PRODUCTION OF ANTERIOR SEGMENT ISCHEMIA*

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INTRODUCTION

WHILE IT HAS BEEN SHOWN THAT ANTERIOR SEGMENT ISCHEMIC CHANGES CAN occur without detachment of any rectus muscles, the most common cause of such ischemic changes of the anterior segment is the removal of too many rectus muscles at one operation.¹ Complete detachment and reattachment of four rectus muscles has been described in the literature as being safe for children, but probably should never be done.² The prototype for most extraocular muscle transposition procedures is that of Hummelsheim which was described in 1908.³ Anterior segment ischemia may follow surgery for strabismus or retinal detachment, usually resulting from occlusion of the long posterior ciliary arteries and/or disinsertion of three or four rectus muscles with the inevitable interruption of the blood supply from the anterior ciliary arteries.^{1,4,5}

As early as 1941, Leinfelder and Black,⁶ in their muscle transposition experiments with Rhesus monkeys, reported one eye lost due to infection, several cases of mild iridocyclitis, one case of heminecrosis of the iris and persistent localized dilation of the pupil following transposition of the four rectus muscles. Linder,⁷ in 1943, advised against disinsertion of more than two muscles at any one time during retinal detachment surgery.

Stucchi and Bianchi,⁸ in 1957, reported on four cases of traumatic sixth nerve paralysis which were treated by muscle transplantation, and which showed postoperatively a depigmentation of a sector of the iris. They stated that the iris atrophy was preceded by an iridocyclitis.

In 1958, Borley⁹ mentioned the completion of heminecrosis of the iris in his operation for high myopia. Forbes,¹⁰ in 1959, reported a case of traumatic paralysis of the lateral rectus in a 24-year-old man. This was treated by retroplacement of the medial rectus, resection of the lateral rectus, and transplantation of the temporal halves of the vertical recti. Early complications consisted of striate keratitis, a fixed eccentric pupil,

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white deposits on the anterior capsule of the lens, and high compound myopic astigmatism. Late complications consisted of heminecrosis of the iris and eccentric pupil.

In 1960, Boniuk and Zimmerman¹¹ reported on three patients in which necrosis of the iris and ciliary body followed scleral buckling operations with encircling polyethylene tubes. The only previous histopathologic description of necrosis of the iris and ciliary body following a retinal detachment operation was that of Wilson and Irvine¹² in 1955. This complication was observed in 21 out of 150 eyes enucleated following one or more retinal detachment operations as reported later in 1961 by Boniuk and Zimmerman.¹³

Chamberlain refers to two animals with irregular dilated pupils following postoperative iritis after muscle transplants.¹⁴ This was a part of the study of the ocular motility in the horizontal plane of the primary and secondary horizontal rotators of the Rhesus monkey.

Orzalesi and Saba¹⁵ reported a case of segmental iris atrophy produced after a muscle transplantation operation according to the Hummelsheim - O'Connor method.^{16,17}

Alan B. Scott states in a letter in January 1971, that he has seen severe iritis in some eyes with absolute glaucoma after only one or two muscles were moved in strabismus surgery. Robert S. Jampel agrees in a letter in January 1971, that there is a relationship of muscle movements to anterior segment necrosis, but feels that the muscular branches to the anterior segment are important principally in susceptible individuals. Edward A. Dunlap according to a letter in 1970 had one localized zone of hemorrhagic necrosis inside plastic tubing a year following the placement of the plastic tube around a muscle. According to a letter from Eugene M. Helveston in 1970, he had a patient with anterior segment necrosis following rectus muscle surgery who developed external sloughing of tissue and loss of functional vision.

Anderson⁵ used albino rats and applied diathermy to both long posterior ciliary arteries, or to one long posterior ciliary, and did a tenotomy of three of four rectus muscles with both techniques. He was able to produce ischemia or anterior segment necrosis leading to phthisis bulbi. Unless diathermy was applied, he could not produce such a reaction from muscle surgery alone.

