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, 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."

REFERENCES.

- ¹ Lewis Jones, H.: *Ionic Medication*, 1913. London, Lewis, p. 20.
- ² Turrell, W. J.: *Proc. Roy. Soc. Med.*, 1921, xiv, No. IX, p. 52.
- ³ Lewis Jones, H.: *Ionic Medication*, p. 1.
- ⁴ Leduc, S.: *Electric Ions and their Use in Medicine*, 1908. London, Rebman.
- ⁵ Finzi, N. S.: Some experiments with ionic medication. *Arch. Roent. Ray*, 1912-13, p. 423.
- ⁶ Inohley, O.: *Journ. Pharm. and Exp. Therap.*, 1921, xviii, pp. 241-255.
- ⁷ Friel, A. R.: *Electric Ionization*, 1920. Bristol, Wright, p. 17.
- ⁸ Kendall, E. C.: *Journ. Biolog. Chem.*, 1920, xliii, p. 155.
- ⁹ Thoburn, T. W., and Hanzlik, P. J.: *Journ. Biolog. Chem.*, 1915, xxiii, p. 175.
- ¹⁰ Friel, A. R.: *Electric Ionization*, p. 35.
- ¹¹ Watson, W.: *A Textbook of Physics*, 1899, p. 798.
- ¹² Stockman, R.: *Rheumatism and Arthritis*, 1920. Edinburgh, Green, p. 51.
- ¹³ Turrell, W. J.: *Proc. Roy. Soc. Med.*, 1921, xiv, No. IX, p. 45.

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

osteophytic growths and erosion of the articular surfaces, but showing practically no tendency to ankylosis. In this type the changes are rather of a degenerative nature.

Treatment of rheumatoid arthritis may be classified under three headings—namely: (1) Elimination of the focus of infection; (2) increasing the resistance of the patient to the infection; (3) local treatment to the joint—(a) to prevent deformity; (b) to alleviate pain; (c) to preserve movement of the joint.

Frequently, however, the focus of infection is difficult to locate, and, although routine search was made in all cases under our care, in most no such focus could be found. It is in these cases, in which the preparation of the vaccine from the focus of infection was impossible owing to a definite focus being absent, that the protein shock method by the intravenous use of *B. coli* vaccine was employed. Our search for foci of infection was necessarily limited owing to our patients (all except one) being out-patients during the treatment, except when admitted for the actual injection for twenty-four to forty-eight hours.

The normal defences of the body in the average case of rheumatoid arthritis are low, as is shown by the absence of leucocytosis in most cases, even in those in which a pyogenic coccus can be demonstrated in the focus of infection. The object of the protein shock is to make a sudden call on these defences with the idea of arousing them from their apathy. The *B. coli* vaccine was used owing to its being a form of protein suspension convenient to administer, and the material for its preparation is always easily obtainable. Possibly there may also be a specific action as well in some cases, in that *B. coli* may be the infection of some of those in which no focus of infection could be discovered.

The vaccine was given intravenously in doses varying from 50 to 200 millions for a first dose, the patient being admitted for twenty-four hours, as it was considered that the reaction was too severe for the patient safely to remain an out-patient whilst it was in progress. A certain amount of difficulty was experienced in judging a suitable initial dose. This should be as large as possible, and we found that the general condition of the patient was a much better guide to the initial dose than the condition of the joints.

The reaction usually consisted of a rise of temperature occurring a few hours after the injection, the temperature varying from 100° to 103° F., and frequently accompanied by a rigor. Nausea and vomiting may also occur. The duration of the reaction varies from twelve hours to two days. If any improvement as a result of the treatment is to take place it does so rapidly, and, as a rule, within two days, though in one case (F. S.) there was very little immediate improvement, but this occurred three weeks after the injections. If the reaction is too severe it can be checked by giving min. 5 of 1 in 1,000 adrenaline chloride solution intravenously; but in none of our cases did we find this to be necessary. Those cases with the severe reaction showed the best results.

Case 1.

Mrs. W., aged 43. Attended July 10th, 1922, complaining of swelling and pain of finger-joints of eight years' duration. On inquiry she stated that she had slight vaginal discharge.

Examination showed swelling of wrists and finger-joints, and a good deal of tenderness and limitation of movement. Heart: Mitral regurgitation present, but good compensation. Vagina and cervix uteri: No evidence of discharge found, and no cervicitis.

One hundred million *B. coli* vaccine were given intravenously with moderate reaction. Marked improvement followed; pain disappeared, and the swelling diminished considerably; stiffness was, however, still present.

On July 27th 500 million were given with moderate reaction and good result to joints.

The patient still has slight swellings of the joints, but movement is practically normal and painless.

Case 2.

Doris M., aged 26. Attended June 21st, 1922, complaining of pain and swelling in finger-joints for some time, and recently pains in shoulders and knees.

