

III. — Observations and Experiments on the Use of Opium, Bromide of Potassium, and Cannabis Indica in Insanity, especially in regard to the effects of the two latter given together. By T. S. CLOUSTON, M.D., Medical Superintendent of the Cumberland and Westmoreland Asylum, Carlisle.¹ U

So many cases of insanity consist of simple brain excitement, and in so many more is excitement the most distressing symptom, that if we could discover any agent which would subdue this excitement, and at the same time not interfere with the improved nutrition of the brain which rest, tonics, and good diet will effect, and on which complete recovery of its normal functions depends, such an agent would be a most incalculable blessing. There are many cases in which a physician knows that if he could tide over his patient for a few weeks of excitement, that recovery would come as the natural termination of the attack. Much distrust of strong narcotics prevails among the profession since Dr. Anstie's work on 'Stimulants and Narcotics' appeared. And yet how is such a case of maniacal excitement to be managed without them out of a lunatic asylum? The exact condition of the brain cells in mania being as yet quite unknown, we cannot apply a direct antidote. At best we can only work very empirically. But our empiricism may be founded on a rational and scientific examination of the effects of the drugs we use, and the natural history of the disease we treat, or it may be a mere haphazard employment of some agent recommended by some one who had no rational ground for his recommendation at all. Maniacal excitement is so essentially in many cases what has been hitherto called a functional disease, that it offers more hopes of benefit from drugs than most other complaints. A patient is rational and coherent in mind one hour and is furiously maniacal the next, and the excitement passes off as quickly. Surely such a condition may be reached and remedied by some therapeutic agent. We have many drugs more or less "narcotic" and "sedative," but hitherto the effects of those drugs have been far more carefully studied when given to persons previously free from excitement, than when given to those acutely maniacal. I do not mean to undervalue the observations which have been made on this subject, but all physicians know and strongly feel the want of accuracy and definiteness which prevails in this department of medicine. The following observations were undertaken almost entirely with the view of obtaining a little more accuracy in my own knowledge of the effects of certain medi-

¹ *The Essay for which the Fothergillian Gold Medal for 1870 was awarded by the Medical Society of London.*

cines on maniacally excited patients. They consist of two parts: the first, experiments made chiefly on incurable patients in whom simple brain excitement existed; the second, clinical observations on the effects of the same medicines on recent and curable cases of excitement. The experiments were undertaken to show, first, the effects of single doses, and second, the effects of long continued courses of the medicines.

The action of the bromide of potassium in cases of maniacal excitement especially deserves careful study. It acts differently in many respects from most of the vegetable narcotics. Given along with at least one of them, it seems to intensify and prolong its effect on the nervous system, without at the same time affecting injuriously the digestion and the nutrition of the body. The investigation of this point will be one special object of this paper.

The action of opium on disordered function of the cerebrum is better known than that of any other drug, though very much remains to be accurately ascertained. So much confusion exists as to its physiological action on a healthy subject, and its therapeutic action on a diseased one, so little is really known as to the tolerance of the remedy in certain disorders of the brain, there has been such a tendency to apply Dr. Anstie's theory as to the identity of narcosis and brain paralysis, where it is quite inapplicable, that any carefully recorded facts bearing on any part of this subject must be of value. Then the action on the healthy brain of a pure stimulant, such as whisky, has been carefully studied, but observations on the tolerance of large doses of such a stimulant in disordered brain functions are much needed. Any effect which food has in such cases we are accustomed to regard, and I believe truly, as beyond question directly towards health. To compare the effects of these various drugs with the effects of a highly concentrated food, therefore, on a given number of cases of brain disorder, can scarcely fail to be instructive.

Effects of single doses.—To ascertain the effects of single doses I at first selected eight patients (four men and four women), all labouring under great excitement, and from two hours and a half to three hours after breakfast, after taking their pulse and temperature and noting their mental state, I gave to each of them the dose of the drug or stimulant I was experimenting with. They were then sent out in the open air, from which they had been taken in, except the day was very cold, and in that case they were kept in the house, and in an hour I again took their pulse and temperature, and noted their mental state. Their condition during the afternoon was also observed. The next day I gave another drug, and this was continued till all had been gone over, when I began again, repeating the experiment four times, with most of the substances used, and twice with the others. I gave these patients in this way drachm doses of tincture of opium, drachm and two drachm doses of bromide of

potassium, drachm doses of tincture of cannabis Indica ('British Pharmacopœia'), and a mixture containing one drachm of bromide of potassium, and one drachm of tincture of cannabis. I performed the same experiments, only instead of the medicine giving each patient four ounces of good Scotch whisky one day, and a pint of beef tea made from a pound of good beef another. I made experiments on myself and my assistant, using smaller doses, and not repeating them so often.

The reason I did not keep the patients in the house in a room of a uniform temperature was, that I wished to see the effect of the various substances on them in their ordinary circumstances at that hour. Two of them I did keep in a bedroom of uniform temperature during most of the experiments, but I found that this did not materially alter the results. I was not able to continue the experiments on all the patients continuously, on account of some of them being free from excitement on certain days, and other causes. On such days I usually substituted other patients who were also excited. They laboured under the most various forms of mania, but the element common to all of them was great excitement and disorder of the functions of the brain. None of them laboured under any bodily disease.

