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1,200,000 units over a course of 10 days. On dark-ground examination the spirochaetes were found to have disappeared from the sore within 12 hours. The initial cleansing of the chancre was likewise dramatic; it became a sterile ulcer at the end of 12 hours. Healing was very slow indeed and the chancre did not finally disappear until about 3 weeks later. It is now 5½ months since that case was treated. The Wassermann was negative 32 days after the completion of treatment, the Kahn was negative a few days later and the cerebrospinal fluid was normal both before and after treatment.

Neurosyphilis.—The other case of syphilis which was treated was one of advanced tabs dorsalis and the patient had a perforating ulcer of the foot. He was given intrathecally increasing doses of penicillin, by means of repeated lumbar punctures, during 10 consecutive days. An initial concentration of 500 units per cubic centimetre was given and when 2,000 units per cubic centimetre had been administered he could not take any more. That concentration seems to be toxic to the theca, as a few meningeal reactions developed; there was an increase in the amount of protein and of the number of cells. The perforating ulcer of the foot was connected with a small sinus which was suppurating. Penicillin was introduced into the sinus after all other treatment had failed. The penicillin treatment was successful in getting rid of the pus and the foot is now completely healed.

Interpretation of results

The question remains as to whether we have here for the first time a drug which is effective in both syphilis and gonorrhoea. If penicillin only masks the symptoms of syphilis and fails to eradicate the disease, we may be faced with a new problem. For example, a patient suffering from both gonorrhoea and syphilis, contracted at the same time, might quite conceivably not be recognized as suffering from syphilis, owing to the action of penicillin in masking the disease.

Another feature worth mentioning concerns the treatment of failures. Although patients sometimes failed to respond to a moderate dose of penicillin, when a second course of a similar dosage was given they generally got well; further, in cases of gonorrhoea, if failure was experienced after the first dose and the patients had already been found to be sulphonamide-resistant, if they were subsequently treated with sulphanamides they appeared to get well. It would not do to be too definite, but it is felt that gonorrhoea can always be cured by the use of penicillin; with regard to syphilis, however, it remains to be seen whether or not such an optimistic verdict can be pronounced.

Discussion on the Preceding Papers

Brig. Osmond (the President), said that it had been very interesting to hear these two addresses, because it seemed as though penicillin were going to solve a great many of the problems of venereal disease. At any rate, it was encouraging to know that the gonococcus was one of the most sensitive organisms. As regards the dosage in gonorrhoea cases, from the small experience he had had, he had gathered that about 20,000 units every 2 or 3 hours up to a total of 100,000 gave the best results. Syphilis was curable and so, he was told, were granuloma inguinale and chancreoid.

One of the problems which would have to be solved by the experts was to find some means of delaying the excretion of the penicillin. He had heard of a case in which penicillin was given intentionally at a time when the patient’s kidneys were not working too well. In that case a comparatively small dose worked just as well as—or better than—a large dose was expected to do. It was just one case but was rather significant.

With regard to penicillin-fastness, he hoped that the medical profession would not have the same experience as they had had with the sulphonamides, and that everybody would use penicillin in adequate doses. If penicillin-fast cases were to occur, it would be the result of under-dosage. The statement that sulphonamide-resistant cases which were afterwards treated with penicillin appeared to react better than did cases treated with penicillin from the outset was interesting, because the surgeons had found that penicillin plus sulphonamide used locally in wounds was far more effective than either of the two alone.

The other point he would like to emphasize was the fact that penicillin given by intramuscular or subcutaneous injection did not get into the cerebrospinal fluid in anything like the same amount as into the blood. That might be very important in treating meningo-vascular syphilis. He had
seen a number of cases of early syphilis treated in America and could confirm what had already been said about this work; but he thought that venereologists ought to be very chary of expecting much in the way of results from the use of penicillin in conditions like tabes and general paralysis of the insane. After all, when there was destruction of nerve tissue it could not be expected that penicillin would cause new nerves to form.

