one of the best diuretics we have. A dose of urea, 10 to 15 grams each morning, will often get rid of obstinate oedema.

It should be noted that there is no excess of urea in the blood during uraemia; if there were there would be a good diuresis and no uraemic convulsions.

To sum up, I would advise that a patient with nephritis should have a slop diet for about ten days, and that the diet should gradually be increased to include fish, eggs, and meat, although there is still albuminuria. Also do not keep a nephritic patient in bed too long. A certain amount of exercise in a warm room helps to lessen the oedema, besides giving the child a happier time.

IONIC MEDICATION.

BY

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THAT particular branch of therapeutics known as ionic medication or ionization is one about which very little information can be obtained in any recognized textbook of pharmacology and therapeutics. Yet the subject is not a new one. Lewis Jones states that Leduc, in one of his publications, gives references to a great many papers on the subject, and mentions one published in 1833.¹ Turrell goes even farther back and declares that the theory of ionic medication was enunciated by Verratti in 1747.² The general application of this theory as a practical question in therapeutics appears, however, to date from the publication of a series of papers by Leduc in 1900. In spite of this most textbooks ignore the subject. A few mention that there is such a method of treatment, but offer little or no criticism of its efficacy.

The reason for this reticence on the part of authors is fairly obvious. The majority of those who practise this method of treatment acclaim with enthusiasm the wonderful results which follow. Those who criticize it exhibit an almost equal degree of vehemence in their condemnation. It is difficult for the therapist, who may have little or no practical experience of the method, to know where the truth lies. It seemed to me, therefore, that it might serve a useful purpose to undertake a critical examination of the whole subject, basing my views on a considerable number of experiments and clinical observations.

The first difficulty which arises is in the definition of the term "ionic medication." According to those who speak with authority on the subject the term embraces (1) the introduction of drugs into the body through the skin or a mucous surface by means of an electric current, and (2) the modification of the chemical composition of parts of the body by the setting up of chemical changes throughout the tissues.³ If the second part of the definition means that the chemical composition of the tissues is modified by the drugs introduced, then it is understandable. If, however, as is generally held, it means that this modification is the result of the passage of a current through the body, without any reference to the drug introduced, it is very difficult to see how this process can be termed "medication." It is obvious, in any case, that the two parts of the definition involve quite different conceptions, and will require to be considered separately.

The first question therefore which has to be considered is: Can drugs be introduced through the skin by means of an electric current? The answer to that question is undoubtedly in the affirmative. In animals Leduc showed that it was possible to introduce strychnine ions through the skin of a rabbit in this way.⁴ Finzi proved that the ferri-cyanide ion could be carried through the skin of a monkey.⁵ Inchley repeated these experiments on cats, rabbits, and guinea-pigs, and showed further that it was possible to introduce a number of other alkaloids, some metals, and certain negative ions.⁶ In man exact records of experiments are few, though numerous writers have mentioned that it is possible to prove the penetration of the iodine ion. In my experiments I have been able to confirm this, and I have further been able to demonstrate quite conclusively the presence in the body of another anion, the salicylic ion, and of two cations, pilocarpine and atropine, after they have been carried through the human skin by a current of electricity.

The next question is: Has the ion thus introduced into the body any special pharmacological action in virtue of its being

so introduced? If we are to believe the ionic theory of the action of drugs—namely, that soluble salts exist in the body mainly as ions, and that each ion possesses an independent pharmacological action—then we must believe that the method of administration will make no difference to its intrinsic action. That this is so has been shown by the experiments of Leduc and Inchley on animals. The strychnine ion introduced electrically exhibited its ordinary action on the spinal cord and caused convulsions, while the atropine ion exhibited its ordinary action by producing paralysis of the cranial autonomic nerves. In man it can be shown quite easily by using a solution of pilocarpine nitrate underneath the positive pole. After the current has passed for some time the individual exhibits salivation, sweating, and disturbance of vision—in other words, the ordinary signs of the action of the pilocarpine ion. It may seem that I elaborate this point rather unnecessarily, but the suggestion has frequently been made, or at any rate implied, that by introducing an ion through the skin by means of an electric current you thereby endow it with some peculiar properties. That this is not so is obvious. The essential pharmacological action of any particular ion is the same whether it be passed through the skin into the body by inunction, a hypodermic needle, or an electric current.

