

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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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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were made with a 2 c.c. Record syringe and fine needle. The rabbit was sometimes anaesthetised with intravenous nembital, but in later experiments, as skill increased, it was often found quite easy to use local cocaine anaesthesia alone. The needle (without the syringe) was introduced into the anterior chamber, usually at the limbus above, and the aqueous (between 0.1 and 0.2 c.c.) allowed to drain off. An equivalent quantity of the penicillin solution was then injected through the same needle. Approximately 0.15 c.c. could be injected without difficulty, though the exact measurement of the quantity used was not possible. The strength of the solutions used was expressed in units of penicillin per c.c. Thus, when 10,000 unit solutions were used the amount which entered the eye was approximately 1,000 to 1,500 units. In some cases weaker solutions containing 2,000 units per c.c. were used, 200 to 300 units then entering the eye.

The effect of the injection was watched with a slit-lamp at half hourly, hourly and then daily intervals for from one to three weeks. A few rabbits were kept for many months to eliminate the possibility of any late effects.

The changes observed began with the injection. The pupil contracted at once, but this was due to draining the aqueous and was not a specific effect of the penicillin, though with the more irritating samples its observed persistence for some hours may have been due to the chemical composition of the injection, though not necessarily to the penicillin itself.

The pH of all the samples which were tested was 6.5 and they were made up in normal saline. Almost immediately after the injection a coagulum formed on the surface of the iris. With some samples it appeared at once, with others only during the first hour. Only a few samples (*e.g.*, one batch of Pfizer 500-600 U/mg., 10,000 unit per c.c., and Eli Lilly 402 x 350326Z) failed to produce a coagulum during the first hour. In some cases it was a dense gelatinous transparent mass covering the whole of the surface of the iris. In others it entirely filled the anterior chamber as a thin jelly in which minute foreign bodies, such as fibres from filter paper, were suspended immobile. Our earlier samples contained many of these minute particles; later the solutions improved greatly in quality. In other cases the coagulum occurred in localised areas only. It was then attached to some part of the iris, sometimes to the anterior surface, sometimes to the pupil margin; occasionally it adhered to the corneal endothelium at the site of the needle puncture. In practically all cases the aqueous continued to circulate normally throughout the observations. The amount and density of the coagulum formed bore no relation to the units of penicillin actually introduced into the anterior chamber, being very slight or absent with 1,000 units or more of various Pfizer samples

and very marked with only 300 units of some Glaxo samples and also of a 7,500 unit tablet (B. and W.) supplied for intravenous injection. It would therefore seem to depend on the presence of impurities and not on the concentration of penicillin. In two cases (samples KB 43/25 and 150 unit/c.c. Ca salt) immediately after the injection the anterior chamber was seen to be filled with minute bright yellow glittering crystals. These were soon caught and held by the jelly-like coagulum which contracted into a small clot in an hour and a half. The yellow crystals disappeared in three to four hours. Both the eyes in which the crystals were observed exhibited a severe reaction but finally cleared up. The nature of the crystals is unknown. It is unlikely that they were a penicillin salt since they took nearly four hours to dissolve. A bright yellow flocculent deposit similar in colour to the crystals was observed in a third rabbit on which a solution made from a tablet supplied for intravenous injection had been used. In this case also the eye showed a severe reaction and did not clear up completely for 24 days. The presence of any yellow particulate deposit in the first few minutes would therefore seem to indicate the presence of irritating impurities.

Usually in uncomplicated cases the coagulum began to shrink in about an hour and in four hours it had practically disappeared, traces of it as rolled up shreds of faintly greyish appearance remaining sometimes for three or four days.

The eyes began to look red and irritable at or before 18 hours after the injection. There was usually conjunctival congestion and slight mucous discharge. Epithelial and endothelial bedewing were present and in five eyes there was definite oedema of the substantia propria. Free cells were circulating in the anterior chamber and the shrunken coagulum could be seen. An aqueous flare was present in most cases and in a few an intense exudative iridocyclitis. In four cases, however, the reaction was so slight that only a faint flare was present at 18 hours and even this had disappeared in less than two days.

