

Postscript. 29th June 1924. Illustrative Cases.

Case A.—Patient, a mechanic in the R. A. F., attended the electrotherapy room on June 12th, 1922. He stated that for the past six days he had noticed a thick discharge from the penis. He did not seek advice as he thought it would gradually get well. He stated that he had had gonorrhœa eight years before in England. He admitted exposure to infection on June 1st, 1922. A slide examination was made, and proved positive for gonococcus, with large numbers of pus cells in the field. He was immediately put on zinc ionization, the guard and spiral electrode being used. The positive pole having been applied to the urethra, a current of 2 milliamperes was passed for fifteen minutes, then reduced to zero, the poles then reversed and again re-applied for the same period. A slide taken after the third daily treatment was negative for gonococcus. The discharge was thicker and less in quantity. On June 20th the discharge was still present but remained thick. Ionization was continued and during the following week the discharge became thinner and had ceased on June 29th. Prostatic massage and microscopic examination yielded no evidence of the disease. I saw this patient six and nine months afterwards. He had been constantly on full duty. There had been no recurrence and he was extremely pleased with the result.

Case B.—The patient, a British soldier, attended for ionization on September 19th, 1921. He gave a history of exposure to infection on May 7th, 1921. He had previously received irrigation with potassium permanganate but did not respond. He was a youth of good physique and sound constitution. This was his first attack. Microscopic examination confirmed the diagnosis. After the third ionization the discharge became thicker, but on September 30th, had almost entirely disappeared. A slide taken after prostatic massage on October 7th proved negative, as had been the case on September 30th. The patient was sent back to duty and had no recurrence during the following year.

Case C.—Patient A. C., 2 R. A. F., had contracted gonorrhœa three months before, i.e., about October 25th, 1921. Examination revealed profuse purulent discharge, the microscopic findings being positive for gonococcus. On his first attendance he complained of pain in the back, lumbar region, and also in the left knee-joint. Ionization was carried out as before, radiant heat exposures and diathermy being given for his back and knee symptoms. On January 27th, i.e. two days after his first attendance, he stated that his back felt much easier and the pain in his knee-joint was practically gone. Four ionizations were necessary for the urethra. He received one dose of gonococcal vaccine (10 millions) after the first ionization and was discharged cured on February 6th. Subsequent to this it was thought advisable to give him two further doses of gonococcal vaccine at weekly intervals. There was, however, no recurrence of urethral symptoms.

General Observations.

- (1) The complications mentioned above appear to be definite contra-indications for ionization.
- (2) Minute currents $\frac{1}{2}$ to 2 m.a., for not longer than a total (including reversal) of 30 minutes are most suitable.
- (3) Current reversal is essential with this electrode to enable extraction.
- (4) The electrode is simple.
- (5) A standard electrode of this type should enable several workers to compare their results.
- (6) Glancing through the literature of the subject one is struck by the wide difference there is between results claimed by different workers. The cause of this is probably due to the use of different instruments and

different technique. Each advocate plys his own weapon in his own particular way.

NOTES ON THE LOCAL CONCENTRATION OF DRUGS.

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In the spleen and liver only does the blood come into actual contact with the elements of the body, that is cells and fibres of the tissues. In all other situations the lymph is the medium concerned in the nourishment, repair, and delivery to the tissue elements of drugs administered, or substances naturally formed in the body in the presence of disease. When Bier's congestion treatment is applied, say to a tubercular limb, swelling and oedema take place and the diseased tissue elements are flooded not with blood, but with lymph, containing the natural defence anti-tubercular substances. This is a classical example of the local concentration of remedial substances in a selected part of the body, and the object of this article is to suggest means whereby the idea underlying Bier's congestion treatment may be further extended, for, if a specific drug could be introduced instead of the rather feeble natural tubercular anti-bodies, and the same local concentration method employed, it would be reasonable to expect a more rapid progress towards cure.

A drug circulating in the body is diluted by both blood and lymph. The amount of blood is about $1\frac{1}{15}$ th of the body weight, but the amount of lymph is an unknown figure. It may be presumed however, that at any one time the quantities of blood and lymph present bear a certain definite ratio to one another, and hence for practical purposes the term "dilution index" is proposed, the figure of which, while really being the proportion of drug to blood only, will act as a convenient index of the proportion of the drug to all the body fluids. Thus a man weighing 150 lbs. possesses 10 lbs. of blood and the dilution index of 10 grs. of quinine injected intravenously will be $1\frac{1}{9000}$ approximately. While this is actually the degree of dilution of the drug in the blood, it serves at the same time as an index of the dilution of the quinine in all the body fluids. The majority of diseases, local or general, due to organisms, are treated by drugs introduced by the mouth, hypodermically, or intravenously. In each case the drug enters the general circulation and, greatly diluted, is expected to produce its effect. Many substances, if administered in doses large enough to produce a high degree of concentration in the general circulation, will destroy disease organisms, but such concentration would in most cases prove fatal to the patient.