Gp. capt. McElligott said that his experience had been very much the same as that of Sir Alexander Fleming, but that in the interests of economy smaller doses had been used in many cases. Still, of the comparatively small number of cases that had been treated, an apparent success rate of 80 per cent had been achieved with dosages of 60,000 and 80,000 units; this had improved to over 90 per cent with the use of 120,000 units. Even among the failures many were apparently cured by further sulphonamide treatment or by irrigations. He must add that he had begun to feel a little shaken after reading a recent article by Koch, Mathis and Geiger. (See page 174.) These workers had shown that 30 per cent of a large number of cases of gonorrhoea, apparently successfully treated with sulphathiazole, remained culturally positive up to a period of three months, and that 5 per cent were found to be positive after that time.

Dr. D. Nabarro said that he regarded Sir Alexander Fleming as a benefactor to mankind; he discovered the action of penicillin in 1928, and showed his original culture plate at a meeting of the Pathological Society. Recently penicillin had been taken up and more thoroughly investigated by the Oxford pathologists and it had been shown to be a drug with marvellous properties. It was useful not only in syphilis and gonorrhoea but in many other diseases and it excelled even the sulphonamides in its potency. Dr. Nabarro had known Sir Alexander Fleming for nearly 40 years; he had been one of a group of able and keen disciples of Sir Almroth Wright. As one of those present probably knew, Fleming many years ago devised a modification of the Wassermann test, in which he utilized the haemolsyn normally present in most samples of human blood. He also used arsphenamine in its very early days. Dr. Nabarro was glad to have this opportunity of congratulating Prof. Fleming on his work, and members of the Society would be pleased to learn that he had been honoured recently by the bestowal of two Fellowships—those of the Royal Society and of the Royal College of Physicians. It was his innate modesty which had kept him in the background for so long, but it at last his work had become appreciated; it was destined for more appreciation as time went on. When for years one had been treating syphilis and vulvovaginitis in children—a slow and laborious task—and then suddenly saw penicillin appear, with its wonderful power and potentialities, one could only say that miracles had not yet ceased on this planet.

Dr. A. H. Harkness stated that he had treated 3 cases of sulphonamide-resistant gonorrhoea successfully with penicillin; one was treated with 80,000 units of the sodium salt in 5 intramuscular injections given 4-hourly, and 2 cases (in which there had been premedication with sulphathiazole) with 48,000 units, when the injections were given 3-hourly. He, too, had observed the giant forms of gonococci in one case 3 hours after the first injection, but smears also showed organisms normal in size which were successfully cultured; no giant colonies appeared. In not any cases were gonococci detected in smears or cultures after the second injection and in all cases the discharge increased after the first injection and did not disappear entirely until 48 hours after the completion of treatment.

Dr. Harkness had also treated one sulphamone-resistant case locally with 100,000 units of an impure calcium salt. After micturition had occurred the anterior urethra was washed out with more sterile water and then distended with part of a solution containing 30,000 units in 20 cubic centimetres of sterile distilled water, the fluid being retained in the urethra by compression of the external urinary meatus. These injections were repeated at half-hourly intervals, on two occasions the fluid being milked into the posterior urethra. Treatment was continued on these lines with a further solution containing 70,000 units in 20 cubic centimetres. In all the treatment lasted 5½ hours. There was neither pain nor discomfort during treatment but 5 hours later there was marked swelling of the penis with pain during micturition. When the patient was seen 22 hours after the completion of treatment, the swelling had entirely disappeared and the pain on micturition had lessened; there was a slight muco-purulent discharge and smears showed giant gonococci, many of the organisms being in chain formation; cultures were sterile. Urethroscopy revealed scattered areas of lymph on the mucous membrane of the anterior urethra, and the prostate, vesiculae seminales and Cowper’s glands did not show any signs of inflammation. The pain on micturition may have been mechanical in origin and due to the 5½ hours’ continuous distension of the anterior urethra, or it may have been due to the drug or to its impurities. If any more of the substance became available, the experiment would be repeated with smaller dosage and the duration of treatment would be lessened.