The majority cleared up entirely in three days, the aqueous and anterior part of the eye becoming normal slightly in advance of the clearing cornea. In three eyes the corneal oedema did not subside and marginal vascularisation occurred on the fourth day. This subsided in two eyes within seven days, in the third it was severe for 12 days, and did not disappear for 17 days. Even this eye, which showed the worst reaction of all, did eventually recover, no abnormality being detectable in 24 days.

It is thus seen that the result of injection of various solutions of penicillin is to produce a reactive aseptic anterior uveitis of varying severity. It appears that even 100 per cent. pure penicillin produces some reaction. A small sample of practically pure sodium

penicillinate (approx. 1,670 u/mg.) was obtained and tested on one rabbit. A thin gel formed in the anterior chamber in eight minutes but no precipitate or particulate matter was noted. The gel was observed for two hours but disappeared almost completely overnight. The eye was practically well in twenty four hours. The variation in reaction severity is produced by the presence of impurities and is not related to variation in strength of penicillin. This suggested that injection into the anterior chamber of a rabbit might provide a rapid method of judging the toxicity of a given sample. A batch, (G 86 Glaxo) which had been found to produce a severe reaction when injected intramuscularly in man, was tested against two other batches, known to be satisfactory, (G 89 Glaxo and Eli Lilly 402 x 350326Z) with this in mind. It produced a more severe iritis than the other two samples, one of which showed only a small coagulum and the other practically none at all. The differences between the three were detectable within half an hour and most marked at 17 hours after injection. Not every batch which gave iritis in rabbits proved toxic to man and more work must be done before this method could be used as a standard test.

#### B. *Injection into the vitreous.*

Ten rabbits were used, some acting as controls since the effect of interfering with the rabbit's vitreous was not known.

The right vitreous of one of the control rabbits was punctured and a minute bubble of air injected. The left vitreous was injected with 0.1 c.c. sterile normal saline. In both cases the breaking of the vitreous gel showed immediately as a localised opacity seen with the ophthalmoscope. In the right eye this opacity remained localised, the air bubble disappeared and no effect was observed on the retina or optic nerve. The opacity was still visible and apparently stationary  $6\frac{1}{2}$  weeks after injection.

The saline injection in the left eye caused a larger and more diffuse opacity, appearing to spread slowly and to radiate from the original droplet. It was visible as streaky black opacities  $6\frac{1}{2}$  weeks later. No effect was observed on the retina or optic nerve. A small lens opacity developed close to the needle track and it is probable that the posterior surface of the lens was slightly damaged by the needle. No inflammatory reaction developed in either eye. The saline injection was repeated on two other eyes. No effect was produced other than the formation of a localised vitreous opacity. In one this disappeared in 4 days; in the other it could still be seen a month later. In neither was there any inflammatory reaction or fundus change.

It therefore seems that merely breaking the vitreous gel may cause permanent opacity in the rabbit but no detectable effect on the state of the retina. Opacification of the vitreous observed after penicillin injection is not therefore to be regarded as at all specific for the penicillin.

The nine rabbits used to study the effect of penicillin on the vitreous were all injected with a fine needle inserted well back alongside the edge of the superior rectus. Pfizer penicillin 10,000 units per c.c. was used in the first five as from the previous experiments this appeared to be one of the least irritating brands. Approximately 0.1 c.c. (1,000 units) was injected into each eye.

The course of events was similar in the first ten eyes studied though not of equal severity in all. Five eyes were excised early for assay of remaining penicillin. The other five were observed for varying periods up to 13 months.

The immediate effect was the formation of a localised vitreous opacity, with the track of the needle leading up to it. In two days the eyes were still quiet and the opacity still localised. Occasionally a few free cells were seen circulating in the aqueous or adhering to the lens. Between the third and fifth day diffusion appeared to occur from the original droplet and the vitreous opacity spread and became less dense. This thinning and spreading continued for about a month, after which the opacity shrank slightly and remained permanent. It was observed in one case for over a year.