Much research therefore has been carried out in the direction of producing complex drugs such as salvarsan, and here for example we are able to introduce into the body a large and otherwise poisonous dose of arsenic. In other words we have increased the concentration of arsenic circulating in the body fluids to a degree which is lethal to the disease, but not to the patient. It will be observed that the effort has been directed towards obtaining a drug which will act when pervading all the fluids of the body, and the question naturally arises "is it necessary in the treatment of a local disease to dilute our remedy with all the fluids of the body;—cannot the remedy be concentrated (for a time at least) at the diseased spot?"

The only remedy for most cases of Madura foot is amputation, and six cases offered an opportunity to test the idea, which shortly explained is that "the drug is injected into an artery and the circulation is at once dammed by a tourniquet." All the cases were Arab Mahomedans who most strongly objected to amputation, and were more than willing to submit to any procedure which might save their limbs.

The fluid injected into the artery—unless a colloid preparation or an anti-serum—must conform to certain conditions:—

1. It must be neutral or alkaline.
2. It must not coagulate the blood.
3. It must not cause pain.

A suitable stock solution is distilled water containing 0.5 per cent. novocaine and 0.5 per cent. citrate of soda. The novocaine is not always necessary as all drugs do not cause pain when injected into an artery (*vide infra*). The drug selected for administration is dissolved in 10 c.c. of the above fluid which, if now acid, is neutralised by the addition of a few drops of sodium bicarbonate solution in distilled water. Colloid preparations and anti-sera may be injected without alteration or additions.

With appropriate modifications the following technique, which was used in the cases of Madura foot, can be adopted for other diseases in other parts of the body. Asepsis is taken for granted.

1. Prepare and place in readiness a few ounces each of the following solutions:—

- (a) 0.5 per cent. novocaine in normal saline.
- (b) 0.5 per cent. citrate of soda.
- (c) Normal saline solution.
- (d) Stock solution as above.

2. Add the selected drug to 10 c.c. of the stock solution already described. Draw this into a 10 c.c. syringe, attach a very fine and sharp needle, and place in readiness on a towel.

3. Throw a rubber tourniquet loosely round the leg about six inches above the ankle.

4. Select the artery for injection. For Madura foot cases the posterior tibial opposite to or just above the ankle is the most convenient, as the anterior tibial is often surprisingly difficult to find.

5. Infiltrate the line of the proposed incision with 0.5 per cent. novocaine solution superficially and deeply, producing an anaesthetic area at least 1½ inches broad.

6. After ten minutes expose the artery and sheath, but do not open the latter at this stage. Infiltrate around the artery with the novocaine solution.

7. Double a long piece of tape, and—avoiding the companion nerve—pass the doubled loop under the sheath of the artery.

8. Cut the loop, and of the two slings thus formed give the distal to an assistant and grasp the proximal yourself.

9. Pull on the slings and the vessel will come up into the wound. At a point between the two slings expose the artery wall through a very small opening in the sheath, and flood the wound and artery wall with 0.5 per cent. sodium citrate solution.

10. Thrust the needle of the charged syringe into the lumen of the vessel at a very acute angle (so as to make a valvular opening). Release the proximal sling slightly, and if the puncture is successful blood will appear in the syringe. When this is observed tighten the proximal sling and relax the distal. Make the injection quickly, and as the last drops leave the syringe a second assistant tightens the tourniquet just above the wound.

11. Leaving the needle *in situ* disconnect the syringe and fill it with normal saline. Reattach to the needle and inject a little saline so as to wash out its bore.

12. Withdraw the needle, coil up the tapes and place them in the wound. Wash the sodium citrate out of the wound by normal saline solution, and if bleeding occurs apply pressure.

13. Dress the wound with B. I. P. P., keeping the skin edges as far apart as possible.

14. Remove the tourniquet from half to one hour later.

At second and subsequent injections, after infiltrating with novocaine solution the tapes are simply pulled upon as above described and the injection performed in exactly the same manner. Several points concerning these procedures will be discussed in connection with the results obtained, after description of the actual cases so treated.

Case No. 1.—Madura disease of many years standing, sinuses involving the whole foot from heel to toes.

