

# PENICILLIN IN THE TREATMENT OF VENEREAL DISEASE: A YEAR'S EXPERIENCE IN A CIVILIAN CLINIC

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## GONORRHOEA

IN the past twelve months 116 cases of gonococcal infection in men and 26 cases in women and children have been treated with penicillin. Various dosages have been used and every case has been cured, if not by the first course, a further more intensive course has been sufficient.

The greatest cure rate has been given by multiple intramuscular injections of saline solution of penicillin in varying dose at three to four-hourly intervals. Single injections of a dose of 100,000 Oxford units (O.u.) in saline solution and single or multiple injections of 50,000 to 100,000 Oxford units in suspension in beeswax and nut oil have not given such a high rate of cure. The presentation of the penicillin in beeswax-nut oil suspension was designed to delay the rate of absorption (and therefore also the rate of excretion), thus maintaining for a longer time an adequate concentration of penicillin in the blood stream, prolonging its action on the gonococci, and, by so doing, enhancing the prospect of cure.

The ideal method of treatment for out-patients is a single intramuscular injection giving a high rate of cure. So far this ideal has not been attained, but at the moment a single injection of a large dose (200,000 units) in saline solution is being tried to see if this will give a sufficiently high rate of cure to justify its use.

*Gonorrhœa in Men.*—Varying dosages of penicillin, ranging from 15,000 to 200,000 Oxford units, have been given either by single or by multiple intramuscular injection. Multiple (2 to 10) injections either of saline solution or of beeswax suspension, exhibited in 70 cases, yielded a cure rate of 87 per cent. ; whereas single injection treatment, used in 33 cases, gave a cure rate of 60 to 61 per cent. But, in 13 cases, where a single injection of a high dose (200,000 Oxford units) was the method used, the cure rate was 84.6 per cent.

It was found that a course of four injections of 40,000 O.u. at three-hourly intervals gave a cure rate of 100 per cent. in 10 cases, and this dosage was for a time adopted as the standard treatment for a case of gonococcal urethritis.\* This regime was well adapted for use in out-patients, being easily completed in one day, say between 9 a.m. and 6 p.m.

\* Subsequently relapses occurred with this technique and it became evident that a larger number of three-hourly injections, say eight instead of four, of 40,000 units, would be necessary to achieve something approaching complete success in a large group of cases.

Of the 116 cases of gonococcal infection in men, 44 cases had resisted sulphonamide therapy, and 24 cases relapsed on the initial dosage of penicillin, but all were cured by a further more intensive course of penicillin. It could not be shown that cases which were resistant to sulphonamide therapy were either more or less liable to relapse with penicillin therapy than those cases which had had no previous treatment.

The subjoined table shows the results given by the different dosages of penicillin used in the treatment of gonorrhœa in men.

TABLE I  
*Gonorrhœa in Men*

Dose.	Interval in Hours.	Number of Cases.	Number of Cases Sulphonamide Resistant.	Number of Relapses.	Percentage Cure.
<i>Saline Solution.</i>					
1 × 100,000	...	13	5	5	61·5
2 × 100,000	12	1	1	...	...
10 × 10,000	3	1	...	...	...
2 × 60,000	24	1	1	1	...
4 × 15,000	4	11	5	5	54·5
8 × 20,000	3	5	1	...	100·0
4 × 40,000	3 or 4	10	4	...	100·0
5 × 30,000	2	9	4	...	100·0
5 × 20,000	2	2	1	...	...
50, 15, 15, 50,000	4	5	4	...	100·0
1 × 200,000	...	13	3	...	84·6
2 × 200,000	24	2	1	...	...
<i>Beeswax and Nut Oil.</i>					
1 × 100,000	...	20	6	8	60·0
2 × 100,000	9-12	14	3	2	85·7
4 × 50,000	12	9	5	1	89·0