My objects were to ascertain accurately the effect of single doses of each medicine on, 1, the maniacal excitement; 2, the appetite; 3, the temperature; 4, the pulse, and to compare them with each other, and with the effect of a pure stimulant in large doses, and the most concentrated and nourishing of food. It is not surprising that I found the results with each drug were not the same in each patient in the successive experiments. A maniacal patient is so changeable and uncertain in his state with or without medicine, he varies so much as to the amount of muscular exercise he takes, and his whole system is so affected by these variations, that one cannot wonder at anomalies in the experiments on particular days. It was to obviate these uncertainties as much as possible that I took so many patients labouring under various forms of excitement, and repeated the experiments so often. In that way, I think, the results may be re-

TABLE I.

Substances given.	No. of Patients.	No. of Experiments.	Excitement aggravated at first.	Excitement subdued.	Excitement not subdued.
Tinct. Opii	9	29	2	19	10
Potas. Bromid. and Tinct. Can. Ind.	8	29	5	26	3
Potas. Bromid.	7	13	0	7	6
Tinct. Can. Ind.	7	15	0	12	3
Whisky	10	21	13	14	7
Beef tea	9	15	0	1	14

garded as trustworthy as to the *general* indications they give. I shall endeavour now to summarise the daily observations which I made.¹

Excitement.—The effect of any medicine on maniacal excitement cannot be at all so exactly measured or defined as its effect on the temperature or pulse. The general and decided effects of the drugs I gave I have shown in Table I. From this it is seen that the combination of bromide of potassium and tincture of cannabis subdued the excitement in the greater number of cases, and certainly its effects were more patent and lasting than any of the others. Of the twenty-nine times in which it was given it decidedly subdued the excitement on twenty-six occasions, or in 90 per cent. of them. Opium was the next drug in potency of effect, though it only subdued the excitement in nineteen of the twenty-nine experiments, being 66 per cent. The bromide of potassium alone allayed excitement in about one half the experiments in which it was used, but its effects were very much less decided in the extent to which it allayed the excitement. Its effects usually lasted, however, for the remainder of the day on which it was given. In one half of the experiments two drachms were given, and this dose it was which had the effect on the excitement in five of the seven experiments in which any effect was observed. The Indian hemp produced abatement of the mania in twelve out of the fifteen experiments, but in almost all these cases its effects were comparatively slight, and seldom lasted for more than three hours. The whisky was followed by marked cessation of the excitement in fourteen out of twenty-one experiments, and its effects, contrary to what might have been expected, lasted usually for seven or eight hours. The beef tea had no appreciable immediate effect on the maniacal excitement in most cases. In only one case did a patient become more free from excitement after getting it, and this was the weakest of the number.

In regard to the length of time each drug took to act, and the mode of action of each, I found that the sedative effect of the opium was got most speedily. Aggravation of the excitement previous to the sedative effect was observed five times in the case of the mixture of the bromide and cannabis Indica, twice in the case of opium, and thirteen times in the case of the whisky, and this aggravation was so great and troublesome in the case of the last as to put it out of the question as a sedative for maniacal excitement. The sedative effect usually began to appear in from half an hour to two hours after the mixture of bromide and cannabis Indica, though in some of the experiments this was delayed for three hours. The preliminary stage of aggravation, when it occurred, lasted for about two hours in the case of the drugs, and for about one hour and a half in the case of the whisky.

¹ The daily records themselves were appended to the original essay, but they are too long for insertion here.

It was only the milder cases which were affected by the bromide or the cannabis Indica separately; the opium and whisky affected some of the worst cases at times, while the combination of the former affected the most excited on the largest number of occasions.

A very striking fact is seen at a glance at the records of the observations themselves, and it is the extreme *uncertainty* of action of almost all the medicines on successive days on the same cases. One day the drachm of Tincture Opii subdued the excitement and caused no loss of appetite. Another day in the case of the same patient the same dose was followed by no such effect at all. It is this which renders any such therapeutical inquiry so apparently unsatisfactory, but which gives additional value to any drug whose effects are most free from this element of uncertainty. It shows how many things have to be taken into account, and how very many accurate observations will have to be made before anything like reliable generalisation can be attempted. We can only at present follow the *prevailing tendencies* of action of a drug.

In none of the experiments, even when the patient was most fully under the influence of any drugs, was there anything like a narcotic action. The nearest approach to this was the drowsiness and sleep that sometimes occurred. But it seemed quite natural sleep. It would surely be a misnomer to apply the word "paralysis" to any result of those drugs in these cases. If an acute maniac is talking incoherent nonsense and moving about incessantly, his reasoning powers and intelligence being in abeyance, and if after a dose of bromide of potassium he ceases to talk and move about so much—all the other functions of the nervous system being undisturbed—and he makes some nearer approach to reason or intelligence, we must find some other name than either "narcosis" or "paralysis" for such a result. Dr. Anstie implies that the effect of a large dose of opium on maniacal excitement must be "narcotic." In the cases above related, the action was truly "stimulant" in his sense, though the doses were "narcotic doses."

As regards the food action on the excitement, it was in all these cases so inappreciable at the time that no comparison can be made

TABLE II.

Substances given.	No. of Patients.	No. of Experiments.	No. of times appetite taken away.
Tinct. Opii	9	29	7
Potas. Bromid. and Tinct. Can. Ind.	8	29	1
Potas. Bromid.	7	13	0
Tinct. Can. Ind.	7	15	1
Whisky	10	21	1
Beef tea	9	15	0

between it and the drug action as regards immediate effect on the excitement.