Copper sulphate was injected as follows:— $\frac{1}{2}$ gr., $\frac{1}{2}$ gr., $\frac{1}{2}$ gr., $\frac{1}{2}$ gr. in 10 c.c. stock solution at intervals of from four days to a week. After the second injection the bright green colour of the copper began to appear in the sinuses, and this colour deepened as the injections proceeded, showing that a part of the drug at least was being excreted via the blood, lymph, and discharge.

The sinuses became drier but no further improvement took place, and at the request of the patient who wished to return to his distant home, amputation was performed. Section through the amputated foot showed that the green copper colour was pervading all the tissues. This injection caused no pain.

Cases 2 and 3.—In condition these were similar to No. 1. The drug here injected was colloid antimony in doses of from $\frac{1}{2}$ to 3 c.c. administered at intervals as before. After a slight temporary improvement relapse occurred and the drug was given up. It was noted that as soon as the tourniquet was removed acute nausea occurred (checked at once by intramine). This symptom rather tends to show that the colloid did not leave the vessels in any quantity and become deposited in the tissues as with the copper. This injection was painless.

Cases 4, 5 and 6.—It was observed that Madura foot improves under simple saline dressings alone, and my last three cases were treated by injections of sodium chloride. One declined further treatment after two injections which he said were painful, and left hospital. After this the novocaine solution was employed.

In the second case the whole of the sole of the foot was involved, but the bones were unaffected. After six injections administered over a period of three weeks the condition cleared up completely, and as far as the Madura disease was concerned a definite cure could be claimed. Doses of sodium chloride given were 15 gr., 20 gr., 30 gr., 15 gr., 15 gr., 15 gr. Thirty grains appears to be too large a dose, as in this case a small patch of gangrene appeared over the skin on the inner side of the ankle. The last case was an advanced one, all the bones and soft tissues being involved, and no cure in the real sense could possibly be expected. In Madura disease very little natural reaction towards cure takes place. Eight injections of sodium chloride were given,—10 gr. every third day. This dosage is a safe one and I think that 15 gr. should be the maximum for this drug. Under the stimulus of the injections, the foot inflamed and the tissues began to break down. In the end a large abscess formed. On incision this gave vent to a quantity of granules and broken down tissue debris. The abscess cavity was treated with a simple dressing, and soon the whole foot began to assume a healthy aspect. The bony destruction however was found to be too great to give a good weight-bearing (though deformed) foot and amputation was required.

Although the results obtained with sodium chloride are encouraging and suggestive, I wish to make it quite clear that no claim to the discovery of a cure for Madura disease is made. But certain important data have been elicited which require consideration—

1. The degree of local concentration attained and obtainable, and the effect thereof on the artery and tissues.
2. Suitable drugs and dosage.
3. Efficiency of the tourniquet.

Although all the figures given in this article can only, in the nature of things be but roughly approximate to the truth, still a practical mental conception of what is taking place is obtained. Taking the weight of the arm or foot of a man weighing 150 lbs. to be 5 lbs., then ten grains of sodium chloride concentrated locally will give a dilution index of 1|160 as compared with one of 1|9000 when the same dose is injected intravenously. Half a grain of copper sulphate in local concentration gives a dilution index of 1|3200. These are high degrees of concentration, and in neither case did any harm result to the tissues or arteries. Thrombosis did not take place, for in each of the Madura foot cases at the end of the courses of injections the vessels beyond the site of punctures were found to pulsate as freely as ever. Barrett in the *British Medical Journal* of 5th April, 1924, states that injuries to veins are not followed by thrombosis if sepsis is absent. This is in accordance with my findings with regard to arteries. It is true that a small patch of gangrene did occur in one case, but this I think was due to blocking of a small branch where the circulation is naturally poor after an injection of too large a dose of sodium chloride, —(gr. 30, representing a dilution index of 1|50).

Specific anti-sera would appear to be specially suitable for this form of treatment, for it is difficult to imagine that any harm would result from the administration of doses as large as those which can be given hypodermically or intravenously. Colloid preparations ought to be useful as large quantities can safely be given, and a correspondingly low dilution index obtained. It is possible, however, that these may not act so well as the simpler drugs for reasons indicated in the description of the cases treated with colloid antimony. Much further research is necessary to determine which class of drug—colloid or otherwise—is most suitable for this form of medication, and it is hardly possible at this stage to lay down rules for dosage or spacing of the injections. At present each drug would have to be considered separately, although the cases treated with copper sulphate and sodium chloride give one something to go upon. A few remarks, however, may be made regarding iodine, as I have frequently given over gr. 1 in the form of the tincture (in 40 to 60) intravenously without the slightest ill effect. Such an amount concentrated locally in the 5 lb. limb would give a dilution index of 1|1600. This is probably excessive as 1|50000 will kill *B. coli* in 2½ minutes. It is suggested therefore that the initial dose given in watery solution via the arteries should not exceed 1|10th gr. (dilution index 1|14000). If, however, the colloid form of iodine is used a much larger dose may be injected.

