

COMMUNICATIONS
FIBROSING RESPONSE TO AQUEOUS*
ITS RELATION TO GLAUCOMA

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SIMPLE open-angle glaucoma in the South African Bantu races is an even graver disease than in Europeans. Should the disease progress, as it usually does, so that drug therapy no longer controls the pressure and surgery becomes inevitable, the results of drainage operations are strangled by the relatively rapid fibrosis that develops. Generally this has been attributed to the keloid tendency of these races. Thus the very surgical trauma involved in raising a conjunctival flap seemingly automatically condemns the operation to failure.

In the hope of obtaining drainage with the minimum of trauma, the following method was devised. Polyethylene (polythene) tubing was drawn in a hot oven to capillary dimensions. It was then thin enough (about 0.15 mm. in diameter) to pass easily through a No. 26 hypodermic needle. The actual bore of the capillary cannot be discerned with the naked eye but becomes obvious when it is filled with a coloured liquid or examined microscopically.

The shaft of a No. 26 hypodermic needle with the hub removed and additionally sharpened to have a fine triangular cutting point was soldered to the end of an old cataract knife-handle to form a slightly obtuse-angled L. A well-fitting stylet acted as a plunger, so that a short length (8 mm.) of the polythene capillary in the needle could easily be expressed.

It is a relatively simple procedure to pierce the conjunctiva about 8 to 10 mm. from the limbus and gather it on to the needle. The point then engages the sclera a few millimetres from the limbus, and penetrates the anterior chamber (A.C.) in the angle just anterior to the iris. With sufficient of the needle point in the A.C., the stylet plunger is depressed until about 2.5 mm. of the polythene projects from the needle. Then, as the latter is withdrawn, the internal lips of the limbal wound grip the polythene, retaining it *in situ*. Thus a section of about 2 mm. projects into the A.C., 2 mm. lies within the limbus, and the rest is subconjunctival. Fixation of the globe is best obtained with a double-fixation forceps (*e.g.* Monnoyer). The immediate effect is the formation of a subconjunctival bleb, the A.C. being retained.

Experiments in rabbits showed that short lengths of polythene placed subconjunctivally caused no reaction whatsoever either macro- or microscopically. When the polythene was introduced into the A.C., a subconjunctival bleb formed but this had disappeared by the following day. Again, however, there was no reaction. The cessation of drainage was considered

* Received for publication March 2, 1959.

to be due to the normally very high fibrinogen content of rabbit aqueous which would naturally lead to clotting and block the tubing.

When it was ascertained that the tubing itself caused no harm, a capillary was introduced into the A.C. in a European patient with absolute glaucoma who had requested enucleation because of the pain. A large diffuse bleb formed. A small piece of tubing, about 4 mm. long, was also introduced, subconjunctivally only, into the opposite fornix. There was no untoward reaction to the polythene and the following day the eye was white and the drainage bleb was very satisfactory. The ocular tension, which had risen to over 90 mm. Hg, dropped to between 15 and 20 mm. Hg, and the result was most gratifying. After one month the eye was still draining very well and with everything seemingly satisfactory this operation was performed on the worse eye of an African native with advanced glaucoma. Again the immediate result was most pleasing. After a few months, however, it became obvious that the bleb was more circumscribed and tenser, and after a further month it had become solidified and thereafter contracted. The ocular tension rose and other procedures had to be tried. In the European

