Experimental serous and hemorrhagic uveal edema associated with retinal detachment surgery. Thomas M. Aaberg.

A study of the effects of hypotony, cryotherapy as the adhesive modality and vortex system obstruction in repair of experimental retinal detachment in the owl monkey is reported. The presence of serous uveal edema (detachment) correlated mainly with the degree of vortex obstruction. Hemorrhagic extravasation appeared to be a more exaggerated manifestation of such vascular stasis.

Serous or hemorrhagic accumulation of fluid in choroidal tissue and the suprachoroidae, most commonly known as choroidal edema in Europe or choroidal detachments in the United States, has been said to occur routinely in retinal detachment surgery. Some authors believe the expansion of the suprachoroidae occurs to some degree after all retinal detachment operations. Serum choroidal edema appeared clinically on the first or second postoperative day in 25 per cent of the series reviewed by Hawkins and Schepens. Actual hemorrhage into the choroid and suprachoroidae occurred most commonly at the time of drainage of subretinal fluid, occurring in one per cent of cases.

In an experimental study on squirrel monkeys, Hawkins and Schepens showed the combination of scleral diathermy, vitreous aspiration, and destruction of two vortex veins produced serous choroidal detachment. Diathermy and vitreous aspiration alone also produced suprachoroidal edema but to a lesser degree. These animals did not have retinal detachments, however, and thus did not correspond to the human situation.

Hayreh and Baines produced uveal venous stasis ischemia in rhesus monkeys by selective catarization of vortex veins. Occlusion of three or all vortex veins caused eventual anterior segment ischemia and atrophy.

The present study was undertaken to study the effects in retinal detachment surgery of hypotony, cryotherapy as the adhesive modality, and obstruction to the vortex system to determine the importance of each factor when combined with scleral buckling techniques, using a model mimicking the human retinal detachment situation.

Methods. Rhegmatogenous retinal detachments were produced in owl monkeys by the technique of Machemer and Norton. Four weeks after production of the total retinal detachment, retinal surgery was performed utilizing either a segmental meridional buckle, without obstruction to a vortex ampulla, an encircling buckle placed over an anterior tear with minimal vortex obstruction, a posterior encircling buckle compromising all vortex flow, or insufflation of the vitreous using air and no scleral buckle, the latter providing virtually no obstruction to vortex supply. Cryotherapy was constant in amount and extent, treating only the tear with lesions placed encircling the hole. In each of the surgical categories, the eye was left in a hypotonous state at the end of surgery to give the maximal chance for uveal edema. If, on histologic examination, uveal edema was found to be present, a similar series of animals in that category was investigated with care taken to avoid hypotony during or after the operation. Therefore, only surgical categories in which uveal edema resulted with hypotony had further investigation regarding uveal edema without hypotony. This was done in order to keep the experiment to a workable number of animals. No attempt was made to judge the effect of hypotony or cryotherapy alone since the exp...
Experiment was designed to study factors present in repair of retinal detachment as combined with scleral buckling techniques.

The 27 animals in this experiment protocol can be divided into four broad groups (Tables I and II). Only the first group had no retinal detachment created. Groups 2 through 4 had an experimental retinal detachment procedure initially; Group 1, without retinal detachment present, had an encircling buckle placed in the posterior equatorial region after anterior chamber paracentesis to isolate the effect of vortex vein obstruction without cryotherapy or hypotony, and without the effect of pre-existing retinal detachment. Group 2, with a retinal detachment, had no buckle but had cryotherapy over the quadrant of the hole with drainage of subretinal fluid and insufflation of vitreous by air to tamponade the hole and attach the retina. Group 3 had a meridional buckle without encircling element, in the horizontal meridian where holes had been created away from the vortex ampulla. Cryotherapy was utilized and hypotony was present from drainage of the fluid with only a meridional buckle employed. Group 4, also with retinal detachment, consisted of two subgroups, an encircling buckle placed anterior to the equator in animals where holes had been created very anteriorly, and a second subgroup with the buckle placed posterior to the equator over the vortex ampulla. These two groups were, in turn, divided into groups with and without cryotherapy and with and without hypotony.