Appetite.—No effect of a drug is more important on a maniacal patient than its effect on his appetite for food. If that is much interfered with, the good effects of the medicine will have to be great and manifest indeed, to counterbalance so indisputable an evil.

I have in Table II shown the number of times in which the patient's desire for food was clearly interfered with after each medicine given. Opium stands in bad pre-eminence at the head of the list as that which most frequently produced this result. In seven out of the twenty-nine experiments with opium, the patients could not be got to take the next meal. This was never the case after bromide of potassium at all, and only once after cannabis Indica and its combination with the bromide. This was one of acute excitement, with complete incoherence and absence of reason, being that most like the acute delirium of fever. In his case it caused on two occasions dryness of the tongue and lips as well as loss of appetite.

Temperature.—The temperature of the body in maniacal excitement has been far too little attended to. It often rises in a direct ratio to the brain excitement present, it is most important as a diagnostic of organic disease, and it affords most valuable indications for treatment in many cases. In Table III I have recorded the results of my observations in regard to temperature. The tendency of opium was to raise the temperature slightly; that of the bromide and cannabis Indica combined to depress it; of the bromide alone to raise it rather more than opium; of the cannabis Indica alone

TABLE III.

Substances given.	No. of Patients.	No. of Experiments.	Average Temperature.		Average gain in each experiment.	Average loss in each experiment.
			Before medicine.	After medicine.		
Tinct. Opii	9	29	97·6°	97·8°	·2°	...
Tinct. Can. Ind., Potas., and Bromid.	8	29	98°	97·7°	...	·3°
Potas. Bromid.	7	13	98·1°	98·4°	·3°	...
Tinct. Can. Ind.	7	15	97·5°	97·6°	·1°	...
Whisky	10	21	97·9°	97·3°	...	·6°
Beef tea	9	15	98·16°	98·14°	...	·02°

to raise it very slightly; of the whisky to lower it most of all, and of the beef tea to lower it in the most trifling degree possible. It must be remembered that the temperature of the body in such maniacal patients is higher than in health. I think we must look on the action of opium, bromide of potassium, and tincture of cannabis, therefore, in this respect, as being away from the healthy

standard, while that of a mixture of the bromide and tincture of cannabis is in the opposite direction. There can be no doubt about the lowering of temperature caused by the whisky being too great. Its effect in this direction was almost uniform in nearly all the experiments. Even when it aggravated the excitement at first, and there was much more muscular motion, the temperature was usually found lower. A loss of 2.3° in the temperature of the body in an hour (when that temperature had not been very abnormally high to begin with) means devitalization, and that was the case once after the whisky. We may fairly in this case, then, take the effect of the beef tea as our standard of what we might expect from a drug which most readily approached the reparative action of food. The effect of opium was in the wrong direction altogether; that of the mixture of the bromide and cannabis Indica in the right direction, but perhaps going too far; and of the whisky in the right direction, but going too far.

The different effect of the mixture of the bromide of potassium and the cannabis Indica from each of them given separately is worthy of notice, as it confirms my experience that in all respects this mixture acts differently from either of its constituents.

The effects of smaller doses on my assistant and myself differed from those above mentioned in the bromide lowering the temperature, the cannabis Indica raising it considerably, and the mixture of both raising it very slightly, while the beef tea also raised it slightly. The lowering of the temperature by whisky was very marked.

TABLE IV.

Substances given.	No. of Patients.	No. of Experiments.	Pulse before getting medicine.	Pulse after getting medicine.	Average gain in each experiment.	Average loss in each experiment.	No. of times pulse decidedly irregular, or intermittent.
Tinct. Opii	9	29	85	84	...	1	3
Potas. Bromid. and Tinct. Can. Ind. }	8	29	84	95	11	...	7
Potas. Bromid.	7	13	83	79	...	4	1
Tinct. Can. Ind.	7	15	83	89	6	...	3
Whisky	10	21	81	82	1	...	0
Beef tea	9	15	80	79	...	1	0

Pulse.—In Table IV the effects of the different substances on the pulse are seen. That of opium was to lower it to a most trifling extent. The bromide did so in greater degree, and the beef tea about the same extent as the opium. The tincture of cannabis Indica, on the other hand, caused an average increase of eleven beats, and the tincture of cannabis alone of six beats. The tendency of the mixture was also slightly to lessen the force of the pulse; and as is seen from

the table, to cause irregular action to a greater extent than opium. In seven of the twenty-nine experiments an irregular or intermittent pulse followed a dose of this mixture, while in only three of the twenty-nine was this the case after opium. It is known that cannabis Indica quickens the action of the heart; but why the bromide, which itself tends to reduce its action, should actually strengthen the accelerating action of the cannabis, is only explicable by the theory that all the effects of the latter are greatly added to by giving it with the former.

On myself and my assistant the effects of smaller doses on the pulse were the same as the results shown in the table.

Taking all the effects of these medicines into account, I think the balance of good is decidedly on the side of the mixture of bromide of potassium and cannabis Indica. The greater certainty and longer duration of its sedative effect on the excitement, and the absence of any bad effect on the appetite, are good results which are not materially interfered with by its action on the heart.

