Effect of aqueous-venous shunt on rabbit eyes

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The response of the normal rabbit eye to an aqueous-venous shunt has been briefly described in a previous report. The procedure consisted in establishing a shunt between the anterior chamber and an extraocular vein located under Tenon's capsule by means of a fine polyethylene tube. The animals were observed for a period of no longer than 12 weeks. Results were encouraging enough to warrant studies over a longer period of time, modifications of technique, and an investigation of the effect of this operation on rabbit eyes with hereditary buphthalmia.

Fourteen pigmented normal rabbits and 6 New Zealand albino rabbits with hereditary buphthalmos were used. Two of these 6 rabbits had unilateral buphthalmos. The materials used and the procedures followed have been described except for the following modifications.

The polyethylene capillaries had an outside diameter of 0.17 to 0.4 mm. anteriorly and 0.1 to 0.2 mm. posteriorly. The inside diameter was 0.08 to 0.2 mm. anteriorly and 0.05 to 0.1 mm. posteriorly. The polyethylene capillary was threaded through a polyethylene fixation sleeve with an outside diameter of 0.3 to 0.5 mm., and a length of 1 to 2 mm. The sleeve had a fixation ear with a groove located at the posterior end of the sleeve (Fig. 1). The capillary and sleeve were glued together with Eastman 910 adhesive, nonmedical grade. In order to anchor the implanted capillary to the sclera, two double arm 7-0 black silk sutures were used. One was placed in front of the fixation ear, in the groove. The other was located in front of the fixation sleeve and was intended to prevent migration of the capillary into the anterior chamber.

The length of the plastic capillary in the anterior chamber was 2 to 3 mm. In the vortex vein it did not go beyond its intrascleral course, usually 3 to 4 mm. The pressure inside the tube was increased after its insertion into the vein by clamping the vein. This forced out of the capillary any air bubble or tissue fragment which might obstruct it. When a blood clot was noted within the capillary lumen, it was flushed with a 1/5,000 solution of heparin sodium. A mixture of 10 per cent phenylephrine hydrochloride and 1 per cent cyclopentolate was used as a topical mydriatic at the end of the operation.

Controls were obtained by leaving one eye of each rabbit unoperated. The eye
Fig. 1. Modified surgical technique for aqueous-venous shunt. Above: Enlarged sketch of polyethylene tube with fixation sleeve (D) and ear (C). Z = anterior end of polyethylene tube. Y = posterior end. Below: Modified aqueous-venous shunt completed. A, point of exit of the vortex vein from the sclera; B, location of the incision in the vortex vein; E, portion of the tube which is in the anterior chamber at the end of operation.

with more advanced buphthalmos was operated upon in 4 bilateral buphthalmos cases. Enucleated globes were fixed in a 10 per cent formalin. The globes were opened and examined with a dissecting microscope. The specimens were then embedded in paraffin and the sections were stained with hematoxylin and eosin.

All data in this report were evaluated by testing the mean and standard deviation by the chi square method. Results were considered statistically significant when the probability was less than 5 per cent that the event considered was due to hazard.

Results

Effect on aqueous dynamics. An aqueous-venous shunt was created in 14 normal rabbit eyes, and in 6 rabbit eyes with hereditary buphthalmos in at least one eye. Five of the 14 normal eyes were excluded from this report because of accidental deaths 2 to 8 weeks postoperatively. This left 15 eyes on which observations could be completed. The postoperative follow-up period ranged from 8 weeks (2 rabbits) to 18 to 24 weeks (13 rabbits). Of 15 eyes, 8 showed a decrease of intraocular pressure and increase of outflow facility by tonography 24 weeks after operation (Tables I and II). The change in aqueous dynamics was more marked in the eyes with hereditary buphthalmos than in normal eyes. Results were divided into two groups: those in which the aqueous-venous shunt was patent, and those in which the shunt was not patent after operation.

Cases where the shunt remained patent. Eight rabbits, 3 normals and 5 with buphthalmos, were followed for 24 weeks and had an aqueous-venous shunt which remained patent. The average value of aqueous outflow facility in 3 normal eyes was 0.32 μl per minute per millimeter of mercury prior to operation, and 0.44 μl per minute per millimeter of mercury after operation, which is a statistically significant difference.