Animals were examined daily during the postoperative period. Schiötz tensions were measured at 24 hours. Animals (in which there was to be no hypotony) that had a difference of more than 5 mm. Hg between fellow eyes were not used in the series. Indirect ophthalmoscopy was performed daily, and the eyes checked for degree of inflammation or intraocular hemorrhage. On the fourth to fifth postoperative day, the average time of clinical choroidal edema, all eyes were enucleated and prepared in Koliner fixative as described by Machemer. The interval before enucleation was chosen because of previous findings of Hawkins and Schepens showing it to be the maximum period of choroidal edema.

Results. Dilation of the large veins near the suprachoroides, and to some degree in the choroid and ciliary body itself, occurred in all eyes and is not interpreted as uveal edema. Such pathology was noted anterior to the buckle, posterior to the buckle, and even contralateral to the buckle in cases of segmental meridional implants. In some cases, there was a minimal amount of eosinophilic noncellular material immediately adjacent to a vessel which may or may not be a minimal stage of serous uveal edema. In such cases, the fluid merely covered a portion of a vessel between it and the uveal lamella without a recognizable pocket of fluid. Erythrocytes sometimes extravasated in these areas. Serous uveal edema, for the purposes of this study, is a layer of eosinophilic fluid which is at least the width of an adjacent suprachoroidal vessel. With this definition in mind, it was found that Groups 1, 2, and 3 did not produce serous uveal edema (Table I).
Table II. Serous uveal edema (detachment) experiment groups

<table>
<thead>
<tr>
<th>Encircling anterior equatorial</th>
<th>Encircling posterior equatorial</th>
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<tr>
<td>With cryo</td>
<td>Without cryo</td>
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<tr>
<td>Hypotony 0/3</td>
<td>Hypotony 0/3</td>
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Group 4 consisted of two subgroups, those of anterior and posterior equatorial encircling buckles (Table II). When the buckle was placed anterior to the equator, which or without cryotherapy and with hypotony, serous uveal edema was not present in six eyes. When buckles were placed posterior to the equator, thus obstructing the vortex flow, serous uveal edema was present in all subcategories although not in all eyes in each subgroup (Fig. 1). Nevertheless, the group with cryotherapy and hypotony with encircling posterior equatorial buckle had the greatest percentage.

Venous engorgement with cellular (erythrocyte) extravasation (hemorrhagic uveal edema) occurred to a varying degree in all eyes with posterior equatorial encircling buckles but was not seen in the other categories. Extensive hemorrhagic uveal edema occurred in one eye of this category in the subgroup of hypotony with cryotherapy (Fig. 2). Extensive hemorrhage was present in the posterior and anterior chamber as well as the choroidal, ciliary body, and iris.

Discussion. The presence of serous uveal edema in this study depends on its definition. If any eosinophilic noncellular material surrounding dilated vessels is taken as the definition, then all of the animals in categories 2 through 4, i.e., those with retinal detachments preceding the procedure, had uveal edema. In order to determine which components of retinal detachment surgery contributed the most to the production of chorioidal fluid, this definition was not plausible. Therefore, the arbitrary definition of a layer of serous proteinaceous material the width of an adjacent suprachoroidal vessel was set prior to undertaking this study. Using this definition, only those animals with an encircling buckle posterior to the equator, thus obstructing all vortex flow to at least a partial degree, developed serous uveal edema. Both animals with cryotherapy and without cryotherapy in this group developed such edema. The possibility that hypotony increased the likelihood of serous uveal edema appears to be indicated although a greater number of animals in the subgroup would be necessary to establish this fact. The fact that uveal edema did not occur in Group 1, i.e., posterior encircling buckle but no pre-existing retinal detachment, either means the associated retinal detachment itself is a factor in creating the edema or else the drainage of SRF allowed a tighter buckle.

The manner in which pre-existing retinal detachment may contribute to the pathophysiology is uncertain, but hypotony and low-grade inflammation are often concomitantly present. The presence of uveal edema with retinal detachment prior to surgery has recently been emphasized.

It is well recognized that serous uveal edema (detachment) can occur from any of the components investigated, i.e., from hypotony alone, as after cataract extraction; after creating an irritative pigment epithelial adhesion, as seen after photocoagulation without scleral buckling; or after meridional retinal detachment plombage without vortex compromise. Nevertheless, in the experimental owl monkey model, it appears that compromise of the vortex outflow is one of the most significant factors, with the irritative phenomena of cryotherapy and hypotony adding to the likelihood of serous uveal edema.