From the fifth to the seventh day a severe exudative retino-choroiditis began, accompanied by various vascular changes. The first sign was the appearance of wide-spread areas of pallor, suggesting intense retinal oedema followed by sheets of whitish exudate lying in front of the retina and obscuring it. This became split and torn with reddish areas visible in the cracks; in the lower part of the eye the retina was either detached or raised up by choroidal exudate. At the same time the nerve head became swollen and the outlines of the fibres in the optic streak blurred. Large and small haemorrhages were seen on and around the papilla. In most cases these were from the veins and suggestive of a thrombosis of the central vein. In one eye both the veins and arteries were narrow and pale as from an embolus of the central artery, although there were also small scattered haemorrhages. The pupils showed no light reaction after the seventh day and all the eyes except one appeared to be blind. This one eye showed only small areas of retinal exudate and no definite haemorrhages. It partially recovered with slight blurring of the disc, pigmented retino-choroidal scars and small areas of organised exudate on the lower part of the retina, still visible a year later. The other four eyes continued to get worse. By the twelfth or thirteenth day the nerve fibres normally visible round the disc had disappeared as had also the greater part of the retina and the chorio-capillaris. The disc region showed as a round fluffy blob, protruding slightly from a smooth whitish fundus traversed only by the larger choroidal vessels. When the exudate had settled to the bottom of the eye large masses of dense black retinal and choroidal pigment, apparently extracellular, could be seen. Between the second and third

week an outgrowth of new blood vessels in thin leashes appeared from the region of the disc. They stretched into the vitreous and formed organised strands, some projecting from the papilla itself and others from the ends of the optic streak. The condition was one of combined retinitis proliferans and complete retinal and optic atrophy. Between the fourth and fifth week a degenerative iritis began. The aqueous flare reappeared, the uveal border of the pupil disintegrated and posterior synechiae formed. In two eyes lens opacities began at the fifth week and cataract with water clefts was complete between the third and fourth months. In the other three eyes the lens remained clear.

Sections of a moderately severe case taken at two months were examined. The cornea, iris and ciliary body appeared normal. The choroid was grossly thickened approximately to the extent of four to five times its normal thickness. The outer layer of the choroid, consisting of large vessels, was easily recognisable and the vessels contained blood. The choriocapillaris had, however, been replaced by a thick layer of fibrous tissue and no trace of normal capillaries could be found. In many places the choroid contained pigment cells and also large macrophages, their cytoplasm packed with pigment granules. These were more numerous in the lower part of the eye.

The retina had entirely altered in appearance. Near the ora serrata it was recognisable but the outer layers were entirely converted into cellular fibrous tissue and the ganglion cell layer and nerve fibre layer were disintegrating. Nearer the equator and all over the posterior pole the tissue was unrecognisable as retina. In some places it consisted of layers of fibroblasts, which could be seen laying down collagen in flat sheets among the remains of the neural elements and the pigment-containing macrophages. In other parts, especially near the optic disc, the internal and external limiting membranes could be seen, enclosing between them a fine fibrous tissue entirely devoid of nuclei. In some places this fibrous layer was thick, in others tenuous. Its appearance suggested that of the intercalary membrane which lines a coloboma and is similarly formed of fibrous and degenerate retina, devoid of choroidal blood supply.

The optic nerve was vacuolated and did not appear to contain nerve fibres. The disc itself was almost entirely fibrous and at its margins the choroid and the remains of the retina were welded into a continuous fibrous scar-like tissue. A few retinal vessels were seen in the centre of the disc but did not extend much beyond this. The sclera was normal as were the ciliary nerves.

The condition would thus seem to be a most complete neuro-retinal degeneration followed by fibrosis and accompanied by thickening and fibrosis of the choroid. Whether this was caused

by the penicillin itself or by the toxic impurities was not clear, and a further four rabbits were injected with the 1,670 (approx.) unit practically pure sodium penicillinate used in the investigation of the aqueous.

