may be a guide in other cases. They show what a large angle can thus be overcome, and the almost daily improvement obtained by orthoptic training after the operation. My only regret is that I did not have a photograph of the children taken before the operation, so that I could have another taken afterwards. In his paper of May, 1944, J. A. Magnus states that his case had little or no power of abduction after the operation, but in my first case the child has developed this power, and it seems possible that the second may also do so. As regards the advisability of recessing the internal rectus in these cases, this point must be left to the individual judgment of the particular surgeon, who should base his conclusions on the synoptophore readings taken before the operation. For myself, I am far from convinced that an advancement should be ever performed without a recession of the opposing muscle, though the recession may have to be only part of the way between the insertion and the equator.

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PENICILLIN IN OPHTHALMOLOGY*

With special reference to its application in treatment outside hospital

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THE scope of penicillin in the treatment of diseases of the eye has been widely discussed in recent papers by Milner (1944), Robson (1944), Florey and Florey (1943) in this country, and von Salmann (1943, 1944) and others in America. It is our purpose here to record our experiences in its use which has been largely directed towards ascertaining its value in self administration by patients

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in their own homes. We have by this means been able to eliminate the necessity for admission to hospital in many cases and to shorten the patient's stay in others. In these days of severe shortage of beds, this is no mean advantage. We also record here methods of application of penicillin and some points of laboratory technique which we have found convenient.

During the last six months we have used penicillin in the treatment of over 150 patients.

Clinical application

We have used solutions, cream and powder, but chiefly cream, which we prefer for the simplicity of its application.

1. Solutions. Normal saline was used as the vehicle throughout, and though not isotonic with tears, has proved entirely satisfactory. The use of solutions, however, necessitates the confinement of the patient in hospital.

Solutions are put up in E.M.S. perforated screw-capped bottles and are stored frozen as far as possible. We have not been able to show any deleterious effect on the solution by contact with the rubber washers in the few experiments made. Solutions of more than 100 units per c.c. retained their potency for many weeks in the refrigerator and for at least a fortnight at room temperature, providing they were not contaminated. To avoid contamination, we found it satisfactory to instruct the nursing staff to withdraw the penicillin into a syringe with a fine hypodermic needle, both needle and syringe being sterilised by boiling.

Solutions were applied as follows :—

(*a*) Instillation into the conjunctival sac of penicillin 250-500 U/c.c. This was used in cases of acute conjunctivitis with secondary corneal ulcers. It can only be applied to in-patients for the reason mentioned above, *i.e.*, the necessity for ensuring asepsis. Instillations were made two hourly during day and night for the first 72 hours, and after this period during the daytime only. Signs of improvement were observed after two or three days treatment with complete cure in 5-7 days.

(*b*) Instillation into the conjunctival sac of a solution of 1,000 U/c.c. was given in four cases of serpent ulcer of the cornea. The solution was instilled two hourly during day and night for the first five or six days and continued by daytime only after this. The treatment was combined with irrigation of the lacrymal passages with a less concentrated solution (250 U/c.c.) twice daily. Cure was obtained in 10-14 days. In all but one case, a fine superficial scar remained; the exception healed without any visible scarring. Hypopyon was present in all cases.

Two cases of gonococcal ophthalmia—one a child of four and

one an infant of two weeks—were treated in a similar manner. All discharge of pus ceased after three days treatment in both cases. The patients were allowed home on cream and came up for examination once every two days. Complete cure ensued in one week and the bacteriological findings were negative fourteen days after all treatment was stopped. No corneal involvement occurred in either case.

(*c*) A concentrated solution of penicillin was used in a case of penetrating wound of the sclerotic before suturing the wound. The wound healed by first intention in five days, but low-grade iritis supervened in about a month and it was felt advisable to remove the eye owing to the risk of sympathetic ophthalmia. It should be pointed out that at no time was there any evidence of infection.