In regard to the dose of bromide of potassium, which is equivalent in sedative effect to opium or henbane, it is very difficult indeed to come to an exact conclusion. If there is much excitement, no single dose of the bromide up to two drachms will be at all equal to one drachm of the tincture of opium. To produce sleep in milder cases my experience is, that one drachm of the bromide will have the same soporific effect in most cases as half a fluid drachm of laudanum, or two drachms of the tincture of hyoscyamus. With regard to the dose of a mixture of the bromide and tincture of cannabis, which will be equivalent to laudanum, I have had more experience. The experiments as to single doses throw some light on this, and in many other cases I have given the two medicines alternately to see the effects; while in others, to whom I now give the bromide and tincture of cannabis to allay excitement, I used formerly to give opium, hyoscyamus, and tincture of cannabis alone. In only two out of thirteen cases did I find one drachm of the bromide with one drachm of the tincture of cannabis to have a less sedative effect than one drachm of tincture of opium. In two cases its effect was about the same, and in the other nine it was unequivocally more decided, while in two it was more decided than ninety minim doses of the laudanum. My experience has been, that about forty-five grains of the bromide, along with forty-five minims of the tincture of cannabis, will have the same sedative effect as a drachm of laudanum. In one violent case of periodic mania, with whom opium did not agree, I find that drachm doses of the bromide, and a drachm of tincture of cannabis, have rather more than the same effect as half-ounce doses of the tincture of hyoscyamus, and that by adding drachm doses of the bromide to one drachm of the tincture of hyoscyamus, the same sedative effects were produced, or by half-ounce doses of the latter alone. In another

case drachm doses of each of the bromide and cannabis have as much effect as six drachms of the tincture of hyoscyamus. In another case half-drachm doses of each of the former have about the same sedative effect as two-drachm doses of the latter.

The experiments with single doses which I have related quite bear out my previous experience as to the decided increase in the effect of a combination of the bromide and the Indian hemp over the effect of either of them used separately. Over and over again I have found that half-drachm doses of each were more powerful than drachm doses of the tincture of cannabis, or than two-drachm doses of the bromide. This seems to me one of the peculiarities of the bromide of potassium, that, combined with a sedative drug, it powerfully increases the usual effect of such drug. I cannot speak so certainly of this effect when combined with opium, but with hyoscyamus and Indian hemp it is most decided. In my own case, the effect of fifteen minims of tincture of cannabis along with half a drachm of the bromide was very much stronger than half a drachm of the former alone, and incomparably stronger than a drachm of the latter. In very many cases I have given a combination of the two medicines where I had been giving sometimes the one and sometimes the other previously, and I have always found that half quantities of each combined were as powerful as double the amount of the cannabis, and more powerful than double the amount of the bromide given alone.

It was one of the effects of Indian hemp specially mentioned by O'Shaughnessy in his first experiments with the drug, that it caused an increase of appetite, and I found that when giving the bromide of potassium to my epileptic patients, it increased their appetites. Certainly no sedative or narcotine drug that I have ever used in large doses in the case of maniacal patients affected their appetites so little as the two given together. In doses under a drachm of each I never saw any diminution of appetite at all, and in large doses it was only after a long time that I found the appetite sometimes lessened.

My own experience of the kind of effect produced by mixture of the bromide and the Indian hemp as distinguished from the effect of each of those taken separately when I took them myself was this. Half a drachm of the bromide produced a slight drowsiness in about an hour, which lasted for about two hours, but the effect was almost imperceptible. A drachm of the bromide produced a more decided drowsiness, and after about two hours a feeling of coldness and slowness of the pulse. Half a drachm of the tincture of cannabis produced in an hour a feeling of confusion and fulness in the head, then a sort of preternatural acuteness of hearing, then the impression of a great length of time between acts performed within a minute of each other described by Christison, and in two hours great drowsiness,

which lasted for four hours, leaving a feeling of confusion in the head and incapacity for continuous mental exertion. Fifteen minims of the same tincture along with half a drachm of the bromide, caused in an hour first a tingling in the calves of the legs, then numbness of the legs extending gradually all over the body, then confusion of ideas and the impression of lengthened time and sense of fear, then a tendency to jerking and unsteadiness of the muscles. In about two hours all these sensations became merged in a sensation of fullness in the head and great drowsiness, which lasted for six hours. Its effect was also strongly diuretic. It produced quickness and irregularity of the pulse for the first three hours. I do not attach very much importance to the experiments on myself and my assistant, as no true comparison can be made between a therapeutical and a purely physiological experiment. Curiosity alone prompted me to take the drugs myself.

Effect of the sedatives when given regularly for long periods.—Opium in large doses having been hitherto regarded as the most powerful, and in the majority of cases the most reliable sedative in uncomplicated maniacal excitement, I selected nine chronic maniacs, all labouring under great excitement of long duration, and on them tried the effect of opium given continuously for a length of time. I knew the natural history of the disease in them all, for they had all been under my observation for periods of from three to five years, with little or no medical treatment for long periods. I regarded them all as quite incurable. Whatever effects on the bodily health and organic functions the brain excitement could produce, had taken place, and they were nearly all, as it were, *in statu quo* as regards body and mind. I had no reason to suppose that any of them had such organic disease of the brain as softening, tumours, or any other progressively fatal lesion. In three of them there were remissions of the excitement at regular times, but the periodicity in each of them was regular and quite well known to me. My reasons for taking such cases were, first, that they were incurable, and therefore the experiment could not do any harm to them; second, that in them I had simple brain excitement in known amount, against which I could, as it were, match a sedative drug; and third, that in them I could observe the effects of that drug on the bodily functions, the temperature, the weight of the body, the pulse, &c., with the certainty that any changes that might occur were the effects of the drug, and were not happening in the natural course of the disease.