These giant forms of organisms might be a clue to the mode of action of penicillin. They were first observed in cultures by Gardner in organisms both sensitive and insensitive to penicillin (when the dilution of penicillin was insufficient to inhibit growth completely) and Dr. Harkness had not until that day known them to be reported in the examination of smears taken from a patient during treatment.

More than two months had elapsed since the one patient was treated locally and the urine remained clear without any threads. A further patient, who was resistant to sulphonamide therapy, had been treated successfully on similar lines with 50,000 units in 25 cubic centimetres of...
sterile distilled water over a period of 24 hours and in that case the solution was not milked into the posterior urethra. Not any urinary symptoms ensued.

Lt.-col. Campbell said that the local application of penicillin had been mentioned. He had had experience of 2 outstanding cases, both very unusual, of ophthalmia in adults. One was the case of a soldier who had been evacuated with an acute ophthalmia; he was sent to an ophthalmologist who employed penicillin locally. The immediate result was excellent, but the speaker did not know the details of the case. The second case was one he had seen himself. This was a case of gonorrhoea which was undergoing treatment. The patient had received sulphonamide treatment of various kinds and had not reacted at all. He had infected his own eye and the results were dramatic—the worst the speaker had ever seen. The doctors in charge of the case despaired of saving the eye; but again, with the use of penicillin locally for about 4 days—the treatment almost amounting to continuous drip—the eye was saved and the sight was restored except for very slight nebulae at one corner.

Dr. Shanson asked whether penicillin had been tried out in cases of congenital syphilis.

Dr. Nabarro said that he had heard that day of a case at the Hospital for Sick Children, Great Ormond Street, in which treatment had been started only the previous day, but he regretted that he could not give details. It was the first case of which he had heard.

Captain Bowditch said that she had had experience of the treatment of 2 cases of syphilis with penicillin. Both cases had all the manifestations of secondary syphilis and a positive Wassermann reaction. Eight days' treatment at 3-hourly intervals was given. She could not state the dosage, but the lesions quickly cleared up. She did not know how soon the blood tests became negative, but she believed it was within a 40-day period.

Sir Alexander Fleming, in summing up and replying to the discussion, said that there was very little to which he had to reply. Most of the questions asked had been already answered. As to the dosage of penicillin, one worker in the Mayo Clinic cured staphylococcal septicemia with smaller doses than those commonly used—continuous intravenous drip with 40,000 units a day, which was less than half the ordinary dosage. This worker stated that he could not discover any penicillin in the blood. It must have been there, but it would have been in such small quantities that the tests which were employed did not reveal it.

There seemed to be no real reason why the sulphonamides should not be combined with penicillin. They certainly worked in different ways, and a case might very well be cured with much smaller amounts of penicillin if this were done.

Attention had been drawn to the curious forms of bacteria which were found after contact with penicillin. They did take most extraordinary forms when grown in the presence of minute amounts of penicillin. This phenomenon was not peculiar to penicillin and the same change in the appearance of the micro-organism took place after exposure to various other antiseptics.

The question of fastness was very important. It was quite easy to make organisms penicillin-fast. He had not tried to do this with the gonococcus, but he had not the slightest doubt that the principle held good with that organism also. With other organisms there was not the slightest difficulty in making them penicillin-fast in the laboratory. Some workers had reported making them fast in the body, but this he had not seen. He remembered one woman who had large ulcers, not venereal, in which staphylococcus was demonstrable, and who was treated for a long period with local applications of penicillin. The staphylococcus persisted in certain parts, but these staphylococci at the end of treatment were just as sensitive as at the beginning, and when she was given systemic treatment by injection the whole infection cleared up.

One of the great advantages of penicillin was that it was non-toxic, so that when it became available in larger quantity doctors would not be frightened of using large doses. The question of the development of fast organisms through insufficient dosage should not, therefore, arise.

Dr. J. Suchet, also in reply, said that there was nothing in the literature as yet concerning the treatment of congenital syphilis by means of penicillin. The real trouble was the lack of symptoms or signs whereby one could judge the progress of a particular case and, so far as congenital syphilis went, unless active lesions were present it was very difficult to assess the value of the treatment.
DISCUSSION ON THE PRECEDING PAPERS

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