Thus it seems probable that the majority of all postero-internal zone fibres take origin in the grey matter. And when it is remembered that the fibres do not put in an appearance until the sclerosis of the heads of the horns is in a large measure replaced by proper grey elements, it does not seem improbable that they take origin in the most dorsal portion of the grey matter.

This disposes of three of the tracts of the posterior column whose fibres are by most investigators thought to be of endogenous origin, and which persist in all lesions exclusively confined to afferent root fibres, but which are the earliest to succumb to any morbid process which primarily affects the grey matter.

The fourth and remaining one is Schultze's descending comma tract. In the normal cord, like others of intracordal origin, this tract is of mixed composition, containing fibres that degenerate when the posterior roots are severed, and others that atrophy only when the grey matter is diseased. But it is generally believed that fibres which depend for their nutritional activity on the cells situated in the grey matter largely preponderate over those whose trophic centres are in the cells of the posterior spinal ganglia.

In view of the fact that three tracts of acknowledged intramedullary origin have persisted even in the presence of considerable chronic poliomyelitis, there arises a natural desire for an explanation of the presence of degeneration in this tract (see Figs. 2, 3, and 4 c) whose main origin is similar. For, as already intimated, the comma tract is in a state of almost absolute fibrosis from its usually assigned upper to its lower limits. (See Figs. 2, 3, and 4 c).

An explanation which has presented itself is that being of more mixed origin than the other endogenous tracts it has suffered doubly as a result of a chronic degeneration in its centres in the cord and in the posterior root fibres.

Yet I have not been able to convince myself into accepting so easy an explanation. It seems to me that there must be some specific reason for this contradictory degeneration, that there must be some special groups of cells whose fibres enter into the posterior external columns and congregate as the descending comma tracts, and which in this case have been so severely affected by the atrophic process at work as to cause abolition of these fasciculi of fibres.

The only groups of cells, however, which show extreme degeneration are Clarke's (see Fig. 6 a). Is it possible that cells of the vesicular cylinders, besides being the authors of the direct cerebellar tracts, also give origin either directly from some of the cells themselves, or as collaterals from the cerebellar fibres to the descending comma tracts?

In a normal cord fibres may be seen passing from the grey matter mesial to Clarke's columns, where they exist, into the postero-external columns to about the position of the comma tracts. Fibres corresponding to these cannot be observed in this cord; and that these fibres, Clarke's cells both large and small, and the comma tracts are all degenerated, appears to be above coincidence, and to point to some anatomical association.

Again we know almost precisely the vertical extent of the vesicular cylinders. Day-by-day evidence is being adduced which tends to prove that the descending comma tracts are of about the same vertical extent as the cylinders, and it seems probable that before inquiry stops it will be determined that there is an exactness in the range of both structures.

It appears unlikely, in view of what we know of cell associations, that an almost continuous column of cells of the extent of Clarke's are unassociated by commissural fibres; and taking into consideration the nearness and apparent association of the vesicular cylinders with the fibres leading from their neighbourhood to the vicinity of the comma tracts, and the likeness in vertical extent of both the cylinders of cells and fasciculi of fibres, it does not appear improbable that the latter function between upper and lower levels of the former. If such an anatomical connection exists, there is at once found an explanation of the persistence of fibres in three tracts of intracordal origin and the abolition of the greater part of the fibres from others of like origin.

NOTE.—Since the above was read at the 1897 meeting of the British Medical Association, Dr. Bruce has published an interesting case showing the connection of Flechsig's median

triangle and Gombault and Phillip's sacral fibres which together he has named the septo-marginal tract. This case is certainly strong negative evidence in favour of Bruce's contention regarding the extent of the septo-marginal tract. The disappearance of the lower and more peripheral portion of the latter in this case, which corresponds to Gombault and Phillip's fibres, while the upper portion corresponding to Flechsig's triangle persists, is no doubt due to the greater degeneration in the grey matter of the sacral posterior horns.

THE CROONIAN LECTURES

ON

SOME POINTS CONNECTED WITH SLEEP, SLEEPLESSNESS, AND HYPNOTICS.

Delivered before the Royal College of Physicians of London.

By JOHN BUCKLEY BRADBURY, M.D. CANTAB.,

Fellow of the College; Downing Professor of Medicine in the University of Cambridge; and Senior Physician to Addenbrooke's Hospital.

LECTURE IV.

I CONCLUDED my last lecture by stating that attempts had been made to find a less dangerous and equally effective substitute for morphine. To two such compounds I now wish to draw your attention.

