Original Articles.

A STUDY OF HAIG'S URIC ACID THEORY.

BY GERTRUDE W. VAN PELT, M.D., BOSTON.

THE medical world owes to Dr. Haig, I think, a profound debt of gratitude for his thorough and patient study on the excretion of uric acid. Whether his theories, in whole or in part, be true or not, he has collected with infinite pains a vast array of facts which must be studied and explained in some way, which cannot fail to advance our knowledge of disease.

The most important facts which he seems to have proved are, that uric acid is always formed in a definite relation to urea (according to his observations, about 1-35); that its action when present in excess of that relation is to increase arterial tension, locally or generally, and thereby to decrease the urinary flow; and that uric acid is present in the blood in inverse ratio to its acidity, and can be altered at will by affecting its acidity. It follows from this that excretion of uric acid below the relation of 1-35 implies a storing up of it in some part of the body, and Haig's theory is, that it is the liberation from time to time of this stored-up uric acid which causes the attacks of migraine, epilepsy, and many other nervous disturbances. According to his experience, sodium salicylate is the drug most to be depended upon to rid the system of this excess. These points he has supported by careful and prolonged experimentation, which he has reported in his book on uric acid. Its action on pulse tension he has studied under various drugs, at different hours of the day, and in a variety of pathological conditions, by the aid of the sphygmograph, in connection with auscultation of the heart; also, where possible, he has driven uric acid out of the circulation and then taken the pulse tension for comparison. It seems to me, as I shall explain later, that this is the most important point on which to be clear, and that it should be established beyond a shadow of doubt, before we can estimate the value of his work.

In speaking of this part of the subject, he says: "If my premises are good, and my deductions sound, and if uric acid really influences the circulation to the extent which I have been led to believe that it does, it follows that uric acid really dominates the function, nutrition and structure of the human body to an extent which has never yet been dreamed of in our philosophy, and in place of affecting the structure of a few comparatively insignificant fibrous tissues in which it is found after death, it may really direct the development, life history, and final decay and dissolution of every tissue, from the most important nerve centres to the most active glands, to the matrix of the nails, and the structure of the skin and hair."

Such claims for a comparatively innocuous substance sound extravagant, and yet, I do not see why, if its effect on arterial tension be true, much of the rest may not follow; and his theories have appeared to me so plausible, so carefully worked out and so suggestive, that I accepted them for the time being as proven, and used them as a working hypothesis.

Since interested in this subject I have made between three and four hundred urinalyses from a number of cases, which, though not enough to enable me to confirm or reject such important studies as Haig's, have been enough to increase my interest in the subject, and convince me that there is at least some close

connection between these excretions and a great variety of pathological conditions; though his explanations of why this one substance manifests itself in such a variety of ways, has not seemed to me satisfactory. Although I have nothing to report which can in any way be considered as proof, I think I have watched a few cases with sufficient care to make them valuable as testimony one way or the other.

In making the analyses, I have used the same methods that Haig does, and have tested for urea, uric acid, and acidity, generally taking the specific gravity, and often examining for sugar and albumin. The arterial tension I have only observed by feeling the pulse, and as such a method can have no value for any one else, I will merely mention that I have made no observations on that subject which contradict those of Haig.

CASE I, twenty-six years of age, came to consult me for a general condition of ill health extending over years, which had during the past few months culminated in six or seven curious attacks that had alarmed her. These always appeared soon after breakfast. They began by a feeling of sudden drowsiness, with a pain on the top of the head, after which she passed into a semi-conscious condition lasting three to four hours. On recovery she found her eyelids swollen, and her face of an ashen color. Memory had failed since the beginning of these attacks. Her general symptoms were: mental and physical depression; nervousness; insomnia; sudden awakening about 4 A. M., with sometimes extreme nausea, sometimes slight dyspnea, sometimes much gas in the intestines, and frequent urinations between 4 and 6 A. M. Appetite was variable; bowels irregular. She was troubled with acne. She was usually worse in the morning, best in the afternoon, and the evenings were variable. The worst time of the year was spring. She had had malaria as a child, and her symptoms had often been attributed to that cause: therefore, her blood was examined for the plasmodium, but it was not found.

