SCLERAL CAUTERY WITH IRIDECTOMY— AN EXPERIMENTAL STUDY*

BY *Ellen F. Regan*, M.D.

IN 1958 SCHEIE[1] described a filtering operation for glaucoma which he called peripheral iridectomy with scleral cautery. Since that time we have employed this operation with increasing frequency and we have been impressed with the consistency with which filtration occurs. For this reason it seemed interesting to study the eyes of monkeys on which the operation had been performed.

Attempts to produce filtering blebs in the eyes of experimental animals have been notoriously unsuccessful. The introduction of Elliot's trephination stimulated interest in the production and function of filtering cicatrices. Kummell[2] in 1913 performed trephinations upon rabbits and found that by the tenth postoperative day fibrillary connective tissue was closing the surgical defect. From inspection of the cats' eyes removed twenty-six and thirty-two days after trephination, Rochon-Duvigneaud and Ducamp[3] concluded that if fistulization occurred it was from the presence of some heterogeneous substance between the wound edges. In 1914 Ellet,[4] studying the trephination operation on rabbit eyes, thought that in one instance a subconjunctival cyst indicated possible filtration, but neither Clausen[5] nor Holth[6] could demonstrate filtration, and Wilmer[7] in 1927 stated that in his experience trephinings on dogs' eyes showed a great tendency to heal completely, although microscopic examination in nearly all cases indicated the possibility of drainage under conditions of increased intraocular pressure. In 1932, Spaeth[8] studied iris inclusion operations performed on rabbits and concluded that the presence of iris pigment within the wound promoted filtration. Spaeth observed that by the thirteenth day after operation a thin space developed between the incarcerated iris and the contiguous cut surface of the sclera. The iris stroma then

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gradually atrophied, leaving a pigment-epithelium–lined tract between the anterior chamber and the subconjunctival tissue.

About 1950 Dunnington and I[9] performed a series of trephining and iridencleisis operations on monkeys' eyes, seeking to ascertain (1) the presence or absence of filtration after such procedures and (2) the technical factors which tend to produce a properly devised antiglaucomatous operation. These attempts to determine the presence of microscopic filtration were unrewarding. India ink or Prussian blue was injected into the anterior chambers of the monkeys' eyes at varying intervals after trephination or iridencleisis but no filtration was demonstrable. In either type of operation, a prompt proliferation of fibrous tissue from the episcleral and subconjunctival region grew down to fill the corneoscleral aperture. This was in keeping with Kronfeld and McGarry's[10] gonioscopic and slit-lamp study of a large number of eyes after antiglaucomatous operations. These investigators concluded that many failures following technically correct procedures were caused by an overactivity of the tissues at the outer end of the trephine canal or the iridencleisis incision.

Closely related to the present study is an experimental investigation made by Neame[11] on the effect of electrocautery puncture and diathermy puncture into the anterior chamber. Neame was interested in Preziosi's operation which consists of a puncture made with galvanocautery into the anterior chamber from beneath a conjunctival flap.[12] In this procedure no iridectomy is performed and the conjunctiva is closed by suturing. One week after performing this operation upon rabbits Neame[11] could demonstrate a gap in the corneosclera at the site of perforation. The edges of the incision appeared acellular and inflammatory cells were present beyond this area. In addition the local destructive effect produced by electrocautery was greater than that arising from the diathermy needle.

PRESENT INVESTIGATION

PROCEDURE

All monkeys were anesthetized with intravenous Nembutal and tetracaine ½% eye drops were instilled. Sodium sulamyd ointment 10% was instilled at end of the operation. No dressings were used. In all monkeys iridectomy with scleral cautery was performed upon one eye and either iridectomy alone or iridectomy with posterior sclerectomy was performed upon the second eye. In all eyes the iridectomy was complete, because previous investigations showed that in the

presence of peripheral iridectomy the iris frequently became incarcerated in the incision. The operative procedures used were complete iridectomy, posterior sclerectomy with iridectomy, or scleral cautery with iridectomy.

