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COMMUNICATIONS

THE VALUE OF PENICILLIN IN THE TREATMENT OF SUPERFICIAL INFECTIONS OF THE EYES AND LID MARGINS *

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Introduction

THE purpose of this investigation was to determine the clinical and bacteriological results of local application of penicillin in cases of conjunctivitis, corneal ulceration and blepharitis.

Clinically, four groups of cases were selected :

1. Conjunctivitis, of some severity, showing well-marked injection and discharge but without secondary involvement of the cornea.

2. Conjunctivitis, again of some severity, with additional secondary corneal infiltrations, either superficial and diffuse, or marginal.

3. Conjunctivitis with a single large secondary corneal ulcer or infiltration. The clinical picture was here dominated by the localised corneal infection.

4. Blepharitis, chronic in type and severe in character. All these patients were prone to frequent and disabling subacute exacerbations of the infection.

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No cases of corneal ulceration unassociated with conjunctivitis or other causative factors were available for the investigation. Such cases are commonly seen in age-groups higher than that of the services, and in specialised occupations such as coal-mining.

Certain cases in each group showed skin lesions of the face which were thought to play an important part in the aetiology of the eye condition. No specialised treatment of the skin was carried out during the investigation.

In none of the cases selected was there associated infection of the lacrymal passages. A number had received previous treatment, in some cases for long periods, but this appeared to have no influence on the efficacy of the penicillin therapy.

Methods of Investigation

The sodium salt of penicillin was employed. It was supplied to us in sterile tablets of 7,500 units each.

From these tablets two preparations were made:—

(1) Drops. These consisted of a sterile aqueous solution containing 250 units per c.c.

(2) Ointment. The base used was 30 per cent. lanette wax (SX quality) in water. Penicillin was added to this to give a final concentration of 250 units per gram.

Each batch of material was distributed in small quantities in sterile screw-capped bottles and kept frozen solid until required for use. Only one bottle of each preparation was actually in use at one time. Between treatments this bottle, though not frozen solid, was kept in a refrigerator at 0-5°C. A single bottle lasted only 1-3 days, depending on the number of cases under treatment, and no significant deterioration occurred during this time.

Routine Treatment.—Drops were used on cases in Group 1, as in these the discharge tended to be profuse. In Groups 2, 3 and 4 ointment was used. No other method of therapy was employed throughout the investigation.

The drops or ointment were instilled in the lower fornix of the affected eye at four-hourly intervals, both by day and night. The amounts used were not measured: one or two drops, and a piece of ointment the size of a match-head were the average quantities. No attempt was made to aid absorption of the preparation by iontophoresis or a corneal bath, nor did the cases of blepharitis receive any additional application to the lid margins.

Allowing for wastage in containers and pipettes and on applicators the consumption of material was at the rate of approximately 1 c.cm. of drops or 1 gram of ointment per eye per day with this procedure. This gives an average consumption of 20 c.c. or 20 grams for a bilateral case treated for ten days; and represents a total of 5,000 units of penicillin for an average case.

About one-half of the patients complained of smarting pain for some 10 to 20 minutes after instillation of the drops or ointment, but no case of damage to the corneal epithelium was noted. As a routine the penicillin was instilled for 7 days after the bacteriological cultures from the conjunctival sac had become negative. If, however, by this time the eye had not made a full clinical recovery the treatment was continued for a further 7 days. On completion of the instillation of drops or ointment all treatment was withheld and the patient was retained in hospital a further two weeks for observation. He was then sent to a convalescent home for four weeks, and from there he was re-admitted to hospital for a further examination before discharge. Thus each case was under review for either six or seven weeks.

Certain precautions were taken to prevent the occurrence of cross infection. The men were not nursed in isolation but were retained in one ward, to which no other cases were admitted. The day and night nursing staffs were particularly careful to avoid the transference of infection and were not engaged on any other duties during the investigation. The men were permitted to associate with other ambulatory patients in the recreation rooms, but were not allowed to enter other wards.

Bacteriological Methods.—Conjunctival swabs from the affected eyes were examined before commencement of treatment, daily during treatment until repeated negative results were obtained, seven days after cessation of treatment, and at various later dates. The swabs were inoculated immediately on to warm blood-agar plates and into nutrient broth. These media were incubated for 48 hours and the nature of any growth determined. Every organism isolated was tested for penicillin-sensitivity and all staphylococci were tested for coagulase production.

