of urine. It then walked with arched back and gingerly steps along the table, but there was no sign of paralysis. At 10.40, the injection was repeated, and again we noticed the same spastic gait, and afterwards slight prostration. At 11 a.m. the prostration following on this injection was more marked, and on taking the temperature we found it had fallen to 99°. At 11.20, no definite symptom was produced by this injection, nor after the three that followed at intervals of twenty minutes. In all 32 grains were given. At 1 p.m. it was noted that the animal, though inclined to rest, could walk easily and take food. Its temperature was now 98°. At 2 p.m. the animal had recovered and was hopping about in a natural manner.

Natural salicylic acid, 5 grains, was dissolved in 20 minims of rectified spirit, and injected into a rabbit through a hypodermic syringe. There was no result, and twenty minutes afterwards the injection was repeated, and at the expiry of an hour from the last injection we noted that "it was eating cabbage, and moving about easily. Urine passed gave characteristic reaction with the perchloride of iron."

Artificial salicylic acid, 5 grains, dissolved in 20 minims of rectified spirit was injected into a rabbit on the same day, and twenty minutes afterwards "it was observed to be slightly seedy, but could take food." The injection was repeated, and ten minutes afterwards it was observed to be very weak about the legs, so weak that when the legs were stretched out it could not recover its position. Succeeding rapidly came flexor paralysis of hind and fore limbs, and subsequently supervened violent convulsions, head arched backwards, and snapping of the jaws.

In an hour and twenty minutes from the first injection death occurred after a very severe convulsion.

Salicin.—On July 2nd, 10 A.M., a grey rabbit was anaesthetised, and 18 grains of salicin in solution in warm water were introduced into the stomach. The temperature was 101.8°; at 10.45 A.M. the temperature was 100.8°, and at 11.15 100.4°. There was no evidence that the animal was affected in any other way by the salicin. An hour and a half after it had been administered a large quantity of urine was passed, which gave the characteristic reaction with the perchloride of iron.

On July 4th, to another rabbit 30 grains of salicin were similarly administered at 11 A.M. At 11.30 the temperature was 100.6°, but there was no sign of the animal being in any way injured. Urine passed two hours after the administration of the salicin gave the reaction with iron.

These experiments prove: 1. That salicin in a dose of 30 grains seems to have no injurious influence on the life of a rabbit of above weight, but that it diminishes the temperature about 1°. 2. That salicylic acid obtained naturally by oxidation of salicin, or from the oil of winter green in 10-grain doses, has also no deleterious effect. 3. That salicylate of sodium obtained from the natural salicylic acid, in 32 grains, is not lethal, but that it causes prostration and lowers the temperature.

On the other hand, it is conclusively demonstrated that: 1. Salicylic acid, artificial, in a 10-grain dose, causes, first, paralysis of flexors; secondly, death by violent convulsions. 2. Salicylate of sodium, artificial, in 18-grain doses, is lethal; in 4-grain doses it causes paralysis of the hind limbs; in 8-grain circular and rotatory movement, with paresis and dragging of the hind limbs; further in 12-grain doses it causes pronounced paralysis of the hind limbs, and marked progressive prostration and that 18 grains cause not merely paralysis of the hind limbs, but a paralytic condition of the fore limbs, and entire loss of control of muscle movements, and death supervenes in a short time.

The deductions from these experiments indicate that artificial salicylic acid and its salt of sodium are dangerous and, in large doses, fatal to animals. While salicin, natural salicylic acid, and its salts of sodium are not. Now, on what does this difference depend? Doubtless on some impurity in the artificial acid, and corroborative evidence, though not yet completed, is afforded by the following letter which we have received from G. G. Henderson, M.A., B.Sc., of the Chemical Laboratory of the University of Glasgow:—

"I find, on examination, that the sample of artificial salicylic acid you left with me is not pure, but contains a small quantity of another acid, which I have no doubt is the cause of the appearances observed after the use of artificial salicylic acid. I attribute the presence of this impurity to the fact that the phenol used in preparing salicylic acid synthetically is not pure, but always contains other substances (cresol, etc.), of some one of which the acid found in salicylic acid is probably a derivative. I had not enough of

the impurity to make a further examination of it, but it is certainly not salicylic acid. I should add that no trace of this substance is to be found in natural salicylic acid."

