or left handedness, ocular dominance being of secondary importance. A right handed man engaged in work such as chopping wood, would tend to bring his right eye automatically into the main danger zone, in so far as foreign bodies flying more or less upwards were concerned: the analysis showed for this type of work a definite preponderance of injured right eyes. On the other hand if he is using a hammer and chisel, he tends to stand on the left side of his work, twisting the right side of his body downwards and forwards, bringing the left eye into the main danger zone: the analysis showed for this type of work a definite preponderance of injured left eyes. Foreign bodies may naturally fly off at various angles, rendering the matter of danger zones of equal importance to assistants and neighbouring workmen: a number of injuries thus incurred, appeared in the group. In this connection I was interested on the occasion of a visit to one of the small granite quarries in the Dublin mountains, to note the "safety" positions, relative to one another, adopted by the workmen. The owner informed me that these positions were firmly established in accordance with long tradition.

In the course of investigations in respect of the protection of the workman I have learnt to appreciate the importance of the foreman. A good foreman is the best possible interpreter of safety measures to his own group of men.

In conclusion I wish to acknowledge my indebtedness to Mr. William McCrea for his invaluable pathological reports. I would have asked him to supplement this paper with a comprehensive statement were he not already contemplating publication in respect of his work in the laboratory as a whole. I wish also to acknowledge my indebtedness to Mr. Harris Tomkin, who works with me in the same hospital department, for his permission to include in the series such of his patients as were admitted for treatment during the period under review.

A NOTE ON INTRA-VITREOUS PENICILLIN*

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SINCE clinical opportunities of administering penicillin by the intra-vitreous method are fortunately rare, these few cases may be of interest. The retinal changes described in experimental cases (Sorsby 1946, Mann 1946) and in some clinical cases (Rycroft 1945,

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Brown 1946, Mann 1946) make one hesitate to use the method at all, but most of these were treated before the articles mentioned appeared. A successful vitreous case following anterior chamber introduction (Cameron) and three similar successes (Neve, 1946) have been reported but are omitted from the discussion on account of their indirect introduction. At least twelve months have elapsed since the treatment was given and it was decided to try this method since it was felt that under the usual treatments (including penicillin in adrenalin sub-conjunctivally, Sorsby 1946), most of the eyes would have been lost.

The cases fall into four types, prophylactic, post traumatic vitreous infection, post operative vitreous infection and vitreous infection of unknown origin.

Prophylactic

CASE 1. S. J. aged 48 years. Large magnetic intra-vitreous foreign body entered by scleral wound; highly probable chance of infection; removed by wound of entry; 1,000 units pure penicillin in 0.1 c.c. distilled water given via wound of entry into the vitreous; 50,000 units subconjunctivally with adrenalin, repeated once; usual intensive treatments; corr. V.A. on discharge 6/18, twelve months later, 6/9 J.I.

CASE 2. H.V. aged 5 years. Stone injury; wound in cornea, ciliary body and sclera (9mm.), iris incarcerated in c.b. and some prolapse of iris and vitreous; lens had disappeared; scleral sutures, excision of prolapses, conjunctival flap; 1,000 units given as in case 1.

This eye settled without any symptoms but because there was doubtful projection and the intra-ocular damage could not be assessed on account of intra-vitreous haemorrhage, and the effects of vitreous penicillin with regard to sympathetic ophthalmia were unknown, it was enucleated on the ninth day.

CASE 3. K.R. aged 28 years. Magnetic f.b. intra-vitreous ($7 \times 6 \times 5$ mm.) via corneoscleral wound (6 mm.); iris and vitreous prolapse, lens not seen, removal by enlarged wound, corneal sutures, excision prolapse, and conjunctival flap. No vitreous was lost during the extraction of this large foreign body, probably indicating that the eye had already lost too much. Treatment was the same as in case 1, except that the vitreous penicillin was 2,000 units in 0.2 c.c. with 80,000 units subconjunctivally. Although the eye was symptomless and had good projection at times, it was enucleated because the projection varied and it was felt that the damage had been too great for useful vision. The eye was found to have only 1 c.c. of vitreous left, no lens, but no signs of infection or detachment.