Six eyes were used. The solution (10,000 u/c.c.) which was colourless, was made by dissolving 2.8 mg. of the white powder in 0.5 c.c. sterile normal saline. The pH was 5. Approximately 0.1 c.c. was injected into the vitreous in each case. Sometimes the aqueous was run off before injecting in order to avoid a rise of intra-ocular pressure, in others it was not. This did not appear to affect the results. In all the eyes tested with the pure penicillinate the course of events was much more mild and none of the eyes became blind. In three of them no effect whatever was observed, beyond the formation of a localised vitreous opacity. In three, pathological changes were observed but retrogressed. In these a patch of whitish exudate formed in the vitreous apart from the opacity due directly to the penicillin droplet. In one of these the exudate appeared at the pupil margin, coming forward from behind and disappearing in four days. In the other two it remained in the vitreous, shrinking slowly, and in one of these sychisis scintillans appeared in  $3\frac{1}{2}$  weeks. This eye showed a single small retinal haemorrhage at the margin of the disc on the fourth day, which cleared up in 17 days. A doubtful patch of retinal oedema was also observed on the fourth day. It cleared up in 12 days. All the eyes showed normal fundi in three weeks.

It therefore appears that the serious results obtained with the impure penicillin samples were not due to the penicillin itself but to something else, unidentified, which produced the intense pathological change. Whether this change was initiated by a primary thrombosis of the retinal vessels leading to a secondary neural degeneration, or whether it involved the retinal elements directly could not be determined. Failure of blood supply, degeneration and fibrosis were the salient features of the picture and were absent or minimal and transitory in the six eyes tested with the pure salt. It seems obvious that only pure samples should be used for injection into the vitreous until our knowledge of the nature of the common impurities is greater.

The next series of experiments was designed to discover how long and in what concentration penicillin persisted in the eye after injection.

*SERIES 2. Studies on the persistence of penicillin solution injected into the aqueous and the vitreous of normal and inflamed rabbit eyes.*

I am indebted to Dr. E. S. Duthie for carrying out the assays and for his help over this part of the experiment.

*Methods.*—Aqueous humour was withdrawn directly into small sterile capillary tubes which were then sealed. The cornea in the limbal region was pierced with the broken pointed end of the tube, and the fluid allowed to run in by capillary attraction. The penicillin content was later measured using the slide cell technique with the Oxford H strain of staphylococcus showing complete inhibition at 0.03 units per c.c., as in the method described by Garrod and Heatley (1944). The bacteria usually grew well as colonies in the aqueous humour, but in the first cell this was supplemented by the addition of a small volume of serum and all subsequent dilutions were made in serum. Specificity of inhibition was checked by the addition of penicillinase to one cell containing undiluted humour, and failure of the bacteria to grow in the presence of penicillinase was taken as evidence of another inhibitory factor. This happened in one case, and the result was not recorded. Results are recorded as units penicillin per c.c. Thus complete inhibition at a dilution of  $\frac{1}{4} = 0.12$  units per c.c. penicillin.

In order to decide whether intra-ocular injection of penicillin was likely to be of therapeutic value we endeavoured to find out how long it remained in the eye after one or after two injections. Since changes in the composition of the aqueous might influence its rate of circulation and drainage, some normal eyes were used and others in which an aseptic iritis (aqueous flare and congestion of iris and ciliary vessels) had been induced by dropping hydrogen peroxide on to the cornea twenty-four hours before the injection.

