THE PRESENT-DAY TREND OF TREATMENT OF GONORRHŒA, WITH SPECIAL REFERENCE TO CATAPHORETIC APPLICATION OF COLLOID SILVER.

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After the discovery of the causative organism of gonorrhoea drugs were applied to the urethral mucous membrane with the intention of killing the organisms with which they come in contact. Later, when it was realized that no antiseptic could reach the organisms which are buried in crypts and follicles and are beneath the surface epithelium, lavage with weak antiseptics became the routine procedure. But as this treatment meant merely waiting until the patient cured himself, various methods of attack have been devised within the last fifteen years. A number of metal instruments have been added to our armamentarium, some of them are of value in diagnosis and others are of use in destroying the local foci of disease which delay cure.

At the beginning of the present year, the staff of the Military Hospital, Rochester Row, came to the conclusion that two lines of investigation might be tried: (1) to try to bring antiseptics into contact with the gonococcus through the blood-stream, and (2) to drive antiseptics into the deeper foci beneath the surface layers of urethral epithelium.

Lieutenant-Colonel T. E. Harty, D.S.O., R.A.M.C.(R), had carried out a series of intravenous injections of acriflavine at the Military Hospital, Portobello, Dublin, in October, 1921. In the fifty-five cases treated, he

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reduced the stay in hospital to 37.1 days. He noted that those cases which reacted to treatment did so early, while others continued to show gonococci for one month after beginning the treatment. The number of days under treatment before the disappearance of gonococci was thirteen. The method employed was intravenous injection of 0.2 grammes of acriflavine dissolved in 200 cubic centimetres of physiological salt solution. This dose was increased to 0.3 grammes in 300 cubic centimetres saline solution on the fifth day and repeated on the tenth day. During this course the urine was kept alkaline.

In October, 1922, a similar series of cases was given this form of treatment at the Royal Herbert Hospital, Woolwich. The average time in hospital for eighty-six men was 59.71 days. As the colour of the skin of the men became a lemon yellow as soon as the injection was within the veins, it was thought that the coloration of the skin and rapidity of elimination might be prevented if the drug could be given into the muscles or under the skin. The first attempts were not successful owing to the bulk of the injection used, 0.3 grammes in 100 cubic centimetres, and the inflammatory reaction which followed. Moreover, it was found during tests for toxicity on rabbits, that the animals died from acid intoxication when given a lethal dose of acriflavine. Numerous experiments were then undertaken to solve the problem of the removal of the acid in the preparation, which equals 3.5 cubic centimetres of normal hydrochloric acid for every gramme of the acriflavine, and to make the injection under the skin small in bulk and painless. This was done by adding 3.5 cubic centimetres of normal sodium bicarbonate to one gramme of acriflavine and diluting with distilled water up to twenty cubic centimetres to bring down the content of sodium chloride to one per cent. Two to seven cubic centimetres of this solution may be injected under the skin, just over the muscle fascia, with no great pain resulting. Two sites have been used for the injection, one between the shoulder-blades, the other behind the great trochanter of the femur. Three doses have been given as a course with a five-day interval. The investigations are still being continued. The figures accumulated up to date are of little value owing to their small numbers, but indicate a stay of 39.1 days in hospital. In chronic gonorrhoea some most successful cases have been met with. To quote one case as an example. A soldier was transferred from another station with a history for one year of a urethral discharge, containing gonococci; three deep subcutaneous injections cured the disease and he has been free from recurrence for the past six months.

One difficulty remains unsolved. This neutral solution does not keep well; it must be prepared freshly at least once a week, otherwise it becomes irritating to the tissues.