The following is an analysis of the urine, which was turbid with urates, and from which that passed between 2 and 7 A. M. was omitted through forgetfulness:

Amount in cubic centimetres (estimated between 2 and 7 A. M.)		1,000.00
Specific gravity		1.015.00
Acidity in grammes of hydrochloric acid		1.70
Urea in grammes		19.00
Uric acid in grammes		0.90
Relation between urea and uric acid		1-21

I ordered sodium salicylate, twenty grains, four times daily. The effect was like magic. Although she had only had disturbed nights with the use of trional, which she had been taking for many weeks, she had a good night without any hypnotic, and awakened feeling decidedly better. The urinalysis the next day was as follows:

Amount in cubic centimetres		1,000.00
Specific gravity		1.024.00
Acidity in grammes of hydrochloric acid		1.20
Urea in grammes		20.00
Uric acid in grammes		1.25
Relation between uric acid and urea		1-16

In four days she reported that her appetite was much better and that she felt calm and languid instead of irritable and nervous as she had for so long, and I decreased the sodium salicylate to twenty grains thrice daily. The improvement was almost constant. Menstruation took place normally, though it had been

much disturbed. She never had another one of her attacks. In two months she felt perfectly well, all her symptoms had disappeared, and I stopped all treatment. Her face at this time was entirely free from acne, and her color had changed from a yellowish to a pink tint. In the light of subsequent experience, I think treatment was stopped too early, though probably salicylates had done all they could for her at that time. She left the city soon after and I could not follow her, though she wrote me once that her symptoms were beginning to return. I examined her urine frequently while she was under my care. The uric acid excretions for a time were higher than before treatment, and then decreased, though they were always in excess. The average amount of water increased, and symptoms began at once to disappear, which would seem to show that the arterial tension was lower while the uric acid was excreted in combination with the salicylates.

CASE II. I have selected next a case of rheumatism. The affected joints were the knees and to a slight extent the fingers. This, with the only other symptom — constipation — had existed for years. It was severe enough to cause much stiffness and at times some pain. For a few months before beginning treatment it had been painful and made the effort of walking exhausting.

I prescribed sodium salicylate, fifteen grains thrice daily, but her knees grew so rapidly worse that, remembering Sir William Roberts's opinion that sodium favored the deposit of quadriurates in the joints, I tried in turn salicylic acid and salicylate of colchicum, regulating the acidity of the urine with potassium citrate. She made a certain amount of improvement. The relation of uric acid to urea increased from 1-33 to 1-21.5; but as improvement seemed to come to a standstill at the end of forty days, I decided to try sodium salicylate once more, and gave fifty to sixty grains as could be borne. She improved at once. In two days the excretions of uric acid to urea were 1-14.5. She continued on this treatment for six weeks. Her knees slowly improved and her bowels began to move regularly without cathartics. Once during this period the urinalysis showed a ratio of uric acid to urea 1-11. Then as the patient seemed weakened somewhat and looked pale, and her knees were so much better, I gave her syrup of hydriodic acid and later iron. Her strength increased rapidly, though her knees were still stiff and at the end of two weeks the ratio of uric acid to urea was 1-30.

The points of interest in this case are: one, that there were no general symptoms known as those of uricacidemia; two, that her improvement always coincided with an increased excretion of uric acid; three, that she excreted without constitutional disturbance as much as seemed to cause it in others, of which I shall give an example later; and four, that the symptoms were aggravated the first time sodium salicylate was given. This last might be explained according to Haig's hypotheses as follows: she had uric acid stored up elsewhere in the system than in the joints, in such places as caused no inconvenience, and in such combinations as had greater affinity for sodium salicylate than the combination in the joints. It was, therefore, taken up rapidly into the circulation, and in coming in contact with the irritated joints, which on account of this irritation were relatively acid tissues, some of it at least was immediately re-precipitated. It seems to

me probable that if I had continued with this treatment in the beginning, the improvement would have been more rapid. When sodium salicylate was used the second time, much stored-up uric acid had been dissolved away, and what was excreted was taken presumably directly from the joints.