Examination showed early rheumatoid changes in fingers, with swelling and limitation of movement. No swelling, but slight limitation of movement of right shoulder-joint. No oral, nasal, or other septic foci discovered.

On June 26th she was given 100 million *B. coli*. There was a severe reaction, with marked fever (103° F.) for three to four days, intermissions, pallor, asthenia, and sweating. Within twelve hours of the injection there was distinct improvement of the joint condition. The swelling and pain disappeared, and movements became free. Five weeks later there was some return of symptoms, and the patient was readmitted and given 500 million intravenously, with improvement. The patient has remained well since.

Case 3.

F. S., aged 59. Admitted June 6th, 1922, with extremely marked rheumatoid changes of about five years' duration in all the joints of both upper and lower limbs. There was inability to extend the elbows beyond the right angle, practically no movement in wrists, inability to extend knee-joints above 150 degrees; she was unable to walk, but could stand with difficulty. Patient had previously had treatment at various spas, including vaccine treatment, subcutaneously by vaccines from teeth. The teeth were found to be very septic, and marked pyorrhoea was present, but there were no dental abscesses.

Weight extension was applied to the knee-joints, extraction of all teeth was performed, and three doses, of 500 million, 1,000 million, and 2,000 million respectively, of *B. coli* vaccine were given intravenously at intervals of ten days. The reactions were mild, though after the second dose an additional soft swelling appeared in the metacarpo-phalangeal joint of the right index finger, and persisted a few days before disappearing. Immediate improvement in the joints was practically nil, but since her discharge considerable improvement has occurred, and when last seen (September, 1922) she could walk moderately well with the aid of two sticks, and she was then able to extend both knee-joints. The pain was less but still persisted; subsequently, however, except for slight recurrences during damp weather, this disappeared.

Case 4.

L. G., aged 37. Attended February 2nd, 1922, complaining of pain and stiffness in fingers and wrists. On examination there was found to be considerable swelling of all the small joints of the hands, with marked stiffness. No Heberden's nodes were present. Some pyorrhoea alveolaris was present in the mouth. Dental sepsis was healed by extraction, and a trial made of potassium iodide and guaiacol carbonate by mouth, with little or no improvement.

On March 30th the patient was given 50 million *B. coli* intravenously. The reaction was slight and consisted of two days' pyrexia. The affected joints became less swollen and freely movable. A relapse occurred about six weeks later, and 150 million were given on April 13th and 250 million on April 18th, the latter dose being given because the former failed to produce sufficient reaction. A slight reaction was produced by the second dose and the results to the joints were good. Since then the joints have remained free from pain and stiffness, but slight spindle-shaped swelling of the fingers persists.

Case 5.

A. R., aged 44. Attended May 4th, 1922, complaining of "rheumatism" for two months. Examination showed rheumatoid arthritis in smaller joints of the hands, oral sepsis, and septic tonsils. The teeth and tonsils were treated by extraction and antiseptic paints respectively, and the patient was given a mixture containing potassium iodide and guaiacol carbonate, but no improvement resulted. She was then given 50 million *B. coli* vaccine intravenously, and there was immediate improvement in the affected joints; the swelling subsided and the pain was relieved. Seven weeks later there was some return of the symptoms, and 200 million *B. coli* were given intravenously and improvement again resulted. Since July 6th the patient has not reported to the hospital.

Case 6.

E. B., aged 52. Attended on February 21st, 1922, complaining of pains in wrists and legs for two months. Examination showed swelling of small joints of hands and right knee; some oedema of ankles present. Some dental sepsis present.

The patient was under treatment for five months with local applications and medicine, and dental sepsis was treated. On June 22nd the patient was admitted and was given 100 million *B. coli* vaccine intravenously, with very good results to the joints and a moderate reaction. Since this the patient has reported fortnightly, and now states that she is practically free from pain, and that, whereas prior to treatment she was unable to dress herself, she can now do so.

Conclusions.

The number of cases under review is small, so that it is premature to draw any hard and fast conclusions. However, though we do not claim in any way that this treatment is a final and lasting cure for the condition, to us the treatment does appear to have definite value, especially as an adjuvant to the more recognized methods of treatment. It is also too early to state whether any benefits that may have resulted are permanent.

We consider it to be indicated under the following conditions: (1) Cases in which no definite focus of infection can be located. (2) Cases in which the more recognized methods have failed. (3) Early cases in which the process in the joints is still active, especially if swelling and effusion be present. Case 3 indicated that little can be hoped for when adhesions are present in the joints.

A great difficulty experienced with the treatment was to estimate the dose of vaccine required to produce a beneficial reaction which would not be too severe for the patient. We are of the opinion that we erred on the side of leniency in this respect and that too small doses were given.

In conclusion, we desire to express our indebtedness to Dr. Woodwork for the loan of beds for our cases during the period of reactions.