Before beginning this series, however, an experiment was done to confirm the already accepted fact that penicillin injected intravenously does not appear readily in the aqueous. A normal rabbit was injected through the ear vein with 5,000 units of penicillin (Pfizer). After half an hour a sample of blood and a sample of the aqueous of the right eye were taken. After a further half hour the aqueous was drawn off from the right and left eyes, the rabbit was killed and the vitreous removed. The results were as follows :

After $\frac{1}{2}$ hour.	R.E. (aqueous) = 0.06 u/c.c.
	Blood = 0.5 u/c.c.
After 1 hour.	R.E. (aqueous) = 0.03 u/c.c.
	R.E. (vitreous) = nil.
	L.E. (aqueous) = 0.06 u/c.c.
	L.E. (vitreous) = nil.
	Blood = 0.12 u/c.c.

This would seem to show that intravenous injection would be of little if any value in infections of the aqueous or vitreous.

The series of injections into the normal aqueous was then begun. The results were as follows :



- 1,000 units injected. After  $\frac{1}{2}$  hour 80 u/c.c. remained.  
 1,000 units injected. After 1 hour 80 u/c.c. remained.  
 1,000 units injected. After 6 hours 0.5 u/c.c. remained.  
 1,000 units injected. After 12-18 hours Nil remained.  
 1,000 units injected. After 24 hours Nil.

It would appear that strong inhibitory action can be expected for at least six hours but that persistence for much longer is unlikely.

Injections into eyes irritated by dropping in  $H_2O_2$  twenty-four hours previously, gave somewhat similar results. The effect of  $H_2O_2$  (5 volumes or over) is to produce within twenty-four hours an aqueous flare and ciliary congestion. This normally passes off in a few days unless the application is repeated several times when a keratitis may be produced as well. The object of this part of the experiment was to find out whether an aqueous altered in constitution would retain penicillin longer, since the drainage of albuminous aqueous might not be as rapid as normal. We obtained no real evidence that this is so. On the other hand we did not produce any iritis severe enough to stop the circulation of the aqueous or to produce synechia.

The results of this series were as follows:

- 1,000 units injected. After 6 hours 0.5 u/c.c. remained.  
 " " " After 12 hours Nil-0.12 u/c.c. remained.  
 " " " After 24 hours Nil-0.6 u/c.c. remained.

Finally, 0.1 c.c. of a similar penicillin solution was injected into the vitreous and the amount present estimated in the aqueous and the vitreous at varying intervals. The figures given below appear to indicate that penicillin diffuses from the vitreous into the aqueous and disappears from the vitreous less rapidly than it does from the aqueous. On the other hand the effect of high concentrations of anything but chemically pure penicillin on the retina and choroid is so bad that, if we judge from the results in rabbits, it is inadvisable to use this method of treatment. It is, however, possible that the human vitreous, when infected, may tolerate at any rate weak solutions, the purer the better.

#### *Injection into Vitreous*

<i>Time</i>	<i>u/c.c. in vitreous</i>	<i>u/c.c. in aqueous</i>
1 hr.	180 u/c.c.	80 u/c.c.
18 hrs.	8 u/c.c.	5 u/c.c.
24 hrs.	8.5-21 u/c.c.	0.16-0.8 u/c.c.
48 hrs.	0.7 u/c.c.	0.06 u/c.c.
4 days	0.2 u/c.c.	0.06 u/c.c.

(2 injections given)

#### **Section II.—Use of penicillin intra-ocularly in man**

Twenty-nine eyes have been treated by intra-ocular injection of penicillin. These were all perforating injuries except one and were

mostly war wounds. There was an intra-ocular foreign body in 23 of the eyes. This was magnetic in 17 cases and was removed. One non-magnetic intra-ocular foreign body was also removed. In six cases therefore an intra-ocular foreign body remained. In one case this was a piece of "Dural." In the other five the nature of the foreign body was unknown. Four of the remaining six cases had severe perforating wounds without an intra-ocular foreign body. Two of these were injuries with wood. The other two cases were respectively an infected cataract operation and corneal ulceration with hypopyon.