After a very careful analysis, Mr. Henderson isolated the impurity referred to. It was in the form of a buff-coloured powder, and it was found to be more soluble than salicylic acid; 1 grain of it was injected into 20 minims of rectified spirit, and injected into a rabbit weighing 6 lbs., but without any visible effect. After the expiry of half an hour, 2 grains similarly dissolved were injected, and in ten minutes, and without any rotatory movements, the breathing became very rapid, the arteries of the ear were alternately dilated and contracted, and the animal lay prostrate, with its fore and hind legs stretched out. Again, in half an hour, the same quantity—2 grains—was injected, and the prostration became more intense, the respirations lower, and a fine tremor was detected in the muscles of the face. In the course of two hours there was a slow improvement, but never a complete or even partial recovery, and ultimately the rabbit died, after thirty-six hours, being unable during that time to eat anything.

The action of this impurity seems to be of the nature of a slow but certain poison, and the lethal dose is relatively much less than that of salicylic acid. The rabbits in the previous experiments weighed only 14 ounces, and in this case 6 lbs., so that the lethal dose would correspond to about 1 grain for a 1 lb. rabbit.

The obvious conclusions from these experiments are that artificial salicylic acid contains an impurity or impurities, and until this or these can be extracted by the aid of chemistry the internal administration of it or its salt of sodium should be discontinued. Large and repeated doses of the sodium salt are necessary in the treatment of acute rheumatism, and hence we may account for the restlessness, the confusion, and the delirium sometimes attendant on its use, which have been testified by clinical experience. It is more than probable, too, that the retarded convalescence occurring in some cases of acute rheumatism after the salicylate treatment is due to the great and protracted prostration which the impurity or impurities give rise to. It is to be remembered in connection with these symptoms that prescriptions of the salicylate of sodium are invariably made up, unless otherwise indicated, from the artificial and not the natural salt.

In a further communication we will state the physiological action of the acid from which the impurity has been removed, and also the effect of pure salicylic acid made artificially.

THE INFLUENCE OF OPIUM AND MORPHINE ON URIC ACID CONSIDERED WITH REFERENCE TO THEIR ACTION IN HEALTH AND DISEASE.

Read in the Section of Pharmacology and Therapeutics at the Annual Meeting of the British Medical Association held in Leeds, August, 1889.

By 'A. HAIG, M.A., M.D. OXON., M.R.C.P.,

Physician to the Royal Hospital for Children and Women, Waterloo Road; Assistant Physician to the Metropolitan Hospital.

As the action of morphine in uræmia and in uræmic and puerperal convulsions has recently been attracting some notice,¹ and as its effect on arterial tension has been previously pointed out by others, I propose in this paper to give the results of my investigations on its influence on the excretion of uric acid.

These results show, I believe, that it causes retention of uric acid, and that the result of this is a fall of arterial tension, the effect being exactly the same whether the retention is produced by opium, by acids, or other substances, so that my results with it completely confirm the previous observations of others.²

I shall further bring evidence to show that the effect of morphine on mental depression and other mental states and conditions, as already well known, is the result of its action on uric acid and arterial tension, or is at least the exact parallel of the action of other drugs which affect the excretion of uric acid and arterial tension in the same way, and that it is thus possible to produce what is practically the same result by several drugs. And I shall also point out that the effect of opium and morphine on uric acid and arterial tension may explain the good effects

¹ JOURNAL, i, 1889, 588 and 943; also Debate at Medical Society, April 8th, 1889; see JOURNAL, i, 1889, 837.

² Loc. cit.; JOURNAL, February, 1889.

they have been observed to produce in uræmia and uræmic and other convulsions.

It will be seen at once how closely connected these subjects are, and how importantly they bear on my previously published work on *Uric Acid as a Cause of Headache, Epilepsy, Mental Depression, and High Arterial Tension*, I shall hope to be able to make abundantly evident.