COMPLETE IRIDECTOMY. A 5-millimeter limbal-based conjunctival flap was prepared with scissors. A keratome incision was made into the anterior chamber at the limbus in the twelve o'clock meridian. A complete iridectomy was performed and the conjunctival flap and Tenon's capsule were closed using a continuous 6–0 plain surgical gut suture.

POSTERIOR SCLERECTOMY WITH IRIDECTOMY. A 5-millimeter limbal-based conjunctival flap was prepared to extend from eleven to one o'clock. Taking care not to produce a bevel, a keratome incision was made at the limbus at twelve o'clock. With a scissors about one millimeter of sclera was excised tangentially from the posterior lip of the wound. The section removed included the full thickness of the sclera. A complete iridectomy was performed and conjunctiva and Tenon's capsule were closed using continuous 6–0 plain surgical gut.

SCLERAL CAUTERY WITH IRIDECTOMY. A 5-millimeter limbal-based conjunctival flap was prepared to extend from eleven to one o'clock. Using a knife, a groove approximately four millimeters in length was made at the limbus. The posterior lip was treated with cautery and when the groove had thus been deepened to at least two-thirds the depth of the incision it was completed with a sharp instrument. In the case of the monkey which has a widely open angle, this was done with a keratome, again taking care not to bevel the incision. A complete iridectomy was then performed and the conjunctiva closed with a continuous suture of 6–0 plain surgical gut.

The monkeys were sacrificed at intervals of one, two, three, and four weeks, and four, six, and eight months. The eyes were enucleated, fixed in celloidin, sectioned serially, and stained with hematoxylin-eosin.

RESULTS

IRIDECTOMY. In all instances the wounds healed in a normal manner with no clinical or histologic evidence of filtration. Nor was there any evidence of iritis or cataract formation.

POSTERIOR SCLERECTOMY. In no instance was there clinical evidence of filtration, and in only one eye, one week after operation, could one possibly imagine filtration occurring if the intraocular pressure were raised. Histologically it usually appeared as if the anterior lip of the incision had fallen inward to come into apposition with the inner

layers of the scleral lip. This created a large anterior triangle which was first filled with rather loose connective tissue and in time with closely packed fibrous connective tissue from the episclera and subconjunctiva. Occasionally there was iris adherent to or caught into the posterior lips of the incision, but the surrounding tissue reaction bound the iris firmly in place. There was no undue cellular reaction within the anterior chamber nor were any cataractous changes observed in the lenses.

SCLERAL CAUTERY WITH IRIDECTOMY. Rather to our surprise, we frequently observed clinical evidence of filtration. This took the form