Post-traumatic infection

CASE 4. W.B. aged 14 years. Magnetic foreign body, intra-vitreous ($4 \times 2 \times 1\frac{1}{2}$ mm.) via limbal wound 6 mm., early traumatic cataract. Magnet removal, no intra-vitreous penicillin; twenty-four hours later ocular pain, ciliary injection, hazy vitreous and poor projection suggested a vitreous infection. 2,000 units intra-vitreous penicillin given via wound as in case 1, with usual intensive treatment but no subconjunctival penicillin. In twenty-four hours symptoms had subsided, aqueous was macroscopically clear, projection fair. Five days later on sitting up a 'quiet' hypopyon appeared; lens continued to swell, but the eye still remained quiet with, however, only poor projection; enucleated on the fifteenth day, since it was felt that even if it stood a chance of recovery, the only fair projection combined with the unknown end result of intra-vitreous penicillin therapy might mean a liability to early sympathetic ophthalmia.

CASE 5. A.J. aged 33 years. Admitted with hypopyon, severe iritis and yellowish cloudy vitreous suggesting vitreous infection, apparently seven days old in a previously myopic eye of -18.0 D.sph; found to have a magnetic intra-vitreous foreign body; removal via limbal section; treatment as in case 1, but with 10,000 units in 0.2 c.c. given in region of ora; symptoms subsided in twenty-four hours; tension low on discharge; twelve months later projection poor, secondary cataract, eye soft, but no signs of active disease. Refused enucleation.

CASE 6. M.S. aged 21 years. Admitted with hypopyon ulcer; found to have intra-vitreous magnetic foreign body ($2 \times 1 \times 0.5$ mm.); vitreous haemorrhage, limbal wound, lens undamaged; magnet removal; usual intensive treatment (but without subconjunctival penicillin); hypopyon and symptoms began to subside; three days later a patch of exudate was seen behind the lens in the region of the wound, which gradually increased until five days later it had extended 5-6 mm. toward the posterior pole of the lens and the hypopyon had reappeared; 500 units penicillin given into the vitreous and 1,500 units subconjunctivally; hypopyon had gone by the next day, retro-lental exudate remained; 500 units repeated two weeks later on reappearance of hypopyon (the exudate had decreased only a little); discharged after six weeks with corr. V.A. 6/24. Readmitted two months later with 'quiet' hypopyon, no 'k.p.'; intensive treatment (but no subconjunctival penicillin); hypopyon went but reappeared seven days later; exudate still seen on lens; hypopyon cleared again only to reappear symptomlessly three months later; similar intensive treatment but with the addition of 50,000 units subconjunctival penicillin b.d. for two days. Evisceration advised because of probable chance of sympathetic ophthalmia. At

the evisceration the vitreous was removed intact with the anterior segment. The patch of exudate was found to be attached to a diffuse area of sterile pus in that region of the vitreous extending backward for about 6-8 mm. The rest of the vitreous was in good condition with an intact surface and no fluid.

CASE 7. S.R. aged 41 years. Admitted with five days history; yellowish vitreous haze; fibrous jelly like exudate in a.c. Marked iris exudate; bare P.L. Limbal removal of magnetic foreign body ($5 \times 2 \times 1$ mm.); 1,000 units intra-vitreous penicillin in 0.2 c.c. given at the ora; P.L. improved to poor projection in five days; exudate in a.c. began to clear; enucleated on account of poor projection and possible subsequent danger on the fourteenth day.

Post-operative infection

CASE 8. S. T. aged 70 years. Attempted intra-capsular extraction in which the capsule ruptured. Four days later severe iritis; intensive treatment begun including 50,000 subconjunctival penicillin with adrenalin; the next day a vitreous haze appeared, two days later the vitreous haze increased and became yellowish, projection became poor and a half size hypopyon had appeared: 1,500 intra-vitreous penicillin given via the ora and 90,000 units subconjunctival (adrenalin); symptoms and hypopyon had gone in 24 hours, vitreous still cloudy; discharged after three weeks with doubtful projection; three months later correction V.A. 6/60; twelve months later 2/60. He now shows a decrease in field corresponding to the injection area and the most dependent part of the vitreous, of which the apposite portions of the uvea show complete atrophy, and a single negligible floating vitreous opacity. The disc is atrophic to an extent suggestive of more damage than would be caused by arteriosclerosis (B.P. 200/100), when compared with the other eye, although this is not seen well on account of incipient cataract. Both have slight myopic changes (-5.0 D. sph.). There is a central patch 5 mm. diameter in Descemet's membrane. It is probable that these degenerative changes are all the result of the infection and treatment.