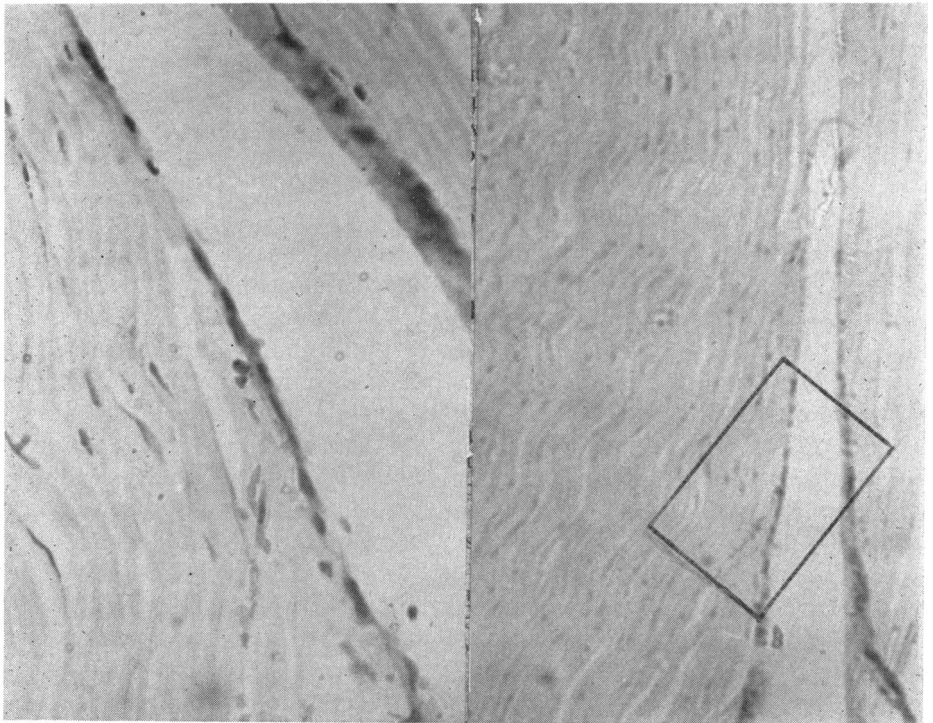


FIG. 1.—Tunnel through limbus. The polythene has been dissolved or displaced during preparation of the section. The tunnel is lined by ? endothelium ? fibroblasts. There are no inflammatory reactions.

the same changes occurred, and with the rise in tension and return of pain enucleation was again requested.

Fig. 1 illustrates the freedom from reaction round the tube in the limbus.

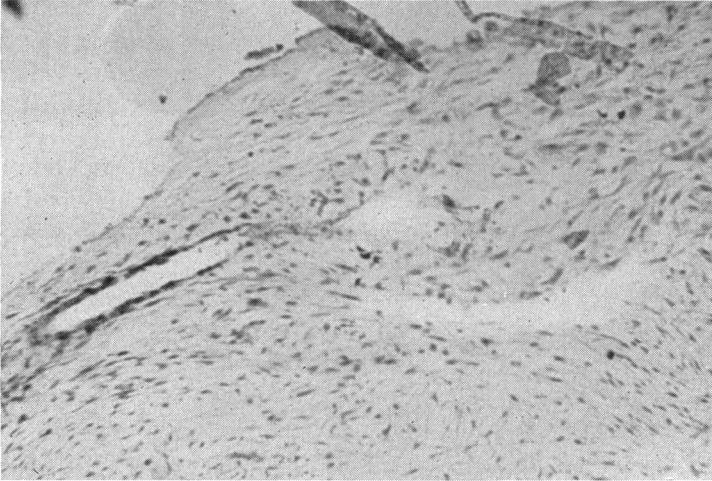


FIG. 2(a).—Subconjunctival fibroblastic reaction round the polythene.

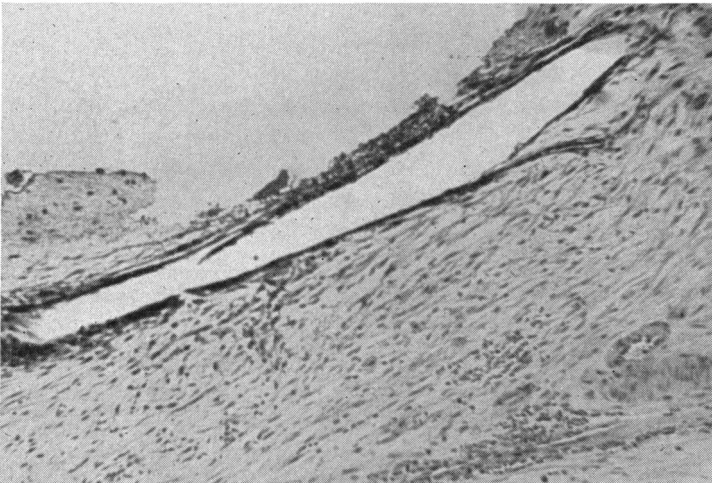


FIG. 2(b).—Similar subconjunctival reaction in the African native. The polythene and fibrous nodule were easily removed when other procedures were tried to relieve the raised ocular tension.

Fig. 2 shows the fibrosis round the subconjunctival end of the capillary. In the preparation of the sections the polythene is dissolved or displaced. Sections of the region where the small fragment of tubing had been intro-

duced, subconjunctivally only, showed no reaction and it was difficult to decide where the polythene had been, only a small gap being observed.

From these observations it is concluded that the aqueous excited a proliferation of fibroblasts which gradually thickened the walls of the bleb, then bridged the gap, and eventually sealed the end of the polythene capillary. The same result occurred in three other cases, including one of neglected acute glaucoma originally produced by acute angle closure. This suggests that the aqueous in open-angle glaucoma is not especially deficient in a possible fibrolytic enzyme.

