominant rôle of visual images in the dream, in comparison with the much greater part played by verbal images in waking life. It is as if a more primitive part of the cerebral organisation were in action—a part which deals in visual rather than in verbal symbols; just as in cultural evolution pictograms appeared before the more recondite symbols of the alphabet.

Fatigue, from the psychological standpoint, is not so important as the feeling of fatigue, which acts by interfering with attention. Some of the psychologists are ambitious. According to Hollingsworth, sleep is an unnecessary stupor, a "vestigial instinctive habit to be overcome by a race of supermen in the future."

Summary.—A consideration of the facts experimental and clinical, normal and pathological, set forth in the previous chapters, and of the theories that have been in this chapter briefly discussed, shows that a description and, so far as it is possible, an " explanation " of sleep must take account of data from many fields. Only in this way can at present a complete understanding be distantly approached.

That sleep has a saving function in the economy of the organism is strongly suggested by physiological investigation of the basal metabolic rate and of the circulatory and other phenomena. That it has actually a restorative function is more doubtful, but is rendered probable by such knowledge as we have—clinical, experimental, and microscopic —of the effects of sleeplessness. The alternation of wakefulness and sleep is from this point of view only one instance of the many in the animal body, and therefore in the animal kingdom, of the alternation of a predominance of catabolic and of anabolic processes. The value of all rhythmic alternations of this kind lies in the greater rate at which energy expenditure can occur while the organism is actively at work. The alternation of systole and diastole in the cardiac cycle is an unusually clear instance of rhythmic alternation as an essential property of muscular action.

Similarly it is probable that the cellular mechanics of the organism in general, by their very nature, imply a long-period alternation of greater and lesser activity in the form of wakefulness and sleep. What these mechanics may be has been discussed at some length in dealing with cellular activity and particularly with the physical conditions of cell-membranes.

Rhythm is characteristic of practically all vital activities, and no less of sleep. While rhythm is probably related in a general way, as has just been suggested, to the alternations of catabolic and anabolic changes in the cell, and more immediately to its mechanics, the particular form of rhythm adopted is dependent on external as well as internal factors. It has been pointed out that the daily return of sleep is probably a function of the alternation of darkness and light in the environment, the relationship being gradually established in the course of evolutionary time. An observation that supports this is the lesser metabolic change that occurs in sleep in darkness compared with sleep in light. Like all rhythms, the sleep-rhythm is capable of being disturbed. There seems to be no reason to suppose that a man could not be trained to sleep, say, only every second or third night, just as his bowels may be trained to move

only every second or third day. Similarly, in proportion as sleep involves in some degree a large number of bodily functions, it is capable of being disturbed in a large number of ways.

The neural pattern, being constituted of associated functions, is capable of showing dissociation of these functions, so that while one part is active the other part may be asleep. It seems probable in fact that a neutral phase is abhorrent to the central nervous elements. Each element tends to be active in some way—in a state of excitation, or in a state of inhibition; where the latter is not induced by some activity of its own, it tends to come about by " induction " from neighbouring elements which happen to be active. The phenomena considered in the chapter on the pathology of sleep gave many instances of this—dreams, somnambulism, dissociated states (*e.g.*, " sleep-drunkenness "), and partial awaking on the one hand, narcolepsy and catalepsy on the other.

The point is that inhibition is not a mere state of rest; it presupposes as definite a cellular change as excitation does. Nothing that has been said above of the known measurable physiological conditions in sleep is incompatible with a conception of sleep as simply the external manifesta-

tion of the lowest degree of general vital activity found in the organism in the course of the 24 hours. But what has been said of the properties of the pattern, and especially the nerve-net which is the central feature of the pattern, implies something more than mere diminution of activity. The functions of the central nervous part of the pattern are adaptive, in such a way that an excitatory stimulus like a noise, which usually produces an increase of function, becomes a stimulus to the state of sleep which implies on the whole a diminution of function. Some process not of mere diminution must have intervened. A similar conclusion forces itself from a contemplation of the relations of fatigue to sleep. Fatigue, as has been shown, may lead to sleep in two ways: via the psychical route in the conscious animal, the sensation of fatigue stimulating the animal to rest, and rest passing, but not by a direct continuity, into sleep; or by a route which can be stated entirely in physical terms, as in Pawlow's experiments where repeated stimulation of the same part of the cortex leads inferentially to fatigue of that part and to an inhibitory process, which tends to generalise itself as sleep. A process qualitatively different from mere diminution in activity in the central nervous system is suggested by these data, and