For a month I had these patients weighed every week, noting their weights, their morning and evening temperature, and their morning and evening pulse. Then for twelve weeks I gave them opium in the form of tincture opii of the 'British Pharmacopœia' in increasing doses, noting every week their mental state, their weight, temperature, and pulse. For the first two weeks I gave them twenty-

TABLE V.

Name.	Age.	Weight before taking opium.	Weight after taking opium.	Average morning temperature before medicine.	Average evening temperature before medicine.	Average morning temperature after medicine.	Average evening temperature after medicine.	Average morning pulse before medicine.	Average evening pulse before medicine.	Average morning pulse while taking medicine.	Average evening pulse while taking medicine.	Patients' mental state.
J. G. . . .	61	lbs. 133	lbs. 123	97°	98°	97·8°	97·6°	77	89	93	71	Chronic mania; 4 years' duration; excitement severe; no remissions; intelligence not quite gone.
E. M. . . .	42	128	122	98·2°	97·7°	97·2°	97·6°	78	93	81	77	Chronic mania; 4 years' duration; exacerbations, but not regular; mental powers very much impaired.
M. T. . . .	34	148	140	98·6°	97·8°	98·5°	97·4°	74	74	82	73	Chronic mania; 10 years; regular periodic exacerbations; great excitement; mental powers not so much impaired as any of the others.
J. H. . . .	26	134	127	97·8°	97·5°	97·5°	97·2°	100	77	91	74	Chronic mania; 10 years; mind much impaired.
C. M. . . .	30	113	114	98·4°	97°	97·5°	97·5°	104	93	90	79	Chronic mania; 3 years; tendency to phthisis; great impairment of mental powers.
S. R. . . .	35	116	103	96·9°	97·7°	96·6°	97·4°	81	78	80	71	Chronic mania; 4 years; great excitement and violence; mental powers considerably impaired.
E. S. . . .	39	105	103	98·4°	97·7°	97·5°	97·6°	103	94	93	89	Chronic mania; 10 years; one lung tubercular; mind quite impaired.
Aggregate weights and average temperature and pulse		877	832	97·9°	97·6°	97·5°	97·5°	88	85	87	76	

1870.]

On the Use of Certain Drugs in Insanity.

503

five minims three times a day, for the next two weeks one fluid drachm three times a day, for the next eight weeks one fluid drachm and a half three times a day.¹ Of course the patients during all this time were in the same circumstances with regard to diet, clothing, and other conditions. The reason I kept up the drachm and a half doses so long was, that this is about the limit of the doses commonly used in mania, and I wished to ascertain the effects of such ordinarily employed doses. At the end of the twelve weeks the medicine was stopped. Of the nine I found that the opium caused such persistent sickness and total absence of appetite in two, that I could not continue it for more than a few days. There were only seven, therefore, in whom the experiment was continued to the end.

Excitement.—As regards the maniacal excitement, I found that in none of the cases did the twenty-five minim doses subdue it in any degree, and during the fortnight they took this dose there was no perceptible change in their appetites, weights, temperatures, or pulses.

During the fortnight they took drachm doses there was a very perceptible difference in the maniacal excitement in all of them but one, who at the time was passing through one of the regular exacerbations which characterised her case. In three of them there was a decided tendency to drowsiness through the day. In one case the partial subsidence of the excitement which characterised the first week did not last through the second, for by the end of it she was about as excited as ever. Five of them had begun to lose in weight, though the absolute loss was small, being only eleven pounds in the five. There was a slight fall in the temperatures of most of them.

When the dose was raised to a drachm and a half the excitement was very markedly lessened or altogether overcome in all of them. This effect was not lasting, however, in all the cases, for by the end of six weeks two of them were nearly as excited as ever, and the one who was subject to exacerbations had one of these during this period, and was almost as bad as when she was free from the influence of any drug. The most careful examination into the character of the cases did not show any reasons why one case should have been more and longer affected by the opium than another. To refer to Table V, J. G. and C. M. became almost as bad as ever when taking the medicine, and M. T., during one of the exacerbations of her malady, was but little affected by it. One of these patients was old, the other two young. In one case the mental powers were very much affected, in the other two not so much so. Two of them were robust, the third had a tendency to phthisis.

The results of the treatment in all of them are shown in Table V.

¹ They got the first dose of the opium at seven o'clock in the morning, and the temperatures were taken at half-past ten. I wished to avoid the immediate effects of a dose of the drug.

Weight.—They all lost weight while taking the large doses of the drug. In some of them the loss was considerable, in others trifling. The greatest loss was thirteen pounds, the smallest one pound. The aggregate loss in all the cases was forty-five pounds. The patients whose excitement was most subdued did not lose most, nor did they lose least. It may be thought that the total amount lost in weight by them all is very small indeed, but it must be remembered that all those patients had no doubt lost greatly in weight when they first became excited, and were mostly at the minimum consistent with such health as they enjoyed. The opposing tendencies of the excitement of the brain and the reparative powers of the food they ate had found their balance, as it were, in each of them, and the effect of the opium was to give some more strength than had previously existed to the exhaustive forces.

