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COMMUNICATIONS

PENICILLIN AND VITAMIN C IN THE TREATMENT OF HYPOPYON ULCER*

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IN pre-penicillin days, as the result of a paper by Keith Lyle and D. W. McLean in the *Brit. Jl. of Ophtha!* (June, 1941), the routine treatment used by me for hypopyon ulcer, had been cauterisation, carbolic acid, mydriatic, short-wave diathermy, and daily injections, intravenously, of 500 mg. of vitamin C. The great value of vitamin C was brought to my notice by the following case, which unfortunately, I can no longer trace, and of which I can produce no paintings. A young man in the early thirties had a hypopyon ulcer in one eye, which gradually but surely went downhill, and in fact, got to the stage when excision seemed to be inevitable, when to my horror, the other eye started with a small ulcer and hypopyon. It was then that (having read this paper) injections of vitamin C were given, and within 48 hours, our anxieties had gone and in two to three weeks' time, the patient was discharged from hospital with a useful standard of vision. This dramatic result was very impressive and cases were treated by this means (not many, it is true) without a failure.

In August 1944, Major-General Ogilvie very kindly placed at my disposal, the waste penicillin—200 units per c.c.—from the

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large amounts made up for injections at Colchester Hospital. As a result of this, my friends sent me any hypopyon ulcers they came across. Although at that time, bed restriction in the E.M.S. was very acute, thanks to the kindness of the Hospital Officer at Cambridge, the County Medical Officer of Essex and the co-operation of the Medical Superintendent of Oldchurch Hospital, cases were admitted and treated.

The ulcers were at first carbolicised immediately after the artist had made the initial drawing. The penicillin drops, which were kept frozen in the refrigerator, were instilled every hour during the day and three-hourly at night. In addition, gutt. atropin. gr iv or other mydriatic, three times a day, constant hot pad, a treatment with short-wave diathermy, 12 hours after admission or sometimes straight away, and an injection of Redoxon (Roche) 500 mg., were given. The pathological investigations were, unfortunately, not satisfactory, owing to the tremendous strain placed upon that department at that time, and their inability to undertake the frequent investigations.

The cases treated can be divided into two categories:

A—Those that were regarded as hopeless from the start, and

B—The case in which there was a reasonable expectation of treatment producing a satisfactory result.

(A.1). *S.M., aged 53 years.* This patient came in with a large hypopyon ulcer in an only eye. Although she had been under treatment, vision was reduced to perception of light, and in ordinary circumstances the eye would have had to have been eviscerated. In addition to her full ordinary treatment for hypopyon ulcer, penicillin was used, first as drops every three hours, and later one hourly in the day and three-hourly at night. As the eye remained rather red in this case, although very greatly improved, penicillin was stopped on August 5, 1944 and restarted on August 25, 1944, in the meantime treating the remaining ulcer with carbolicising and painting of the lids with silver nitrate. Penicillin was again stopped on September 2, 1944, and on September 6, 1944, the eye was white and the ulcer completely healed, with only a small residual dense scar. Vision was reduced to shadows, which was mainly due to the fact that an almost complete cataract was present, which was then seen for the first time. The pupil was visible and appeared to be bound down in places, which was what one would expect.

(2) *T.R., aged 83 years.* This man was in hospital for hypopyon ulcer from May 2, 1944. Several paracenteses were done and the eye got steadily worse. As a last resort, penicillin was added to his treatment. A rapid improvement occurred immediately, and he was discharged from hospital in July, 1944, with a perfectly quiet, comfortable eye, although not seeing. In

this case it had been decided to eviscerate the eye before penicillin was started. Unfortunately a Descemetocoele developed, becoming large on August 28, 1944, and the eye was eventually excised on September 6, 1944. I think the Descemetocoele was due to gross thinning of the cornea, and not to progression of the ulcer, which was healed.