Some time ago I was much struck by the way in which a good dose of tinct. opii relieved a severe headache in a patient under my care at the Waterloo Road Hospital, suffering from chronic nephritis. After many other more orthodox remedies had been given without avail, the resident medical officer (Dr. Johnson) suggested a dose of opium, and the effect was wonderful.

I then came across the writings of MM. Ball and Jennings,³ showing that in chronic morphinism, when feelings of misery are present between doses, the pulse tension is high, and that when a new dose of the drug brings ease and comfort, the tension is natural or low. It at once occurred to me that there was here an important parallel between the well-being produced by opium and the well-being which I can produce by acids or other drugs causing retention of uric acid.

In both cases the feelings of well-being are accompanied by a pulse of low tension, and the feelings of misery and depression by one of high tension. For my part I believe that this relation of mental condition to pulse-tension is not in any way a coincidence, but I think that the high tension pulse, or the conditions which produce it, are the absolute and essential causes of the mental condition acting through their effect on the cerebral circulation; but I shall return to this point again.⁴

I at once set to work to test the effects of opium and morphine on the excretion of uric acid on arterial tension and mental depression and on the uric acid headache, in which latter trouble its value had previously been noted by some sufferers.

My results show clearly and distinctly that opium and morphine cause retention of uric acid, that during the retention the arterial tension is reduced just as it is when the retention is produced by other drugs, that after the retention, as the effect of the opium passes off, there is a rebound, with an excessive excretion of uric acid, and very marked high tension, these being often accompanied by headache and mental depression, and constituting the unpleasant after-effects of opium already well known.

I am thus able to confirm the observations of MM. Ball and Jennings⁵ with regard to arterial tension, and to show that they hold good not only for chronic morphinism, but even for quite small single doses of opium and morphine; and I am led to believe that the seductive feeling of well-being—to obtain which opium is so largely consumed—is due to its effects on the excretion of uric acid and arterial tension, and that the wished-for result may be brought about to a large extent by other drugs; and conversely that the headache and miserable feeling of depression which follow some ten to twelve hours after a dose of opium, and which MM. Ball and Jennings have noted as being accompanied by a high tension pulse, are the result of the passing-out through the blood of the uric acid previously kept back, and that precisely the same results follow the retention and well-being produced by acids, iron, lead, and other drugs, or occur independently of drug action before, during, and after an attack of headache or epilepsy; and the causation of epilepsy by lead is a case in point, the lead retaining a store of uric acid which, when it comes to be swept out, is for a time in excess in the blood, and causes, among other things, the convulsions.

Fig. 1 shows the effect of two doses of one-sixth of a grain of tartrate of morphine on the acidity, uric acid, and urea.

I purposely chose the tartrate so as not to complicate the problem by having a mineral acid present; because I had previously found that opium and morphine raise the acidity, and as I believe their action on the excretion of uric acid and on arterial tension is all the result of the rise of acidity they occasion, I was anxious to try the effect of morphine, apart from a mineral acid, in such a salt as the hydrochlorate or sulphate, even though the amount could be very small.

The result shows, I think, clearly that two doses of one-sixth of a grain of tartrate of morphine were able to cause a very marked rise of acidity which, as urea is falling, is clearly due to the drug, and when the morphine effect passes off on the fourth day acidity falls, even though urea is rising.

I shall have something to say further on as to the way in which opium and morphine raise acidity, and it is only a special application of what I have already said on the matter of acidity in previous papers.

The effect of opium or morphine on acidity is very marked and prompt, and where only one dose is taken the rise and fall are both over in about twelve hours, and as the one nearly balances the other, they show very little in a twenty-four hour chart; but in the experiment in the figure the morphine was specially taken with the object of affecting the alkaline tide of the third day, so as to show as much as possible in a twenty-four hour chart. No doubt, with larger doses continued over twenty-four hours, a larger fluctuation could have been produced, but some of the symptoms might have been inconvenient.