For swabs taken during the course of penicillin treatment special media were used in which was incorporated a preparation of penicillinase (Harper, 1943) to inactivate any penicillin carried over into the medium by the swab.

Comparative assays of the material were carried out by the cylinder technique described by Abraham et al. (1941).

Persistence of Penicillin in the Discharge.—A number of tests were made to determine the duration of penicillin activity in the discharge from the eye following the application of both drops and ointment. The capillary tube technique (Fleming, 1943) and the modified slide-cell technique (Florey and Florey, 1943) were employed, and the tests were recorded as positive if there were definite inhibition of the standard Oxford staphylococcus in the discharge diluted with an equal volume of normal human serum. These results are recorded in Tables I and II. They demonstrate the superiority of the ointment over the drops in its powers of persistence in the conjunctival sac.

TABLE I

Persistence of Penicillin in the Discharge after application as Drops

Time after application	Number of examinations	Penicillin positive	Penicillin negative
1 hour	6	5	1
2 hours	6	3	3
3 hours	6	1	5
4 hours	3	0	3

TABLE II

Persistence of Penicillin in the Discharge after application as Ointment

Time after application	Number of examinations	Penicillin positive	Penicillin negative
2 hours	4	4	0
3 hours	6	6	0
4 hours	6	4	2
5 hours	6	3	3

Analysis of Cases

Group 1.—The important clinical and bacteriological features of the cases comprising Group 1 are set out in Table III.

SUMMARY.

a. No case was encountered due to a penicillin-resistant organism.

b. All the cases were readily and completely cured within an average of 5 days.

c. Cases which had proved resistant to other forms of therapy (Nos. 1, 2, 3, 6 and 7) responded as well and as rapidly as previously untreated cases.

d. Associated skin lesions (Cases 2, 4 and 5) appeared to have no effect on the penicillin therapy.

e. Particularly encouraging were results on a severely infected socket of four years' duration (No. 6) and a severe conjunctival infection following a squint operation (No. 7).

f. One case (No. 4) relapsed clinically during the period of observation.

TABLE III.—GROUP 1. Cases of Conjunctivitis without Corneal Involvement.

Case	Clinical condition before treatment	Clinical response to treatment	Bacteriological condition before treatment	Bacteriological response to treatment
1.—Gds. T. ...	Left conjunctivitis. Duration, 3 weeks. Similar infection in right eye two weeks previously	Cured in 3 days	Moderate growth Staph. aureus from both eyes	Swabs became sterile after 3 days. No recurrence
2.—Cfn. L. ...	Severe bilateral conjunctivitis. Duration, 2 months. Comprehensive previous treatment. Seborrhoeic dermatitis of face with entropion of lower lids	Cured in 10 days	No growth of organisms was obtained at any time in this case	—
3.—Sgt. B. ...	Right conjunctivitis. Duration, 4 weeks. Comprehensive previous treatment. Simultaneous conjunctivitis with superficial punctate and marginal keratitis in left eye. (Included in Group 2)	Cured in 4 days. (Full subsequent observation not completed)	Heavy growth Staph. aureus	Sterile after 1 day. No recurrence
4.—L.A.C. O.	Right conjunctivitis. Duration, 2 days. Simultaneous conjunctivitis with superficial punctate keratitis in left eye. (Included in Group 2) Acne rosacea of face.	Cured in 3 days. Recurrence 7 days after cessation of treatment. Again rapidly cured on resumption of treatment	Heavy growth of Staph. aureus	Sterile after 1 day. Diphtheroid bacilli appeared after cessation of treatment, and no other organisms were found at the time of the clinical relapse
5.—Pte. G. ...	Right conjunctivitis. Duration, 2 days. Left conjunctivitis with marginal keratitis 4 weeks previously. (Included in Group 2) Left otitis externa	Cured in 4 days	Moderate growth of Staph. aureus	Sterile after 1 day. No recurrence
6.—Cpl. B. ...	Subacute exacerbation in chronically infected left socket. Duration, intermittently, since excision of eye 4 years previously. Comprehensive previous treatment.	Cured in 5 days	Heavy growth of Strep. haemolyticus in pure culture	Streptococci disappeared after 2 days. Diphtheroid bacilli present for 2 days, then culture negative till 6 days after cessation of treatment when heavy growth Staph. aureus obtained. This persisted at all later examinations.
7.—Cfn. S. ...	Right severe purulent conjunctivitis following squint operation. Duration, 6 days. Unsatisfactory response to usual methods of treatment	Cured in 8 days	Heavy growth of Staph. aureus	Sterile after 5 days. No recurrence

