slow improvement in jaundice and urine. Of the fatal cases, I doubt whether any treatment would have saved the two who died of suppression of urine (one treated, one not treated); the third case was not thought severe enough to need penicillin, and this patient died of auricular flutter on the 21st day: this should have been averted if there had been a specific treatment.

Lieut.-Col. L. H. Howells and Major R. R. Hughes made an intensive study of seven cases, six of which they treated with penicillin. Their conclusions were as follows:

1. Penicillin in adequate doses appeared to shorten the general effects of the disease as assessed by the duration of the fever; it had an effect on the number of febrile relapses, and these results bore a direct relation to the dosage.

2. Penicillin did not seem to influence the degree and duration of the cholaemia as estimated by the icteric index and the van den Bergh test, or to affect the rate of disappearance of icterus from the skin or of bile from the urine.

3. Penicillin did not influence the degree of nitrogen retention as estimated by the blood urea, or the degree or rate of disappearance of albuminuria.

4. Apart from the objective evidence mentioned in paragraph 1 there remains only the very definite clinical impression that cases treated with penicillin, especially with high doses, improved dramatically within 36 hours.

5. It is considered that penicillin should be given in cases of Weil's disease as soon as possible and in high doses. Once liver and kidney damage has occurred penicillin does not appear to minimize the results of this; hence it would be interesting to observe the effects of the drug during the pre-icteric phase.

Results

The results in the present series of cases of Weil's disease are as follows:

Total cases	39
Penicillin-treated	16
8 severe, 7 moderate, 1 mild. (14 confirmed by agglutination tests.) 1 died of uraemia	
Untreated	23
2 died—1 of myocarditis on 21st day, 1 of uraemia soon after admission	

Discussion

I have presented the results of the treatment with penicillin of 16 cases of Weil's disease. It would appear that there has been an effect on the speed with which the temperature falls and on the number of febrile relapses, while all the observers claimed an improvement in the patients' general condition within 36 hours. These are scanty pieces of evidence on which to base definite conclusions.

In another theatre of war penicillin treatment, in my opinion, has been considered as ineffectual, but the dosage used was inadequate—15,000 units 3-hourly. It is known that certain strains of leptospira are penicillin-sensitive *in vitro*.

In view of these facts it is felt that further work on this subject should be pursued; it is essential to give treatment early, and the dosage should be high.

I have followed this work throughout, and have seen most of the patients; nevertheless my part in this paper is that of compiler on behalf of the following physicians of 21 Army Group: Lieut.-Cols. C. L. Cope, G. G. Gillam, L. H. Howells, R. L. Mackay, I. McGolrick, I. Murray, R. E. Tunbridge—all R.A.M.C.; Lieut.-Col. J. H. Geddes, R.C.A.M.C.; and Majors H. A. Dewar, R. R. Hughes, S. B. Karani, and Capt. J. A. Lorimer—all R.A.M.C.

More than 250 hospitals in England and Wales are now using rehabilitation methods—including physiotherapy, remedial exercises, outdoor games, and handicrafts. This is nearly twice as many as a year ago, when the Ministry of Health made a special appeal to civilian hospitals to establish a rehabilitation department as soon as possible. Some hospitals are using local halls; others have been supplied by the Ministry of Health with prefabricated huts for remedial exercises and other activities. The Ministry also lends equipment for gymnastics, sports, and occupational therapy. The majority of some 400 hospitals covered by a Ministry of Health survey have appointed a member of the staff as a rehabilitation medical officer. Many of these doctors have attended special courses at selected rehabilitation centres. Other courses have been provided for physiotherapists, handicraft teachers, and others. To help with the resettlement of disabled persons in industry, large firms in the neighbourhood of certain hospitals have established special workshops in which disabled employees may be restored to working capacity by exercising the affected limbs in suitably adapted work under proper supervision.

LOCAL PENICILLIN THERAPY IN OPHTHALMIA NEONATORUM*

BY

ARNOLD SORSBY, M.D., F.R.C.S.

AND

ELIZABETH HOFFA, L.R.C.P.&S.Ed., D.C.H.

Unlike the sulphonamides, penicillin remains effective in the presence of pus. It therefore has possibilities for the local therapy of ophthalmia neonatorum as an alternative to general sulphonamide treatment of this affection. To investigate this possibility 47 infants at the Ophthalmia Neonatorum Unit at White Oak (L.C.C.) Hospital were treated with penicillin. Table I brings out the salient features in summary form.