The results also are so constant that one may argue with absolute certainty from the mental well-being and the reduced arterial tension to the raised acidity of the urine and the retention of uric acid. Not that opium any more than other drugs can act in total disregard of the conditions present at the time it is taken, but I shall have to point out presently that it generally of itself controls one of the most potent causes of a fall in acidity—namely, increased peristalsis.

Fig. 2 shows the pulse of the well-being of morphine, in a trace taken two hours and forty minutes after a dose of one-sixth of a grain of the tartrate; and, if anyone will refer to the BRITISH MEDICAL JOURNAL of February 9th, 1889 (Fig. 3), he will see that it very much resembles the pulse of well-being caused by acids, which, indeed, as I have said above, it really is, though in this instance the morphine produced the acid.

Fig. 3 is the trace of a pulse on the morning after a dose of morphine, when the alkaline tide is beginning to wash out the uric acid previously retained, and its excess in the blood is causing high tension, mental depression, and threatening of headache. The trace clearly shows high tension, and is very similar to those previously given in the BRITISH MEDICAL JOURNAL.⁶

I have previously said that some people have found opiates of use in migraine or the uric acid headache, and since I began to experiment with opium I have often used it in slight headaches, and have found it even more effectual and certain than an acid; and, just as with an acid, as the headache and mental depression are passing off, there are marked pricking and shooting pains in the joints, showing, as previously pointed out,⁷ that this is one of the places where uric acid is retained; and with a high tension pulse, such as that in Fig. 3, together with its concomitant mental depression and headache, it is a simple matter to replace all these conditions by their opposites by repeating the dose of morphine; and we have here in miniature the vicious circle of chronic morphinism, in which a man is continually driven to repeat the dose to save himself from the evils produced by the previous one.

And now as to the way in which opium and morphine raise acidity. It is well known that opium delays or stops intestinal peristalsis and checks diarrhoea, and in a paper on a case of gout⁸ I have pointed out the effect of constipation in raising the acidity of the urine, diminishing the excretion of uric acid, and precipitating an attack of gout; and have suggested that, when peristalsis of the large intestine is hindered in any way, its contents, which have an acid reaction, linger in its pockets, and that, along with the fluid which is then absorbed from the fæces, some of the acid which gives them their reaction passes also into the circulation.

If this be granted, the action of opium and morphine on acidity is simple and easy to understand; and I have already said that I believe their action on acidity explains that on uric acid, and thus again their effect on arterial tension, which in turn controls the cerebral circulation and produces the conditions of mental brightness and well-being or their opposites.

I have previously shown that I can produce all these conditions with an acid, and we see in Fig. 1 how powerfully morphine affects acidity; a further consideration of this factor may explain the somewhat different action of morphine in different people and under slightly different conditions; for it is obvious that if any organic condition prevented the morphine from delaying peristalsis in the large intestine, and causing increased absorption of acid from its contents, its effect in removing a headache or fit of mental depression would be very greatly diminished.

I have further pointed out that increased peristalsis, with

³ *L'Encephale*, 1887.

⁴ See also JOURNAL, February, 1889, and *Practitioner*, November, 1888.

⁵ *Loc. cit.*

⁶ *Loc. cit.*

⁷ JOURNAL, vol. ii, 1888, p. 12.

⁸ *St. Bartholomew's Hospital Reports*, vol. xxiv, p. 226.

diminished absorption of food and acid, is an important and frequent cause of a fall of acidity and its results, as headache and mental depression, with their concomitant high tension pulse; hence the common relation of dyspepsia to high tension pulse, mental depression, and headache, and an explanation of the fact that a purge given at the time a sick headache is present often does harm;⁹ but the effect of morphine in preventing slight relaxation of the bowels is generally prompt and decided, and, so far as my experience goes, it is a very certain remedy both for headache and mental depression.

The mental brightness and well-being produced by opium is a matter of great interest, and it might seem to anyone unacquainted with what can be done in this way, by means of acids and other drugs which influence the excretion of uric acid, that this condition is peculiar to the drug under discussion, and that it is probably due to its direct action on the cerebrum; but anyone who gets marked results with opium or morphine in driving away mental depression or a headache, or in causing mental brightness and well-being, will, I think, be able to convince himself that he can produce practically identical results with acids, and probably, also, with lead or iron, and some other drugs.