Panophthalmitis of unknown origin

CASE 9. S. C. aged 70 years. A controlled diabetic of some years, recently taken ill severely with no obvious cause; vitreous slowly became cloudy in one eye; followed exudate in pupil and dark cloudy aqueous; no treatment helped; only symptoms, lassitude and occasional pain; light perception eventually failed; evisceration attempted but choroid found firmly attached to a wrinkled sclera; enucleated. Following slow convalescence the remaining

eye affected similarly six months later; full medical investigations again negative; when perception had almost gone 500 units penicillin in 0.1 c.c. given via the ora; a.c. became clearer in 48 hours; vision returned to hand movements; no further improvement followed; death followed from an unknown cause three months later.

Method of administration

A retrobulbar injection of 1 per cent. novocaine and 1/10,000 adrenalin is given into the anterior part of the muscle cone in all cases. In the traumatic cases 2,000 units pure penicillin in 0.2 c.c. distilled water are given into the affected region via the wound of entry or other suitable surgical opportunity.

In cases with no open wound a wait of five to ten minutes is essential to allow the capillary bed to contract. This will allow an intra-ocular space of approximately 0.1–0.3 c.c. Using a Record tuberculin syringe with a 20 bore needle a spot is selected about 8 mm. from the limbus at a point most appropriate for the lesion. The needle is twisted like a trephine until it sinks gently into the globe. Theoretically for future visual reasons it is better to allow the needle to sink only 5 mm. Should the cornea become slightly cloudy during injection the pressure is stopped and then the plunger is withdrawn slightly. This may not happen with 0.2 c.c. and no more should be given in any case. The needle is then withdrawn and the usual treatment resumed.

Discussion

1. *Established infection.* The results of cases 6 and 8, the latter a man of seventy discharged with doubtful projection recovering to 6/60 in three months even including his subsequent central degeneration—and even cases 1, 3, 4 and 5 afford more hope than one would expect from previous results, owing perhaps to greater purity of the drug.

The almost inert physiology of the vitreous (Duke-Elder, 1932, Berens, 1936) serves as an incubator, but also allows a small amount of directly introduced antiseptic to be as effective as a large amount would be in any other tissue. It has been shown that no amount of systemic or local penicillin outside the vitreous will enter in sufficient strength to deal with more than a small infection which has been present more than 24 hours—(von Sallman, Meyer, di Grandi, 1944, Sorsby, Ungar, 1946), the most that can be expected is that the constant extra supply of infection exuding from the focus incubating in the vitreous will be kept in check as it reaches the uvea or aqueous—the vitreous meanwhile deteriorating chemically. Conversely, it would seem from these cases that to attack

the focus with a small enough dose to avoid general retinal and vitreous destruction, yet control the focus, may render the focus an inert mass which will be absorbed eventually like haemorrhage. Projection should theoretically be doubtful in cases which are really not so bad as they seem, since there will be a vitreous mass causing considerable light diffusion. Supporting this clinically, poor projection is sometimes seen in vitreous haemorrhage, and even in an a.c. exudate with a clear vitreous.

Isolated examples such as endophthalmitis have been cured by systemic treatment (Duke-Elder, 1947), some traumatic vitreous infections by protein shock, and one detachment with vitreous infection cured (6/6) by 150,000 units impure penicillin given orbitally in the operative region (Janus, 1945), but it is probable that the majority of cases of direct infection which have had no prophylaxis will be lost if no subconjunctival or vitreous treatment is given. Even subconjunctival therapy cannot be confidently used since the evidence probably appears after the incubation has reached a stage when only direct attack will suffice (Case 8).

Cases 1, 6, 8 suggest that on these principles retinal degeneration and optic atrophy might be avoided in otherwise normal eyes if treated early, useful vision remaining and justifying intra-vitreous penicillin in some infected vitreous conditions.

2. *Prophylaxis.* Is it justified however prophylactically? Many severely damaged eyes do recover without such treatment; cases, with large corneal wounds involving one or both ciliary regions and the vitreous, usually heal with an almost opaque cornea (partly due to sutures), and no lens. Since the life expectation of these individuals should see grafts commonly performed it is worth keeping these badly damaged non-irritant eyes even if they have only perception (sympathetic ophthalmia is discussed later). Infection occurred in this series of severe injuries in 20 per cent. probably corresponding to Desvignes and Boudon series. Since case 1 suggests that no deterioration will result (either due to the small quantity, purity, or dilution of the drug by the re-establishment of the circulation of the aqueous) and there is thus a chance of saving the infected 20 per cent., prophylactic treatment would seem justified.