In 1890, Stockman, in conjunction with Dott,¹ published experiments made on some derivatives of morphine. They introduced into the morphine molecule various alkyl and acid radicles and chlorine, and also modified it by the addition of methyl chloride. Morphine contains two hydroxyl groups, and the hydrogen of one of these, probably united to an aromatic nucleus, is more easily replaced than the other. When this is replaced by methyl, ethyl, or amyl, the morphine action still remains, but the compounds thus produced are more toxic, their narcotic power is less, their tetanising power greater, and they have a greater effect upon the motor nerves. On the whole, their experiments do not seem to give much support to Schröder's law, as they say: "Theoretically, there is possibly a difference in the actions of the three substances, but it must be entirely quantitative, not qualitative, and our methods of investigation were not sufficiently fine to detect it (if it really exists)." Von Mering's recent observations are even more convincing. From clinical observation he found propyl-morphine, isobutyl-morphine, and amyl-morphine distinctly feebler than methyl- and ethyl-morphines.² When acetyl and benzoyl radicles were introduced, and acetyl-morphine, di-acetyl-morphine, benzoyl-morphine, and di-benzoyl-morphine were thus produced, a similar effect was obtained. The narcotic effect, however, was present after small doses (1 mg.— $\frac{1}{2}$ gr.—of acetyl morphine in the case of rabbits), but it did not appear to increase with increase of the dose, tetanic symptoms developing instead. "The depressant action of small doses on the cord, and especially on the respiratory centre," Stockman and Dott say, "is very much greater than that of morphine." From this statement we should not expect any of these to be of value as substitutes for morphine. But the case is otherwise regarding codeine, as they say that, compared with codeine, "they (the acid derivatives) induce an equal narcotic effect with about one-tenth of the dose, while a dose about three times as large is necessary to cause tetanus. Their depressing action on motor nerves is about the same; the nausea and diarrhoea occurring in dogs is quite as great as after codeine." Thus as a substitute for codeine we might expect one of these substances to be of value. Quite recently Dreser,³ from researches mainly on the respiration, has introduced diacetyl morphine, under the name of "heroin," into therapeutics. According to him it is more powerfully sedative, and correspondingly less toxic than codeine; it lengthens the time of inspiration, increases the gaseous exchange, and does not affect the sensibility except in diminishing any tendency to over-extension of the lungs. So far the clinical results have supported Dreser's experiments, but as yet they have been too few to decide the position this drug will hold in therapeutics.

But von Mering has found that monoacetyl-morphine—in which the acetyl replaces the hydrogen of the alcoholic

hydroxyl of morphine—is more sedative and less toxic than diacetyl-morphine, and he states that he has used this substance with success in cases of advanced pulmonary tuberculosis in which codeine and diacetyl-morphine had proved of little effect.⁴

The other derivative of morphine which has been introduced as a substitute is benzyl-morphine, the hydrochloride of which— $C_{17}H_{19}NO_3 \cdot O.C_6H_5.CH_2.HCl$ —is called "peronin." This was introduced into practice by von Mering, who found it slightly less active than morphine, but freer from ill-effects. According to Schröder,⁵ it occupies pharmacologically a position between morphine and codeine, producing more restful sleep than the latter, and no symptoms of stimulation. Mayor's more recent investigations⁶ do not, however, support this. Small doses given to rabbits produced a certain amount of torpor, but the animals reacted to the least stimulus, and if the dose was increased convulsions were produced. If artificial respiration was performed, death resulted from cardiac paralysis. The lethal dose he found smaller than codeine, being in rabbits—peronin, 0.023 to 0.025 gram, and codeine, 0.063 gram per kg. body weight. My own investigations support these results.

In a rabbit after a dose of 0.01 gram per kg. injected intravenously, convulsions occurred; in a rat (155 grams) 0.02 gram (0.13 gram per kg.) injected into the peritoneal cavity produced depression, slow deep respirations, clonic convulsions, and death in 9 minutes. Codeine 0.0143 gram given to a rat weighing 114 grams (0.125 gram per kg.) under similar conditions produced convulsions, but was not fatal; but in one case 0.15 gram per kg. caused death in 8 minutes. Fish, too, are more susceptible to peronin than codeine, minnows dying sooner in 1 to 50,000 of the former than 1 to 7,500 of the latter.

Stursberg⁷ also appears to have found peronin more active than codeine and further removed from morphine pharmacologically, but, like myself, he also seems to have found it somewhat more sedative than codeine. From an experimental point of view, however, there seems little to recommend it in preference to codeine, as its increased sedative action does no more than counterbalance its increased toxic effect. But its true place in therapeutics must be settled by clinical observation, and at present this is insufficient.

The other derivatives of morphine do not possess any practical interest.