We observed two cases of endophthalmitis, one part of a pneumococcal pyaemia, the other after a penetrating injury previously treated outside the hospital and sent in after ophthalmitis had developed. In the first case—a patient aged 78 years—10,000 U/c.c. was applied to the anterior chamber through a keratome incision. It was repeated on the next day, but this being unsuccessful, we changed the treatment to systemic penicillin. Hypostatic pneumonia developed and the patient died two days later. The eyeball was full of pus and there were signs of involvement of the orbital tissues and we could not observe the slightest improvement. The second case was one of a penetrating wound of the cornea with traumatic cataract and secondary iridochoroiditis —culture of the aqueous yielded a profuse growth of Neisseria meningitidis. The patient had three applications of 20,000 U/c.c. penicillin to the anterior chamber. This treatment was combined with one intravenous injection of T.A.B. vaccine. The hypopyon was syringed out of the anterior chamber with the penicillin solution on each occasion and enough of the solution was allowed to remain to keep the anterior chamber reformed. Complete cure was obtained in 10 days.

(*d*) Injection into the tissues was carried out in all cases of acute dacryocystitis where there was no definite abscess formation, and also in cases of minor suppurative affections of the lids, such as styes, suppurating Meibomian cysts, etc. Solutions of 1,000 U/c.c. were used and cures were obtained in 24-48 hours. This method can only be applied either under light anaesthesia, or with previous injection of 2-4 per cent. novocaine, started from an inflamed surface of the skin and injected very slowly. The latter method is more satisfactory because penicillin causes severe pain for ½-1 hour if injected into the tissues—the more so in the case of a cellulitis. Novocaine anaesthesia, however, lasts long enough

to render the above described procedure entirely painless. As adrenalin has been reported as having an inactivating effect on penicillin, it should be omitted from the local anaesthetic in these cases.

(*e*) Irrigation with 250 U/c.c. solution was applied in the after-treatment of an abscessed dacryocystitis after opening. It was done through the wound and through the lacrymal canaliculus. It was found that the cavity ceased to suppurate and assumed a healthy appearance in a much shorter time than is usual in these cases.

2. Cream. The modified Halden base of 30 per cent. lanette wax in water has been used. We found that one batch of this base became strongly acid (pH 3) after autoclaving, resulting in the destruction of any penicillin mixed with it and causing pain when applied to the conjunctiva. It is, therefore, necessary to adjust the pH of the base to 7·2 after sterilizing and we then find that it can be autoclaved for a second time without further change taking place. This difficulty of which we were previously unaware was first suggested to us when patients began to complain that the application of the cream was painful. Investigation of the cream made from this batch showed not only that it was acid, but that penicillin was completely absent. It is, therefore, essential that the potency of each batch of cream should be assayed bacteriologically. Penicillin solution is added to the sterile melted cream and after rapid mixing is poured immediately into tin applicator tubes of 4 gm. capacity, which have previously been plugged with cotton wool and sterilised by autoclaving. The open ends are closed with flamed forceps and the tubes are at once cooled in the refrigerator where they are stored until required. While it is doubtless desirable to add the penicillin to the cream at the lowest practicable temperature, we have been unable to show any loss of potency after penicillin cream has been immersed in a boiling water bath for 10 minutes, and as the pouring of the cream is naturally greatly facilitated by the higher temperature, we do so at one of 80-100 deg. C.

The application of cream seems to be so far the only method for out-patient treatment. We use a standard strength of 250 U/gm. The screw-capped applicator tube prevents contamination from outside and the small quantity given to the patient is used up before it becomes inactive by being kept at room temperature in the patient's house. A great number of patients received such treatment. Typical cases were as follows:—

Acute conjunctivitis with or without corneal ulcers. Chronic conjunctivitis. Marked ectropion with severe chronic infection of the conjunctiva. Blepharitis. Recurrent styes. Eversion of the lacrymal punctum.

In all cases, treatment was preceded by culture from a swab and sensitivity test, usually performed directly by placing two or three dabs from an applicator around the periphery of the plate.

In acute conjunctivitis, complete cure was obtained in 8-12 days with four hourly application of penicillin cream to the conjunctival sac. Considerable improvement was noticed as soon as the third day of treatment. In cases of marginal corneal ulcers, treatment was combined with one daily instillation of 0·25 per cent. scopolamine solution for 4-8 days.

We treated three cases of marked ectropion with severe chronic infection of the conjunctiva and had two cases of eversion of the lacrymal punctum under observation—all over 70 years of age. Cultures showed staphylococcus pyogenes in all cases and penicillin cream was applied. The two eversions healed completely in two weeks with the eyelid back to its original position. No recurrence was seen within two months. Of the three cases of severe ectropion, two healed in 4 weeks and the eyelids returned to their original positions. In one case, Snellen sutures were inserted and penicillin applied. The sutures were removed after 10 days and penicillin continued for 4 weeks with success. No recurrence was seen within 6 months.