In another case of painful absolute glaucoma in which the patient had requested enucleation, two polythene capillaries were inserted through a cyclodialysis approach by means of a similar introducer but with a blunt cannula, to try to establish drainage between the A.C. and the suprachoroidal space. To avoid probable haemorrhage into the A.C. by the sudden complete decompression of the eye, which would most likely occur with this type of operation, the pressure was first reduced very gradually by the slow aspiration of fluid from the eye by means of a very fine needle. Within a few days of the operation the pressure began to rise and after 4 weeks the eye had to be enucleated, the tension being as great as ever. Before the rising pressure clouded the cornea, the parts of the tubes visible in the A.C. were noted to be patent on slit-lamp examination. After enucleation, the A.C. was opened and one polythene tube was withdrawn. The posterior part of this tube was also found to be patent. The failure of drainage suggests either that there was obstruction round the end of the tube or that this route did not favour rapid enough absorption and therefore adequate drainage. Serial sections showed a few foreign-body giant cells in the ciliary body in the region of the scleral spur round the passage of the polythene, but further posteriorly, in the suprachoroidal space, where the ends of the polythene tubes were expected to have been, no reaction, fibrosis, or other cause of obstruction was found (Fig. 3, opposite).

In two other cases of advanced glaucoma, the same procedure was tried without success. It was therefore concluded that the success of cyclodialysis in some cases of glaucoma is not due to aqueous absorption *via* the suprachoroidal space. Hydrostatically one would not expect the aqueous to penetrate any distance into this space, as the pressure within the vitreous would maintain the choroid in apposition to the sclera at the same or even at a slightly higher pressure than that of the aqueous in the angle trying to enter a dialysis cleft. Furthermore, the prolonged persistence of choroidal detachment that can occur suggests that this is not a very good absorptive surface. The most likely mechanism is the breaking of peripheral anterior synechiae and the re-establishment of the normal drainage mechanism, whence its greatest value in glaucoma after cataract surgery.

The fibrosis of the subconjunctival bleb as described above is probably comparable with the subcutaneous thickening that follows long-standing

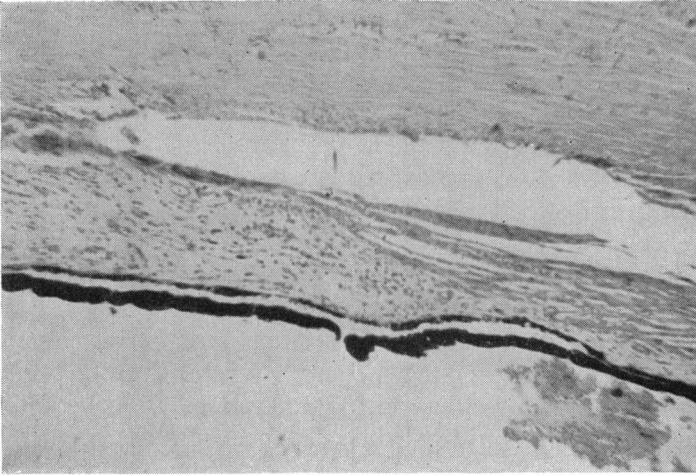


FIG. 3(a).—Suprachoroidal space, showing foreign-body giant-cells round the polythene passage in the region of the scleral spur and anterior peripheral iris synechia. Further posteriorly no reaction is visible where the polythene must have been.



FIG. 3(b).—Short oblique section of polythene is visible, but is displaced a little and has disrupted the adjacent tissue—an artefact caused by the sectioning.

lymphoedema, as occurs in elephantiasis and sometimes after surgical block-dissections.

The persistence of a bleb after drainage operations such as trephining and iris inclusion can only be explained by the growth of endothelium to line the cavity, at least in part. The absorption of fluid from such a cavity will depend upon the fortuitous connexion with aqueous veins, and upon the slow diffusion through the endothelial lining and tissues as occurs with

normal lymph flow. The contraction of the bleb that always occurs after drainage operations shows how slowly the endothelium lines the cavity. The subsequent extension of a thin bleb on to the cornea, or its generalized thinning, indicates the failure of absorption and the stretch that occurs as the pressure rises. The bleb then probably acts as a small saccular "aneurysm" of the A.C. that distends easily with rises in tension and obviates the adverse effects of this pressure on the circulation and structures in the nervehead.