Kornbleuth¹⁸ showed that the rate of flow of aqueous diminished following surgery on the rectus muscles in rabbits due to a decrease in the rate of formation of aqueous through damage to the blood supply of the ciliary body by severance of the anterior ciliary arteries. Nauheim¹⁹ reported that benign corneal lesions occur at the limbus (delen) after

horizontal muscle surgery and felt that it was due to interrupted blood flow from the anterior ciliary vessels and prolonged conjunctival edema resulting in embarrassment to the corneal circulation. Vancea, Vaighel, and Vancea²⁰ reported upon five cases of trophic complications of ulcers near the limbus next to the operated upon muscles in 9-14 days following a double advancement of the lateral rectus. Fotsch²¹ described a 31-year-old patient with bilateral paresis of the lateral recti who, after operation, showed pigmented keratitic precipitates and sector iris atrophy of the iris stroma with a distorted pupil and later pigmentary glaucoma. Bagolini²² found a decrease in intraocular pressure after one or more muscles were operated upon. It averaged 8-12 mm Hg for one-two muscle operations and became maximal after 12-15 days, but approached normal values in two to six months.

Borsello²³ proved there is a change in corneal curvature of a significant amount following rectus surgery which tends to normalize after passage of time. McNeer²⁴ described a case in which a woman underwent two muscle operations to correct an exotropia. Ten years following the first operation, a resection of the right medial rectus was performed. Approximately three months following surgery, a slight iris atrophy in the superior nasal quadrant associated with a mildly peaked pupil in that quadrant was noted.

METHODS AND MATERIALS

Prince²⁵ has shown that in humans, the blood supply to the anterior segment and the iris and ciliary body consists of two long posterior ciliary arteries plus the anterior ciliary arteries coming from the muscles; the lateral rectus muscle having one vessel, and all the other recti having two vessels. The dog anatomy is somewhat similar in that there are two long posterior ciliary arteries with the anterior ciliary arteries coming from the rectus muscles. In the cat, there is an external circle from which eight main arterial branches arise and go to the anterior segment. For this reason, the dog was chosen as the animal on which to begin the initial studies.

The cat or rabbit was not chosen because there is little blood supply by the anterior route to the uvea. The dogs were adult dogs weighing 30 to 35 pounds each. The Rhesus monkey was also chosen to study because it closely resembles the human in that all the recti muscles have two vessels on the borders except the lateral rectus which has only one. The Rhesus monkeys were young adult female monkeys.

SURGERY

After preparation and general anesthesia, polymyxin B-neomycin-gramicidin (Neosporin) drops were inserted into the conjunctival sac and a canthotomy was performed laterally. A peritomy approximately 3 mm from the limbus was performed occupying approximately one quadrant when one or two muscles were to be isolated and 360 degrees when all muscles were severed. After care was taken to only expose the muscle stump and not to clean it as in muscle surgery, a suture of 5-0 mild chromic catgut was inserted into the tendon near its insertion. The tendon was severed from the globe and then reinserted onto the sclera. Closure was with 6-0 plain catgut in a purse-string fashion as needed. Neosporin drops were then applied again.

In one monkey, two recti were severed in the first operation, then at the second operation, approximately 42 days later, the other two recti were severed to study the effect of the time interval between the two operations. Also, in one monkey in which all four recti were severed, methylprednisolone acetate (Depo-Medrol) was injected at the time of operation to assess its effect on the duration of the reaction. Four dogs eyes received Depo-Medrol, also.

FOLLOW-UP

The follow-up consisted of examination on the first, third, seventh, 14th, 28th, and 56th day, and then periodically thereafter if the animal had not been sacrificed. The examination included the use of a loupe with the gross reaction rated +1 to +4. Intraocular pressure was taken if indicated, and slit-lamp examination was performed on all animals using the hand-held slit-lamp. External photography was used periodically to record the reaction and was later studied and correlated with other clinical findings. (Fig. 1) Neosporin was used only if external infection occurred. The general status of the animal was also evaluated. At the time of sacrifice of the animal, a modified exenteration was performed in that Tenon's capsule was kept intact as the eye was removed. Then it was closely teased from the globe to avoid damage of any underlying surgical reaction. The specimen was examined grossly and then placed in formalin. After satisfactory fixation and sectioning, microscopic slides were prepared with hemotoxalyn and eosin, Masson's trichrome, and Mallory's stains.