If that be so the critic will very naturally ask: Wherein lies the particular merit of this method of introducing drugs into the body? The technique is expensive, complicated, and wasteful of valuable drugs, compared at any rate with the hypodermic needle or inunction. What advantages does it possess to compensate for these very obvious drawbacks? The answer is given that "in treatment by ionization a cloud of ions is introduced into the place where the disease exists";⁷ that the ions are limited to the diseased region, and that therefore the local concentration is high. As a result the action is more intense, and the effect consequently greater.

If we examine these statements we must inquire: (a) What quantity of drug can be passed through the human skin by means of the currents used for therapeutic purposes? (b) What evidence is there of a local concentration of the drug? (c) How deeply can the drug be made to penetrate in this way?

I have investigated the first question with special reference to the iodine and salicylic ions, which are the two remedies most extensively employed in the treatment of medical conditions in this way. The method adopted was to "ionize" a number of patients, using a 2 per cent. solution of potassium iodide or sodium salicylate under the negative electrode. The process was continued for a period of thirty to forty minutes, and the urine was collected for analysis during the twenty-four hours following the experiment. The method described by Kendall⁸ was employed to estimate the amount of iodine present in the urine, and the amount of salicylic bodies was estimated by Hanzlik's method.⁹ The following table gives the results when potassium iodide was used.

Current in milliampères	25	50	100	200
Milligrams of iodine in 24 hours' urine	30	55	98	146

It must be pointed out, of course, that it is not possible to raise the current all at once to the amperage indicated. For the comfort of the patient that has to be done gradually, and accordingly the currents mentioned were not acting during the whole period of the experiment. The rapidity with which the current could be raised varied with different individuals, but the quantities of iodine noted in the table were the maximum found for each particular current. In the case of the current of 200 ma. the duration of the experiment was forty minutes, the current being raised from 100 to 200 ma. during the last thirty minutes of the period. The duration in the other cases was thirty minutes.

It is known that from 60 to 80 per cent. of the amount of iodide taken into the body by any channel is excreted in the urine in twenty-four hours. From the figures given it is possible therefore to estimate approximately the amount of the iodine ion which has entered the body. Taking even the lowest percentage, the maximum amount of iodine which was introduced into the body by each current was 50, 92, 160, and 243 mg. respectively. In other words, it will be seen that, with the ordinary currents used in therapeutics, and for the ordinary duration of treatment, the total amount of iodine introduced was not greater than 0.77 grain, 1.4 grains, and

2.46 grains. Even with the huge current of 200 ma. the amount was only 3.74 grains.

When sodium salicylate was used the amount of salicyl bodies excreted in the urine, after the employment of ordinary currents, was so small that it could not be estimated with any degree of accuracy. Using a current rising to 170 ma. during a thirty-minute period, the total amount of salicyl bodies found in the urine was only 9 mg. It is interesting to note that this result coincides with that of Inchley, using a cat as the subject of experiment.⁶ He found only very small amounts of salicyl bodies in the urine, and comments on the fact that the salicylic ion is not carried through the skin to the extent that enthusiastic writers on the subject would lead one to suppose.

Objection may be taken to this process of reasoning. It may be argued that the amount excreted would give no true indication of the amount passed through the skin. The objection has very little weight, but it can easily be overcome by considering the results when pilocarpine nitrate and atropine sulphate were used. With pilocarpine nitrate, using a current rising to 50 ma. over a period of twenty minutes, there was produced in the subject of the experiment salivation, sweating, and slight disturbance of vision. All these effects could be produced on the subject and to the same degree by injecting 1/5 grain hypodermically. In the case of atropine sulphate it was not considered advisable to use large currents because of the poisonous effects of very small quantities of that drug. But using a current of 5 ma. for thirty minutes resulted in sufficient atropine being introduced to produce a rapid pulse (135 a minute), marked dryness of the mouth and throat, and paralysis of accommodation lasting for eighteen hours. All these symptoms could be produced by injecting hypodermically 1/30 grain of atropine sulphate. In these experiments the amount of the drug introduced into the body was estimated, not from the amount excreted, but by its physiological action, and in each case it will be seen that this amount was small. It will be noted, further, that the action of these drugs differed in no way from what is seen when they are given hypodermically.