In the 5 eyes with hereditary buphthalmos, the average value for aqueous outflow facility was 0.06 μl per minute per millimeter of mercury prior to operation and 0.16 μl per minute per millimeter of mercury 24 weeks after operation, which is a statistically significant difference. The corneal edema improved soon after operation and this improvement was maintained during the period of observation (Fig. 2A and B). The control eyes showed no significant change either in outflow facility or in the corneal edema.

In another series of cases, the patency of the shunt was tested postoperatively by means of a fluorescein injection into the anterior chamber. The dye appeared in the lumen of the vortex vein soon after injection. In the current series, hypotension was created by means of repeated tonometry in 2 of 5 buphthalmic eyes with a patent shunt 24 weeks after operation. When the eye rapidly became very soft, a backflow of venous blood into the anterior chamber via the implanted tube was clearly seen.
Fig. 2. Hereditary buphthalmia before (A), above and 3 months after (B), below, aqueous-venous shunt. The improvement of the buphthalmia is indicated by improvement in corneal transparency.

At the present time, these 8 rabbits (3 normals and 5 buphthalmic) are in a long-term postoperative evaluation program. Therefore, microscopic dissection and histopathologic studies have not been performed on this group of animals.

Cases where the shunt was not patent. The shunt was not functioning in a total of 7 eyes (6 normals and one with buphthalmos). In 6 eyes of normal rabbits the intraocular pressure and outflow facility returned to their preoperative levels. This occurred after 8 weeks in 2 eyes, after 18 weeks in 3 eyes, and after 24 weeks in one eye. In none of these 6 eyes had the tube slipped into the anterior chamber. Microscopic dissection showed that in all cases the posterior end of the plastic capillary had perforated the wall of the vein and was located outside the venous lumen. In 3 eyes, the posterior end of the capillary was encapsulated, and in 3, it was surrounded by conjunctival cicatricial tissue. In all cases, there was some degree of neovascularization at the site where the plastic capillary had been introduced into the lumen of the vortex vein. The experiment in these eyes was terminated after dissection. The differences between preoperative and postoperative values for average intraocular pressure and outflow facility were statistically insignificant.

In one eye with buphthalmos the implanted plastic capillary had moved further into the anterior chamber 18 weeks after operation. Dissection showed that the posterior end of the capillary was outside the vein and partially encapsulated. New vessels were present at the site where the plastic capillary had been introduced into the vortex vein. The vein itself, however, was reoperable in spite of mild stasis. The outflow facility in this eye was 0.03 μl per minute per millimeter of mercury prior to operation and 0.15 μl per minute per millimeter of mercury prior to terminating the experiment; this probably indicates that the plastic capillary had migrated recently or that aqueous was still flowing through it into Tenon’s space.

In this group, no change in either average intraocular pressure or outflow facility was found in the control eyes.

Effect on depth of the anterior chamber. In 3 normal rabbits and in one buphthalmic animal, the depth of the anterior chamber was measured with the Zeiss anterior chamber depth micrometer 12 weeks postoperatively. Each measurement was an average of 10 readings. The average value for the anterior chamber depth in 3 normal rabbit eyes was 3.41 mm. after operation, and 3.14 mm. in control eyes. Anterior chamber depth in the buphthalmic rabbit was 4.66 mm. after operation and 5.46 mm. in the control eye. The number of eyes measured was too small to evaluate the significance of the differences observed.

Factors influencing patency of the shunt. Dissection before killing the animals showed
that the implanted polyethylene capillary was harder and more rigid than at the time of implantation. It occurred to the authors that proper placement of the polyethylene tube might play an important role in the patency of the shunt. In 14 of 15 eyes the placement of the tube was recorded and divided in two groups. In 9 eyes the tubes were properly placed. In all of these the plastic capillaries were in position 18 to 24 weeks after the operation. The shunt was still patent in all but one eye. In 5 eyes the tubes were placed improperly. In all cases, the plastic capillary had perforated venous wall and the shunt was not functioning 18 to 24 weeks after the operation (Fig. 3). These findings stress the importance of the proper placement of the tube during the operation.