TABLE I.—Showing results in 47 Cases of Ophthalmia Neonatorum Treated by Various Concentrations of Penicillin.
(+ = Successful Treatment; — = Failure)

Organisms	Concentration of Penicillin: Oxford Units per c.cm.							
	500		1,000		1,500		2,500	
	+	—	+	—	+	—	+	—
Gonococci	2	2*	2	0	2	3*	5	0
Staphylococci	1	1	1	—	1	—	9	—
Diphtheroids	—	—	1	—	1	—	1	—
Staphylococci and bacilli	—	1†	—	1	—	—	3	—
Unidentified diplococci	—	—	—	—	1	—	—	—
No organisms or inclusion bodies found	—	—	—	—	—	—	2	—
Virus: assumed from the presence of inclusion bodies	—	1	—	2‡	—	—	2	—
Total	3	5	4	3	6	4	21	1

* Including one case which relapsed.

† Relapsed after clinical cure in 6 days.

‡ Both initially clear after 8 days and 4 days respectively when relapse occurred.

The Series as a Whole

(a) Initially, penicillin was used in a concentration of 500 Oxford units per c.cm. Eight cases received this treatment, one drop of the solution being instilled hourly during the first 24 hours, and continued two-hourly subsequently. Only three of these eight cases were cured. Two more showed an initial recovery, which, however, was not maintained. The three cured cases required treatment for 2 days, 3 days, and 6 days respectively.

(b) A second series of 7 cases were treated with penicillin in a concentration of 1,000 units per c.cm., the method of application in three cases being as in the first series, and in the remaining four cases the penicillin was instilled at half-hourly intervals for 24 hours and hourly subsequently. Four of this series of 7 cases showed clinical cure in 2, 4, 2, and 5 days respectively; one case did not respond to treatment; while the remaining two cases both relapsed after an initial recovery.

(c) A further 10 cases constituted a third series treated with penicillin, this time in a concentration of 1,500 units per c.cm. (the drops being instilled half-hourly during the first 24 hours and hourly subsequently). Six of these 10 cases showed an excellent response, clinical cure being obtained in 18 hours in one case, in 2 days in four cases, and in 3 days in the remaining case successfully treated. Two cases showed a poor response in spite of treatment for 4½ and 5 days respectively; in one case penicillin treatment was discontinued after 3 days as progress appeared inadequate; in the remaining case of this series an initially satisfactory response which gave a clinical cure within 2 days was followed by a relapse which did not respond to further penicillin therapy.

(d) Twenty-two infants were treated with penicillin in a concentration of 2,500 units per c.cm., the drops being instilled half-hourly for the first 3 hours, then hourly for 24 hours and two-hourly subsequently. In all but one case there was an

* A report to the Penicillin Trials Committee of the Medical Research Council.

excellent clinical response, recovery in some instances being a matter of a few hours, as can be seen from the following summary:

Time taken for a Clinical Cure		Number of Cases
3 hours		
7 "		1
12 "		2
18 "		1
24 "		1
	3-24 hours	6
27 "		1
36 "		1
37 "		1
40 "		3
43 "		1
	27-43 hours	7
50 "		1
60 "		1
70 "		1
78 "		1
100 "		3
	50-100 hours	7

One case is omitted from this table, as the complication of corneal ulcer—present on admission—delayed a return to normal.

One point deserves stressing. Rapidity of clinical cure does not seem to depend altogether on initial mildness of the condition. Of these 20 cases, 4 were severe; they cleared up in 36, 40, 40, and 37 hours respectively, while all the 7 cases that required 50 to 100 hours were either mild or moderate.

Differential Susceptibility of the Causal Organisms to Penicillin

Of the 25 cases in the first three series only 13 showed clinical cure, 5 more relapsed after apparent clinical cure, and 7 gave a poor response or none at all. The distribution of organisms in these different cases is summarized in Table II.

TABLE II

Organisms	Number showing		
	Clinical Cure	No Result	Relapse after Apparent Cure
Gonococci	6	3	2
Staphylococci	3	1	—
Diphtheroids	2	1	—
Staphylococci and bacilli	1	1	1
Unidentified diplococcus	1	—	—
Inclusion bodies	—	1	2

No fine conclusions can be drawn from these results. So far as this series goes it would appear that none of the organisms met in ophthalmia neonatorum are completely resistant to penicillin. A rather surprising feature emerges with the three cases of inclusion blennorrhoea present: theoretically no result would be expected, but in two cases there was an initial recovery, only to be followed by a relapse.