While the salient feature of all these results is that the amount of drug introduced is very small, there was another feature which is of considerable importance and which bears on the question of local concentration. In "ionizing" a patient with potassium iodide it was possible to demonstrate iodine in the saliva collected during the first twenty minutes of the period of treatment. Again, when pilocarpine nitrate was used, salivation made its appearance twelve minutes after the current was started; exactly the same time as after hypodermic injection. Where, then, is the evidence of local concentration? It must be quite obvious that as soon as the ion is carried through the skin it is whisked off in the blood stream and that therefore no local concentration ever takes place. Otherwise how is it possible to explain its appearance so quickly in parts of the body so far removed from the seat of entry, and in such amounts as to produce its physiological action on these parts?

The next question to consider is the depth of penetration of the ions. In man it is difficult to produce any experimental evidence to bear on this question, but the discussion in the previous paragraph throws some light upon it. If the ions introduced through the skin appear so rapidly in distant parts of the body, it must be obvious that they are set free from their function of carrying the electric current as soon as they pass through the skin. That they penetrate deeply is therefore unlikely. It should be noted further that although, until it passes the barrier of the skin, the current can be conveyed only by the ions of the solution underneath the electrodes, as soon as this barrier is passed the ions of the body fluids will take on the task of carrying the current. That fact renders even more unlikely deep penetration of the foreign ions introduced. A number of experiments have been related to prove that ions penetrate deeply. These experiments are, however, useless for this purpose. They only show that it is possible for considerable penetration to take place in dead or isolated tissue and in parchment. In the living body there is quite a different state of affairs.

In the few cases where attempts have been made to show deep penetration of ions in man they have signally failed. Finzi, in monkeys, claimed that he had been able to obtain penetration of the ferri-cyanide ion into the knee-joint.⁸ Grave doubt has to be cast on this experiment because of the possibility of the ferri-cyanide ion found in the joint being carried there by diffusion after the animal was killed. Finally, Inchley, repeating this experiment on a rabbit, found

that there was no deeper penetration into the joint than could be obtained by simple subcutaneous injection of the drug under the skin covering the joint.⁸ The whole weight of experimental evidence in living animals goes to show that the penetration of ions is not deeper than the subcutaneous tissue.

It would appear, therefore, that the following statements are true:

1. The amount of any drug introduced in an ionic state into the body by currents which can be used therapeutically is very small.

2. The drug, as soon as it is carried through the skin, is swept away in the blood stream and produces its specific action on the system generally. There is therefore no local concentration.

3. There is no evidence of deep penetration. On the contrary, in animals the experimental evidence is all against the drug penetrating farther than the subcutaneous tissue. In man it seems to be quite clear that a similar state of affairs exists.

We have now to examine the second part of the definition—namely, that in the process of ionization chemical changes are set up in the tissues, and that the resulting modification of the chemical composition of the body produces a therapeutical effect. That statement, as will be obvious, has really nothing to do with medication, but is a claim for the action of a constant current of electricity. An example of this is the claim that there is a "lytic" action underneath the negative electrode, and that this "lytic" action affects principally exudates and recently formed bands of lowly organized tissue.¹⁰ It is quite true that, when an electric current is passing through the body fluids, there will be movement of anions towards the positive pole and of cations towards the negative pole. But it does not follow that any chemical changes are set up in the tissues between the poles. Faraday demonstrated long ago that when a current is passed through a solution of an electrolyte no apparent change occurs in the fluid, and that chemical changes take place only at the electrodes. To take a concrete example: when a current is passing through a solution of sodium chloride no chemical change can be observed in the solution, although the ions are in motion to their respective poles. At the negative electrode the sodium ion will give up its electrical charge, become a sodium atom, and combine with water to form a caustic alkali which will act on any tissue in contact with it. But that is at the electrode and, in the cases considered, on the skin. To suggest that any ion of the body fluids can produce a "lytic" action on the tissues underneath the skin before it has reached an electrode is manifestly absurd. There can be no "lytic" action except on the skin underneath the negative electrode. Further, it is difficult to conceive, and there is no evidence to suggest, that the mere migration of an ion, which is normally a constituent of the body fluid, to another part of the fluid can cause any chemical change which would have a therapeutical effect.