TABLE IV.—GROUP 2. *Cases of Conjunctivitis with Diffuse Superficial or Marginal Keratitis.*

Case	Clinical condition before treatment	Clinical response to treatment	Bacteriological condition before treatment	Bacteriological response to treatment
8.—Dvr. J. ...	Right conjunctivitis and marginal keratitis. Duration, 3 days	Cured in 10 days	Heavy growth of Staph. aureus, both eyes	Sterile after 2 days. Later cultures yielded only diphtheroid bacilli
9.—Pte. W. ...	Right conjunctivitis, superficial punctate and marginal keratitis. Duration, 6 days	Cured in 7 days	Heavy growth of Staph. aureus	Sterile after 1 day. No recurrence
10.—Gnr. M.	Right conjunctivitis and superficial punctate keratitis. Duration, 6 weeks. Comprehensive previous treatment	Cured in 7 days	Heavy growth of Staph. aureus	Sterile after 1 day. No recurrence
11.—Cpl. B.	Left conjunctivitis and superficial punctate keratitis. Duration, 2 weeks. Comprehensive previous treatment. Simultaneous right uncomplicated conjunctivitis. (Included in Group 1). Acne rosacea of face.	Cured in 6 days. (Full subsequent observation, not completed)	Heavy growth of Staph. aureus	Sterile after 1 day. No recurrence
12.—L.A.C.O.	Severe left conjunctivitis and superficial punctate keratitis. Duration, 2 months. Comprehensive previous treatment. Simultaneous right uncomplicated conjunctivitis. (Included in Group 1). Acne rosacea of face	Cured in 6 days	Heavy growth of Staph. aureus	Sterile after 1 day. Diphtheroid bacilli appeared after cessation of treatment
13.—Pte. G.	Left conjunctivitis and marginal keratitis. Duration, 4 weeks. Comprehensive previous treatment. Developed uncomplicated right conjunctivitis 4 weeks later. (Included in Group 1). Left otitis externa	Cured in 7 days	Moderate growth of Staph. aureus	Sterile after 1 day. Staph. aureus appeared after cessation of treatment
14.—Sgt. B.	Left conjunctivitis and superficial punctate and marginal keratitis. Duration, 3 days. Simultaneous right uncomplicated conjunctivitis. (Included in Group 1)	Cured in 10 days. (Full subsequent observation not completed)	Heavy growth of Staph. aureus	Sterile after 1 day. No recurrence
15.—Tpr. H.	Right conjunctivitis and superficial punctate keratitis. Duration, 2 weeks. Seborrheic dermatitis of face	Cured in 8 days. Recurrence 2 weeks later	Heavy growth of Staph. aureus	Sterile after 1 day. Staph. aureus reappeared 2 weeks later

TABLE V.—GROUP 3. *Cases of Corneal Ulceration or extensive localised Corneal Infiltration secondary to Conjunctivitis*

Case	Clinical condition before treatment	Clinical response to treatment	Bacteriological condition before treatment	Bacteriological response to treatment
16.—Pte. P.	Right recurrent marginal corneal ulcer. Duration, 2 months. Comprehensive previous treatment	Cured in 10 days	Moderate growth of Staph. aureus	Negative after 1 day. Staph. albus appeared after cessation of treatment
17.—Pte. C.	Right recurrent marginal corneal ulcer. Duration, 4 days	Cured in 9 days	Pure growth of Diplobacillus liquefaciens of Petit, showing slight penicillin-sensitivity in culture	Sterile after 2 days. Diphtheroid bacilli appeared after cessation of treatment
18.—Pte. W.	Right marginal corneal ulcer. Duration, 2 weeks	Cured in 8 days	Cultures yielded a growth of diphtheroid bacilli only	Sterile after 1 day. No recurrence
19.—Tpr. H.	Right paracentral corneal infiltration and marginal corneal ulcer. Duration, 1 week. Seborrhoeic dermatitis of face	Cured in 9 days	Heavy growth of Staph. aureus	Sterile after 1 day. No recurrence