The drug next in interest to opium as a hypnotic is cannabis indica, and as the most recent researches on this substance have emanated from our Cambridge school I intend to dwell somewhat in detail upon it. Three years ago Messrs. Wood, Spivey, and Easterfield began to investigate the chemistry of this plant, and as charas was its most active product they decided to work with this. Previously various substances had been stated to be the active principle. A resinous compound was isolated by O'Shaughnessy, Robertson, T. and H. Smith, and other more recent investigators; an oily substance was obtained by Personne, alkaloids by a few experimenters, and to each of these the activity of Indian hemp was thought to be due. I will dispose of the alkaloids first. Only minute quantities of an alkaloid have been found by some of the most recent workers, and many have failed to obtain any. None was obtained by Wood, Spivey, and Easterfield from charas, although it was carefully looked for. As the alkaloid first isolated appears to have been nicotine, and as most recent investigators have failed to obtain more than traces of an alkaloid, and these not possessing the peculiar action of the drug, the hypothesis that the activity of Indian

hemp is dependent upon this class of bodies must, for the present at least, fall to the ground. Personne's cannabene has been found to be an impure sesquiterpene and not the active principle, so I need say nothing more about it. We are therefore left with the resin, and all the most reliable observations point to this as the active substance. The brothers Smith appear to have obtained it in a fairly pure form more than half a century ago, and in reality little more was added to our knowledge of this substance until recently. In 1894 Leib Lapin⁸ obtained by a very lengthy process a still purer substance which he termed cannabindon, and still more recently the chemists at Cambridge isolated what was thought to be a pure substance and called it cannabinal.⁹ These investigators, by extraction with various solvents and subsequent distillation, obtained several substances, as will be seen in the table below taken from the *Cambridge Philosophical Transactions*, ix, p. 144.

These substances, with the exception of the hydrocarbon, were passed on to my late assistant for pharmacological examination. He found that the resin cannabinal was decidedly active and produced most of the symptoms attributed to Indian hemp.¹⁰ The terpenes, in much larger doses, had no such effect. In rabbits their administration was followed by slight excitement and in men by slight diuresis. These substances may possibly aid in increasing the rapidity of absorption of the active principle, but as far as the cerebral effect of Indian hemp is concerned this is probably all they do, and this only to a slight degree.

The resin in doses of 0.1 gram ($1\frac{1}{2}$ grain) produced marked intoxication, weakness in the legs, loss of memory, loss of time sensation, a peculiar tendency to laugh, a sensation of dryness of the lips, and an increased viscosity of the saliva. The pulse was increased in frequency and the pupils became slightly dilated. After smaller doses similar though less marked effects occurred, but the limit was reached with 0.01 gram, no distinct effect being produced by doses of this size. Sleepiness as an individual symptom was not always present, but there was always cerebral depression and sleep came more easily than under normal conditions. This was especially the case if the drug was taken in the evening. In dogs and cats similar symptoms were induced, but proportionately much larger doses were required, and of the two species cats were the more susceptible. The symptoms were nervous depression, ataxia, anorexia, and sleep. In rabbits the only symptoms were slight depression, a fall in the frequency of the pulse and in the temperature. After very large doses death occurred.

As regards the time of onset of the symptoms, in man these usually appeared about an hour after the administration of the substance, but the time depended to a great extent on the condition of the stomach; in one experiment the onset was delayed for three hours. This slowness of action is due to the comparative insolubility of the drug in aqueous media. In very dilute acids the resin appears to be quite insoluble; in dilute alkalies very slightly soluble. Marshall¹¹ believes that it is mainly in alkaline solution that it is absorbed, and according to him the late appearance of the symptoms is partly due to the fact that the substance must ordinarily be passed on into the intestines before solution can occur.

Owing to the gradual loss of activity with age and perhaps other causes, different preparations of cannabis indica often

Charas 2 kilos.				
Residue insol. in ether, 755 grams = 38%		Ether Extract.		
Ash = 53%	Organic matter = 47% N. = 2.5%	Boiling below 300° C. 200 grams = 10% Steam distilled distillate.	Boiling at 270°—200° at 20-60 mm. pressure 650 grams = 33%	Non-volatile residue, pitchy. 150 grams = 8%
	Terpene, B.P. 150°—180° 30 grams = 1.5%	Sesqui-terpene, B.P. 258°—259° 40 grams = 2%	Crystalline paraffin $C_{29}H_{60}$? 3 grams = 0.15% M.P. 63.5°—64° (64) B.P. at 15 mm., 285°—290° (285)	Red oil Cannabinal $C_{19}H_{34}O_2$ B.P. 265°—270° at 20 mm. 630 grams = 31½%
				Di-nitro Mono-acetyl and Mono-benzoyl With H.I. and P. non-nitrate Hydrocarbons.

show marked variations in physiological activity. Even different specimens of cannabinol show a difference in physiological effect. To determine the cause of this various experiments were undertaken. Temperature in itself was found to have little influence, but the resin was found to be easily oxidised, and it is very probable that its growing inactivity is due to gradual oxidation, but this cannot at present be regarded as absolutely proved.