CASE III. I refer to this case because, first, it is an interesting contrast to the preceding, being a case of severe rheumatism and presenting at the same time marked constitutional symptoms; and second, it illustrates well the peculiar action sodium salicylate seems to have in numerous cases. The rheumatism was general, both in the joints and muscles, and once for a period of six months was severe enough to necessitate crutches and a daily treatment of massage. The general symptoms were a confused feeling in the head, which was often so great as to make her afraid to go out alone; occasional loss of power of motion, even to the extent of inability to grasp an object; extreme nervousness and apprehensive feelings. The urine before treatment was thick with urates, and the analysis as follows:

Amount in cubic centimetres	1,000.00
Specific gravity	1.026.00
Acidity in grammes of hydrochloric acid	2.44
Urea in grammes	25.00
Uric acid in grammes	1.27
Relation between uric acid and urea	1-20

She was immediately put upon sodium salicylate (grs. xv t. i. d.), which *decreased* the excretion of uric acid. She felt a little better, however, and at the end of twelve days the analysis was as follows:

Amount in cubic centimetres	875.00
Specific gravity	1.021.00
Acidity in grammes of hydrochloric acid	1.17
Urea in grammes	17.50
Uric acid in grammes	.30
Relation between uric acid and urea	1-19.1

It will be noticed there was a diminished flow of urine and amount of urea, which suggests a higher arterial tension; also that the acidity is reduced more than one-half, and the actual amount of uric acid diminished, though its relation to urea is little changed; also that the per cent. of uric acid is elevated, that is, that we have a more concentrated solution. This state of things continued as long as sodium salicylate was used (which was some weeks), though the figures varied constantly one way or the other. The patient improved sufficiently as to general symptoms to prevent discouragement, though the rheumatism did not improve at first, and later grew worse. She is still under treatment, and although considerably better, the results are not definite enough to report.

The following seems to me a possible explanation of the action of sodium salicylate. It makes of the blood a too good solvent of urates. And when the tissues are loaded with uric acid, all the salicylates quickly combine, throwing much more uric acid into the circulation than would otherwise have been there, and quite probably the blood, with its acidity diminished, may be capable of holding in solution a varying amount of uric acid besides that which satisfies the salicylates. This enormous quantity of urates immediately raises the arterial tension, decreasing the urinary flow and excretion of uric acid. The large amount of uric acid in the small amount of urine suggests that sodium salicylate is attempting to act as usual, namely, to facilitate excretion, but that it is prevented by the action of some other force. But as

the patients generally feel a little better, there is confirmation of Haig's idea that salicylic acid *per se* is less irritating to the nervous system than the ordinary form, called by Sir William Roberts, quadriurates. It is certainly more soluble, for a specimen containing salicylic acid is clear when one containing a smaller amount of quadriurates is turbid. This effect of sodium salicylate I have noticed over and over again, whatever the explanation may be. And if, under such circumstances, arterial tension be lowered by raising the acidity of the blood, or by some other means, the excretion of uric acid will increase. Haig perhaps alludes to the same thing when he says that sodium salicylate acts much better when combined with an acid.

CASE IV. This a case of uricacidemia, which suggests the presence of other poisons. She has been an invalid for about twenty years, has a poor inheritance from both parents, and has never been strong. She has been all over the world for health, and has had all kinds of treatment. Dyspepsia was a prominent symptom; and the gastric analyses, according to the method of Winter and Hayem, showed a condition of hyperpepsia with fermentation. Besides this, she suffered from neuralgia, at times in almost every part of the body, and often very severe; headaches, which sometimes confined her to a dark room; extreme nervousness; irritability; periods of insomnia; biliousness; constipation; dysmenorrhea; and often an inability to use herself in any way without bringing on some sort of an attack. Her urine was always *very* scanty and often loaded with urates. After she had been under my care for two years, I became interested in Haig's theories, and my first real interest in them grew out of the light they threw upon this case. It seemed to me she had not a symptom which might not be explained by them. A urinalysis, after she had been taking sodium salicylate for two and a half months, and eaten no meat for one month, was as follows:

Amount in cubic centimetres	1,750.00
Specific gravity	1.011.00
Acidity in grammes of hydrochloric acid	1.15
Urea in grammes	10.50
Uric acid in grammes	.90
Relation between uric acid and urea	1 11

Under this treatment she was less miserable, the quantity of the urine averaged about 1,250 c.c., and the usual disturbance at the menstrual period had almost disappeared, but the success was not great. For three months she ate no meat, and the excretion of urea ran gradually very low, although I tried to supply its place with gluten. It several times sank below six grammes and once was as low as two and a half grammes. The average relation of uric acid to urea during these three months was 1-14.4. The urine was always pale and very faintly acid. I was unable to increase the food or to give any drug I knew of, such as iron, arsenic or iodine, to raise acidity, because the stomach could not bear it. Hydrochloric acid did not have that effect, and moreover did not seem reasonable treatment in a case of hyperpepsia. Being convinced in this case that elimination was even more important than feeding, I decided to try pilocarpine hydrochlorate. I gave a hundredth of a grain three times a day for three days, stopping all else. The character of the urine changed at once. For the first time it was highly colored with a brick-dust deposit. The analysis was as follows:

Amount in cubic centimetres	750.00
Specific gravity	1.011.00
Acidity in grammes of hydrochloric acid	.78
Urea in grammes	9.38
Uric acid in grammes	.846
Relation of uric acid to urea	1-11

The urea, although so low, was double what it had been for some time, and I felt as if I had at last, perhaps, found something that would unlock the system and allow metabolism to go on. This drug, however, made her so nauseated and bilious that I only continued it two days longer. Before beginning it she had for some period been suffering unusually with neuralgia. The day after having stopped it, she reported that she felt better than she had for weeks, more alive, and had almost no pain. Once a week, for some weeks, I gave her pilocarpine in the same doses, and always with similar results. Finally I continued it for ten days in spite of the most painful symptoms, headache, nausea, loss of appetite, severe neuralgia and rheumatism. In five days these subsided, and metabolism constantly increased. Urinalysis was as follows:

Amount in cubic centimetres	1,500.00
Acidity in grammes of hydrochloric acid	2.19
Urea in grammes	17.25
Uric acid in grammes	.798
Relation between uric acid and urea	1 21.7

This was the best I had ever found for her, and her improvement in strength for that short time was remarkable. It will be noticed that the effect of pilocarpine was not so much on the excretion of uric acid as of urea. In other words, by some means, her metabolism was increased and her symptoms improved, though the relation of uric acid to urea was the same as it had often been before. The depression was not caused by pilocarpine, inasmuch as it disappeared with a continuance of the drug, and the question is, Was it not caused by subtle poisons which the pilocarpine enabled the system to rid itself of?

I have had at least five other uric acid cases, in which the action of pilocarpine has suggested the same question. A comparison of cases of which these are types suggests to my mind the following four points:

(1) Not all cases of uricacidemia suffer from general symptoms, even when uric acid is in the circulation. It may show itself as rheumatism and be excreted from time to time without causing disturbance, for example, Case II reported. That may be explained by supposing that in such cases the nervous centres are less irritable to uric acid, or, by supposing that these general disturbances are caused by some other factor or factors usually but not always associated with uric acid.

(2) When there *are* general symptoms, they generally bear a relation to the excretion of uric acid. This is not always easy to show by a glance at the figures, as often complicating circumstances must be considered before they can be interpreted, for example, different symptoms are produced when equal amounts are excreted with or without salicylates. Then again, it seems probable that there is not always a relation between uric acid excreted and that in the circulation. This must be the case when the amount of urine is very small and that which is passed is a very concentrated solution. This is the effect which is alluded to in Case II, which can be produced under suitable conditions by sodium salicylate. But I think the relation will become apparent to any one who studies the excretions with this idea in view. As illustrative of it,

I will give a few analyses, made from the urine of a neurasthenic :

and caused death. At the same time he made studies of the uric acid and treated the patient for that, as he

	March 21st.	April 7th.	April 9th.	April 10th.
Amount in cubic centimetres	1,500.00	1,000.00	185.00	875.00
Acidity in grammes, hydrochloric acid	1.65		.74	1.43
Urea in grammes	23.25	8.90	6.57	14.88
Uric acid, grammes	.645	0.435	.168	.588
Relation of uric acid to urea	1 to 36	1 to 20.5	1 to 39	1 to 25+
Symptoms	Just after a period of great depression. Feeling relatively well, though weak.	Feels tired and exhausted, and stiff all over.	Excessively irritable and depressed, with feeling of exhaustion.	Better than yesterday, though with same symptoms.
Remarks	During the next two wks. the pendulum swung so rapidly, often changing several times in 24 hrs., that it was impossible to follow it.		Uric acid higher than figures, so much sediment not accounted for.	

It will be noticed that on the 9th uric acid, though low, was great for this amount of urine, and the small amount of urine and urea imply very high tension and a large amount of uric acid in the circulation which is retained. On the 10th, tension was not so high and metabolism was improving.