supported by the phenomena of differential activity (dissociation) which have been mentioned. The cortical irradiation which the work of Pawlow's school so strongly suggests speaks also for the spread of a special process; so also do the facts that sleep occurs in the absence of fatigue, and that the latter is but one of many determinants. That this special process is a neural inhibition, occurring principally in the central neural part of the physiological pattern, and self-propagating, is strongly suggested by the experiments of Pawlow, especially those which have been alluded to in slight detail (delay of reflexes, and differentiation of reflexes). Evidence of the propagation of the inhibitory process, even to the lowest levels of the central nervous system, is furnished by the observation that when the "spinal dog" (a dog with a transection of the cord below the medulla) is asleep, the tendon reflexes of the lower levels are not changed from the waking state, whereas in the intact sleeping animal they are diminished. The tonelessness of the muscles beyond anything obtainable in the completest waking rest also suggests an inhibiting influence, since the loss of tone is paralleled only by the tonelessness of the obvious, because sudden, inhibition of narcoleptic and cataleptic attacks. Similarly the

rise in the sensory threshold and the dissociation-phenomena of somnambulism, and of dreaming, suggest an inhibition of sensory nerve processes, a "sensory blockade." Wakefulness and sleep are corresponding opposites; epileptic and narcoleptic attacks are also corresponding opposites; the two latter are episodic paroxysmal exaggerations of the former. An epileptic convulsion is the acme of the neural excitation of which waking activity is the normal expression; narcolepsy, on the other hand, is the extreme case of that spread of inhibition of which normal sleep is the usual manifestation. It seems not unlikely that the physiological conditions of sleep and of the epileptic-narcoleptic problem are closely bound up with each other. Two important processes of the physiology of the central nervous system—inhibition and irradiation, whether of excitation or of inhibition—are concerned in the explanation of both.

These suppositions are strengthened when the changes that underlie the general conditions of inhibition are considered. Contributions to this problem from the pharmacology of hypnotics, from the chemistry of the blood-serum, from pathological and clinical observation, and from experiments, have already been set forth.

If it be accepted that the neural process in

sleep is essentially inhibitory, then if the physiological processes involved in central inhibition were known, the problem of the intricate mechanism of sleep would be solved; for sleep would simply be a special case of inhibition—and special only in the sense of being diffusely irradiated. But the minute physiochemical changes that constitute inhibition are only guessed at, while, on the other hand, the studies on sleep that have been mentioned may contribute something to the solution of the general problem of the nature of the inhibitory process in the central nervous system.

Speculations in calcium metabolism are highly adventurous, but that the distribution of calcium-ions may be bound up with the intricate physical chemistry of sleep is suggested on several grounds. In normal sleep the concentration of ionic calcium in the serum of the peripheral blood is found to be diminished, in comparison with waking life. Certain patients (chronic encephalitics) with a derangement of the central nervous system, on some occasions, as the result of overbreathing, develop signs of tetany, a condition which is known to be associated with a diminution in the ionic calcium concentration of the serum; others with a similar affection, on overbreathing, develop attacks of sleep; while attacks of sleep

occur also spontaneously in the chronic encephalitic patient. Demole's experiments, of injecting calcium in cats into the region which is most frequently and most severely affected in chronic encephalitis, produced phenomena indistinguishable from normal sleep.

It has been suggested that the fall in calcium in the peripheral blood is compensated by its accumulation at the base of the brain.

The action of hypnotics, which are chemical substances inducing a state of sleep with great readiness, is probably on cell-membranes, in view of the lipoid composition of the latter, and of the direct relation between the lipoid solubility of these substances and their hypnotic action. The mechanism of their action on physiochemical systems of similar composition has lately been demonstrated. It consists in reversing the physical constitution of an emulsion from an oil-in-water one to an emulsion of water-in-oil. The electrical conductivity across a membrane composed of such an emulsion will clearly be much diminished by the reversal. The change in the emulsion is itself reversible, unless an excess of hypnotic substance is used.

Now calcium (the portion of it which is in the ionised form, in any solution) also is known from experiment to have a potent influence on cell-

membranes. Clinically moreover it has a reputation in limiting effusions of all kinds (*e.g.*, in urticarial conditions and the like), presumably by diminishing the permeability of cellular membranes to water. Pearce, in an unconfirmed experiment, has claimed to demonstrate that the absence of calcium converts the vasoconstrictor effect of adrenalin into a dilator one—*i.e.*, an excitatory effect is reversed into an inhibitory one. These three lines of evidence point to an influence of calcium on cell-membranes in the direction of causing a decrease in permeability.

It is accordingly tempting to surmise that what hypnotics do for the sleepless or indeed for any subject by lessening membrane-permeability in the central nervous system, a slight excess of calcium does in normal sleep, by initiating an inhibited condition of the nerve-cells in the grey matter at the base of the brain. The inhibition then irradiates, by a process of which the details are not yet elucidated, over the rest of the central nervous system. It is possible that while normally a diminished conductivity of the central nervous system is brought about by this means, the essential lowering of membrane-permeability may be in other cases brought about differently. Exercise (leading to fatigue) may work, as Crile suggests, by inducing polarisation of the surfaces