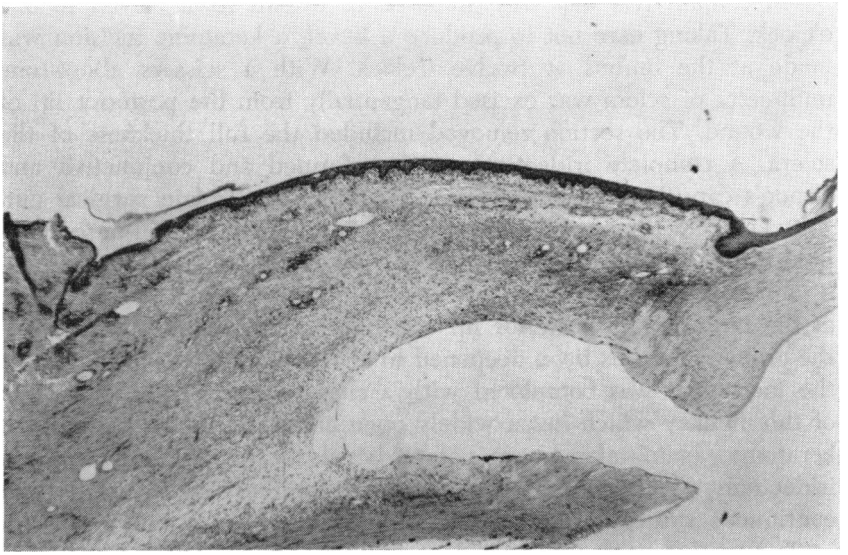

FIGURE 1. EYE OF A MONKEY ONE WEEK AFTER IRIDECTOMY WITH SCLERAL CAUTERY SHOWING WIDELY SEPARATED CORNEAL AND SCLERAL WOUND EDGES, ROUND CELL INFILTRATION OF THE CONJUNCTIVAL FLAP

that Kronfeld[13] and Scheie[14] so graphically describe as a "succulent" diffuse bleb. The anterior chamber was always present by the second postoperative day and at no time were there any clinical signs of iritis or of lens changes. Microscopically there was usually evidence of filtration. Our criteria for filtration were that the scleral and corneal lips of the wound were separated and that this dehiscence was covered by loose connective tissue under a conjunctival flap.

One week after iridectomy with scleral cautery, the scleral and corneal lips of the limbal incision stained a bright pink color and there was a loss of cells and structural markings in this area (Figure 1).

There was often a very thin single layer of cells more or less covering the anterior lip of the wound. These cells seemed to be continuous with the endothelium. The conjunctival flap was thickened with dilated blood vessels and moderate round cell infiltration. There was very little evidence of fibroblast proliferation.

Two to four weeks after operation the corneoscleral incision showed only slight changes and no evidence of wound repair. The anterior half was largely lined by a single layer of cells while the overlying subconjunctival tissues showed increased vascularization and round cell infiltration. There was fibroblastic proliferation in the adjacent episcleral tissue. At the end of four weeks a loose connective tissue occasionally was found to extend about halfway through the lips of the corneoscleral incision, but in general the limbal track was free from cellular infiltration.

Eyes examined at the end of four, six, and eight months showed no further healing. The edges of the corneoscleral incision were now somewhat fragmented, with some cells in the intervening spaces (Figure 2). Usually, although not always, a single layer of cells continuous with the endothelium lined the anterior half of the incision. The posterior half of the wound remained uncovered and consisted

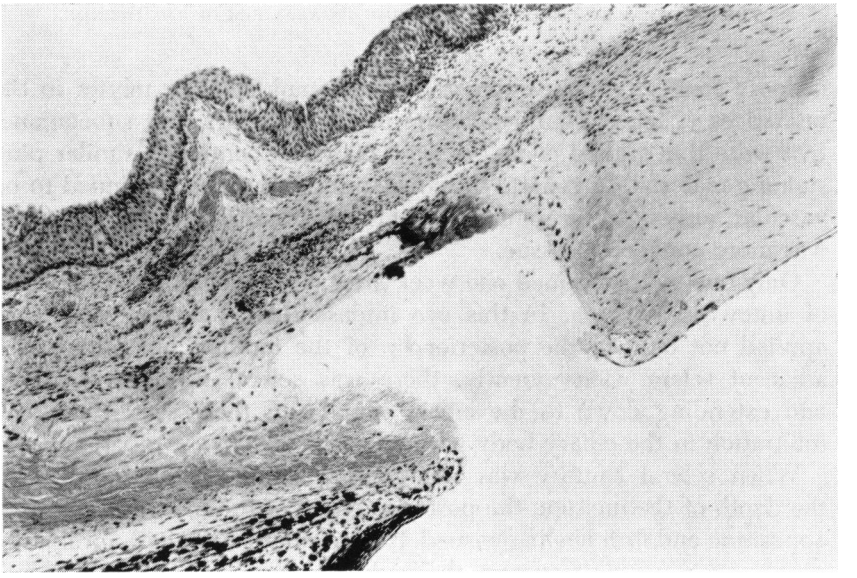

FIGURE 2. EYE OF A MONKEY SIX MONTHS AFTER IRIDECTOMY WITH SCLERAL CAUTERY SHOWING FRAGMENTATION OF SCLERAL FIBERS AND LITTLE IF ANY CELLULAR LINING TO THE FILTERING CICATRIX