Operatively the small vitreous volume even of 0.2 c.c. is less upsetting to a soft eye with a large corneal wound than a subconjunctival injection of 0.5 c.c. which occupies quite a large space and can deform the eye for a sufficient time to retard good immediate healing at the very time (first hour) it is most desirable. The normal physiology in any case is also greatly disturbed and the concentrations may not be as high as experimental evidence (Sorsby, Ungar, 1947) suggests. In small corneal wounds, of course, subconjunctival injections will be the best, and the concentrations will be in accordance with experimental evidence.

As a result, until further evidence is available a small prophylactic vitreous injection would seem justified in severe injuries.

Cases 5, 6 and 7, incidentally had impure penicillin.

3. *Vitreous Grafts.* Case 3 is of interest because in spite of hardly any vitreous remaining it settled with some projection. Had there been more vitreous it might have recovered. The only real objection to vitreous grafts in such cases would be infection. Perhaps it could be controlled by penicillin in protective solutions of small concentrations of, for example, 100 or 200 units per c.c.

4. *Uveitis.* It may be that the disappointing results in uveitis (Yasuna) are partly due to a certain amount of infection passing into the peripheral vitreous and acting as a constant focus. The rapid improvement shown by Weve's evacuation of "vitreous" exudate of localised patches of choroiditis by diathermy punctures (Weve, 1939) would suggest this. Intra-vitreous penicillin in generalised uveitis may perhaps be a future line of treatment rather than one to be avoided. Case 9, would appear to support this.

5. *Sympathetic Ophthalmia.* Perhaps it is unjustifiable to discuss sympathetic ophthalmia in relation to this small number of cases but since enucleation is mainly carried out with this in mind a few notes and queries are justified. First, in the prophylactic cases in which the penicillin may mask early sympathetic ophthalmia, is one justified in removal on purely varied projection? Will it be safe to wait until some irritant signs develop?

Similarly in the infected type the disconcerting suddenness of the cessation of symptoms and the continued quietude which follows, associated with the sepsis, presents a difficult prognostic problem. If the bases for the septic superstition were that either the local reaction was so severe that phthisis follows, or that the sepsis was sufficient to upset the infective or biochemical mechanism of sympathetic ophthalmia, then penicillin in these cases can be given no credit as a preventative. Does it follow that a septic case which has settled with penicillin is even better protected and can definitely be left until certain signs, preferably irritable, can be seen? Or should one assume that penicillin has stopped the septic prophylaxis before the process has been completed and the eye is therefore as prone to sympathetic as if sepsis had never been present?

In case 8, the waiting policy produced useful vision and it does not seem unreasonable to leave any case which was treated as soon as the vitreous infection was diagnosed to continue its course until definite irritative signs develop—none of which appeared in these cases although treatment was instituted later than it would be in a future case.

In all cases the advantage of the retrobulbar injection must be given credit. The near ischaemia during surgery is as useful as an

orthopaedic tourniquet, and the subsequent return of full circulation as a slow decompression is also useful, while the anaesthesia is incomparably better than a general.

Conclusions

This series is of course far too small for any conclusions but the somewhat better results than most previous cases have shown, suggest a more hopeful future than has been expected. The following suggested treatments with pure penicillin are therefore purely a working basis for use until further evidence is available.

1. *Prophylactic.* In any trauma with a large corneal wound in which there is a probability of vitreous infection as judged from the circumstances of the injury.

2. *Post-traumatic and post-operative vitreous infection,* In any post-traumatic and post-operative vitreous infection that does not subside immediately with subconjunctival penicillin (adrenalin).

3. *Vitreous infection of unknown origin and generalised uveitis.* In any progressive vitreal condition which suggests an infection even of low grade, that is not amenable to subconjunctival (adrenalin) penicillin.

4. *Vitreous graft.* The possibilities of vitreous grafting controlled by penicillin might be considered.

5. *Dose.* 1,000–2,000 units of pure penicillin in 0.1–0.2 c.c. distilled water.

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