We now come to the question of the active principle of Indian hemp. Is cannabinol the active ingredient? Marshall is inclined to think that it is. That cannabinol is probably the active principle was arrived at by a process of exclusion. All the other products, pure or impure, isolated from charas were inactive or much less active than this, and this being the case it is difficult to come to any other conclusion. At first the substance was thought to be pure, or, if impure, it was said that "the impurity could only be due to a stereochemical isomer or a compound with closely similar composition and properties." Since this was written the compound has been found to be composed of at least two substances, one having the empiric formula $C_{21}H_{35}O_2$ (to which the name cannabinol is now restricted),¹³ the other a lower carburetted compound not yet isolated in the pure state. The former substance was isolated by means of its acetyl compound, which was obtained in a crystalline form. From this the cannabinol was obtained by deacetyllising. It presented nearly all the physical properties of the original substance, but it possessed scarcely any physiological activity. Whether the residual substance possesses greater physiological action has not been determined. So far it has been impossible to free it altogether from the higher compound, but probably this will be accomplished in course of time.

At present the chemists have turned their attention mainly to the analysis of this new substance. From the old cannabinol by treatment with nitric acid they obtained a body previously isolated by Bolas and Francis, and termed oxy-cannabinol. This substance is a nitro-body and a lactone, and Wood, Spivey, and Easterfield propose the provisional name of nitro-cannabinol-lactone for it. By successive conversion into the amido- and iodo-bodies, these observers have obtained cannabinol-lactone, and by subsequent treatment they have obtained from this iso-phthalic acid. From their analysis they have come to the conclusion that oxy-cannabinol is nitro-meta-tolyl-butyl-lactone; and thus has been established the first step in the determination of the chemical constitution of an active cannabis product. With the further determination of the constitution of these bodies, probably more light will be thrown upon the physiological activity of cannabis preparations.

Several derivatives of the original cannabinol have been tried physiologically, but none of these are of therapeutic interest. It was hoped to obtain a more soluble active product, but experiments in this direction have not been attended with success.

Our present position, therefore, with regard to cannabis indica is this. We have obtained a more or less pure body with active physiological properties, but varying as regards these within rather wide limits. As alcoholic and oily extracts of charas are as active, if not more active, than cannabinol, there seems to be some undetermined factor, unless the difference in effect is due to difference in absorbability. It seems probable that the loss of activity is due to gradual oxidation of the active principle, and consequently all preparations should be kept as much as possible from light, heat, and air.

Other hypnotics derived from the vegetable kingdom which have aroused interest in recent years are hyoscyne and pellotine and their allies. Hyoscyne, as you know, belongs to the belladonna group of alkaloids, most of which are what Ladenburg termed tropanes. These are substances consisting of a base tropine united to an organic acid. This drug (hyoscyne) has been said to be identical with scopolamine, and the question is not yet settled. A number of other tropanes are known, most of them having been synthetically produced, but only one of these—homatropine—is of therapeutic importance, and this mainly from an ophthalmological point of view. Hyoscyne is more sedative than hyoscyamine, and more reliable as a hypnotic. Indeed, it has almost totally replaced hyoscyamine for this purpose. As a type of the comparative effect of the

two drugs we may take a series of cases reported by Wetherill.¹³ He used the drugs in a series of mental cases, and from 268 administrations of hyoscyamine a good night's rest was only obtained in 73; in 68 a fair night's sleep followed, and in 87 a poor one; in 40 no sleep whatever was obtained. Hyoscyne, on the other hand, in much smaller doses produced a good night's rest in 246 instances out of 348, and totally failed only in 14 cases. The ill-effects also were less numerous.

For the treatment of insomnia in general hyoscyne will probably never come into use, but its solubility in water, and its applicability to hypodermic medication, make it of extreme value in many conditions, particularly in the insane. In exhaustion from any cause, and in advanced heart disease, it is said to be contra-indicated.

The other drug I have mentioned is pellotine. It is an alkaloid derived from the anhalonium Williamsii, and it was suggested as a hypnotic only a few years ago. There are two species or varieties of anhalonium which have attracted attention during the last few years: Anhalonium Williamsii and anhalonium Lewinii or mescal button. These have been investigated most extensively by Heffter.¹⁴ He isolated pellotine from the Williamsii, and mescaline, anhalonidine, anhalonine, and lophophorine from anhalonium Lewinii. Mescaline in frogs produced decided cerebral depression, lophophorine distinct stimulation. Between the two in action are arranged pellotine, anhalonidine, and anhalonine. In these a narcotic stage is followed by a tetanic one. Anhalonidine produces the most prolonged narcosis, anhalonine the shortest. In warm-blooded animals, however, these effects were not observed, and in experiments on himself no marked narcosis was produced. Anhalonidine (0.1 g. to 0.25 g., or $1\frac{1}{2}$ grain to $3\frac{3}{4}$ grains) caused some sleepiness and heaviness of the head, and anhalonine (0.1 g., or $1\frac{1}{2}$ grain) produced slight sleepiness, but neither of these seems likely to prove useful as hypnotics. Pellotine is the only one of these alkaloids which has been put to practical use, and this in only a few instances. Jolly¹⁵ and Pilcz¹⁶ have recorded cases treated by this drug. In 58 administrations Pilcz obtained from one-third of a grain a satisfactory night's rest in half the cases; in 21 per cent. it failed. Jolly had to use larger doses, and in excitable and delirious patients he only obtained a calming effect. Giddiness was also complained of. He gives its relative strength as, pellotine 0.06 g., trional 1 g., chloral hydrate 2 g. Wilcox¹⁷ is inclined to believe that it may be of considerable value.