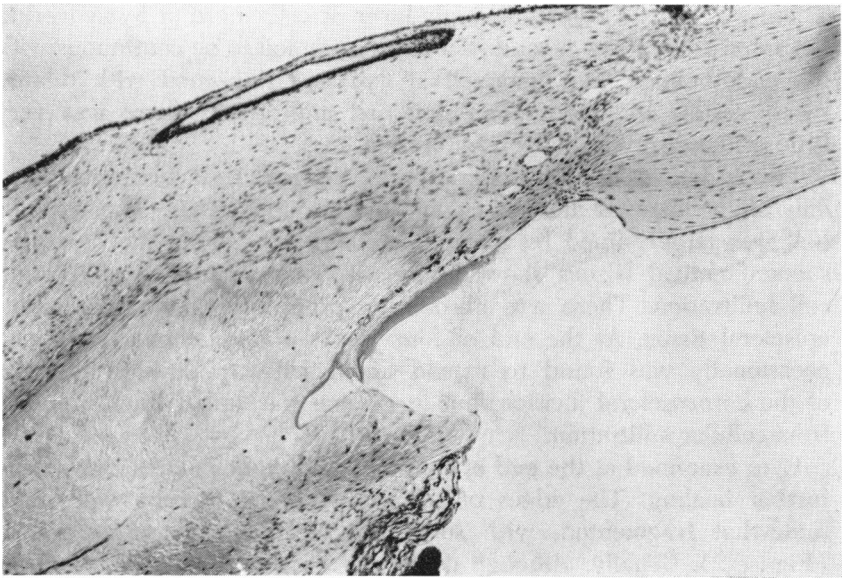

FIGURE 3. EYE OF A MONKEY EIGHT MONTHS AFTER IRIDECTOMY WITH SCLERAL CAUTERY SHOWING AN OPEN CORNEOSCLERAL INCISION WITH SCLERAL FRAGMENTATION AND AMORPHOUS MATTER FILLING MUCH OF THE SUBJUNCTIVAL SPACE. THE CELLULAR LINING COVERS ONLY THE CORNEAL RIM OF THE OPENING

of loose connective tissue sometimes with pink staining matter in the interstices (Figure 3). In the surrounding episclera and subconjunctiva were thin walled channels some of which contained similar pink staining material. In general the subconjunctival tissue continued to be vascular, although the round cell infiltration had decreased and there was more connective tissue.

Only one eye, examined one week after operation, showed evidence of untoward reaction. In this eye intense scleral cautery had been applied not only to the posterior lip of the incision but also to the adjacent sclera. Consequently, there was scleral necrosis overlying and extending down to the ciliary body, and there was round cell infiltration in the ciliary body and iris.

When scleral cautery was not applied to at least two-thirds of the depth of the incision, the posterior edges of the incision came into apposition and firm healing ensued. Neovascularization and fibroblastic proliferation were present at the end of a week if cautery was not sufficient to affect the limbal structures.

Inasmuch as the effect of iris inclusion is always a problem it was

noted that when iris incarceration occurred, it did not contribute to the fistulizing process, but rather seemed to stimulate fibroblast proliferation.

DISCUSSION

From these studies it appears that in experimental animals scleral cautery produces filtration more consistently than any other surgical procedure and that when accurately applied it causes no untoward tissue reactions. Histologically, the appearance of an incision after scleral cautery conforms closely with that observed by Teng, Chi, and Katzin[15] in four eyes removed at varying intervals after clinically successful filtering operations. The common characteristics of these clinical and experimental operations are: (1) the frequent appearance of a singular layer of cells lining the anterior part of the corneoscleral opening; (2) degeneration or fragmentation of the sclera where it is not covered by such a lining; (3) "spongy" connective tissue in the uncovered episcleral or subconjunctival area; and (4) endothelium-lined channels in the episclera.