All of these twenty-nine cases had severely injured or highly infected eyes and judged by ordinary clinical standards would have been lost. Severe cases were chosen for the trial of intra-ocular penicillin because, in order to decide whether penicillin is an improvement on routine methods of treatment, one should theoretically use only cases in which from general clinical experience the prognosis is considered to be hopeless, *i.e.*, unless the eye was excised the pathological process would continue indefinitely. If under this severe test an unusually high proportion of eyes treated with penicillin healed in a reasonable time the inference would be that the penicillin was responsible. Nineteen of the eyes were cultured and the following organisms grown:

Staph. aureus—No. of cases 7	B. coli—No. of cases 1
Staph. albus—No. of cases 4	B. xerosis—No. of cases 2
Staph. albus with other organism—No. of cases 2	Sterile—No. of cases 3

The technique of treatment followed in all the twenty-nine cases of intra-ocular use of penicillin was as follows:

a. *The solution.* This varied from 50,000 units in 0.25 c.c. normal saline to 1,000 units only. Solutions containing 50,000, 25,000, 12,000, 7,250, 2,700, 3,000 and 1,000 units in 0.25 c.c. were tried. 0.25 was approximately the amount which could be run into the anterior chamber, though whether it was all retained was doubtful, some always appearing to escape beside the lacrimal nozzle which was used to run it in through a small broad needle incision. The actual strength used did not appear to matter much, except that it happened that the best results were obtained with the weaker solutions, except in two cases which received 25,000 units each and recovered well. It happened, however, that the stronger solutions were mostly used on the more desperate cases, often being run in through the original wound, sometimes into the vitreous.

In all the cases the prognosis was worse if the lens was injured; in all the eyes in which penicillin came into direct contact with the vitreous the vitreous became opaque and the sight was not regained. Further work with purer solutions is needed before this question of action on the vitreous in man can be finally settled.

In all the cases which recovered there was a reactive iritis lasting four days and subsiding suddenly.

It would appear that in exogenous infections of the anterior part of the uveal tract without injury to the lens or with an intact posterior lens capsule, injection of penicillin into the anterior chamber once or twice is indicated. In two cases it was done three times, but one of the eyes was excised, the other remained blind, so that there appears to be no indication for continuing if the eye does not quieten after two injections.

All these cases were simultaneously treated with a penicillin ointment containing 0.7 units per mg. (7,000 units penicillin dissolved in 1 drop of water and beaten up in 10 gms. of sterile vaseline) applied to the lid margins and conjunctival sac three hourly during the day, in order to maintain sterility of the external parts of the eye.

The results of treatment were that eleven eyes had to be excised as no improvement followed the treatment. Eighteen eyes remain to be considered. Nine of them healed and remained quiet and painless but were blind from the damage done by the original injury. In three of these the penicillin was injected into the vitreous which became opaque and did not clear. One healed but with a cataract which can be extracted later. One regained 6/36 vision and one 2/60.

The remaining six eyes are of greater interest and will be described in detail.

1. Mrs. H., aged 76 years. Infected cataract wound. The eye was seen to be infected 36 hours after the operation. Staph. aureus was grown from the lips of the wound, the conjunctival culture having been sterile two days before the operation. The patient was put on M. and B. 693 by mouth, atropine 1 per cent., and a solution of 125 mg. 110 unit penicillin in 25 c.c. normal saline dropped into the eye two hourly. The eye got steadily worse and the patient started vomiting after two days. The M. and B. 693 was stopped and the synthetic mydriatic, E.3, substituted for atropine as there were signs of irritation. The eye got worse for the next 12 days, pus forming in the anterior chamber. On the 14th day after operation a broad needle incision was made in the cornea and the anterior chamber irrigated with 2,750 units of penicillin (25 mg. 110 unit penicillin (Glaxo) in 0.5 c.c. normal saline: 0.25 c.c. of this was run into the eye with a lacrimal syringe and the excess allowed to run out). The injection was painful and the pain lasted several hours. It was repeated 24 hours later, again causing pain, relieved but not abolished by veganin. For the next two days there was a severe reactive iritis, but on the third day (four days from the first injection) dramatic improvement occurred. The pain disappeared and the eye quietened. The pus disappeared and a week after the

first injection the eye was quite quiet. Needling of the posterior lens capsule was subsequently performed and a visual acuity of 6/6 resulted. No further trouble has occurred during the ensuing five months.