THE TREATMENT OF INSOMNIA.

This, notwithstanding its apparent simplicity, is one of the most difficult subjects in therapeutics. On the one hand, we have a number of drugs which, given in sufficient doses will, we know, in the majority of cases produce a desired result; on the other hand, apart from any immediate ill-effects, we may make our patient a slave to a habit which in the long run will prove more disastrous than the insomnia itself. The great principle of therapeutics—the removal of the cause—should ever be kept in mind; the relief of the symptom being regarded as secondary to this. It is, therefore, necessary to inquire first into

THE CAUSES OF INSOMNIA.

What is sleeplessness to one person may not be so to another. The average sleeping time of an adult is six to eight hours, but the amount of sleep required varies with the individual. It also varies with age. Babies sleep the greater part of their time. As they grow older, gradually less sleep is required until adult life is reached; with the onset of old age more sleep is again needed. The amount of sleep varies, too, with the mental constitution of the individual—idiots and persons of weak intellect often sleep excessively—and with the quality of the sleep, profound and continuous sleep being much more refreshing than superficial and broken.

Considering these variations, insomnia may perhaps be best defined as a loss of the normal amount of sleep. This loss may occur at the beginning or towards the end of the period of sleep, or it may occur through constant awakenings. Thus some people go to sleep directly after getting into bed, but awake every hour for several hours, sleeping well during the rest of the night. Others, especially the gouty, awake punctually at 3 or 4, and are unable to sleep again, or, at any rate, until it is

time to get up. Others, as I have said, find great difficulty in getting off, but once asleep do not awaken until the morning. Occasionally we even see patients who assert that they do not sleep at all, a statement which must usually be accepted with reservation.

The causes of insomnia may be classed under four heads—irritative, toxic, psychical, and those arising from change in the mode of life.

1. *Irritative Causes.*—This class includes all forms of insomnia caused by pain, and milder irritations like uneasiness. In children, teething, indigestion, worms, and so forth are frequent causes. Eye strain—as in hypermetropia and astigmatism—the irritation of an eczema, the inconveniences produced by faucial adenoids and other similar conditions, are also etiological factors of insomnia. After surgical operations, even in the absence of pain, insomnia is not infrequent; and this may be due in part to the constrained position of the patient and some irritability of the wound, in part to toxæmic and psychical causes. Cold feet, vesical affections, asthma, bronchitis, and other diseases, accompanied by troublesome if slight irritations, fall under this head; but the most important causal factor of this group is undoubtedly pain. In all diseases accompanied by pain sleeplessness is a symptom; and although other etiological factors of insomnia may be present, it is the pain which necessitates treatment.

2. *Toxic Causes.*—A large number of diseases are due to or are accompanied by the presence of some toxic agent in the blood, and such diseases are often attended by troublesome insomnia. Alcoholism and nicotism, the exanthems (measles, small-pox, scarlet fever), enteric and other continued fevers, erysipelas, diphtheria, pneumonia, hepatic disorders (the lithæmia of Murchison), dyspepsia, and other gastric and intestinal disorders, rheumatism, gout, and Bright's disease, are some of the conditions which may be mentioned under this head. The insomnia accompanying heart disease and altered vascular conditions (arterio-sclerosis, etc.) may also be included in this division, as its origin appears to be a blood poison. This form of insomnia is also partly due to a deficient blood supply, and possibly to an altered cardiac action. The sleeplessness induced by certain beverages, such as tea, coffee, and cocoa, requires mention here. These, especially if taken in a strong form and late at night, are powerful preventives of sleep in most people. Strychnine and other nervine tonics, when taken regularly, often cause sleeplessness during the earlier part of the night; but in certain conditions, by improving the circulation and other functions, they prove excellent hypnotics. Insomnia is also a symptom of certain drug habits, such as opium-eating, morphinism, and cocaineism.