The following are taken from the same patient at a later period :

said, "not because I believed her symptoms due to uricacidemia, but because, whatever might be the cause of her symptoms, I hoped to get the same good results from treatment that Haig had reported." And as a matter of fact she improved. He also studied, in the same way, normal control cases, epilepsy, grand mal, petit mal, and acute mania following influenza, and found that these were not caused by paraxanthin. He

	2d.	9th.	13th.	20th.
Amount in cubic centimetres	125.00	1,500.00	1,500.00	1,000.00
Acidity in grammes, hydrochloric acid	.32	1.11	1.44	1.36
Urea in grammes	3.06	12.75	18.00	16.2
Uric acid in grammes	.155	.7	.585	.53
Relation of uric acid to urea	1 to 20	1 to 18.2	1 to 30.8	1 to 30.2 —
Symptoms	Extreme depression, neuralgia, nausea, headache, nervousness.	In comparison with 2d, feels well.	Still better.	Not quite so well the last few days.

After the 13th tension began to grow gradually higher, shown by diminishing urine and decreasing metabolism.

I could also select periods from this same patient for comparison with these, which would show similar variations but in which the background of symptoms, so to speak, was very much darker or lighter. In other words, an analysis of the urine does not tell me, even in the patients I am used to observing, how they are feeling unless I have been observing them through that attack, but knowing the history of the previous days, I can often form a correct idea of their condition by watching the uric acid excretions.

(3) The great variety and enormous differences in symptoms between patients excreting the same amount of uric acid make it necessary to suppose some other poison present to produce the results.

In the *Medical News* of May 26 and November 3, 1894, Dr. B. K. Rachford gives the results of some very careful study on this subject, in which he shows that a case of migraine and epileptiform attacks was due to paraxanthin poisoning. He proved this by extracting the poison from the urine and injecting it in mice, in which animals it produced similar symptoms

says, "My investigations show that in a case of migraine and in a case of migrainous epilepsy there was in the urine passed by the patients during their attacks, not only an increase of uric acid and an increase in the ratio of uric acid to urea, but there was also found a very great increase of the poisonous leuko-maines of the uric acid group, and the paraxanthin solution from the migrainous epilepsy produced in mice symptoms very like those from which my patient suffered." This study and such classes of facts at once suggests that the particular poisons causing the symptoms in other uric acid cases have not yet been isolated. It may be observed in this connection that some of my cases treated with pilocarpine were worse in the beginning of treatment, when we may imagine that some hypothetical poison was being excreted freely but that these symptoms abated with a continuance of the drug; moreover, that the variations of excretions of uric acid were out of proportion to the symptoms. These facts, though proving nothing, point to useful directions for study.

(4) The uric acid variations, common to so many conditions, together with certain symptoms accompanying it, point to a relation as well as a difference.

The relations, clinically, have been long noticed. Charcot was, I believe, the first to call attention to it, and it has since been confirmed by many well-known observers. He speaks of the uric acid diathesis as forming a tree, the principal branches of which are gout, articular rheumatism, certain forms of migraine, and cutaneous affections; and of there being another tree comprising neurasthenia, hysteria, epilepsy, all the hereditary forms of insanity, general paresis, locomotor ataxia. And he says that these two trees spring, as it were, from the same soil, communicate by their roots, and are so intimately related that one is tempted to ask if they are not one and the same tree. Even in my small experience I have had cases varying from those characterized by a simple decrease of strength, to those showing alarming mental disturbances. And such apparently different diseases seem to be associated with or a part of this condition that I am ready to consider it one whose causes have become settled in the race, involving more or less most of its members.

In an interesting article by Dr. J. F. Barbour, printed in the *American Therapist*, June, 1894, he quotes Dr. Menalac Sakorrhaphos, of Athens, from the *Progrès Médical*, as saying: "The march of arthritis is slow and progressive; it results after long years in the so-called nervous diathesis. As the lifetime of one individual is not sufficient for the evolution of this disease, it is transmitted by heredity. . . . One may say arthritis — and under this name we include the nervous diathesis likewise — represents, as it were, the human race in its period of decadence; it is a sign of the approaching end of a family, precisely as an acute disease destroys the life of an individual."

This last I quote to emphasize the universality of this condition, and not at all because it seems to me necessary to take so gloomy a view of the situation.