*Comment.*—In those cases which relapsed, the relapse occurred more quickly (average three to four days) after one or two doses, and less quickly (average five days) after multiple (four to eight) injections. Urethral smears became free of gonococci on an average of three to four hours after the commencement of penicillin therapy. Local intolerance, such as pain and stiffness at the site of injection, has been slight, and has to a large extent passed off in from one and a half to two hours after injection. General intolerance to penicillin has been minimal; occasionally slight headaches or disturbed sleep with dreams have been recorded. In over 75 per cent. of all the 116 cases, the urethral discharge ceased after the first day, but, according to the duration and severity of the inflammatory reaction, an increased secretion of mucus might persist for several days. Apart from a relatively high relapse rate from the use of suspensions of penicillin in beeswax and nut oil, the difficulties of administration of this preparation were so great as to render it an unsuitable method for the large-scale treatment of out-patients, and further development

of this technique has been postponed. An attempt is now being made to prolong a bacteriostatic concentration of penicillin in the blood by the employment of adrenaline, according to the method suggested by Fisk, Foord and Alles (February 1945).

*Gonorrhœa in Women and Children.*—Of the 26 cases of gonococcal infection in women and children, only one case relapsed on the initial dosage (four injections each of 40,000 units), and this patient was cured by a further course of penicillin. The results of the different dosages used are displayed in the subjoined table :—

TABLE II  
*Gonorrhœa in Women*

Dose.	Interval (Hours).	Number of Cases.	Number of Cases Sulphonamide Resistant.	Number of Relapses.	Percentage Cure.
<i>Saline Solution.</i>					
4 × 40,000	3	12	7	1	91·6
100,000 50,000 50,000	3	1	1	...	...
100,000 50,000 50,000 50,000	4	1	1	...	...
4 × 15,000	3	1	1	...	...
3 × 20,000	3	1	1	...	...
100,000 50,000 25,000 15,000	6 hours on successive days	1	...	...	...
50,000 (I.M. drip)	...	1	...	...	...
350,000 (I.M. drip—7 days)	...	1	...	...	...
The one case which relapsed received 2 × 200,000 (American) at an interval of 4 hours, and this resulted in cure.					
<i>Beeswax and Nut Oil.</i>					
4 × 50,000	8 hours on successive days	2	2	...	...
100,000 50,000 50,000	4	1	1	...	...
100,000 50,000 25,000	5 and 19	1	...	...	...

*Comment.*—Of the 23 cases in adults, 3 were complicated by pregnancy and one by the puerperium. Other complications included salpingitis (2 cases), secondary syphilis (one case), and neurosyphilis (one case). Concomitant trichomonas vaginalis infestation was present in 5 cases : this protozoal infestation showed a temporary improvement after penicillin, but relapsed quickly. Fourteen of the 23 cases had resisted the action of sulphonamide drugs, usually sulphathiazole. Smears taken daily and not at short intervals became negative on an average less than a day and a half after penicillin. Smears taken at frequent intervals contained no gonococci on an average less than five and a half hours after penicillin.

Three children were treated, one being a case of gonococcal ophthalmia, and two had gonococcal vulvo-vaginitis. The individual dose of penicillin used varied, according to the child's age, from

10,000 units for the baby with ophthalmia to 30,000 or 50,000 units for the girls with vulvo-vaginitis, the number of injections given being four for the baby and for the girl who received the 30,000 unit dose, and three injections for the girl receiving the 50,000 unit dose. In the case of ophthalmia, and in both the cases of vulvo-vaginitis, the smears were negative on the day after commencement of treatment. Both the cases of vulvo-vaginitis had proved sulphonamide-resistant.

### SYPHILIS

Thirteen cases of early syphilis in men (9 sero-positive primary, 3 secondary, and one latent), and 9 cases of early syphilis in women (3 primary sero-negative and 6 secondary) have been treated with penicillin. The scheme of treatment has been the same for both sexes, and has consisted of sixty intramuscular injections each of 40,000 units in saline solution given at intervals of three hours to a total of 2,400,000 units in seven and a half days. In addition, 8 cases of syphilis in men (3 primary sero-negative, one primary sero-positive, two secondary and two latent) were treated with half the above total amount of penicillin, namely 1,200,000 units, in sixty divided intramuscular doses each of 20,000 units, along with eight daily intravenous injections each of 60 mgms. of mapharside. Three cases of congenital syphilis, including one of juvenile paresis, were also treated.