The mechanics of scleral cautery are not clear, but there are at least two factors involved. One is scleral shrinkage from the application of thermal heat. Scheie implies that this is the essential effect for the production of a filtering wound, but experimental studies of retinal detachment surgery indicate that this shrinkage is not permanent.[1,16,17] The second factor is the effect of thermal heat on wound healing. The degree and extent of a burn depend upon the temperature and the duration of the application of thermal heat.[18] Histologically, the first signs of healing appear in the adjacent tissue where recanalization of the thrombosed vessels is followed by neovascularization, round cell infiltration, and fibroblastic proliferation into the necrosed area.[19,20] These steps in wound healing are considerably delayed and in the presence of extensive burns the heparin tolerance is increased.[21] In contrast to a normal case, where healing is well established in five to seven days, it is not until ten to twelve days after injury that fibroblastic proliferation occurs in a thermal burn.[21,22]

The inhibitory effect of aqueous humor upon wound healing has been discussed by many investigators. Albrink and Wallace[23] found that pure aqueous humor from adult cats would support survival but only limited growth of chick fibroblasts. Kornblueth and Tenenbaum[24] made similar findings. In addition Chi, Teng, and Katzin[25] recorded collagen degeneration in non-encapsulated pieces of sclera implanted into the anterior chamber of rabbits' eyes.

A nice, but quite unproven, theory for the efficacy of scleral cautery would then incorporate both the effect of thermal burns and aqueous humor. By causing scleral shrinkage as well as delaying neovascularization and fibroblastic proliferation, scleral cautery enables the aqueous humor to have a more extensive area and a longer time in which to set up the mechanism whereby new connective tissue is inhibited and existing collagen fibers are destroyed.

SUMMARY

When scleral cautery with complete iridectomy is performed upon monkey eyes, histologic examination frequently reveals a filtering wound. A description of such incisions and possible reasons for their formation are presented.

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DISCUSSION

DR. PETER KRONFELD. I have had the opportunity of studying Dr. Regan's paper and some of her histological slides. As I checked one against the other, my first impression was that Dr. Regan is understating her case; as I listened to her presentation this morning, I have this feeling much more strongly. I think her evidence bears more emphasizing than she herself has done. This feeling may have something to do with the fact that I have a very profound enthusiasm about anything that looks like a filtering bleb.

I was particularly pleased to see two points brought out by Dr. Regan's work. First, she recognizes different stages in the development of these postoperative scars. For a good many years, I have been more or less convinced that the postoperative fistulizing bleb does not form overnight, that it takes months to reach a stage of fairly steady function. At that point certain histological changes may still go on, namely regressive changes of certain connective tissue elements underneath the conjunctiva, associated with hypertrophic changes of other connective tissue elements. Secondly, I am particularly pleased to see that the end result in most of Dr. Regan's sclerotomies by cautery is the type of bleb that I consider most desirable. It is the diffuse succulent bleb, the type of bleb that does not show any transformation of the surface layer. The transport of fluid seems to take place entirely in the deeper layers and just where it finally goes is difficult to say from just biomicroscopic observations.

All in all, I believe Dr. Regan's histological findings come so close to what Dr. Teng and his group and other previous examiners of fistulizing blebs

(particularly Dr. Verhoeff) have described that I would consider them identical.

I consider this a very major accomplishment, particularly since all previous attempts to produce such scars have been almost uniformly failures. Naturally, it will be important to establish the function of these scars by the modern methods of aqueous rheology, but I am very confident that perfusion experiments six or eight months after the surgery are going to prove that we are dealing with a highly efficient set of outflow channels.