Up to the present acriflavine is the best of the dye products as a bactericide. This field of research is only opened and further results may be expected from the discovery of new dyes in the future.
Since the month of May, 1923, a new method directed against the gonococcus has been in operation at the Military Hospital, Rochester Row, and continued at the Royal Herbert Hospital, Woolwich, since the closure of the former hospital in July. The origin of the work was the production by electrical methods of a pure silver colloid, which is stable in distilled water, by Major S. H. Long, D.Sc. This colloid was first used at the Indian Station Hospital, Karachi, on cases of gonorrhoea. A silver catheter with multiple perforations was introduced into the urethra and attached to the positive pole of the electric supply. The catheter was filled with the colloid and a small current of electricity was sent through the urethra— that is, the method was assumed to be ionization. The findings were so promising that the matter was referred to the Military Hospital, Rochester Row, for further investigation. Examined chemically, the colloid was found to have no added protective; the particles were of small dimensions; it was not precipitated by 0.5 per cent sodium chloride in three days, and one per cent sodium chloride took three hours to destroy completely the colloid. Electrically, as the medium is a non-conductor, it was found that the colloid particles moved from the negative pole towards the positive pole. Bacteriological experiments, using a culture of staphylococci isolated from the urethra, showed that 1,000 million organisms were destroyed in twenty minutes, and that 300 million were killed in 2½ minutes by the undiluted colloid.

During the above chemical investigations, a week's trial was given of the ionic method of using the colloid, but the method had to be abandoned owing to the pain and discomfort of the catheter within the acutely inflamed urethra. It was then decided to try the effect of using the colloid cataphoretically, that is, applying electric pressure and not electric current through a column of the silver colloid within the urethra.

It is to be noted that the colloid consists of electro-negative particles which move distinctly towards the positive pole when subjected to an electric pressure, as shown by microscopical and electrical tests. Therefore, this method tends to drive the colloidal particles into the urethral mucous membrane when a column of the silver suspension is acted on by a pressure of sixty volts or over direct current through the negative pole, with the positive pole attached to a perineal pad. Sixty volts direct current is the minimum pressure which will set the colloidal particles moving towards the opposite pole.

After some experimental work on details, the following method of carrying out the treatment was adopted:—

A room is wired for the treatment of ten patients from a 106-volt direct current supply. Ten electrical points are distributed round the walls of the room, each with a plug and switch connected in parallel, through a switchboard, with the source of electrical supply. Two wires from the wall plug bring the electrical energy to the patient. One wire is positive, the other is negative, and each wire is marked, after test, with its polarity.
The positive connexion is attached to a wire gauze pad which is wrapped in several folds of washed lint, and on this the patient sits. From the pad an extension is brought forward to enclose the shaft of the penis. The pad is wetted with saline solution. The negative wire is attached to a one-inch length of silver tubing which is inserted into the lower part of the rubber tubing of an irrigation apparatus consisting of a 300-cubic-centimetre funnel and five feet of rubber tubing with a glass urethral nozzle attached. A piece of silver wire is soldered to the inside of the silver tube and extends down to the glass nozzle.

The patient sits on a chair and on the positive pad. The funnel, suspended on a stand, or by a wire beside him, is filled with colloid silver, air is expelled, and the bladder and urethra are filled with the colloid by pressing the nozzle firmly into the urethral meatus.

With the sliding resistance on the switchboard at zero—usually marked "weak"—on the board, the current is switched on. Next the switch at the point on the wall for the patient is put on and the sliding resistance moved towards "strong" until all resistance has been cut out. If ten cases are to be treated, this is not usually done till all the cases are ready. There is practically no rise in current—even with ten patients the milliametre does not register more than one milliampere, but the pressure shown is 106 volts. In order to prevent burning of the patient due to excess of current which might be caused by an accidental short circuit one wireless receiving valve has been introduced into the circuit in series with the supply voltage on the patient's side of the switchboard. This valve acts as an automatic cut-out. Even on a dead short circuit the valve will prevent a current of more than eight milliamperes from passing through the patient, which is harmless even at the high voltage used. So that the use of this high voltage for medical purposes is feasible and can be manipulated by anyone without electrical knowledge once the circuit is installed by following a few simple directions.

