TREATMENT OF EARLY SYPHILIS WITH PENICILLIN*†

BY

R. R. WILLCOX, F. J. G. JEFFERISS, AND G. L. M. McELLIGOTT

St. Mary's Hospital, Paddington, London

Since the last International Congress of Dermatology was held in London in 1952 the use of penicillin alone in the treatment of early syphilis has become even more firmly established throughout the world. European specialists, however, have been somewhat slower to abandon the older, albeit well tried, methods employing arsenic and bismuth than experts in other areas. In January, 1953, a World Health Organization survey of the schemes of treatment in use in the venereal diseases clinics of the world showed that drugs other than penicillin were at that time being used in 34.7 per cent. of these establishments. While all the North American clinics included in the survey relied on penicillin alone, arsenic and bismuth (usually in addition to penicillin) were still in use in 47.8 per cent. of the clinics of Europe (Willcox, 1954).

Though penicillin alone in a total dosage of 2.4 mega units had been used throughout the British Army and the Royal Air Force for the treatment of primary and secondary syphilis since 1944, in the civil clinics it was at first the common practice to follow a course of 2.4 to 4 mega units penicillin with ten weekly injections of neoarsphenamine and bismuth. This routine was followed at St. Mary's Hospital during the years 1946-47 and McElligott, Jefferiss, and Willcox (1948) made a preliminary report on 275 patients with early syphilis treated with 2.4 to 4 mega units penicillin over a period of 7½ to 12½ days plus a course of neoarsphenamine and bismuth lasting from 6 to 10 weeks. 54 per cent. of the patients had been followed for 12 to 18 months or over, and there were ten failures, four of which were considered as being due to re-infection. Toxic effects from the arsenical drugs were not negligible and in ten cases they were severe. This led to the discontinuance of arsenic and, from 1947 to 1950, the short intensive course of penicillin was followed by not more than ten intramuscular injections of an aqueous suspension of bismuth oxychloride, usually given twice weekly.

Jefferiss, Willcox and McElligott (1951) reviewed a total of 744 cases of primary and secondary syphilis treated at St. Mary's Hospital in 1946-48. All of these patients had had an 8-day course of penicillin

(maximum total dosage 4.8 mega units), 561 receiving a single course of a maximum of ten injections of neoarsphenamine and bismuth, and 183 a maximum of ten injections of bismuth only. Up to the time of review 32 patients had needed re-treatment, ten of whom were considered to have been re-infected. Since then no further cases of serological, clinical, or neurological relapse have been noted in this series, which supports the widely-held opinion that relapses, when they occur, usually do so within the first year of post-treatment observation.

Penicillin Alone in the Treatment of Early Syphilis

Since 1951 all cases of syphilis, early and late, have been treated with penicillin alone. Although many experienced workers in the United States consider that the clinical and serological results of the treatment of early syphilis will not improve with total dosages of penicillin higher than 4.8 to 6 mega units, we have felt that, in our present state of knowledge, a serious chronic disease such as syphilis may still deserve to be over-treated. We also believe that the idea of consolidation treatment with sub-curative doses of arsenic and bismuth is mistaken, and that, if any treponemes survive after intensive penicillin treatment, it would seem to be more logical to attack them again with the most efficient treponemocidal agent at our disposal, rather than to administer potentially dangerous drugs in a dosage more likely to be suppressive than curative. Consequently, in 1951, a short consolidation course of penicillin (900,000 units of procaine penicillin in oil with aluminium monostearate (PAM) twice weekly for 5 weeks) was substituted for the bismuth following the initial course of eight daily injections of 600,000 units of PAM.

Though default from surveillance and, occasionally, even from treatment is inevitable among the many itinerant patients in a large city clinic, seventy (58 per cent.) of 120 patients (79 male and 41 female) treated with penicillin alone were followed for 10 to 12 months or more, and 53 (44 per cent.) for 22-24 months or more (Table I). The cerebrospinal fluid was examined as a routine in many of the patients who remained for a second year of observation with uniformly negative results.

* Received for publication November 1, 1957.

† Presented at the XI International Congress of Dermatology, Stockholm, 1957.