Hemorrhagic extravasation appears to be a more exaggerated manifestation of vascular stasis. The eye in this study with extensive hemorrhage into the anterior and posterior chambers (Fig. 2) mimics those eyes reported by Hayreh and Baines in which all vortex veins were cauterized. A scleral buckle, however, produces only partial occlusion of the vortex veins and, therefore, is more unpredictable in the amount of stasis created. Because the serous component may be minimal, the ophthalmoscopic manifestations of choroidal edema may likewise be lacking.

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REFERENCES


The effects of ten antibiotics and two preservatives on the rabbit corneal endothelium were studied by in vitro perfusion. Dose-related effects on corneal thickness were seen with certain antibiotics. No correlation was found between structure, origin, or bacterial sensitivity of the antibiotics and their effect on corneal transplants. Five distinct morphological changes were observed; two were transient and only one was specific. Although clinical dose correlation was not intended, further investigation is needed on erythromycin, bacitracin, chloramphenicol, penicillin, oxacillin, and cephalothin.

The possible role of antibiotics producing alterations in the endothelium is important because of the use of soft contact lenses with drugs, subconjunctival injections, intracameral and intravitreal injection, the new interest in ocular inserts which increase or prolong drug concentrations in the region of the endothelial cell, and the direct application of drugs to the endothelium in perforating ocular injuries.

The present studies were designed to examine the effects of ten antibiotics and two preservatives on corneal thickness and morphology of the perfused rabbit corneal endothelial cell and to determine if there are different responses to different classes of drugs.

Methods. White albino rabbits of both sexes were killed by air embolus. Both eyes were enucleated and mounted within 20 minutes in a separate constant perfusion apparatus. The epithelium was removed and silicone oil was placed over the anterior surface of the cornea. One cornea was perfused with medium alone and served as a control. All perfusion media were modified with glutathione and adenosine, were adjusted to a pH of 7.0, and were maintained at 32° C. Pressure in the perfusion system was eight millimeters of mercury.

Measurements of corneal thickness from the anterior stromal-air interface to the endothelium were taken at ten-minute intervals with the specular microscope. Results were recorded and plotted on a graph as thickness against time. Readings for the first 60 minutes were adjustment times; the last three hours were plotted as a beta-slope representing average change in corneal thickness per minute.

Serial still photographs, still photographs made into montages, and time-lapse cinema photography were used to evaluate morphological changes. Hematoxylin and eosin preparations from 18 experiments were made after perfusion was completed. Flat mounts using Tripan Blue or P-nitro blue tetrazolium were made on a limited number of specimens.

Antibiotics.* Ten antibiotics and two preservatives were studied: Group I: penicillin G, oxacillin, methicillin, ampicillin. Group II: cephaloridine, cephalothin. Group III: bacitracin, chloramphenicol, gentamicin with and without the preservatives methylparaben, propylparaben, erythromycin, and its preservative, benzy alcohol.

Commercial prepared antibiotics were used except when gentamicin was perfused without preservative.

Cephaloridine was the antibiotic most likely to produce corneal thickness changes to osmolarity changes. In nine experiments glucose equivalent to concentrations of cephaloridine were added to the medium to compare osmolarity-induced changes to those of antibiotics. Results. In evaluating corneal thickness changes associated with antibiotics (Table I), comparisons were made (1) between minimum dose and changes observed; (2) among experimental concentrations, therapeutic dosage, and bacterial sensitivity; (3) between drug concentrations and the severity and rapidity of changes observed; and (4) between the minimum and maximum concentration which produced changes. Ninety-five controls showed a mean corneal thickness change of 0.025 microns ± 0.135 per minute. All of the antibiotics in Group I showed dose-related changes in corneal thickness. Penicillin G and oxacillin produced the most rapid and severe effects.

Cephaloridine (Group II) caused changes that were due to osmolarity effects alone. Cephalothin

*Antibiotics used in this study are: ampicillin; Polycillin-N; oxacillin; Prontosil; methicillin; Staphicillin; penicillin G; Penicillin G; gentamicin; Erythromycin; cephalothin; Keflin; cephaloridine; Lincomycin; chloramphenicol; Chloromycetin; gentamicin; Garamycin; bacitracin; Bacitracin.