Further, it is quite clear that the people who take opium as a habit do not do so for its soporific or narcotic effects; and Mr. W. J. Moore says: "A telling commentary on the assertion that opium dulls the mental faculties is the practice of the Chinese, who take their opium before business bargaining."¹⁰ And Dr.

as I have said, an acid; but an acid may apparently in some cases not be absorbed, or, at least, not quickly, owing to conditions present in the stomach at the time it is taken; or, again, in some people, it rather appears as if an acid causes some gastric irritation, and so possibly prevents its own absorption; so that, of the two, opium is to some extent the more certain cure of headache and mental depression, and the quickest way to mental brightness and well-being.

The mental brilliancy and happy feelings are most marked from two to four hours after a dose, and the pulse tension is then also most reduced (see Fig. 2); an hour or two later the narcotic

Fig. 2.—March 31st, 1889, 3.50 P.M. Sitting. Pressure, 4 ounces; pulse, 66; tension slight. Well-being of morphine 2 hours 40 minutes after gr. 1 of the tartrate.

action of opium begins to be felt, and if the dose is not repeated, the feelings of well-being become mingled with a certain amount of drowsiness; later still, as eight or twelve hours after the dose and after sleep, if there has been any, comes the rebound with headache, mental depression, and high tension pulse (Fig. 3), all of which can be quickly removed by another dose; and thus the opium circle becomes established, and can only be broken through by bearing the headache and mental depression without repeating the dose; and after some personal experience, I have ceased to wonder that many are unequal to this effort.

If, however, as I have been trying to point out, the mental brightness and well-being are due to the effects of opium on uric acid, and so on pulse tension and cerebral circulation; and if the mental depression and headache are due also to the passing out of the uric acid previously held back, it seems to me that if we can get a drug which will promote the free elimination of uric acid, while at the same time, by affecting its solubility, it prevents its causing symptoms of mental depression and headache, we shall be easily able to break through the opium circle.

And in salicylate of sodium, we have a drug which exactly answers to these requirements; when uric acid is passing out in the opium rebound, it is held in solution by an alkali, and causes symptoms of its presence in the blood; but I have previously pointed out that uric acid, when held in solution by a salicylate, passes freely out in the urine without causing any symptoms.¹¹ And I should expect, therefore, that the salicylate would effectually break through the opium circle by removing the accumulated uric acid; and, so far as my experience goes, I believe that this is the case.

It may be interesting here to call to mind that nearly all the beverages consumed to any large extent in this country have the same effect on pulse tension that opium or morphine and acids have; thus ale, stout, champagne, sherry, and port are very strongly acid,¹² and do undoubtedly effect all the changes in uric acid excretion and pulse tension that a dose of a mineral acid would, producing at the same time more or less of mental brightness and well-being; and alcohol itself, by dilating the peripheral arterioles, no doubt, has the same effect on the cerebral circulation. Tobacco smoking, again, tends to reduce pulse tension, and produces no doubt in this way the pleasant feelings of calm and well-being, for which it is so highly prized.

Many non-alcoholic beverages in common use, as those made, or supposed to be made, from lemon or lime-juice, have an acidity which, calculated as oxalic acid, is surprisingly high, and have been found by experience to produce the same results; so that I believe that those who resort to any of these beverages obtain practically the same results, namely, the relief of mental depression and causeless worry, and that mental exaltation and well-being is what all are seeking for, not the stupor of alcoholic excess, or the narcotism of large doses of opium; these are so to speak the accidental results of carrying the process too far.

And now to come to the effects of opium and morphine in disease, I cannot but regard it as very important corroboration of my theories of the causation of mental depression and melancholia by uric acid through its effect on pulse tension, and of my above

Farquharson, in the recent debate in the House of Commons, on the opium traffic, mentioned the fact that Wilberforce always put an opium pill in his mouth before getting up to speak in the House. This statement of Dr. Farquharson's excited some laughter; I suppose because it was considered that Wilberforce found it necessary to dull his susceptibilities before getting up to speak; but my strong impression is that Wilberforce must have been aware of a fact about the use of opium of which his contemporaries and many of their successors were ignorant, and that this same fact is well known to the opium-eating Chinese.