*Effects.*—*Spirochæta pallida* disappeared from serum obtained from the chancre or from moist papules or mucous patches in six to nine hours. Unless it was very large, the chancre healed superficially within the eight-day period of administration. The spots of the secondary rash faded and disappeared, or were disappearing, by the end of the seven and a half days' treatment. Provided that the patient was not confined to bed, there was little local intolerance in spite of the number and frequency of the intramuscular injections. General intolerance, usually in the form of headache, was slight apart from a Herxheimer reaction, with transient fever, headache, and intensification of the secondary rash, observed in two of the male cases.

*The quantitative Wassermann reaction (Q.W.R.)* was taken at the commencement of treatment and thereafter daily during the seven and a half days' course. On completion of the course, the Q.W.R. was taken at weekly intervals.

It was found that in the majority of cases the titre of the Wassermann rose during the course of treatment, and in 5 cases was higher at the end of treatment than at the commencement. In the remaining cases the titre of the Wassermann at the end of treatment was the same as or lower than the titre at the commencement. In those cases who attended regularly for observation the Wassermann became negative within two to nine weeks after completion of treatment. In most cases it was found that the higher the titre at the commencement of treatment the longer the time taken for reduction to negativity.

*Comments.*—The three-hourly injections are given both night and day, and it is necessary to take the patient into hospital. The treatment is completed in seven and a half days as contrasted with the six to eighteen months' duration of routine arseno-bismuth therapy. When penicillin is administered in combination with the arsenical, mapharside, the total dose given of each is subcurative, but when they are used together the synergistic curative effect is expected to be greater, possibly greater than a full dose of either. Penicillin is well received by patients who, through an allergic condition such as asthma, are intolerant of neoarsphenamine, and penicillin has been well tolerated by patients suffering from post-arsphenamine hepatitis with jaundice.

None of the cases described has been observed for a period sufficiently long to justify conclusions being drawn as to the permanence of the beneficial action of penicillin, either when given alone or in combination with an arsenical. Penicillin used alone is not attended by the risk of causing any of the disabling and sometimes dangerous toxic effects which occasionally follow treatment by either arsenical or bismuthial drugs.

#### GENERAL COMMENTARY

The advantages resulting from the adoption of penicillin in the therapy of either of the major venereal diseases, gonorrhœa and syphilis, include the rapid abolition of infectivity and reduction of spread of the disease; the absence of toxic reactions involving danger or disability; the minimum loss of working time; and the important fact that the treatment is completely under the control of the doctor who gives the doses, whereas with sulphonamide therapy the patient has to be relied upon to treat himself by taking his oral doses regularly.

#### SUMMARY

A year's experience of the use of penicillin in the treatment of gonorrhœa and syphilis in a civilian clinic is epitomised. One hundred and forty-two cases of gonorrhœa and 33 cases of syphilis are reviewed.

The results of penicillin treatment are described, and displayed in tabular form.

#### CONCLUSIONS

One day's treatment, comprising four or five intramuscular injections of penicillin at three-hourly intervals to a total dosage of 150,000 to 160,000 Oxford units, will effect a cure of gonorrhœa in a very high proportion of cases, whether in men or in women.

Syphilis requires a much higher dosage than gonorrhœa, and the dose sufficient to cure a gonorrhœa may only hinder the recognition of a concomitant syphilis.

Eight days of treatment, comprising sixty intramuscular injections of penicillin at three-hourly intervals to a total dosage of 2,400,000 O.u., will produce apparent clinical cure in early syphilis with reduction or reversal of positive serological tests, in either sex. Penicillin is therefore an exceedingly potent, as it is also a non-toxic remedy, the value of which cannot yet be assessed, but the use of which should serve to shorten greatly the therapeutic schedules of the future.

The year 1944 marked the commencement of the "penicillin era" in the treatment of the two major venereal diseases.

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#### REFERENCE

FISK, FOORD and ALLES (2nd February 1945), *Science*, **101**, No. 2614.