of cells, and so also diminishing conductivity through or across the surface. In the instance where fatigue has been excessive, and sleep is rendered difficult, this may be the result of the interference of another factor, catabolic products not being removed by oxidation rapidly enough, and interfering in some way with polarisation or its consequences. Insomnia, resulting in continuous activity, may have the same effect. Brain tumours, by causing stasis and consequent equalisation of osmotic pressure inside and outside the nerve-cells—*i.e.*, an approximation of the concentration of electrolytes inside and outside the cells, can have an effect equivalent, as far as conductivity is concerned, to diminished permeability. But since the conditions of pressure and its consequences remain constant as long as the lesion is allowed to remain, the change in permeability is not reversible—*i.e.*, the patient remains drowsy even if stimulated. Measurements of electrical conductivity, both of the skin during life while the subject is asleep (Richter) and of the brain after death in animals (Crile) forcibly deprived of sleep, show the increased electrical resistance that might have been expected on the hypothesis here elaborated.

It remains to bring under the general scheme the importance of the grey matter at the base

of the brain as a factor in sleep. Does this region constitute a " sleep-centre " in the sense that it regulates the rhythmic recurrence of its sleep, its continuance, and its cessation, as has been often suggested by those who have used the term " sleep-centre " ?

The clinical facts are conclusive that there is some connection between the " centre " and sleep; but the point of connection is another question.

In the first place, in epidemic encephalitis, in which the lesion is predominantly in the subthalamic region, the acute stage is frequently characterised by insomnia, somnolence following in the later stages; as if irritation of something were followed by paralysis of the same thing, causing first a lack of sleep and then too much of it. In neoplasm of the cerebral grey matter of the third ventricle and the aqueduct, the somnolence increases as the growth progresses; destruction, in other words, is accompanied by an increase in sleep, not by a diminution of it, as would be expected to follow if the lost substance had been concerned with the induction of sleep. Furthermore, pharmacological research has shown that hypnotic drugs are concentrated almost entirely in the basal ganglia, and almost not at all in the cortex (at least of animals) or

in the centres below the diencephalon. Presumably they are found where they act—*i.e.*, in the basal grey matter. The action of hypnotics is essentially depressant; their action in inducing sleep is evidently by depressing the functional activity of the parts where they are concentrated. It seems to follow that these parts cannot be excitors of sleep, else their paralysis by depressant drugs would be expected to cause insomnia, and not the opposite condition.

In brief, the evidence points to the basal grey matter as being a waking-centre and not a sleep-centre. It is not very difficult, in the light of the scheme already propounded, to see how this can be so. The control of the vital vegetative functions, which are incessantly more or less in action—in waking more so, in sleeping less—is centred in the basal grey matter. These vital functions undergo a diurnal rhythmic increase and decrease of function, independently of whether sleep occurs or not, as we have seen. Their activity implies a focus of excitation at the base of the brain, and this excitation will wax and wane correspondingly. Now it has been shown that the activity of the physiological pattern that constitutes the neural basis of sleep depends largely on the presence of environmental stimuli. It has also been pointed out that the

internal as well as the external environment has to be considered. It seems justifiable to conclude that a diminution in the internal stimuli will favour and even provoke the onset of sleep, just as a diminution or cessation of external stimuli appears to do. Hence there is a probability that the rhythmic diminution in the activity of the vital vegetative centres which occurs each 24 hours tends to produce a local inhibiting process which will irradiate over the rest of the central nervous system in suitable—*i.e.*, non-excited—conditions, such as are furnished by rest in darkness and quiet.

In this view the basal grey matter maintains its characteristics as a centre for vital activity, in which episodically a diminution favours the onset of diffuse inhibition known outwardly as sleep. Additional support for this theory seems to be furnished by the relation of emotion to narcoleptic attacks (*vide* Chapter III.) on the one hand, and of the association of lesions of the basal grey matter in epidemic encephalitis with emotional changes, but especially with the loss of emotional response or apathy not infrequently seen in chronic encephalitics who also sleep overmuch. It is our emotions that move us, as James said: lack of emotivity (apathy) produces a state of inactivity; inactivity of the organism

favours the onset of inhibition in its neural pattern; and so sleep tends to occur. The physical substrate of emotion is principally as far as we know in the basal grey matter, especially in the thalamus. Again, there is a trend of evidence pointing to a connection between the relative inactivity of basal neuron-masses and sleep.

The " centre " is therefore conceived as a focus of activity, upon which not only the cortex but the whole organism depends for stimulation, and peculiarly liable, when its own activity diminishes, to serve also as a focus from which inhibition of activity may radiate.

The body of evidence which has been considered supports the conclusion which R. Dubois reached thirty-three years ago, when as the result of experimental work on marmosets, he proved to his own satisfaction that there existed in the floor of the third ventricle a " centre for waking " which was one and the same with a " sleep-centre." The most recent work, by Burggren and Moberg, more precisely locates the centre principally in the infundibular and hypothalamic nuclei of the ventricular floor; but the centre is best conceived functionally as more extensive than this in the direction already indicated.

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Printed in Great Britain for
Baillière, Tindall and Cox, by Billing and Sons Ltd., Guildford and Esher.