(3) *A.H., aged 33 years.* This patient was transferred, having been under treatment from July 6, 1944 to July 26, 1944. On July 6, 1944, he went to hospital, where a foreign body was removed and he was admitted on July 18, 1944, with a hypopyon ulcer and corneal abrasion. The eye did extremely badly, and on July 26, 1944, it was decided to eviscerate the eye. As a last hope he was sent to Oldchurch Hospital for penicillin to be added to the usual treatment. There was a steady improvement after penicillin was started and on August 4, 1944, a large part of the iris could be seen satisfactorily. The eye was less red and there was no pain. The continued redness of the eye with no pain, made me suspicious that penicillin was the cause of the continued injection. It was accordingly stopped on August 7, 1944, and the eye got whiter. Penicillin was restarted on August 12, 1944, and stopped again on August 22, 1944. The whole cornea was then scarred but white, except at the periphery, through which the iris could be seen. He was discharged on August 26, 1944, with a completely white, stable eye. This man was seen again in July, 1945, when he had a completely quiet, white, painless eye. (Fig. a.)

The following cases were never considered hopeless, and were treated with penicillin from the time of admission.

(B. 1) *C.S., aged 71 years.* This man had had recurring corneal ulcers in the right eye for two years, and had been treated for ten days as an out-patient before being admitted on July 29, 1944, with a hypopyon ulcer. A culture was taken on admission, and showed a typical *B.coli* and *streptococcus viridans*. Penicillin was instilled, in addition to the ordinary treatment. Twenty-four hours later, there was a great improvement, and on July 31, 1944, all signs of hypopyon ulcer had disappeared. On August 4, 1944, the eye was still red, owing to the mydraine injection which was given. As *B.coli* was found in the culture, penicillin was immediately discontinued, as that might have been an additional cause for the redness. The eye became completely white within 36 hours and the patient was discharged from hospital. (Paintings of the eye on admission and 24 hours later. Figs 1 and 2.)

(2) *W.P., aged 41 years.* On July 26, 1944, this patient's right eye was scratched by a baby's finger. On July 28, 1944, she developed a hypopyon ulcer, and July 29, 1944, was admitted to hospital, when penicillin was started. Twenty-four hours later, there was a very great improvement which was maintained. On

August 4, 1944, the eye was almost well and the patient was discharged on August 7, 1944, perfectly well. The day after discharge apparently a little trouble occurred with the eye and on August 17, 1944, she was readmitted with a bloodstained hypopyon, although no staining ulcer was present. The clinical state was one almost characteristic of gonococcal infection. A cervical swab was done and gonococcus found. She was then transferred. (Figs. 3 and 4.)

(3) *W.S., aged 35 years.* This man had a corneal abrasion on July 26, 1944, from wood. A very nastily infected hypopyon ulcer developed and he was admitted for penicillin treatment on August 1, 1944. On August 4, 1944, the eye was perfectly well and the man discharged from hospital. No recurrence was observed.

(4) *W.B., aged 46 years.* This man was admitted to hospital on August 3, 1944, with a left corneal ulcer and hypopyon and also bilateral severe conjunctivitis. The left eye had been painful for six days. The left lacrymal sac was blocked and excised on August 3, 1944. The left eye cleared up completely, penicillin being stopped on August 9, 1944, when he was discharged. No further complications were observed, and the culture showed diphtheroids only.

(5) *H.W., aged 67 years.* This man was admitted on August 5, 1944, having been hit in the right eye by an ear of wheat, four days previously. On admission he had a hypopyon ulcer. Culture showed diphtheroids only. Penicillin was started straight away, in addition to the full treatment, with the exception of vitamin C, which was not given until 24 hours later. The ulcer was very much better but the hypopyon had not gone. Vitamin C was then given intravenously, and the hypopyon disappeared in a few hours. As the eye remained very red, penicillin was stopped on August 10, 1944 and recommenced on August 15, 1944. A culture was done in the meantime, and diphtheroids only were grown (*micrococcus tetragenus*). The patient was discharged from hospital on August 22, 1944, and no further trouble occurred. He had a well-healed, fairly dense scar, rather resembling a disciform keratitis. (Figs 5 and 6))

(6) *J.D., aged 20 years.* This patient had a foreign body in the right eye for five days. It was removed on August 5, 1944, and she was admitted to hospital on August 6, 1944, with a hypopyon ulcer. This case, like the last, was treated by a full treatment without vitamin C, and, as in the previous one, a great improvement in the ulcer occurred, but there was not the amount of absorption of the hypopyon that one would have expected. Vitamin C. was then given, and the hypopyon disappeared in a few hours. The eye was a little irritable on

FIG. A.