TABLE I
RESULTS OF TREATING 120 PATIENTS WITH EARLY
SYPHILIS WITH PENICILLIN ALONE

Follow-up (mths)	No. Followed	No. Re-treated	Cumulative Percentage Re-treated
0	120	—	—
1-3	103	—	—
4-6	87	1	1.1
7-9	76	1	2.4
10-12	70	—	2.4
13-15	63	—	2.4
16-18	57	—	2.4
19-21	56	—	2.4
22-24	53	—	2.4
More than 2 years	39	—	2.4

The Tables show that up to the present the results have been excellent.

In only two of the cases followed up has re-treatment been considered necessary. One, a male patient with secondary syphilis to whom PAM 13.8 mega units was given, was re-treated after 7 months on account of persisting sero-positivity, although in fact the serological titre was falling slowly. The other case, a woman with secondary syphilis who had been given PAM 11.2 mega units, was re-treated after 6 months, the positive serum reactions remaining unchanged. It is possible that in one if not both of these cases re-treatment was unnecessary, as serological reversal is often slow in treated cases of secondary syphilis.

The serum findings at the last recorded visit of all the patients are shown in Table II. It will be seen that over 90 per cent. of the patients observed became Wassermann negative by the end of the 7 months observation period and that this rate was maintained thereafter.

TABLE II
SERO-POSITIVITY TO WASSERMANN TEST AT LAST VISIT

Final Follow-up (mths)	No. Followed	Wassermann Reaction			Percentage WR Neg.
		Neg.	Doubtful	Pos.	
0-3	33	11	7	15	33.3
4-6	11	7	2	2	63.6
7-12	13	12	—	1*	92.3
13-24	24	22	1	1*	91.6
Over 24	39	38	1	—	97.4
Totals	120	90	11	19	75.0

*Declining titre.
(Only Wassermann reaction readings taken; those of Harris test ignored.)

The results of the three schemes of treatment are compared in Table III, and it will be noted that the results of using penicillin alone are apparently better than those obtained when adjuvant drugs were used.

There are two possible explanations of this anomaly:

(1) That appreciably higher doses of penicillin were given when no adjuvant treatment was employed;

TABLE III
COMPARISON OF RESULTS BY THREE METHODS

Schedule of Treatment	Penicillin, Arsenic, and Bismuth	Penicillin and Bismuth	Penicillin Alone
Number Treated	561	183	120
Followed One Year or More	No. 307 Per cent. 54.5	76 41.5	56 46.7
Relapses and Re-infections	22	7	2
Percentage Failures of those Followed One Year or More	7.2	9.2	3.6

(2) That, with the declining prevalence of early syphilis, the possibility of re-infection has become progressively less likely.

We had already suspected that some of the cases classed as relapses in the earlier series were in fact re-infections. It is also worth recording that we have observed at various stages in their follow-up period many patients who had been treated on similar lines in other hospitals. These cases are, of course, not included in our figures, but up to the present no instance of clinical or serological relapse has been noted among them.

Summary

(1) The results of the treatment of 864 cases of primary and secondary syphilis at St. Mary's Hospital, London, are reviewed. Of these, 561 received treatment with penicillin and a short course of arsenic and bismuth, 183 were given penicillin and a maximum of ten injections of bismuth, and 120 received penicillin alone.

(2) In the series as a whole the clinical and serological results have been excellent and seem, if anything, to have been better rather than worse when penicillin alone was used. This anomaly may be explained by the higher doses of penicillin given over a longer period when no adjuvant metallothérapie was given, and by the fact that in more recent years the possibility of re-infection must be greatly diminished. Moreover, when penicillin alone was used, side-effects from treatment were hardly ever encountered.

(3) Penicillin alone is confidently recommended as the treatment of choice in early syphilis.

REFERENCES

- Jefferiss, F. J. G., Willcox, R. R. and McElligott, G. L. M. (1951). *Lancet*, 1, 83.
McElligott, G. L. M., Jefferiss, F. J. G., and Willcox, R. R. (1948). *Brit. J. vener. Dis.*, 24, 45.
Willcox, R. R. (1954). *Bull. Wild Hlth Org.*, 10, 579.