FIGURE 1
Monkey with three rectus muscles severed. A: 3 days (OU),
B: 7 days (OD), and C: 60 days (OD) postoperative.

RESULTS

Criteria for a positive gross reaction included edema of the lids, chemosis of the conjunctiva, edema and haze of the cornea, and most importantly, cells and flare in the anterior chamber. Corneal edema, posterior synechiae, rubeosis irides and pigmentary disturbances were all recorded. (Table I & II).

DOG

Various combinations of three and four muscle operations were performed in 20 dog eyes. There was a gross reaction found in all eyes although only five showed a significant reaction. A minimal gross reaction often cleared by 14 days and by 30 days almost all of the eyes were grossly quiet. However, the microscopic reaction lasted from 14 to 90 days, but the microscopic reaction was minimal compared to the gross findings. There were no posterior changes found microscopically. There was no relationship between the number of muscles or the particular muscles operated on.

TABLE I: EVALUATION OF DOG EYES FOLLOWING MUSCLE SURGERY

Dog Number	Eye	Enucleation in Days Following Surgery	Procedure	Gross Reaction	Microscopic Reaction
1	OD	44	4 recti	+1	<+1
	OS	44	4 recti	+4	+2
2	OD	53	4 recti	+1	<+1
	OS	53	4 recti	+3	<+1
3	OD	43	SR, LR, IR	+1	+1
	OS	43	SR, MR, IR	+1	+1
4	OD	43	4 recti	+2	+2
	OS	43	4 recti	+2	+1
5	OD	30	4 recti	+2	0
	OS	30	4 recti	+2	<+1
6	OD	46	SR, LR, IR	+4	+3
	OS	46	SR, MR, LR	+2	<+1
7	OD	42	LR, SR, MR	+1	<+1
	OS	42	LR, IR, MR	+1	<+1
8	OD	31	4 recti D	+1	<+1
	OS	31	4 recti D	+1	<+1
9	OD	7	4 recti D	+1	0
	OS	7	4 recti D	+1	0
10	OD	90	4 recti	+3	1
	OS	90	4 recti	+3	1

D = Depo-Medrol

TABLE II: EVALUATION OF MONKEY EYES FOLLOWING MUSCLE SURGERY

Monkey Number	Eye	Enucleation in Days Following Surgery	Procedure	Gross Reaction	Microscopic Reaction
1	OD	77	4 recti D	+2	+1
	OS	77	LR & IR	0	
		42 d. later	SR & MR	0	+1
2	OD	75	SR,IR,LR	+3	+1
	OS	75	SR,LR,MR	+1	+1
3	OD	67	SR,LR,MR	0	0
	OS	67	IR,SR,MR	+1	+1
4	OD	63	4 recti	+1	+1
	OS	63	IR,MR	0	0

D = Depo-Medrol

In only three eyes was the microscopic reaction rated significant. The four eyes receiving Depo-Medrol showed no significant difference from the ones without Depo-Medrol.

MONKEY

Various combinations of two and three rectus muscles were severed and in three eyes all four recti were severed. In the left eye of monkey (1), there was a 42 day interval between the severence of two rectus muscles followed by the other two and no gross reaction was noted between or after the two procedures. As can be seen from Table II, there was a significant gross reaction in only three of the eight eyes, but a minimal reaction in two others. However, the microscopic reaction was minimal compared to the gross reaction, and was significant in only one; the right eye of Monkey (2). (Fig. 2) Some minimal changes could be seen in five other eyes. The eye receiving the Depo-Medrol revealed no difference in reaction from the others.

PATIENTS

Our first patient was a 45-year-old white man who was in an automobile accident and sustained a paralysis of the right lateral rectus muscle. After the passage of months, he was found to have 40 diopters of esotropia with a small right hypertropia of 6 diopters. A Hummelsheim procedure was performed consisting of a right medial rectus recession of 4 mm and one-half of the right inferior rectus and one-half of the right superior rectus moved to right lateral rectus insertion. However, the remaining

FIGURE 2
Monkey with 3 rectus muscles severed OD. A: whole eye, B: anterior segment, C: angle,
and D: iris (with pigment, debris, and round cells).