Recurrent styes respond excellently to penicillin treatment. We treated the cases until the marginal redness cleared up completely and instructed the patients afterwards to repeat the applications for 3-4 days, at intervals of 2 weeks.

Cases of chronic blepharitis appear to be the most resistant to treatment. A large number were observed. In these cases, interrupted treatment proved to be the best. Application, as in the case of styes, was advised three times daily at first, with an interval of 10 days, and twice daily when resumed.

We have to report here two cases of serpent ulcer with hypopyon who refused admission to Hospital, thus leaving us with no alternative but out-patient treatment—with penicillin cream. Atropine was prescribed and the patients were instructed to apply the cream at three hourly intervals. Before the patients left hospital, we irrigated the lacrymal passages with penicillin solution and repeated this when the patients came for re-examination. Both cases were cured in three weeks. Nevertheless, we obviously do not think that cases of hypopyon ulcer should be treated as out-patients—at least for the first week—as the varying intelligence and skill of the patients would allow of too much hazard.

We have investigated the stability of penicillin creams at room temperature and at 2-4 deg. C. It appears that creams containing penicillin in the region of 1,000 U/gm. retain their potency for

at least 3 weeks at room temperature and 14 weeks in the refrigerator. Similar results were obtained with cream containing 100 U/gm. but one of 10 U/gm. deteriorated rapidly after 3 weeks. We also tested creams which had been issued to patients and had been returned to us at the end of the treatment.

The results were as follows :—

Stability of penicillin creams—creams made up to contain

Weeks	1000 U/Gm.		100 U/Gm.		10 U/Gm. *	
	Room temp.	Frig.	Room temp.	Frig.	Room temp.	Frig.
0	16	15	12	12	2	5
1	17	17	12	12	4	5
3	16	17	11	13	3	5
7	12	16	10	12	0	4
14	10	15	4	10	0	0

* Discrepancy between the initial zones was due to uneven distribution of penicillin in the original sample.

The creams used by patients and returned showed—

	Content U/Gm.	Days in Frig. before issue	Days used at Room temp.	Zone of Inhibition
1	1,000	1	43	9
2	400	3	13	12
3	400	16	—	15
4	250	1	21	10

NOTE 1.—The figures indicate zone of inhibition of the Oxford H. Staphylococcus in millimetres.

NOTE 2.—Tube No. 3 serves as a control to Tube No. 2.

In view of these results we put up tubes of not more than 2·5–3 Gm. penicillin cream which is sufficient for 7—10 days of treatment. A number of tubes were put up with 1 per cent. phenoxetol as a preservative.

3. Powder. Powders are made up in sulphathiazole powder, containing 5 per cent. magnesium oxide, in 50 gm. lots in sterilized 8 oz. flat medicine bottles, as described in the M.R.C.

memorandum. To each bottle 100,000 units of calcium penicillin powder is added giving a final strength of 2,000 U/gm. Potency appears to remain unimpaired for many months when stored in a refrigerator. The powder is issued in small quantities as required in screw-capped bijou bottles.

Powder was used in some cases of corneal ulcers as initial treatment, and in dusting infected areas, such as acute dacryocystitis after incision, and during after-treatment, and also for dusting the cavity and around after dacryocystectomy, in cases of chronic dacryocystitis. Applied to the conjunctival sac, it is a very effective way of treating torpid ulcers. Although the patients complain of prolonged " gritty " feeling, we can strongly recommend this mode of application. Another advantage is its long stability that makes it possible to carry and keep it anywhere without the danger of becoming ineffective.

In one or two cases of chronic conjunctivitis, with suspicion of nasal origin, justified by a growth of staphylococcus pyogenes from a nasal swab, we applied penicillin powder snuff. In both cases the condition improved, but we cannot report any permanent result as yet.

The purpose of this paper is to try to picture the *routine* application of penicillin at the Eye Department of a country hospital. We hope it will be of some practical value when penicillin will be available in commerce and ophthalmic surgeons outside hospital departments will make regular use of it.

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