The routine followed for treatment is that the patient has a dose of 20 million gonococci injected subcutaneously, and his urethra is washed out with lime-water to remove mucus, and then with distilled water to remove electrolyte. The patient then sits on the chair, fills his bladder and urethra as mentioned, and the voltage is applied for three-quarters of an hour to one hour. If during the treatment the amount of fluid in his bladder is causing discomfort, or if the amount of urine secreted into the bladder is sufficient to act as a conductor, the bladder is emptied and again filled with colloid. This treatment is repeated daily for four days until the patient's urethra is dry and free from discharge. He then goes through a test for cure, and is discharged from hospital when no signs of recurrence is brought out by the test.

If it happens that the urine is not clear at the end of the first set of four applications of silver colloid, the patient receives a second injection of antigonococcal vaccine, and has a Kollman's dilator passed, and
immediately after it he is again treated cataphoretically. It has been found that those cases which require further treatment have a number of closed follicles in the urethra, as seen by the urethroscope, and when these are opened, that the cure could be completed by one or two further applications of the silver colloid.

The test of cure consists of a complete examination of the urethra after irrigation with magnesium chloride 1 in 500 solution twice a day for two days, preceded by a 100 to 200-million injection of gonococcal vaccine.

The examination consists of the introduction of a sound, followed by inspection of the urethral mucous membrane by means of the urethroscope; prostatic and vesicular massage with microscopic examination of any secretion expressed from them. The urine must be free from pus, and no pus must be present in the urethra.

As this treatment can only deal with urethral infection, it has been decided that if a preliminary examination of the prostate gland or the vesicles shows that the disease has reached them, or signs of any metastatic disease due to gonorrhoea are found, a deep subcutaneous injection of two or three cubic centimetres of a 1 in 20 solution of acriflavine is given at intervals of from three to five days. The sites chosen for injection are over the deep fascia behind the great trochanter.

The number of cases which have been subjected to the combined treatment are too few for the estimation of its value. The difficulty experienced is in getting into the blood and urine a sufficient concentration of acriflavine to be within the bacterial lethal dose. Tests of some serum and urine show that with a subcutaneous injection of 0·1 gramme the urine concentration was about 1 in 50,000, and in the serum the dilution is ten times greater, which suggests that definite results will be obtained with higher doses; it was also found that the acriflavine concentration was negligible on the third day, it had been so rapidly excreted.

During the test of the electrical colloid treatment daily examinations of microscopic slides have been carried out. Two points looked for are: (1) the presence or absence of gonococci and their number per field; and (2) the proportion of epithelial cells to pus cells present in the discharge. The first gives a rough estimate of the acuteness of the infection, while the second gives an indication of the stage of the disease. If daily microscopic slides are taken of a case of gonorrhoea from the beginning of treatment, it is found that the findings as regards both points can be plotted and the curves run practically parallel. Examination of microscopic slides even when made only twice a week, can thus be used, as a quite reliable indication of the urethral condition and the progress of the case towards recovery. In chronic cases where the finding of gonococci is difficult, the cell ratio gives the clue the patient's progress, and directs the treatment. To obtain comparable results, it is, of course, necessary to take the smears in the same way, and for quickness and reliable counting of the cells the pus should be spread like a blood film for malaria examination or a
differential count. The results of the electrical treatment of 107 cases give the following figures:

- Total number of cases treated and discharged hospital as cured: 107
- Average number of days under electrical treatment: 9
- In hospital under observation after treatment: 28·9
- In hospital, at two large venereal hospitals, in the year 1922: 13
- In hospital, at two large venereal hospitals, in the year 1922: 69·2

It appears to the officers working this method of attack on gonorrhoea that it is more than an experiment, and that it opens up a field of work which promises success when the method is perfected. At present there is further work to be done as to the most efficient voltage required to get the quickest cure. Also, only one non-conducting colloid has been tried, others may give better results, or this colloid may be improved. The object of this paper is to indicate the work done in the hope that others may try the methods described, and that we may arrive by co-operation at the scientific facts on which to base the medical control of gonorrhoea, at which point we have not yet arrived.