3. *Psychical Causes.*—Grief, shock, worry, and mental anxiety are among the most frequent causes of insomnia. In many persons a predisposing factor—a nervous temperament—also exists, and among such persons insomnia may easily be established as a habit. In students overwork, especially if accompanied by irregularity in retiring to rest, and the prospect of an examination, are the most frequent causes. Women at the menopause often suffer from insomnia, partly perhaps owing to the accumulation of toxic products not eliminated by the catamenia. The various forms of insanity are accompanied by insomnia, usually as a premonitory symptom; but there can be no doubt that continued loss of sleep is also a factor in the production of mental aberrations. Cases of severe chorea and of paralysis agitans are also marked by sleeplessness.

4. *Causes arising from Change in the Mode of Life.*—Eating late dinners by those unaccustomed to them, and change of climate, especially to high altitudes, or in some individuals even to the seaside, sometimes give rise to temporary insomnia. Nurses who have been on night duty, after changing to the day frequently suffer from sleeplessness; and the same condition occurs in other people with intermittent nocturnal occupations.

It is evident from the multiplicity of these causative factors that no one line of treatment can be suitable for all cases. As I have said, the first thing to do is to "remove the cause," therefore the treatment of insomnia resolves itself primarily into the treatment of the causative condition. If it is indigestion, acid or gouty dyspepsia, careful attention to the diet, the avoidance of tea and fruit (cooked or uncooked), and of all sub-

stances containing vegetable acids (except in so far as these may be used in treatment), are essential. Fruit, owing to the acid it contains, is, I believe, in many individuals an unsuspected cause of indigestion, gout, and sleeplessness; so are acid wines. In the gouty, much butcher's meat, especially beef, should be prohibited, and white fish, poultry, and game taken in its place. Fried fat, such as that on the outside of fried fish, should also be avoided. An alkaline bitter before meals, an occasional mercurial at bedtime, followed by a saline aperient the next morning; and in the gouty colchicum and magnesium or sodium salicylate should be prescribed. One of my patients found that a little peppermint water, taken at bedtime, gave him a better night than any hypnotic. In the insomnia of the aged and the overtired, and in that due to cardiac and vascular disease, strychnine is a valuable remedy. In cardiac disease and neurasthenics, with low arterial tension, digitalis and the other cardiac tonics may be resorted to. In anæmia iron, nux vomica, and sometimes digitalis, are required; and in a similar way other diseases which are causal factors of insomnia must be treated.

But often this method does not suffice. The removal of the cause does not bring back refreshing sleep. The reason is that the cerebral cells have assumed an irritable condition, and it is necessary to depress their activity to bring them back to a more normal state; in other words, we have to break the habit of sleeplessness, and it is here that hypnotics are of such great value. The best of these for any individual patient will vary according to his condition. There is no absolutely safe one, but experimental investigation and clinical experience show that paraldehyde stands in the first rank. Chloralamide and chloralose are safer but slower in action than chloral hydrate, and of the two I decidedly give the preference to chloralamide. The sulphones are also valuable, and in practice I have found sulphonal the most valuable of the three; but, as a whole, the bromides seem to be the least harmful, and in simple cases uncomplicated by other disease it is my practice, where I think a hypnotic is necessary, to try them before resorting to any other drug.

But, leaving these general indications and coming to the special therapeutics of insomnia, we may divide these into non-medicinal and medicinal. The first, as it is more or less common to the treatment of all insomnias, I shall deal with first. In all cases, where practicable, the bedroom ought to be in a quiet part of the house, well-ventilated, and of moderate temperature. Light should be easily excluded and the apartment scantily furnished. The bed should vary according to the custom of the individual; for young and middle-aged adults a firm mattress is the best, but for the old a softer bedding may be necessary. The covering should be light and warm, but in the use of pillows no general recommendation can be made. Some people sleep better with the head raised, others with it on a level with the body. In heart disease it will be found necessary to raise it, but as a rule this arrangement may be left to the choice of the individual. For broad-shouldered people Whitla recommends the wedge-shaped pillow used by the Germans.

Some people read themselves to sleep, some count; others, like Southey, think of some monotonous discourse. One of my patients used to hang his feet out of bed for some time and then put them in again. Walking about naked or a cold or tepid bath is often useful. Massage is sometimes advantageous. In the case of cold feet, rubbing them vigorously, or the use of a hot bottle, or a footbath with mustard in it is beneficial, or a hot sitz-bath may be used. Attention should also be given to the condition of the stomach. As a rule a light supper is the best, and for many—and especially those who awake in the middle of the night—a little hot milk or meat juice containing a small amount of alcohol is helpful.

Sleeplessness from overwork, and especially literary work, requires mental rest and change of air and scene. Temporary exposure to the cool air of the bedroom, or the wet pack, or a bath is often of use, and so is a glass of whisky and water at bed time, especially in those unaccustomed to the use of alcohol; but if the insomnia continue it is necessary to give a mild hypnotic, such as 20 gr. of sulphonal, or 30 or 40 gr. of bromide of potassium, to break the habit of sleeplessness. Capsules containing 1xxx of turpentine given at bed time are sometimes beneficial in the insomnia of overwork and

worry. The drug acts as a stimulant and derivative, and is stated to act best in plethoric cases. No beverages containing caffeine should be taken after breakfast.