Certain authorities, recognizing the difficulty of explaining their therapeutical results on the basis of chemical changes in the tissues, have claimed that it is the movement of the ions which is the important factor. They suggest that there is a bombardment of millions of tissue ions on the affected part and that this "ionic massage" may be of benefit. In the present state of our knowledge of the forces bound up in matter it is hardly worth while discussing such a hypothesis. Two facts, however, are worth mentioning: (1) Though the number of ions set in motion must be enormous, the total mass of ions acting on any part must be very small; (2) the greatest migration velocity of any ion, the hydrogen ion, with a potential gradient of one volt per centimetre is only 0.0032 cm. a second.¹¹ It is difficult to see how a "bombardment" carried on by a small mass moving so slowly can have much effect. It can be in no way comparable to massage at the hands of a well trained and intelligent expert.

In view of these facts I have endeavoured to examine closely the therapeutical value of this method of treatment in a number of cases in the Western Infirmary, Glasgow. Potassium iodide and sodium salicylate, each in 2 per cent. solution, were the drugs used, and the cases which were treated were patients suffering from fibrositis of the lumbar and other regions, sciatica, and rheumatoid arthritis. As a general rule currents up to 100 ma. for thirty to forty-five minutes were employed; in one case a current of 170 ma. was reached during the last ten minutes of a thirty-minute period of treatment. The results can be briefly summarized. In no case was there any real benefit. The results agree with those

obtained by Stockman in an extensive investigation of the treatment of the same conditions by ionization. These were not published in detail, but an epitome of them is to be found in his book on *Rheumatism and Arthritis*.¹² Nor could it be expected that it is possible to cure such diseases in this way. For iodides and salicylates can be administered by the mouth in doses sufficient to produce a continuous concentration of iodine or salicylic ions in any part of the body far greater than could possibly be produced by ionization. Further, very much greater quantities of salicylic ions can be passed locally through the skin by applying methyl salicylate, and much greater quantities of iodine ions by applying iothion (di-iodohydroxypropan), an oily liquid having the chemical formula $\text{CH}_2\text{I}.\text{CHOH}.\text{CH}_2\text{I}$. Yet none of these methods of treatment benefits the conditions mentioned.

Although no real and permanent benefit followed this method of treatment, in a number of cases there was a temporary relief of pain. This relief persisted for some hours after the process of ionization, but in every case the pain returned, though in a few cases not to the same extent. This diminution of pain could in no way be ascribed to the introduction of the iodine or salicylic ions, for an exactly similar diminution of pain was obtained when the current was reversed and therefore no iodine or salicylic ions were being introduced. Similarly, when a pad soaked in a solution of sodium chloride was used over the affected part the same relief was observed.

It would be of interest to inquire as to the particular factor to which this is due. It has been shown conclusively that it is not due to the specific action of any ion. It must be due, therefore, to the galvanic current. Two different factors will thus require to be considered: (1) the current passing between the poles, and (2) the action of the current at the poles. Turrell suggests that the action of the current passing between the poles has the effect of generating an appreciable increase of temperature in the tissues, and to this increase of temperature he ascribes the beneficial result which follows.¹³ It is true that Joule's law applies to electrolytes, and that therefore all the energy of the current spent when traversing the electrolyte is used simply in the production of heat, and not in causing chemical changes. But the most of the heat produced in this way is on the skin where the resistance to the current is greatest, while that produced in the tissues underneath the skin is small, is slowly evolved, and is dissipated quickly throughout the body. The experiments Turrell brought forward in support of his view merely showed an increase of the surface temperature of the limb to which the electrodes were applied, and that could quite easily be caused by dilatation of the cutaneous vessels. He admitted further that the more powerful heat-producing action of the diathermy current was not nearly so good as the ordinary galvanic current. His attempt to explain this obvious difficulty is not convincing.