At first glance such facts as those shown by Dr. Rachford and Dr. Haig may seem to contradict each other, but I think a more prolonged comparison shows them to be really in harmony. Is not the high arterial tension caused by uric acid the whole key to the situation? If uric acid can lock the kidneys, so to speak, we must have poisons retained in the system just as when the bowels are locked. When the condition appears first in an individual and not in her ancestry, that is, when there is no nervous inheritance to start with, it is apt to show itself merely as rheumatism, and probably in a mild form. This is what Dr. Sakorrhaphos calls the first stage of the disease. There are no marked general symptoms here. The blood probably has a normal reaction most of the time, metabolism proceeds undisturbed, and what excess of uric acid there is, is stored up in the joints, or in some tissue where it causes no inconvenience. Such cases may feel nothing but slight rheumatism all their lives. If they die by fifty they may never feel anything, in the case of its being stored up elsewhere than in the joints; but in advanced years, as the blood becomes more alkaline, they will suffer more or less from uricacidemia or rheumatism or both. This is a Haig case in its incipency.

As the disease proceeds, when for instance, a person starts in life with it, or when for any reason it develops more rapidly, there will be from time to time systemic disturbances of more or less severity. By examining the urinary excretions we shall find, if this theory be true, that these attacks, whatever they may

be, are accompanied by increased excretion of uric acid, and that they subside when the uric acid excretions subside, either naturally or when assisted by treatment. Between these attacks, accompanied by increased excretion, the patient is perfectly well. During them, the arterial tension is high, which will in itself cause certain symptoms. But we may suppose besides, that this state of tension will cause other poisons to be retained, so that, for instance, attacks of migraine, asthma, ordinary headache, acute dyspepsia, or whatever it may be, are due primarily not to altered local arterial tension as Haig holds, but to some ptomaine or poison held in the system because of the arterial tension. For if it is due only to uric acid, why could Dr. Rachford produce in mice similar symptoms to those of the patient, by injecting a substance obtained from that urine, while the injection of uric acid produces no such symptoms? If, on the other hand, uric acid has nothing to do with these symptoms, as many affirm, why do they follow the curve of the uric acid excretions, and why can they be produced at will by increasing this excretion, as Haig has shown? In the case we have been supposing, the patient is well between the attacks. The system is not constantly under the action of these poisons as they are only periodically excreted. But in still more advanced cases, the patient is never well. He has his ups and downs, which will correspond to the fluctuations in the uric acid excretions, but these variations will take place against a background of ill health, which, on its hand, will vary all the way from general lack of strength to grave nervous conditions. These, then, if such be the explanation, are the cases which by degrees have succumbed, which were not able during their attacks to throw off all the poisons accumulated in the intervals, and so a vicious circle has been established, which is capable of transference from father to son.

The causes which bring about this condition must be far spread and deeply rooted, and have perhaps not been even guessed. Haig lays great stress on the eating of meat as a cause, and believes that its permanent cure consists in a vegetable diet. He has, I think, proved, that in some cases this is a fact. I cannot, however, but suspect, that it is more often due to mistakes not so easy to correct. Perhaps it may be a cause more commonly found in England than America. Comparatively few of my patients have eaten much meat. I think most of them from preference have consumed less than the ordinary amount, though perhaps the habits of their ancestors ought to be known in this connection. But if the most important pathological action of uric acid be its power to raise arterial tension, there are surely other causes potent in this direction, which might in that way originate uricacidemia, and run parallel with it. There is, I think abundant testimony to show that anxiety and nervous strain are capable of raising arterial tension, and who can estimate what must be the effect of the eternal competition and eagerness to outdo others, which is such a mainspring of action in this civilization?

As to treatment, I have not found anything which will relieve all, though I have found that by careful and patient study, nearly all can be relieved. As to whether they can be cured or not, my experience is too short to afford me any proof, though I believe they can be. My aim in treatment is to increase the excretion of uric acid as much as possible without pro-

ducing an interference with metabolism and if possible to hold it at this point, and I use mainly, either alone or in various combinations, sodium salicylate, sodium phosphate, pilocarpine, iron, the iodides, salol, acids and alkalies, and prescribe exercise whenever it can be taken. Recently I have used a treatment with potassium permanganate, suggested by Dr. Rachford, which has been so helpful that I hope in a future paper to report my experiences with it.

RECENT ADVANCES IN THE METHODS OF LOCAL ANESTHESIA.¹

BY F. B. LUND, M.D., BOSTON,
Surgeon to Out-Patients, Boston City Hospital.

It cannot be denied that there are certain disadvantages, which may at times assume serious proportions, connected with the administration of a general anesthetic for certain operations.