Temperature.—On comparing the average temperature of each of those patients when taking no medicine, and during the whole time they were taking the opium, we find (Table V) that in every one of them but one it was lower while taking the medicine. The actual fall in each case is seen to vary from 1° to $\cdot 1^{\circ}$ in the morning temperature, and from $\cdot 5^{\circ}$ to $\cdot 1^{\circ}$ in the evening temperature. The total amount of the loss of temperature in the seven was in the morning $2\cdot 7^{\circ}$, and in the evening $1\cdot 1^{\circ}$. This seems small and unimportant, but it must be remembered how much the permanent lowering of one degree of temperature represents of loss in vital energy and reparative action if it is already below the normal amount, and how much of good it may represent if it is above the natural standard.

The average temperature of those patients was higher than most other classes of patients in the asylum, and higher than the average temperature of forty sane persons who were employés in the asylum, which I found to be $97\cdot 5^{\circ}$ in the morning, and $96\cdot 7^{\circ}$ at night. Was it not, therefore, a health tendency, this reduction of the temperature caused by the drug? To answer this we must take into account certain facts in regard to the temperature of the insane. I found from an examination of the temperature of patients labouring under all forms of insanity, that a high evening temperature, as compared with the morning temperature, represents a large mortality in the class where this exists. Any drug that would have a curative tendency must reduce the evening temperature. In the cases experimented on, it is seen that the reduction of the evening temperature is very slight as compared with the morning temperature of the patients, and that, therefore, the average evening temperature is relatively higher while they were taking the opium than when they were not, the difference between the average morning and evening temperature of the same persons was $\cdot 8^{\circ}$, the difference in those seven patients taking no medicine was $\cdot 3^{\circ}$, while the difference after they began to take the opium was nil. It seems to me, there-

fore, that taking the effects of the opium on the weight and temperature of the patients together, we must conclude that it lowered the reparative power of the body below the point at which it could, as it were, cope with the destructive tendencies of the brain excitement.

It will be clearly observed that my experiments, though pointing to ill effects that may result from the use of opium in maniacal excitement for short periods or in single doses, yet tend to show that those ill effects will probably only be slight at first. The necessity or the supposed advantage of temporarily subduing the excitement may be so great or so urgent in any particular case that the physician will decide to do so by opium, notwithstanding those risks.

Pulse.—The average frequency of the morning pulse with opium and without it does not show any constant result in all the cases. But if we look at the evening pulse we see that in every case it was lower after taking the opium than before. The pulse of a chronic maniac is a most variable quantity, especially during the day, when there is much movement of the body, and the indications got from it are not much to be relied on. Taking all the cases there was a lowering of one beat in the general average of the morning pulse, and of nine beats in the evening pulse, the numbers being 88, 87, and 85, 76.

It will be observed that all those effects were the result of a continuous use of the opium in doses that were far from being narcotic in their effects. In no case did any comatose symptoms show themselves. Sickness was not caused in those patients who continued to take the medicine. In those whose excitement was allayed there was no torpor of mind or body produced so that they could not take their food or take their usual exercise. In regard to sleep there is no doubt they all slept very much better when taking the opium than before. The functions of the hemispheres of the brain were disordered, and this in all cases tends to impair or interfere with the healthy nutrition of the body, and opium when given continuously in the doses in which I gave it, whether as in some of the cases it seemed to allay the symptoms of the disordered cerebrum, or whether it did not do this, yet in all cases it still further interfered with the proper nutrition of the body, and pushed it one step further down hill in the direction of death.

The rise in temperature, which was the immediate effect of single doses of opium, was thus seen not to last when the drug was given continuously. The loss in weight among the patients is, no doubt, directly connected with the tendency observed in the experiments with single doses to interfere with the appetite for food. The element of uncertainty in regard to its effect on different cases was seen to exist when it was given continuously just as much as when single doses were given, and an explanation of this was as difficult in the one case as in the other.

In order to compare accurately the effects of a continuous course of a mixture of the bromide of potassium and cannabis Indica with that of opium, I discontinued the use of the latter in the cases of those seven patients, and waited till the same time of year came round as that in which I had made the preceding observations. I then, after having observed their mental state and weighing them, put them on half-drachm doses of each thrice a day, and continued this for a fortnight, but finding that the medicine was having an effect, and showing no signs of losing that effect, I continued its use for a fortnight longer. I then increased the doses to forty-five grains of the bromide and forty-five minims of the tincture of cannabis, and continued this for a fortnight, but as this was having a very decided and continuous sedative effect I could not safely increase the doses any more, except in one or two of the cases, to whom I gave a few doses of a drachm of each, and in whom the effects were decidedly too strongly narcotic to be long continued. I then reduced the doses to a half drachm of each. I found this treatment so beneficial to the patients that I have continued it now for about eight months, with a few days' intermission occasionally in all the patients. In the case of those whose excitement was periodic I gave it during the excited periods only. I have noted some of the results that could be tabulated in Table VI. They are shortly these:—

Excitement.—The half-drachm doses had the effect of allaying the

TABLE VI.