In my experience, opium, far from dulling the mental faculties, renders them sharper and brighter than they would ever be otherwise; the only thing that at all approaches it in this respect being,

⁹ See *Lancet*, vol. i, 1889, p. 1187.

¹⁰ *Standard*, March 26th, 1889.

¹¹ *Med. Chi. Trans.*, vol. lxxi, p. 135.

¹² *M. D. Thesis*, Bale and Sons, 1888, p. 7.

remarks on the influence of opium on these factors, to find that Dr. Ringer has pointed out that a hypodermic injection of morphine is of very great use in some cases of melancholia, and speaks in strong terms of its valuable effects.¹³

In headache, as I have said, opium and morphine act well, though in some patients they cause nausea, or intensify this condition when it is present, and in these cases morphine may have to be given hypodermically, and a hypodermic injection of morphine is recommended by Dr. W. H. Day in the last edition of his work on *Headache*.

With regard to epilepsy, an injection of atropomorphine is advised by Brown-Séquard¹⁴ in cases where there is any warning; and since I noticed the connection of this disease with uric acid,¹⁵ I have several times given acids with the objects of warding off the fits in cases where there was any warning of their approach, and several patients have declared that the fits have been kept off by this means; but there are so many sources of fallacy, that it is not safe to attach any great importance to these statements.

My argument for using an acid was as follows:—An epileptic fit appears to bear the same relation to the excretion of uric acid and mental depression¹⁶ that a headache does, and it is therefore probable that the pulse tension is raised at the time of the fit, though it is difficult or impossible to prove this, as the struggling in the fit tends to remove its signs; if, therefore, there is sufficient warning, one ought to be able, just as in a headache, to diminish or prevent the plus excretion of uric acid, reduce the pulse tension and keep off the fit by giving an acid, and it is interesting to note that atropomorphine has sometimes been found to have this effect, though I suppose the proof that in any given case it has prevented a fit must, as in the case of the acid, rest entirely on the statement of the patient.

With regard to puerperal and uræmic convulsions I stand on less firm ground, but it is certainly an interesting fact that opium, which has been shown to reduce arterial tension, should relieve these convulsions.

If what I have been saying above is correct, and opium reduces pulse tension by its effect on uric acid, we are brought face to face with the question, Are puerperal and uræmic convulsions due to the high tension of uric acid? The answer to this question must depend on the view that is taken of the relation of high arterial tension to nephritis. Is the high tension the result of the nephritis, and only present after the kidney is damaged, or is the high tension present, as contended by the late Dr. Mahomed, for some years before there is any kidney lesion? that is, is it to some extent independent of the condition of the kidney? I have previously pointed out that I am able, by influencing the amount of the uric acid in the circulation, to raise or lower pulse tension at pleasure and to a considerable extent; and I believe that there is little or no difference between the sphygmogram of the high tension thus produced (see Fig. 3), and that of nephritis.

Fig. 3.—May 15th, 1889, 7.30 A.M. Sitting. Pressure, 4 ounces; pulse, 60; tension moderate. Threatening of headache morning after morphine.

Dr. Broadbent, as I have remarked in previous papers, considers that uræmic convulsions are due to high arterial tension affecting the cerebral circulation, and not to a poison acting on the nerve cells; and if this is so, it is obvious that the tension which causes the convulsions must be due to a temporary cause, or a transient exacerbation of tension which is perhaps never quite normal, and it therefore corresponds in every way to the effects of a uric acid storm.