In cases in which a trephine ceases to drain, therefore, the blockage is produced by fibrous tissue forming on top of the opening and eventually capping and corking it rather than by a circumferential proliferation from the wall of the trephine strangling the gap. Several cases of trephines that had ceased draining, with resultant rising ocular tension, have been relieved by introducing subconjunctivally, some distance from the original trephine, a fine needle knife (*e.g.* Grieshaber's), and by carefully cutting and separating the conjunctiva from the sclera. In this way the trephine has been reopened and good drainage has been restored and maintained for, so far, more than a year.

It also seems immaterial how the drainage opening through the limbus is made (trephine, punch, cautery, etc.), provided it is large enough to allow what must be the slow growth of endothelium to line the cavity. Likewise the value of gonio-puncture probably lies in the fact that it acts as a small goniotomy. It is also possible that a subconjunctival aqueous leak may play some part in the growth of pingueculae and pterygia once the abnormal change in the elastic and collagen tissues in these sites has occurred. I have frequently noticed the ooze of aqueous from largish vessels as pterygia have been dissected from the limbus, whereas this is seldom noted when raising a conjunctival flap well on to the limbus as is my wont in cataract surgery.

The failure of goniotomy in adults in cases of open-angle glaucoma suggests that the fault does not lie in the trabecula. Any defect in the endothelium of Schlemm's canal and its efferent vessels would favour fibrosis and obstruction of the lumen by the aqueous action on the surrounding tissues. The efferent vessels, being much smaller than the canal, are thus likely to be blocked sooner than the canal itself. With the hope of establishing new aqueous capillaries the following procedure was carried out:

A broad conjunctival flap based and extending well on to the limbus was raised in the upper hemisphere. A deep trough about 5 mm. wide and extending from 3 to 12 to 9 o'clock was then dissected in the sclera overlying and posterior to the region of Schlemm's canal. As the tissue was removed it became obvious that more and larger aqueous vessels were being opened. The dissection was continued until the general examination and focal slit illumination indicated that only a very thin layer remained. The conjunctiva was then replaced and carefully sutured with 6×0 catgut. The patient was an African with very advanced

glaucoma. Pre-operatively the cornea was slightly hazed and the tension was 70 mm. Hg which miotics and Diamox could reduce only to 40 mm. Hg. One week post-operatively the pressure measured 15 mm. but after 2 months it had risen to 30 mm. The lower hemisphere was then done, and the pressure has since remained at about 20 mm. This patient has now been observed for 7 months since the second operation. The troughs have partly filled in but, as anticipated, there is a marked increase in new blood capillaries. Most of these have now closed but several large aqueous veins can be seen in regions where they are not usually observed. One also gets the impression that the anterior chamber is slightly deeper. This probably is to be expected. The deep lamellar dissection overlying the angle would favour a slight ectasia. This would put the trabecula on the stretch which in turn would open the spaces of the meshwork and also allow Schlemm's canal to balloon out. It is obvious that during the dissection the greatest care must be taken not to enter the anterior chamber.

Although this record is of one case only, it is considered worth reporting so that others might try the procedure.

Summary

Observations in cases of very advanced glaucoma treated by means of capillary polythene tubing extending from the anterior chamber (A.C.) to the subconjunctival tissues indicate that the aqueous stimulates a fibrotic response in the subconjunctival tissues. The failure of drainage by means of a polythene tube from the A.C. to the suprachoroidal space suggests that cyclodialysis when successful is probably re-opening an occluded angle. A possible association between subconjunctival aqueous leaks and the growth of pterygia is suggested. Deep lamellar sclerectomy overlying Schlemm's canal is suggested as a means of stimulating the formation of new aqueous canals.

I wish to express my gratitude to Prof. J. Gillman of the Department of Physiology, University of the Witwatersrand, for giving me facilities for the experimental work on rabbits, to Dr. Christine Gilbert for permission to use the Histology Department, and to Mr. S. Dry for preparing the sections and micro-photographs.

ADDENDUM

Since this paper was submitted for publication, five more eyes with raised tension have been treated with the paralimbal lamellar sclerectomy. In four, one hemisphere only was done, and in all a normal tension was achieved. One had had a filtering sclerotomy that had ceased to drain within a month. The fifth case was that of a young man who had been suffering from intractable glaucoma for 6 months, which had followed a traumatic cataract treated with discission and curette evacuation. Miotics, Diamox, and cyclodialysis had failed to control the tension. The upper hemisphere was done first and after one week the lower hemisphere was also done because the tension appeared to be rising. The eye is now hypotonic and the patient is symptom-free.