The 22 cases treated with penicillin in a concentration of 2,500 units per c.cm. bear out the efficacy of the drug for the variety of causal organisms of ophthalmia. As can be seen from Table I, treatment was successful in the 5 cases due to the gonococcus, the 9 caused by staphylococci, the 3 in which staphylococci and bacilli were present, and in the 2 in which inclusion bodies were found; 2 further cases in which no organisms or inclusion bodies were present also responded to penicillin treatment. No relapses were observed in this series, and the only failure was a case in which no organisms were found in the smear and the culture showed diphtheroids.

It would therefore appear that penicillin is effective over the whole range of causal organisms with the possible exception of diphtheroids—though even here two cases responded to penicillin in a concentration of 1,000 and 1,500 units respectively, and a third case showed a partial response to penicillin (1,500 units per c.cm.).

With the limited material so far investigated it is not possible to assess whether the different causal organisms respond to a varying degree to penicillin treatment. The problem is, moreover, complicated by the fact that it is not always possible to assess the significance of bacteriological findings in ophthalmia neonatorum. *Staph. albus*, diphtheroids, and some other bacilli are generally regarded as non-pathogenic. Yet it is worth noting that three of the seven cases treated with penicillin in a concentration of 2,500 units and requiring treatment for more than 50 hours showed diphtheroids—one of them in association with *Staph. albus*. In no case in which diphtheroids were

found was there a rapid clinical cure. The bacteriological findings in the 7 cases requiring over 50 hours of treatment are of interest (Table III).

TABLE III

Smear	Culture	Inclusion Bodies	Duration of Treatment
Diphtheroids	<i>Staph. aureus</i>	Absent	100 hours
"	<i>Staph. albus</i>	"	50 "
Staphylococcus	<i>Staph. aureus</i>	"	60 "
Negative	Negative	"	70 "
"	<i>Staph. aureus</i>	Present	78 "
"	"	"	100 "

Cases showing diphtheroids or inclusion bodies would therefore appear to be most resistant to penicillin therapy. (*Staph. aureus*, though it appears three times in these 7 cases, is not in itself resistant to penicillin, as was evident from the excellent response in 6 other cases.)

Sulphonamide-resistant Cases

Five cases among the first 25 were treated with penicillin after a poor or protracted response to sulphonamides. Three of these were cases of gonococcal ophthalmia and responded well to penicillin, used in concentrations of 500, 1,000, and 1,500 units respectively. In the fourth case *Staph. aureus*, and in a fifth diphtheroids, were present; in both these cases there was a satisfactory response to penicillin in a concentration of 1,500 units per c.cm. Initially the first case had been treated by sulphathiazole for 12 days, and the four others by sulphamezathine for 5½, 12, 5½, and 23 days, respectively. Clinical cure by penicillin took place in 3, 4, 2, and 3 days respectively in the first four cases and in 18 hours in the fifth case.

Mode of Use

On admission the infant's eyes are irrigated with half-normal saline at room temperature and one drop of penicillin is instilled. Irrigation is also carried out before each further instillation of penicillin so long as there is any discharge. With penicillin in a concentration of 2,500 units per c.cm. irrigation is generally not necessary after 6 hours. Penicillin is continued for 48 hours after apparent clinical cure, at two-hourly intervals during the day and three-hourly at night. The drug is well tolerated by the infant's eye. Occasionally a mild transitory flushing of the conjunctiva is observed.

Comparison with General Sulphonamide Therapy

Until a standardized technique for local penicillin therapy is established no useful comparison with general sulphonamide therapy can be made. Local therapy has obvious advantages, and, moreover, avoids the danger of sensitization that the oral administration of sulphonamides carries. Frequent irrigations are, however, a trial to the infant and a considerable burden on the nurse. The present results promise to reduce these to a tolerable minimum. The dramatic results obtained by the sulphonamides are paralleled by those given by penicillin.

Summary

A total of 47 cases of ophthalmia neonatorum treated by the local application of penicillin in the form of drops is reported. Concentrations of 500, 1,000, 1,500, and 2,500 Oxford units per c.cm. were used.

An increasing proportion of satisfactory results was obtained with increase in the concentration of the drops used, the proportions in the four series being 3 out of 8, 4 out of 7, 6 out of 10, and 21 out of 22 respectively.

In adequate concentration penicillin appears to be effective against all the common causal organisms of ophthalmia neonatorum, including the virus of inclusion blennorrhoea.

It is likely that some forms of ophthalmia neonatorum respond more readily to penicillin than others. On the whole the results are of the same order as those obtained with the sulphonamides.

We are indebted to Dr. E. N. Young of the Southern Group (L.C.C.) Laboratories for her painstaking bacteriological examinations, and to the Matron and Sister Condon of White Oak Hospital for their collaboration. We are grateful to Prof. Sir Alexander Fleming for his interest and help.