At this point the history of a puerperal convulsion may be of some help to us, for it often comes exactly at a time at which, from our previous knowledge, a uric acid storm might be expected; that is to say, at the end of a time, as I have remarked in a previous paper,¹⁷ of large and active nitrogenous metabolism;

the commencement of parturition with pains, vomiting, and inability to take food soon result in a fall of urea and acidity, and the fall of acidity is the signal for a rush of the previously accumulated uric acid into the blood, and so for a marked rise of tension with mental depression, headache, and, possibly, in some cases convulsions, as its signs and results. Again, in cases spoken of as showing chronic high tension of the pulse, my experience would lead me to believe that there are great variations of tension, which, if the pulse is observed only once and at the same hour each day, may, to a large extent, escape notice, though these fluctuations are the possible cause of important symptoms.

My object, however, in this paper is to point out the effect of opium and morphine on acidity, uric acid, and pulse tension, which are of themselves, I believe, very important, and explain a large part of the known effects of these drugs both in health and disease. And it seems to me that if further investigations confirm the value of morphine in these convulsions, and also my explanation of its mode of action, we have here another point from which light may be thrown on the relation of ordinary epilepsy to the excretion of uric acid.

In conclusion, my position with regard to opium and morphine amounts to this. A large number of drugs—iron, lead, the mineral acids and their salts, antipyrin (?) nitro-glycerin(?)—have one effect in common, namely, that of diminishing the excretion of uric acid in the urine, that is, I believe, driving it out of the blood into the liver, spleen, joints, etc. Exactly contemporaneously with the diminished excretion of uric acid due to any of these drugs comes a fall of pulse tension, and a mental condition of brightness and well-being. Uric acid headache or mental depression, if present, are cured, and in their place come pricking and shooting pains in the joints, most marked in those who have previously suffered with gouty arthritis. On the other hand, an alkali, as soda or potash, while increasing the excretion of uric acid, produces symptoms which are the exact reverse of those above mentioned. As these drugs have no obvious properties in common, I have inferred that the results they produce are due to their action on uric acid, which I have pointed out in previous papers. Opium and morphine, as we have seen, diminish the excretion of uric acid, and at the same time reduce pulse tension, cause mental brightness and well-being, cure a uric acid headache, and cause at the same time pricking and shooting pains in the joints; they, therefore, belong to the iron, lead, and acid group of drugs with which their effects exactly correspond, and as they always cause a marked rise of the acidity of the urine, I conclude that their action on uric acid is the result of their action on acidity.

With regard to convulsions, I have pointed out the relation of some cases of epilepsy to the excretion of uric acid.¹⁸ I have now shown that morphine, probably by acting on uric acid, relieves or removes high tension pulse, mental depression, and headache.

It has been noticed that morphine is of much use in certain uræmic and puerperal convulsions which are generally accompanied by a high tension pulse. I now suggest that its curative action in these troubles is also due to its effect on uric acid, and that further investigation may show that these convulsions, like some of those in ordinary epilepsy, have a more important relation to the excretion of uric acid and its effects on pulse tension than has hitherto been suspected.

CASE OF CEREBRAL TUMOUR SUCCESSFULLY REMOVED BY TREPHINING.

Read in the Section of Surgery at the Annual Meeting of the British Medical Association, held in Leeds, August, 1889.

By RUSHTON PARKER, B.S., F.R.C.S.,

Professor of Surgery in University College, Liverpool; Surgeon to the Liverpool Royal Infirmary.

THIS case occurred in the practice of Dr. Austin Williams, of Liverpool, and was attended also by my colleague, Dr. Glynn, both of whom were present at the operation. The patient is a big, strong man, aged 38. The symptoms observed—long-standing headaches, and latterly mental dulness, followed by almost total paralysis of the left arm and distinct weakness of the left leg—pointed clearly to the probability of an intra-cranial growth of some kind; but the administration of iodide of potassium for three

¹³ *Handbook of Therapeutics*, ed. xii, p. 497.

¹⁴ *Quain's Dictionary of Medicine*, p. 450.

¹⁵ *Neurologisches Centralblatt*, March 1st, 1888.

¹⁶ *Neurologisches Centralblatt*, March 1st, 1888, p. 4 of paper.

¹⁷ *JOURNAL*, February 9th, 1889.

¹⁸ *Neurologisches Centralblatt*, loc. cit.