Name.	WEIGHT.				MORNING TEMPERATURE.		EVENING TEMPERATURE.		MORNING PULSE.		EVENING PULSE.	
	Before taking medicine.	After four weeks.	After six weeks.	After eight months.	Before taking medicine.	After six weeks.	Before taking medicine.	After six weeks.	Before taking medicine.	After six weeks.	Before taking medicine.	After six weeks.
	lbs.	lbs.	lbs.	lbs.								
J. G.	128	125	130	123	97°	96·1°	98°	97°	77	87	89	60
E. M.	130	128½	131	134	98·2°	96·5°	97·7°	96·7°	78	86	93	82
M. T.	134	139	138	135½	98·6°	98·7°	97·8°	98·2°	74	83	74	68
J. H.	126	122	122	124	97·8°	97·2°	97·5°	97·4°	100	110	77	80
C. M.	109	107½	105	110	98·4°	98°	97°	97·5°	104	83	93	81
S. R.	106	106½	107	108	96·9°	97·3°	97·7°	96·9°	81	77	78	67
E. S.	102	103¾	101	106	98·4°	98·2°	97°	98·4°	103	98	94	96
Aggregate weights and average temperature and pulse	835	831¾	834	840½	97·9°	97·4°	97·6°	97·4°	88	89	85	76

excitement in all the cases but two. This was quite as strongly marked as the first effect of the drachm-doses of laudanum, and during the nine months it has been given there seems to be no per-

ceptible tendency to lose its effect. This is in most marked contrast to the manner in which the sedative effect of the opium was lessened or lost in a week or two. The effect of each dose is not so soon observed, but lasts longer than each dose of the opium, and is not so apt to cause an approach to narcotic drowsiness in any case. The patients look better, less as if they were under the influence of a narcotic drug, and more as if their maniacal excitement was naturally abated. The forty-five grain and forty-five minim doses were in one of the patients followed by a decided drowsiness and sluggishness, with coldness and paleness of the skin and weak pulse, and this was also the case to a greater extent with the drachm doses. But when the excitement was very intense indeed, even these doses were not followed by any such effects.

Weight.—For the first four weeks, and with the half-drachm doses, the aggregate weight of the patients diminished about four pounds, four having lost in weight and three having gained. It will be remembered that during the same period under the opium treatment they lost eleven pounds. Curiously enough nearly all the patients who lost under the opium gained weight under the other treatment. At the end of seven weeks the patients were beginning to gain in weight, so their aggregate weight was only one pound less than when they began the treatment, and now at the end of eight months their aggregate weight is five and a half pounds more than it was to begin with, five having increased, two diminished in weight, and one remained stationary.

Appetite, &c.—In no case was the appetite interfered with. At very rare intervals the mixture produced sickness in one of the patients. Their tongues all remain clean, and no constipating or purging effect on the bowels has been produced.

Temperature.—As seen in Table VI, the average morning temperature of the patients fell $\cdot 5^{\circ}$, and the average evening temperature $\cdot 2^{\circ}$. The latter result I consider as more favorable than the results of the opium treatment. Taking each patient separately, five of them fell in morning temperature, and four of them in evening temperature. There was no fall in the evening temperature relatively to the morning temperature, in this respect not being different from the opium.

Pulse.—The pulse was slightly increased in frequency in the morning and diminished in frequency at night (see Table VI), the diminution not being nearly as great as that caused by opium. In three of the cases the pulse was slightly weakened.

If we compare the general results of those two modes of treatment it is seen that the maximum of good effects and the minimum of those that are ill in their tendency were obtained by the use of the combination of half-drachm doses of bromide of potassium with thirty minim doses of the tincture of cannabis Indica.

It is interesting to compare the results of the two modes of

treatment I have described with the effects of bromide of potassium alone in large doses on the weight and pulse and temperature.¹ I had been giving it to twenty epileptic patients for thirty-eight weeks in doses rising from five grains three times a day up to fifty grains three times a day, with the following results. They gained steadily in weight for twenty-eight weeks, and their aggregate weight was then fifty-six pounds more than when they began to take the medicine. During the last ten weeks, when they were all taking 150 grains of the medicine per diem, they lost forty pounds. At the end of the time they were still sixteen pounds heavier in the aggregate than they had been to begin with. During the same time the effect of the medicine on their temperature was to lower it steadily until forty grain doses were reached. After that it rose, until at the end of the ten weeks of fifty grain doses it was above what it had been to begin with. Still the difference between the morning and evening temperature was greater at the end of the time than it had been to begin with. The effect on the pulse was to lower its average frequency steadily up to forty grain doses, and then to raise it slightly, but at the end of the time its average frequency was not so great as it had been to begin with. The patients who took the bromide of potassium being epileptics, the effects of the medicines above described cannot be compared with it with perfect precision, but still the general result holds good, that the tendency of the bromide of potassium was at least up to 120 grains per diem, in the direction of health, while from the beginning the effects of the opium were as regards the bodily state in a direction away from health, and the addition of the cannabis Indica to the bromide in the maniacal patients, while it had a good effect on the maniacal excitement, did not seem materially to interfere with the nutritive process.