Postoperative reaction. In the eyes of normal rabbits the postoperative reaction was essentially the same as in the early
Fig. 3A. Proper placement of the tube. A, limbal incision; A', venous incision; T, polyethylene tube; V, vortex vein.

Fig. 3B. Improper placement of the tube. B, B', bent tube.

Fig. 3C. The result of improper placement of the tube. BT, bent tube due to improper limbal placement at the time of surgery; C, posterior end of tube had perforated venous wall and located outside of venous lumen 24 weeks after operation.

series. Mild to moderate congestion, localized corneal edema, localized subepithelial neovascularization of the cornea, and a small peripheral anterior synechia along the implanted capillary were constant findings. No keratic precipitates or lens changes were observed with the slit lamp. Severe reaction occurred when the anterior end of the tube came in contact with the corneal endothelium or iris.

Extrusion of the polyethylene capillary at the site of limbal incision with subsequent epithelial downgrowth into the anterior chamber was observed in one normal rabbit 18 weeks after operation.

A small hyphema occurred following tonometry in one buphthalmic eye 2 weeks
after operation. In this case, backflow of venous blood into anterior chamber via the implanted tube was clearly seen. The hyphema absorbed without complication and the shunt was still patent 6 months after operation.

In buphthalmic rabbit eyes, the congestion of the anterior segment, corneal edema, and the reactivity of the pupil to light were usually improved within 24 to 48 hours after the operation. It was difficult to evaluate the degree of immediate postoperative reaction in these eyes due to the variable degree of corneal haziness and preexisting congestion.

In general, the polyethylene capillary was well tolerated and no medication was required postoperatively either in the normal eyes or in the buphthalmic eyes (Fig. 4).

**Histologic examination.** In 4 eyes (one with a functional* and 3 with a nonfunctional shunt) a histologic examination was performed. One eye was enucleated after 18 days, one after 2 months, and 2 after 4½ months.

Changes in the cornea localized to the area of operation were observed in all eyes. Varying degrees of subepithelial vascularization of the corneal scar, lymphocytic infiltration of the corneal stroma, and adhesion of the iris to the tube were noted.

The episclera showed mild to marked degrees of granulomatous reaction which was characterized by the presence of giant cells, eosinophiles and epithelioid cells. In 3 eyes, there were many polymorphonuclear cells around the suture track or around the polyethylene tube. In all 4 eyes, venous dilatation was present due to episcleral granulomatous reaction.

The vortex vein usually showed an increased thickness of its wall near the implanted tube. In 2 eyes, stenosis, thrombosis, and recanalization, and fibroblastic proliferation have also been observed. In the eye with a functioning shunt, the vortex vein was patent 18 days after operation despite the increased thickness of the venous wall and the presence of many polymorphonuclear cells at the site of venous incision. It is difficult to evaluate the degree of reaction of the vein to the polyethylene tube as there was a considerable variation and the number of eyes available for examination was small.

A nonspecific type of iritis characterized by the presence of lymphocytes and plasma cells within the iris, and a small synechia between iris and tube were observed in all eyes. In one eye, there were many polymorphonuclear cells in the chamber angle despite the absence of clinical evidence of hypopyon. A fibrous membrane and scar were seen in the chamber angle at the site of the incision. The degree of cellular infiltration of the iris varied but was not severe. No detachment or atrophy of the ciliary body was noted. In no case was the lens damaged or cataractous. The vitreous and retina appeared unaffected. A more detailed histopathological study is now in progress.

**Discussion**

Tonographic studies on normal and buphthalmic rabbit eyes showed that the aqueous-venous shunt had a significant effect on the intraocular pressure dynamics
as long as the shunt was functioning. In buphthalmic eyes, the condition of glaucoma usually improved soon after operation and this improvement was maintained during the postoperative follow-up period as long as the shunt was patent. Both the intraocular pressure and outflow facility returned to preoperative levels in eyes in which the implanted tube was not patent. These findings supported the results of earlier experiments with normal rabbits.\(^1\)