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FIG. 4.

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FIG. 2.

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FIG. 3.

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FIG. 1.

FIG. 8. *J. Bayes*

FIG. 7. *J. Bayes*

FIG. 10.

FIG. 9. *J. Bayes*

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FIG. 11.

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FIG. 6.

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FIG. 12.

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FIG. 5.

discharge on August 21, 1944, but this later disappeared and she was quite well without any further treatment. (Figs. 7 and 8.)

(7) *E.J., aged 30 years.* This was a very painful, dirty, phlyctenular ulcer which occurred in a patient in a sanatorium. Treatment with penicillin and atropine only was started on August 16, 1944, at 5 p.m. On August 17, 1944, the ulcer was much cleaner, the eye whiter, and the pain gone. On August 19, 1944, the condition was well and penicillin was stopped. The pathological report before treatment started, showed a moderate number of staphylococcus albus, coagulase positive. There was no hypopyon in this case and no vitamin C was given. (Figs. 9 and 10.)

(8) *R.D., aged 58 years.* This man was admitted to hospital on August 29, 1944, with a hypopyon ulcer of the right cornea, the left eye being useless on account of a large corneal scar. Penicillin was started at once. The eye was much cleaner the next day, but the hypopyon had not gone. Vitamin C was started and all traces of the hypopyon had disappeared on September 2, 1944. On September 5, 1944, penicillin was stopped and the eye was very nearly white, the ulcer being healed.

(9) *F.B., aged 60 years.* This man had a hypopyon ulcer of a week's duration and was treated merely by carbolicising, atropine, constant heat, short-wave diathermy and an injection of vitamin C. In 24 hours, as the painting shows, the hypopyon had completely disappeared, and all infiltration of the ulcer had likewise gone. He was discharged from hospital at the end of a week, with a white eye. (Figs. 11 and 12).

Although very much impressed with the value of penicillin, I feel that this report is incomplete. I have the impression that, if penicillin is used for very long, the eye remains red, due either to irritation by the penicillin itself, or perhaps to irritation by ordinary non-pathogenic organisms thriving on the penicillin and causing the redness. Two or three cases improved from that point of view, very soon after the penicillin was stopped. This suggestion means that a much closer pathological investigation than has ever been contemplated up to now, should be undertaken.

I am also not satisfied that it is advisable to carbolicise all ulcers and feel that it might be far better if, instead of carbolicising, the ulcers were curetted before the instillation of penicillin. The reason for this idea is the dramatic recovery of the case in the sanatorium. (B.7.)

Another point which must be far more carefully investigated is the relative value of vitamin C and penicillin. There seems to be little doubt at present that penicillin heals the ulcers, but does not much affect the hypopyon. It also seems that penicillin and

vitamin C together produced a much quicker result than penicillin alone or vitamin C alone. This statement is only an impression, and should not in any way be regarded as a definite conclusion.

If it were possible for a large number of hypopyon ulcers to be treated in the same department, it seems quite likely that a definite course of treatment might be evolved for hypopyon ulcer, which would mean the loss of far fewer eyes than occurs at present.

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THE INTRA-OCULAR USE OF PENICILLIN*†

BY

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OXFORD

SINCE there appeared to be very little exact knowledge of the effect of penicillin on the intra-ocular tissues and of the fate of penicillin when injected into the eye, it was decided to study its action on the rabbit before proceeding further with its use in man. This paper, therefore, deals in the first section with experimental work and in the second section with the clinical application of this.

Section I.—Experiments on rabbits

Thirty rabbits were used. The experiments were planned from two points of view, in two main groups. In the first series the effect of injection of penicillin from various sources and in various concentrations was studied. The injections were made either into the anterior chamber or into the vitreous. Slit-lamp and ophthalmoscopic examinations were conducted at frequent intervals and in some cases findings were confirmed histologically.

In the second series the concentration of penicillin present in the aqueous or the vitreous at known varying times after injection was studied, both in normal eyes and in others in which aseptic inflammation had been produced.

SERIES 1.—*Study of the effects of intra-ocular injection of penicillin in rabbits.*

A. *Injection into the anterior chamber (16 eyes).* Various samples of penicillin were tried and the effect varied in severity, though not grossly in nature, with the sample used. The injections

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