In nervous and hysterical women, and especially in women at the menopause, the bromides are very useful. I have long been in the habit of giving a mixture of bromide, tincture of sumbul, and tincture of hop, in camphor water at the climacteric; and it has helped to remove the insomnia as well as the mental depression and flushing heats so common at this period.

The sleeplessness of the insane requires careful management. In the early stages of acute mania, the bromides, chloral, hyoscine hydrobromide, and other sedatives are useful, but a hot bath at a temperature of 104° F., and cold water simultaneously poured upon the head, are most efficacious in inducing sleep. In melancholia, where arterial tension is usually high, paraldehyde in doses of $\text{m} \times \text{l}$ to $\text{m} \times \text{c}$, or even more, is a valuable hypnotic. So is morphine, but a grain dose of erythrol tetranitrate, by reducing arterial tension, will frequently act better than anything else. In mild cases of delirium tremens sleep usually comes on after a time whatever treatment be adopted; in the more severe cases chloral and bromides, alone or in combination, are beneficial. Paraldehyde is recommended by some physicians. Opiates may be given, but in most cases hyoscine is probably a more efficient remedy. Among the medical officers of the American army twenty grains of powdered capsicum, in the form of a bolus, is the favourite hypnotic for this complaint. Cerebral depressants should be given as little as possible, and the treatment should be confined chiefly to feeding and tonic measures. In pneumonia sleep comes usually at the crisis; but where this has not occurred I have occasionally seen a hypnotic, such as chloralamide or paraldehyde, turn the scale in favour of the patient. In pleurisy and most other serous inflammations 5 to 10 grains of Dover's powder usually conduce to sleep, mainly by relieving the pain. A hypodermic injection of morphine may be given with the same object in view. In bronchitis chloral and chloralamide are safe hypnotics, and as a rule opiates are to be avoided, as these depress the respiratory centre as I have pointed out. The sleeplessness of asthma is relieved by remedies that cut short an attack, such as chloral hydrate, the fumes of Himrod's and other asthmatic powders, the hypodermic injection of morphine, or in some cases a 5 to 10 gr. dose of citrate of caffeine. Bromides are also useful and so is paraldehyde, which both relieves the asthma and causes sleep. A change of locality, even to another part of the same town, often succeeds. In one case the removal of a student from Downing College, Cambridge, to a house across the street brought relief, and in another of my pupils the change from Caius College to a house in another part of the town brought to an end a most troublesome attack of asthma with its attendant sleeplessness.

The insomnia of heart disease is benefited by digitalis, strophanthus, strychnine, and other cardiac tonics; but in some cases it is necessary to resort to morphine, either by the mouth or, still better, hypodermically, as first suggested by my colleague, Professor Allbutt. Paraldehyde and chloralamide are most useful in my experience. Ice to the head is recommended by Morison, where the vital forces are not too low, or the temperature subnormal. It often produces sleep rapidly, with a more regular cardiac action. Heat may possibly answer in other cases presenting a subnormal temperature.

In chronic Bright's disease insomnia is occasionally very troublesome. Eliminants, such as aperients, should be tried, and if they do not succeed chloral hydrate may be given; the drug is safer in kidney than in heart disease, the reduction of blood pressure being usually beneficial than otherwise. Morphine and hyoscine hydrobromide subcutaneously injected have been recommended in obstinate cases; but their employment requires great caution. Erythrol tetranitrate, by reducing arterial tension, often acts as a charm even when sedatives have failed; and in one of my patients thorough rubbing of the skin by means of a flesh brush induced sleep, and very materially relieved the restlessness of this complaint.

In cases of neuralgia, locomotor ataxy, and so forth, some of the synthetic analgesics—phenazonum or phenacetin—are of

value. These drugs act also as hypnotics in cases where there is no pain, as I have previously stated. Calcium chloride is a valuable remedy in the insomnia due to pruritus. But when pain is the causal factor of insomnia morphine is the best general remedy, and this should be pushed until relief is obtained.

REFERENCES.