The disadvantages of anesthesia by ether and chloroform, the best anesthetic agents we possess, are in large measure inseparably connected with the fact that they act directly upon the centres of thought, sensation, and muscular action. The after-effects—nausea, dizziness, vomiting, etc., are, as in alcoholic intoxication, the results of the toxic action of the anesthetic upon the central nervous system, reflected to the peripheral organs. It seems in the nature of things improbable that a general anesthetic will be found which will be free from the after-effects due to intoxication of the central nervous system. With the fact that there is a certain amount of danger connected with the action of a general anesthetic, it is always the duty of a surgeon to acquaint his patient. While in many, I may say in most cases, this danger is so slight that it may be almost disregarded, there are others—such as those of shock from strangulation of the bowel, respiratory embarrassment from collections of pus in the chest, asthenia from prolonged malnutrition, chronic bronchitis and myocarditis complicating abdominal affections demanding operative treatment, etc.—in which the anesthetic most seriously complicates an operation.

The employment of general anesthesia in operations of short duration, as in minor surgery and in out-patient practice, has the disadvantage of requiring an extra assistant, and if, as is sometimes the case, the operation has to be prolonged beyond the period of primary anesthesia, of subjecting the patient to the disagreeable nausea, vomiting, etc., following the ether, and necessitating either a stay over night at the hospital or sending an attendant home with the patient. Considerations such as these have led to the adoption of a rule in many hospitals that no patients shall be etherized in the Out-patient Department unless they have some one with them to see them safely home. As a result of such rules, many patients have been subjected to the severe pain of operation without an anesthetic, or the already overtaxed wards of the hospital have been further crowded with patients who might perfectly well have been operated on and sent home if they had had some one with them, or if a general anesthetic had not been required.

The desirability of a local anesthetic which should be free from danger—some substance which, without

intoxicating the central nervous system, should temporarily paralyze the sensory nerves supplying the operative field—has led to active endeavor on the part of surgeons to discover some such agent. Up to the year 1884, when Köller, a student of medicine at Vienna, accidentally discovered the anesthetic effect of the drug cocaine upon the mucous membrane of the eye, the only methods of local anesthesia of wide practical application depended upon the numbing effect of cold upon the nerves, and consisted in freezing the part to be operated upon either by the application of freezing mixtures or by spraying with some rapidly evaporating ethereal compound. This method possessed the disadvantages that the process of freezing and thawing is in itself attended by no slight degree of pain, and that it could be safely applied only on regions of most limited area, and sufficed only for the most rapid operations.

The anesthesia produced by cocaine applied to the mucous membranes was found to be attended with no such disadvantages; and although the drug was poisonous, it was found that sufficient local anesthesia could be produced without its absorption in poisonous amounts.

Attempts were at once made to produce local anesthesia of the skin and subcutaneous tissues by the external application of solutions of cocaine, but it was found that sufficient absorption did not take place to produce anesthesia. The introduction of cocaine solutions by electrolysis was tried without success. To an American physician, Dr. Leonard J. Corning, of New York, is due the credit of demonstrating the fact that solutions of cocaine injected subcutaneously along the trunk of a sensory nerve would produce local anesthesia in the area of its distribution. It was found difficult, however, to find a satisfactory technique upon this principle. As applied, it consisted of the injection of a few minims of a two to five-per-cent. solution of cocaine under the skin in four or five places surrounding the operative field, and so situated as to reach, if possible, the branches of the sensory nerves which supplied it. It was found necessary to wait five or ten minutes for the drug to be diffused among the tissues, and so to be brought in contact with the various nerve filaments which supplied the part. Operations performed after this method were often entirely successful, but often for some unknown reason the anesthetic effect failed, to the great chagrin of the surgeon. This failure was due to the well-known fact of the abundant anastomosis of terminal nerve filaments. Although one or more of the nerve trunks supplying the area might be anesthetized, it often happened that one running deeper through the tissues or coming from a different direction, furnished, through its terminal anastomosis, a path for the conduction of pain.

Dr. Corning also demonstrated the fact, that in suitable cases the application of an elastic ligature, by imprisoning the anesthetic fluid in the part, deepened and prolonged the anesthesia.

Sometimes, however, even where this precaution was adopted, the result was unsatisfactory, a fact which was probably due to the circumstance that some nerve trunk sent anastomosing filaments which were not reached by the anesthetic fluid, and served to conduct the sensation of pain.

Another reason for failure was the mistake sometimes made by the surgeon of making the first needle

¹ Read before the Surgical Section of the Suffolk District Medical Society, December 4, 1895.