This case is remarkable for the rapid clearing up of a severe operative infection.

2. G.R., aged 30 years. This patient had a perforating corneal wound, caused by a piece of wire spring, a month before coming to hospital. He had been treated with sulphonamides by mouth and atropine locally. Cultures of the conjunctiva grew corynebact.xerosis. Culture of aqueous humour was sterile. The eye was inflamed, irritable and was suspected of early sympathetic ophthalmia, but as the other eye was blind from an old corneal scar and the anterior chamber could not be examined, this diagnosis was not certain. There was in the injured eye an anterior synechia and fine K.P. One thousand units Pfizer penicillin were injected into the anterior chamber after drawing off the aqueous. The next day there was a further reactive iritis, which gradually subsided. The anterior synechia was divided 19 days after the injection of penicillin. The eye remained perfectly well with 6/5 vision.

This case is remarkable for the complete clearing up of a low grade chronic inflammation and the conversion of a "dangerous eye" into a normal one.

3. S., aged 22 years. This soldier sustained a perforating injury with a large metallic foreign body which was extracted without injury to the lens. The aqueous was sterile on culture, but the eye appeared much inflamed. A solution containing 25,000 units Pfizer penicillin in 0.25 c.c. was used to irrigate the anterior chamber at the time of operation. There was a reactive iritis which subsided within a week. The eye was healed and quiet in 10 days, with a visual acuity of 6/36. This should improve further, as there is no cataract.

4. A.V., aged 40 years. This patient sustained a perforating injury with retention of a small particle of duralumin in the eye. There was a corneal ulcer at the site of perforation, with hypopyon. The conjunctiva grew staph. albus., staph. aureus and diphtheroids. The anterior chamber was sterile. Treatment was at first by sulphathiazole locally and by mouth. The anterior chamber was washed out three times, but the pus reappeared. Seven thousand two hundred units Glaxo penicillin were then injected into the anterior chamber. It produced the usual reactive iritis, but the hypopyon then reformed. No improvement could be traced to the penicillin and six months later the eye recovered spontaneously, though with partial loss of vision. This is consistent with what is known of "dural" injuries in general and the recovery is probably due to the final conversion of all the aluminium into an

inactive form. The interior of the eye probably never had been infected.

5. Miss B., aged 69 years. This patient had a painful blind eye of some years' standing. She attended with three corneal ulcers and hypopyon. Cultures showed staph. albus (coag. neg.), Corynebact. type III. Two thousand one hundred and seventy-five units of penicillin were run into the anterior chamber. The pus disappeared and the ulcers began to heal in two days. They had practically gone in a week, but the eye was excised for pain and was found to contain a malignant melanoma. The penicillin had undoubtedly had a beneficial effect on the ulcers.

6. I.A., aged 52 years. This patient had a perforating injury with a piece of wood. The eye was obviously infected but only staph. albus could be grown. Twenty-four hours after the injury 2,500 units of Pfizer penicillin were used to irrigate the anterior chamber. A temporary improvement occurred but the eye remained irritable and painful and was excised six weeks later. The penicillin here had no effect on an eye in which one might have expected a good result.

It would appear that intra-ocular injection of high concentrations of penicillin is justifiable in severely injured or infected eyes but that the best results are to be expected when the infection is confined to the anterior segment of the eye and where the penicillin does not come in contact with the vitreous. Further work with purer solutions might give better results in these cases.

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## PENICILLIN IN OPHTHALMOLOGY\*†

The bacteriological, experimental, and clinical evidence of its value, including a personal series of 125 clinical cases

BY

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ABERDEEN

### I.—Bacteriology

SINCE the whole of penicillin is based on a proper understanding of its bacteriological properties, these will be briefly referred to first.

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