Eyes of this type will lend themselves to the study of a good many of the factors that interest us as clinicians, the factors which we think may hinder or may further the development of a good functioning bleb.

Dr. Regan asked the question: why does the sclerotomy with cautery succeed when the trephining operation or the posterior lip sclerectomy has failed? To some extent, she has answered the question by proposing an attractive theory. I personally think it is quite conceivable that the small areas of burned tissue give off chemical agents which inhibit the immediate fibroblastic reaction of the surrounding tissues. The normal flow of aqueous, if it can take place through channels which have a lower resistance than the normal outflow channels, can be a very strong factor in permanently establishing new channels. But this is hardly the time for much theorizing. I believe it is safe to say that Dr. Regan's work presents a very major step forward in the establishment of a sound experimental basis for a fistulizing operation.

Dr. Harvey E. Thorpe. It is evident from Dr. Regan's beautiful and timely study and her fine illustrating microphotographs, that endothelium proliferates rather early following excision sclerectomy. However, it is soon outraced by the proliferation of the connective tissue which seals off the planned filtration channel with scar tissue in the operated monkeys. Dr. Regan also demonstrated clearly that scleral thermal cautery burns were followed by delay in the proliferation of the collagenous connective tissue.

Today's projected histological microphotographs of monkey eyes excised after surgery showed a layer of endothelial cells with prominent nuclei lining the apparently viable walls of the thermally created scleral filtration channel.

It thus appears that cautery, as used in the demonstrated material, did not materially delay endothelial proliferation but did inhibit connective tissue growth. This procedure resulted in a patent subconjunctival sclerectomy channel, and leads to the inference that thermal sclerectomy is more likely to remain patent and that it has definite merit over mechanical scleral excision for this type of filtering operation.

Dr. Angus L. MacLean. In this excellent paper, Dr. Regan has shown histologically what we have been observing clinically in patients operated upon by this technique. We have been convinced that cautery to the cut

surfaces of an incision at the limbus establishes spongy tissue in the healing process which, with the loosely arranged subconjunctival tissue, is ideal for filtration.

We have a similar experiment underway on rabbit eyes, but as yet have nothing to report. We are not including iridectomy in the procedure, however. We have been interested only in the effect of the cautery to limbal tissue. After the lips of a groove partway through the limbus thickness have been cauterized, entrance into the anterior chamber is made with the tip of the cautery at one point only without attempting to enlarge the opening enough to perform an iridectomy.

We have been interested in applying this procedure to infantile glaucoma, where, we believe, iridectomy is contraindicated, and to aphakic glaucoma where aqueous alone and not vitreous must be permitted to escape.

Dr. Regan has also shown that one cannot compare the results of trephining in animal and human eyes for we do have success with this operation in human eyes, and here, again, the cautery can be used to great advantage. As Dr. Regan has pointed out, when closure of a trephine opening occurs, it is usually at the external extremity. In my experience this can be prevented by applying cautery to the margins of the trephine opening before the opening is completed. This will stop any bleeding points, improve the efficiency of the filtering fistula, and permit employment of a smaller trephine—never any larger than 1.25 mm. and often 1.00 or 0.75 mm. in diameter. I still think that trephining is the best procedure we have for chronic, open-angle glaucoma in adults where peripheral iridectomy is necessary, particularly if this slight modification with the cautery is used.

Dr. Regan's histological findings have confirmed my belief that limbal lip cautery should be the procedure of choice in infantile glaucoma where iridectomy is probably hazardous and in aphakic glaucoma where escape of vitreous must be prevented.

DR. JOHN M. MCLEAN. Dr. Regan has given us a beautiful demonstration of the microanatomy of the cautery sclerostomy operation. I say "sclerostomy" deliberately, following the arguments propounded by Verhoeff in 1915 in his classic paper on the histology of the filtering operation.