It has been the result of my experience with bromide of potassium given either in epilepsy or in insanity, given alone or in combination with cannabis Indica, that there is a certain dose which may be given with perfect impunity as regards the general health, and with great benefit to the disease for long periods, and that if this dose is increased cumulative effects will show themselves, and all the symptoms of poisoning will come on. The safe and beneficial dose differs in different cases. It would seem as though the kidneys (through which the salt is principally eliminated from the system) can only carry away a certain amount in each individual. I have given twenty-five grain doses three times a day to seventeen epileptics for two years, with a break of only one week, and in only two cases did any constitutional symptoms show themselves, and that was not till the end of a year. The others are all much the better for the medicine, having gained in weight, and improved in general health.

¹ 'Journal of Mental Science,' Oct., 1868.

And when I put twenty-nine epileptics on the medicine in graduated doses, beginning with 15 grains per diem and ending with 150, only the twenty I have referred to stood this treatment for the thirty-eight weeks it was persevered in. At the end of eleven weeks, when they were all taking 75 grains per diem, a boy of fifteen showed signs of being "bromidized;" two men, at the end of seventeen weeks, when taking 105 grains, began to feel bad effects, and two others, at the end of eighteen weeks, with the same doses as the last, showed that the medicine was accumulating in the system. The same phenomenon we shall observe in the clinical observations which follow where the bromide was combined with Indian hemp. In some cases, drachm doses of each were given three times a day for weeks with good effects; in other cases, the same doses could not be continued for more than a few days. This I regard as one of the most important facts yet discovered in regard to the bromides. I have as yet been able to discover no fact by which we can predict beforehand that any particular case will stand large doses for a long period, or that another case will not do so with impunity. Until such a test is discovered we can only give them tentatively in gradually increasing doses in each case until we get up to the maximum of good result without any danger of the cumulative effects of the drug. My experience has been that a strong, vigorous patient, with all the functions of the body performed actively, will generally stand large doses for a longer time than a weaker patient: but to this I have seen exceptions. The salt being eliminated by the kidneys would point to giving a diuretic along with it in cases where it is considered of importance to give large doses, and yet not cause cumulative effects. Indian hemp has been much used as a diuretic. I have given some Spt. Eth. Nitrosi with each dose in such cases, but my experience on this point as yet has not been sufficient to enable me to express any conclusion as to the result.

To test the effects of bromide of potassium alone on acute maniacal excitement, I selected by far the most violent case of periodic mania in the asylum, a woman in whom the attacks of excitement had come on about every month or six weeks for two years, and lasted from a fortnight up to a month. She was a young strong woman in good bodily health. I had tried opium in this case, but it aggravated all the symptoms, and tincture of hyoscyamus in half-ounce doses thrice a day produced but slight abatement of the symptoms. On the occasion on which I made the experiment she became suddenly excited, on the 13th of March. On the 14th she was furiously maniacal, shouting, restless, sleepless, most violent and destructive, with a strong pulse of 90, flushed face, suffused eyes, muscular system in constant activity, and temperature 99.6°. I put her on two-drachm doses every three hours, on this the second day of her excitement. In forty-eight hours, after she had taken four ounces,

she was as excited as ever, but her tongue was beginning to get furred in the centre with a raw line down each side, and there seemed slight muscular unsteadiness. Her pulse too was somewhat weaker. The medicine was given for another day and a half, until she had got seven ounces of it. The maniacal excitement then quite suddenly abated, and her mental state became one of torpid depression. She became pale and pinched-looking, the pupils sluggish, the pulse 108 and very weak, and the temperature fell to 96°. These symptoms increased after the medicine was discontinued, until the co-ordinating power of the muscles was so completely lost that she reeled like a most intoxicated man when she attempted to walk. She slept, almost continuously, for three days. She only took food when given to her, and seemed not to care for it. Her bowels were regular. Her tongue was at first furred with a thick white fur, and then got quite raw-looking. Her breath smelt of bromide of potassium. Her articulation was much affected. She remained in this state for about five days, her temperature remaining at 96°, and it was quite a fortnight from the time it was discontinued before she got over the effects of the drug. As she got better there was slight feverishness with dry tongue and want of appetite. The excitement did not return when the effects of the drug passed off; but the next attack began on the 10th of April, which was sooner than it ought to have come on by a week at least.

This experiment is instructive, as showing, 1st, that the most acute excitement can be subdued by bromide of potassium; 2nd, that this cannot be done without pushing the medicine far beyond what is safe; indeed, almost up to complete paralysis of the cerebrum and sympathetic ganglia of the heart; 3rd, that the action of the drug in such a case is strongly cumulative, increasing in intensity for days after it has been stopped, and lasting for a long time; and 4th, that no permanent improvement is necessarily produced in the morbid cerebral action. I do not regard this a case of cutting short the excitement. It was rather one of half poisoning the patient. If any justification of such an experiment is needed, I must plead the importance of knowing exactly the effects of the bromide on maniacal excitement, the hope that benefit might possibly accrue to the patient, and the absolute want of any precedent to guide me. It seems to me highly instructive, clinically as well as physiologically. Such a case should show the necessity for stopping the bromide at once when its bad effects are first observed, on account of this cumulative action. It illustrates the prolongation of the effects of this as compared with any other drug that has the power of producing the same narcotic or paralytic action on the nervous system. It proves that maniacal excitement gives the same tolerance to the system in resisting the ordinary physiological effects of this drug as in the case of the ordinary vegetable narcotics.

(To be continued.)