It has to be admitted that the passage of an electric current through the tissues will have a general stimulating effect on them which may be of some benefit. But to me it seems clear that it is the action of the current at the poles which is the chief factor in the relief of pain. In every case treated in this way there is some irritation of the skin under the pads, which is evident from the sensations of the patient and from the marked hyperaemia of the skin seen when the pads are removed. This irritation is produced partly by the electrolysis of the substances in the solution employed to moisten the pads and partly by the stimulating action of the current on the skin, and it is sometimes sufficient to cause a tender part of the skin to remain red for several days. Nor is it necessary to use very large currents to produce this irritation. For, while the amount of irritation varies directly as the current, it varies indirectly as the size of the electrode. It is possible, therefore, to get a considerable amount of irritation even with small currents, if small electrodes be used. Here, then, is the ordinary counter-irritant action. It is difficult to account for the manner in which counter-irritants produce their beneficial effect, but that they do relieve deep-seated pain, at any rate temporarily, is undeniable. It seems to me therefore that, while it is possible that the interpolar current has some general stimulating effect on the tissues underneath the skin, the great factor in producing temporary relief of pain is the counter-irritant action on the skin underneath the electrodes.

So far only the medical aspect of ionization has been discussed. As far as its surgical application is concerned, those who practise this method in the treatment of many different varieties of septic sinuses, lupus nodules, and septic diseases

of the vagina and uterus, claim that the results obtained are excellent. I have had no practical experience of its use in these conditions, and can therefore offer no opinion as to its therapeutical efficacy. But, as far as the theory is concerned, attention may be drawn to the following facts. Zinc is the ion which is used in practically all cases. A number of electrotherapeutists use simply a zinc probe, which is put into a sinus, or a zinc sound, which is passed into the uterus, the metal forming in each case the positive electrode. When a current is passed the metal will have a destructive action on any tissue with which it is in contact. The chlorine ions of the tissues will move to the zinc electrode, give up their electrical charges, and the chlorine atoms thus set free will combine with the zinc of the electrode to form nascent zinc chloride. This substance will produce its well recognized caustic action on the tissues and its antiseptic action against any organisms which are present. But that is not "ionic medication." It is simply a method of producing nascent zinc chloride electrolytically in a place where its action may be of value. That a similar state of affairs exists when the zinc rod is placed in a cavity containing a solution of zinc sulphate is most likely, for here there will be constantly produced, electrolytically, nascent zinc sulphate by the sulphuric ions giving up their electrical charges at the zinc electrodes, and the atoms thus formed combining with it. In addition, the irritation of the tissues under the electrode will cause an increased blood supply to the part, which, in the chronic conditions in which ionization is employed, will be of some benefit. That there is any deep penetration of zinc ions is very doubtful, and it is not desirable in view of the powerful coagulating effect which zinc ions have on the albumin of the tissues. It appears to be entirely unnecessary to invoke the conception of the deep penetration of zinc ions in order to explain the therapeutic results which follow ionization. The combined action of the compounds formed electrolytically at the zinc electrode and the irritation of the tissues is quite sufficient to produce all the effects which have been described.

In conclusion, it will be obvious that, if the argument presented above is accurate there is very little scientific basis for the theory of ionic medication, and—as far as, at any rate, as the medical aspect is concerned—for the practice thereof. To those who strongly support this theory I may appear guilty of an excess of zeal in attempting to undermine their hypothesis. In defence I can only draw their attention to the words of Claude Bernard: "In science the word criticism is not synonymous with the word disparagement; to criticize means to seek the truth by distinguishing what is true from what is false."

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RHEUMATOID ARTHRITIS TREATED WITH INTRAVENOUS BACILLUS COLI VACCINE.

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By rheumatoid arthritis we mean the type of chronic arthritis of infective origin attacking the small and large joints, and characterized by proliferative changes in the ligaments and effusion into the cavity of the joints, and going on to ankylosis. Commonly, this type of case is considered to be of chronic infective origin, the infection arising from some hidden focus in the body, common foci being the teeth, tonsils, alimentary canal, and uro-genital system, the latter being particularly common in women. We wish to draw a distinction between this type of case and the type of osteo-arthritis occurring in old people and characterized by