Dr. Regan has assumed, and it is a reasonable assumption, that the situation in the primates on which she worked is similar to the situation in man. I believe that I can, with a few slides, support her assumption, for we recently had occasion to study a human eye which had had a successful cautery sclerostomy operation. There was one difference in technique between what she did and what was done in this eye, in that we made the entire primary incision with the cautery not using any sharp instrument. The patient succumbed a little over two months after operation, with an acute cardiovascular accident.

The first slide will show the eye [slide] as it was taken at autopsy. The entire filtering bleb was obtained in the specimen. [Slide] Sections of the

disc show that the patient did, indeed, suffer from chronic glaucoma. [Slide] The next slide, from the angle, shows that it was primary open-angle glaucoma. [Slide] The next slide shows the operative site. The sections look much like Dr. Regan's except, I would point out, there is no proliferation of endothelial cells on either surface.

The next section shows a higher power view of the corneal side. Note the staining differences in the ends of the corneal fibers, how they seem to be fused together and have lost the cell bodies. This, I believe, does suggest some sort of aqueous collagenase effect on the edge of the wound. [Slide] This is also the corneal side in a trichrome stain showing the same effect, and the fusion of the ends of the corneal lamellae.

[Slide] The next one shows the scleral side where the same type of effect is present and even more pronounced.

[Slide] The next one shows the end of Descemet's membrane and endothelium where the cautery has perforated and does not show any proliferation of endothelial cells to line this fistula.

[Slide] In this slide, I would like to emphasize the bleb. The anterior part of the filtering bleb is composed of very loose, spongy, fibrous tissue with relatively thin epithelium over it, suggesting that there might be a transpiration of aqueous across this epithelial barrier. [Slide] The next one shows a higher power view of the outer edge of the filtering area with this peculiar tissue very much like what Teng and co-workers described as "sludge" and a still higher power [slide] shows the PAS-positive granules in this peculiar sludge-like tissue again, as described by those workers. [Slide] The next slide shows the spongy tissue under the epithelium, where filtration was taking place. [Slide] This is a section taken to one side of the filtering area in the sclera; it does show how the bleb spreads laterally. [Slide] The next slide is the opposite side stained with a tri-chrome stain, again showing the lateral spread of the filtration area as pointed out clinically by Kronfeld. [Slide] As we follow the filtration area backwards, we see that fluid appears to be going in this space immediately above the sclera and under Tenon's capsule. [Slide] The next one shows this space continuing well back to the region of the attachment of the superior rectus muscle.

I would like to compliment Dr. Regan on her beautiful demonstration, and I hope that this material from one human case will serve to complement the material that she presented.

DR. FREDERICK W. STOCKER. This excellent presentation makes me dare to express an heretic thought, namely that I actually do not believe that all those so-called filtering operations really produce filtering. I do not believe there is any evidence of this except in rare cases such as the one Dr. McLean just showed.

In most cases we just create a bulge which is connected with the anterior chamber. As Dr. Regan so beautifully demonstrated in the case of posterior sclerectomy or trephine, this bulge is almost regularly lined by an endo-

thelium-like layer of cells. How do you explain that there could be any filtering through this lining? And yet, we know that the intraocular pressure usually is lowered by these procedures.

I submit that there is a possibility that some of the so-called filtering operations work in that way, that we have an opening into the anterior chamber and fluid escapes into a pocket of soft tissue which is somewhat elastic. This cushion then might rather work by decompression than by actual filtering.

DR. REGAN. Elliot's trephination continues to be very effective operation in open-angle glaucoma. However, in eyes with somewhat narrowed angles scleral cautery with iridectomy is a safer procedure.

The role played by the corneal endothelium in wound healing has not yet been clearly defined. Among the histologic sections I showed today there were none in which corneal endothelium completely lined the cavity. This is in accord with most of the histologic descriptions of successful filtering procedures.

I wish to thank the discussers for their kind and helpful suggestions.