In 2 of 6 buphthalmic eyes, the preoperative intraocular pressures were 15 and 19 mm. Hg respectively, despite their low outflow facilities (0.03 \(\mu\)l per minute per millimeter of mercury in one case and 0.10 \(\mu\)l per minute per millimeter of mercury in the other). The average preoperative values for intraocular pressure (29 mm. Hg) and for outflow facility (0.05 \(\mu\)l per minute per millimeter of mercury) in all 6 eyes did not appear consistent with the buphthalmic condition. McMaster\(^2\) has stated that the aqueous inflow of the buphthalmic eye in rabbits was consistently lower than in the normal eye and that the intraocular pressure was not necessarily elevated even when the outflow facility was decreased. Although the tonographic evidence is only presumptive, it agrees with McMaster’s findings. A more detailed discussion of hereditary buphthalmia in rabbits is not within the scope of this paper.

Failure of the operation was due to one of the following factors: (1) migration of the tube into the anterior chamber, which either brought it in contact with the corneal endothelium, or with the iris, or pulled it out of the venous lumen; (2) perforation of the venous wall posteriorly, due to the increased rigidity of the polyethylene tube, or to improper placement of the tube; (3) obstruction caused by a tissue fragment or a blood clot in the lumen of the tube during the surgery; and (4) thrombosis of the vein.

The anchoring of the implanted plastic capillary has been improved. The incidence of failure, due to slippage of the tube into the anterior chamber, was substantially less in this series (7 per cent) than in the first series of cases (70 per cent). Migration of the tube into the anterior chamber could produce a severe reaction and resulting blindness. While this possibility cannot be disregarded, we believe it to be unlikely if the tube is properly secured to the fixation sleeve and sclera. As yet a postoperative reaction severe enough to cause marked ocular damage or blindness has not been observed in experimental animals. The implanted capillary can be removed easily if the postoperative reaction requires it.

The gradual hardening of the polyethylene capillary after operation has been another factor contributing to failure of the surgical procedure. In order to remedy this problem, proper placement of the capillary at the time of operation is found to be helpful. The less the capillary is bent, the greater the chance that the shunt will remain patent. The smaller its diameter, the less is the incidence of extrusion. Despite these problems, a polyethylene capillary is preferable to one made of silicone because it will not be collapsed by the fixation suture or by the contraction of scar tissue.

Another minor drawback of this procedure is that air, or a small tissue fragment trapped in the capillary, will obstruct the aqueous flow unless the intraocular pressure is high. This occurred in one case. In order to avoid this, the pressure in the vortex vein is built up by blocking the blood flow with a clamp. As a result, blood escapes continuously through the capillary prior to its introduction into the anterior chamber, preventing its blockage.

It has been observed that an increase in the thickness of the wall of the vein, stenosis, thrombosis, and recanalization may occur following an otherwise successful operation. It is not known whether this complication is frequent in the absence of
infection. It is hoped that an answer to this problem can be supplied through current experiments with the monkey.

In his recent report on the seton operation, Richards noted that the decrease in intraocular pressure produced by LaRocca's implant (Polyvinyl U tube) was perhaps due to detachment of the ciliary body. In this series, 4 eyes in which the histological sections were performed showed no evidence of ciliary body detachment or atrophy.

The main advantages of the aqueous-venous shunt are the following: (1) The technique is not difficult and, with experience in microsurgery, the operation can be completed routinely in one hour or less. (2) Subconjunctival scarring is unlikely to affect the patency of the aqueous-venous shunt because the posterior portion of the capillary is lined with venous endothelium. (3) If a reoperation is required, the capillary can be readily exposed and its patency checked in situ. The same vein, or another vein, can be used. However, it should be kept in mind that venous stenosis may occur after operation and this may interfere with the functioning of the shunt.

Observations made with capillary tube of other materials and a more detailed histopathological study are in progress.

Summary
An aqueous-venous shunt was created in rabbits with normal eyes and with hereditary buphthalmia. Modifications of technique and the results of a longer postoperative observation are presented in this series of cases. The implanted capillaries are more stable with the current techniques.

Rabbits with buphthalmia showed a substantial increase in outflow facility associated with marked improvement in the corneal edema after the operation. A significant effect on the intraocular pressure and outflow facility of normal and buphthalmic eyes persisted for as long as the shunt remained patent.

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REFERENCES