- ¹ BRITISH MEDICAL JOURNAL, ii, p. 189. ² Merck's Annual Report for 1898, published March, 1899. ³ Pfüger's Archiv, lxxii, p. 455. ⁴ Loc. cit., p. 10. ⁵ Ther. Monats., 1897, p. 4. ⁶ Rev. Méd. de la Suisse Rom., 1898. ⁷ Einwirk. Einiger Abkömml. d. Morph. Arch. de Phar., vol. iii. ⁸ Diss. Jurgew. ⁹ Journ. Chem. Soc., lxi, 541. ¹⁰ Lancet, 1897, i, 235. ¹¹ Journ. of Amer. Med. Assn., October 15th, 1898. ¹² Journ. Chem. Soc., 1899, i, 20. ¹³ Amer. Journ. of Insanity, xlvii, 28. ¹⁴ Cf. Arch. f. exp. Path. u. Pharm., xl, 385. ¹⁵ Cf. Lancet, 1896, i, 1760. ¹⁶ Cf. Heffter, Arch. f. exp. Path. u. Pharm., 1894. ¹⁷ BRITISH MEDICAL JOURNAL, 1897, ii, 856.

A CASE OF OPHTHALMOPLÉGIA EXTERNA AND PARALYSIS OF BOTH FACIAL NERVES,

AND A CASE OF PARALYSIS OF BOTH FACIAL NERVES WITH SOME AFFECTION OF THE LIMBS, FROM PERIPHERAL NEURITIS; RECOVERY.

By H. SINIGAR, M.D., B.S.LOND.,

Assistant Medical Officer to the Marylebone Infirmary.

For permission to publish these cases I am indebted to Mr. John R. Lunn, Medical Superintendent of the infirmary. I have also to thank Dr. C. E. Beever for his valuable help and for the remarks he has been good enough to add to the report of the cases.

CASE I.—A man, aged 49, was admitted to the infirmary on January 20th, 1898, for loss of power in the hands and feet. He had been a painter until a year before admission, when he had to give up his employment on account of intemperance. He then became a crossing-sweeper. He had dropsy in the early part of 1897. He gave no history of lead colic or palsy and denied syphilis. Three weeks before admission he had what he called cold shivers and went almost blind (this apparently was due to inability to open his eyes). The shivers lasted about a week; he kept to his work, however, until a week before admission, when he became unable to hold his broom and walked with difficulty. No definite account of pain at the onset or of muscular tenderness was elicited.

On admission he was a well-nourished man, but looked older than his years. He could be roused to answer questions, but as a rule was very drowsy. His face was immobile and mask-like; the breathing was quiet and regular. There was double ptosis and complete paralysis of all the external muscles of the eyeball on each side, the eyes being fixed with the visual axes parallel. The pupils were small, the left a little larger than the right, both reacted to light and accommodation. In the left eye there was a corneal opacity and also old iritic adhesions. When his eyelids were lifted he could see fairly well. Ophthalmoscopically there was slight blurring of the nasal side of each disc, but there was no optic neuritis.

The natural lines of the face were obliterated, and the facial muscles were totally paralysed for both voluntary and emotional movements. The orbicularis oris and orbicularis palpebrarum were equally involved; the muscles of mastication were not affected; there was no blue line on the gums; the tongue could be protruded with some slight difficulty and was not tremulous; the soft palate, though not completely paralysed, did not move well on either side; speech was thick and somewhat nasal; swallowing was not easy, as fluids, if drunk quickly, were regurgitated through the nose. He had a very feeble cough, and the pharynx and larynx contained a frothy mucus which he appeared unable to cough up. There were no symptoms of paralysis of the vocal cords, but, unfortunately, the mucus in the pharynx prevented a good view of the larynx being obtained by the laryngoscope. The diaphragm and intercostals were working. The hand grasps on both sides were very feeble, but there was no wrist-drop or obvious paralysis of the muscles of the elbows and shoulders. In the legs the extensor muscles were weak, and there was slight foot drop. He could not stand steadily but could just walk when supported; the toes did not drag and there was no inco-ordination, his gait being simply that of a very feeble man. The knee-jerks and plantar reflexes were absent, nor could the triceps and wrist reflexes be obtained. There was no loss or alteration of tactile sensation. Hearing as tested by the watch was not good, but questions were heard readily. He had complete control over the bladder and rectum. The facial muscles gave no response to faradism, but the limb muscles reacted. There were no signs of organic disease in the viscera. He said he felt well in himself except that he was conscious of being weak.

His condition remained much the same until February 14th, when slight improvement was noticed; he was not so drowsy, and his general condition was better. By February 22nd improvement was very marked. He could then raise the eyelids (the right better than the left), and there was slight up and down movement in the eyes. On February 25th he could keep both eyes open, wrinkle his forehead and screw up the eyes. Vertical movements of the eyes were good, and the internal rectus muscle acted a little on each side. The palate moved better, but was still sluggish. Coughing was performed naturally and vigorously. The hand grasps were wonderfully stronger. The arm and leg muscles reacted well to faradism, while in the face there was slight reaction in the frontales, but no response in the orbicularis oris.

By March 10th all movements of the eyeballs could be performed, but not in a perfect manner. There was nystagmus on vertical and horizontal movements; there was no squint. The right eyebrow, right angle of the