TABLE VI.—GROUP 4. *Chronic Blepharitis*

Case	Clinical condition before treatment	Clinical response to treatment	Bacteriological condition before treatment	Bacteriological response to treatment
20.—Dvr. R.	Non-ulcerative blepharitis. Duration, 5 years. Comprehensive previous treatment	Marked improvement in 2 weeks. Some residual erythema of lid margins	Moderate growth of Staph. aureus, both eyes	Sterile after 1 day. Staph. albus appeared after cessation of treatment
21.—Cpl. W.	Non-ulcerative blepharitis. Duration, 20 years. Comprehensive previous treatment	Marked improvement in 2 weeks. Some residual erythema of lid margins	Morax-Axenfeld bacillus from both eyes. Slightly penicillin-sensitive in culture. Staph. aureus from left eye	Sterile after 3 days. No recurrence
22.—Pte. F.	Ulcerative blepharitis. Duration, 15 years. Comprehensive previous treatment	Marked improvement in 2 weeks. Some residual erythema of lid margins	Heavy growth of Staph. aureus from both eyes	Sterile after 2 days. Diphtheroid bacilli appeared after cessation of treatment
23.—Cfn. N.	Non-ulcerative blepharitis, pustules on lid margins. Duration, 2 years. Comprehensive previous treatment	Marked improvement in 2 weeks. Some residual erythema of lid margins	Heavy growth of Staph. aureus from both eyes	Sterile after 1 day. No recurrence
24.—Pte. S.	Non-ulcerative blepharitis. Duration, 20 years. Comprehensive previous treatment	Marked improvement in 2 weeks. (Full subsequent observation not completed)	Heavy growth of Strep. viridans from both eyes: Staph. aureus from left eye	Sterile after 2 days. Strep. viridans had reappeared in both eyes 7 days after cessation of treatment
25.—Gnr. M.	Ulcerative blepharitis. Duration, 20 years. Comprehensive previous treatment. Chronic dermatitis in right eyebrow	Marked improvement in 2 weeks. Some residual erythema of lid margins	No growth of organisms was obtained at any time in this case	—
26.—Cfn. H.	Non-ulcerative blepharitis. Duration, 2 years. Comprehensive previous treatment	Some improvement in 2 weeks. Marked residual erythema of lid margins	Moderate growth of Staph. aureus from both eyes	Sterile after 1 day. Staph. albus appeared 3 days after cessation of treatment
27.—Gnr. A.	Ulcerative blepharitis. Duration, 25 years. Comprehensive previous treatment. Seborrhoea of scalp and back	Some improvement in 2 weeks. Marked residual erythema of lid margins	Moderate growth of Staph. aureus from both eyes	Sterile after 2 days. No recurrence
28.—Gnr. R.	Ulcerative blepharitis and chronic conjunctivitis. Duration, 2 years. Comprehensive previous treatment	Response during treatment disappointing. At end of period of observation improvement considerable and all ulcers healed, though still some erythema of lid margins and chronic conjunctivitis	Heavy growth of Staph. aureus from both eyes	Sterile after 1 day, but Staph. aureus had reappeared in both eyes 17 days after cessation of treatment

g. Bacteriologically, five of the cases were infections with coagulase-positive staphylococcus aureus, and one with a streptococcus haemolyticus. No organisms were isolated in the remaining case.

h. Cultures became negative after treatment for one day in three cases, and after 2, 3 and 5 days in the remaining cases.

i. There was no bacteriological relapse in this group.

Group 2.—The clinical and bacteriological features of the cases of this group are shown in Table IV.