Efficacy of the Tourniquet.—In a two bone limb the tourniquet does not dam the circulation completely, but it does so sufficiently to produce

the desired effect. The result of the copper injections affords clear proof of this, and moreover a tourniquet applied above the ankle produces distinct oedema of the foot. By suitable padding between the bones the damming can be made still more effective.

Lack of cases put a stop to investigations, and as one of those unfortunates who is fast in the grip of the Moloch of military employment I have had no opportunities at present to test further my ideas. Time passes, and incomplete as my results are, I feel it my duty to give others, who are in the position to do so, a chance to follow up the facts elicited, for I feel convinced that the local concentration of drugs, within its limitations, will prove a practical and useful method of dealing with certain diseases. A few conditions where the treatment might be useful, with suggestions as to drugs and technique will now be given.

1. Tubercular disease of the bones and joints of the extremities.

(a) Ankle. As for Madura disease; if the ankle joint, the anterior tibial artery should be used.

(b) Hand and wrist. Using either the brachial artery at the bend of the elbow or the ulnar above the wrist. The tourniquet may be applied above the elbow and one obtains very perfect local concentration.

Drugs suggested:—sodium morrhuate—(which will presumably destroy the fatty envelope), and iodine the next day, with the idea of killing the now unprotected bacillus.

2. Acute septic conditions of the extremities.

(a) Sepsis of the hand involving the tendons;—as for tubercle. Drugs;—anti-sera in large quantities (to neutralise the toxins), combined with iodine, eusol, or flavine (to destroy organisms).

(b) Acute septic arthritis of the knee-joint, where the only alternative is amputation. Here the femoral artery may be exposed and the same drugs employed as for septic hand, but of course in much larger doses.

3. Meningeal diseases.

Tubercular, pneumococcal and septic meningitis are fatal diseases and a new method of treatment is worth a trial. They are therefore considered in some detail.

It is possible to produce considerable congestion of the head by means of mild compression of the neck by a soft muffler. The surgeon should obtain an idea of how much is required by experimenting on himself. It falls far short of impeding respiration in the least. The ideal method for obtaining local concentration in the meninges would be to inject the external carotid artery and obstruct the veins of the neck. This is hardly practical surgery, however, and an alternative method may be employed.

Suggested Technique.

1. Place a rubber tourniquet loosely round the head just above the ears, and throw a muffler or soft hand towel round the neck.

2. Expose the superficial temporal artery near the zygoma and inject the selected remedy.

3. Tighten the tourniquet and muffler.

4. To obtain *vis a tergo* at the point where the artery passes under the tourniquet, raise the latter off the skull for a couple of pulse beats by means of a small hook.

5. With the flat of the hands knead the scalp firmly, and keep up the constriction as long as it is thought the patient can stand it. The rationale of this method depends on the fact that there is free communication between the scalp and meningeal veins through the veins of the diploe.

Drugs suggested are the specific anti-sera and iodine, sodium morrhuate, eusol, flavine and urotropine in conjunction with the necessary surgical procedures such as opening up a mastoid. Only a partial local concentration can be obtained here, and as such cases are desperate, daily injections would probably be necessary.

Other appropriate conditions will readily suggest themselves. In conclusion I wish to express my sincere thanks to Messrs. Chabukswar and Bhungara of the Indian Medical Department for their able and enthusiastic assistance.

FOUR CASES OF SPOTTED FEVER AT NAGPUR.

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ABOUT four years ago, three cases more or less similar to the ones I am about to describe, were reported by Colonel Chapman, then Civil Surgeon of Nagpur, to Colonel Megaw, I.M.S., Director, School of Tropical Medicine, Calcutta, who is particularly interested in this type of disease, the exact causation of which has hitherto not yet been arrived at, although for clinical purposes it comes under the typhus or typhus-like group of fevers.

The temperature charts of my four cases were as shewn.

Case 1.—Mr. T. P. D., Anglo-Indian, aged 42 years, an engine driver, residing in railway quarters built on a big plain 3 miles from Nagpur.

On the 4th July, 1923, he returned from work with a severe headache, to which he is often subject, and took a powder of caffeine and aspirin.

The subsequent temperature chart is as shewn. The course of the disease was marked by marked constipation and insomnia, the latter often of a severe charac-