SUMMARY.

a. No case was encountered due to a penicillin-resistant organism.

b. In all cases the conjunctival condition was cured and active inflammation in the cornea had subsided within an average period of $7\frac{1}{2}$ days.

c. Four cases (Nos. 10, 12, 13 and 14) had received extensive previous therapy with inconclusive results. The response to penicillin was as satisfactory as in previously untreated cases (Nos. 8, 9 and 11).

d. Three cases (Nos. 12, 13 and 15) had associated skin lesions. All responded well.

e. One case (No. 15) relapsed during the period of observation.

f. All the cases of this group were infections with coagulase-positive staphylococcus aureus,

g. Cultures became negative after treatment for one day in 7 cases and for two days in the remaining case.

h. The clinical relapse (Case 15) was associated with the reappearance of staphylococcus aureus. The reinfecting staphylococcus was fully sensitive to penicillin.

No other bacteriological relapse occurred.

Group 3.—The clinical and bacteriological features of the cases of this group are shown in Table V.

SUMMARY

a. No case was encountered due to a penicillin-resistant organism.

b. The corneal ulcer healed and all local activity subsided within an average period of 9 days.

c. In one case (No. 16) the corneal ulcer had been present for two months. The response was as satisfactory as with those of shorter duration.

d. The one case with an associated skin lesion (No. 19) responded well.

e. No clinical relapse was noted during the period of observation.

f. Two of the cases were infections with coagulase-positive

staphylococcus aureus, and one yielded a growth of diphtheroid bacilli only. The remaining case (No. 17) gave a pure growth of diplobacillus liquefaciens (Petit), which showed slight penicillin sensitivity and disappeared from the eye after treatment for two days.

g. Cultures from the staphylococcal cases became negative after treatment for one and two days respectively.

h. No bacteriological relapse occurred in the cases of this group.

Group 4.—The clinical and bacteriological features of the cases of this group are shown in Table VI.

SUMMARY.

a. No case was encountered due to a penicillin-resistant organism.

b. The blepharitis had been present for some years in each case and all the usual lines of treatment had been extensively employed.

c. In six cases there was marked improvement at the end of two weeks (Nos. 20, 21, 22, 23, 24 and 25). Ulcers were healed and discharge was eliminated but in each some erythema of the lid margins remained.

d. In two cases (Nos. 26 and 27) the response was less satisfactory, and in one case (No. 28) the result during therapy was disappointing, though improvement was noted during the period of observation.

e. One case (No. 25) had an infection of the skin of the right eyebrow and responded well; another (No. 27) with seborrhoea of the scalp and back showed a disappointing result.

f. No clinical relapse occurred during the period of observation.

g. Six of the cases were infections with coagulase-positive staphylococcus aureus, one with the Morax-Axenfeld bacillus and one with streptococcus viridans. The Morax-Axenfeld bacillus showed slight but definite penicillin-sensitivity in culture, and the other organisms were highly sensitive.

In Case 25 no growth was obtained at any time.

h. In four of the cases cultures became sterile after treatment for one day, in three cases after two days, and in one case (the Morax-Axenfeld infection) after three days.

i. Cases 24 and 28 showed bacteriological relapses—the former unaccompanied by clinical relapse. The organisms concerned in the relapses remained penicillin-sensitive.

Conclusions

As a local therapeutic measure for superficial infections of the conjunctiva, cornea, and lid margins, penicillin far excels any therapeutic agent we have hitherto employed. It would seem,

moreover, highly effective in stubborn cases which have proved resistant to the usual methods of treatment.

From the bacteriological viewpoint, penicillin, as employed in this investigation, eradicates sensitive organisms from the conjunctiva in a few days. It cannot, however, prevent reinfection after the cessation of treatment, and we saw no reason to believe that effective therapy with penicillin established any immunity to recurrent infection. In this connection, it is noteworthy that in the cases of this series which showed bacteriological relapse, the organisms causing the relapse were as sensitive to penicillin as were those causing the original infection.

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THE INCIDENCE OF EYE DISEASE IN THE AUSTRALIAN IMPERIAL FORCES, MIDDLE EAST*

BY

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In the *Australian Medical Journal* of January 10, 1942, I published for future medical historians a survey of 6,458 private patients seen in Tasmania between 1931-1939, with 14,317 diseased conditions under 239 disease headings. This gave a ratio of 2.22 diseases per patient. At the conclusion I promised a similar table of eye disease in the Australian Imperial Forces, and now I have pleasure in submitting it. This A.I.F. survey deals with 3,638 patients seen during 1941-1942, with 6,650 diseased conditions under 226 disease headings. This gives a ratio of 1.55 diseases

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