FIGURE 3

Patient #1, 4 days after Hummelsheim procedure OD with edema, folds descemet's membrane, +4 cells and flare.

one-half of the right superior rectus and one-half of the right inferior rectus were moved temporally half a tendon width. On the second day, there was marked edema of the cornea, chemosis, edema of the lids, and a cloudy cornea. By the fourth day, folds were seen in Descemet's membrane and +4 cells and flare in the anterior chamber (Fig. 3). Cortisone and atropine were administered locally on the second day and on the fourth day 120 mg prednisolone was given orally. By the 13th day, less external reaction was apparent, but the cornea was still hazy and the anterior chamber showed +3 cells and flare. Folds were noted in Descemet's membrane. By the 35th day, the visual acuity had returned from hand motion to 20/60 with +2 cells and flare remaining, although the pupil was still dilated and the iris showed signs of atrophy. At the end of three months, the visual acuity returned to 20/30, the pupil was irregular with sector atrophy, and the eye was quiet. The patient proceeded toward total recovery.

The second patient was a 60-year-old white man who had an esotropia from a bilateral lateral rectus paralysis. The medial rectus muscle was recessed to a point 12mm posterior to the limbus. The inferior and superior recti muscles were freed and sutured at the insertion of the lateral rectus muscle. On the second postoperative day, severe corneal edema, ciliary injection and chemosis occurred. An aqueous flare and +4

FIGURE 4

Patient #2, 4 days after 3 recti muscles severed with edema, ciliary injection, chemosis, and iritis.

cells indicated a severe iritis and was evident even by gross examination (Fig. 4). By the 8th day a cataract could be ascertained. This reaction remained for a period of weeks before there was a gradual subsiding of the iritis with subsequent clearing of the eye with only iris atrophy and the posterior subcapsular cataract remaining as residuals.

DISCUSSION

The changes which occur after muscle surgery are extensive. Among the changes which have been listed and observed are corneal edema, cataract, uveitis, corneal curvature change, decrease in intraocular pressure, a decrease in aqueous flow, glaucoma, and frank necrosis.

The reaction called anterior segment ischemia or necrosis is a variable reaction. It is well known that it is more severe in adults than in children. This has also been shown to be true in adult monkeys versus young monkeys.³⁰ It is also more severe if diathermy or other similar modalities is used to cause further destruction to the circulation of the long posterior ciliary arteries.

The reaction in the dog and monkey are similar which lends further support to the similar anatomy of the circulation in these two animals.

The reaction subsides with time, with or without treatment, and persists up to three months microscopically, although it tends to clear grossly much sooner than this. We could see no relationship between the particular muscle combinations which were severed in the dog or the monkey and the reaction produced. In fact, the reaction was sometimes more severe when three muscles were severed than when four were severed. This points to an individual variation as to susceptibility to this reaction. Furthermore, the reaction in animals when Depo-medrol was used was no different than in animals without Depo-medrol. Girard and Bedtravera²⁶ described one adult animal in which three rectus muscles were removed and reinserted and continued to show a reaction for several days. However, the animal was kept 180 days at which time the eye was removed and there was no microscopic abnormality. This was in keeping with our findings in that the gross reaction was more pronounced than the microscopic. If we had removed the eyes earlier, we would probably have found a more severe reaction present.

There are still many unanswered questions about anterior segment necrosis which are difficult to answer. For example, which combination of muscles are likely to produce a reaction? It would take so many animals to study this reaction, due to its variability, that it would be extremely difficult to give further answers to this question. To study the duration of the reaction would also require many animals. Likewise, the time interval between repeat muscle operations on the same eye to avoid the necrotic reaction is a very critical question. It seems to be a consensus that six weeks between operations is adequate time. However, McNeer²⁸ reported a five month interval between operations and even then the necrotic reaction occurred. Of course, the effect of corticosteroids and cycloplegic agents on the severity of the reaction would be expected to be less. However, again, because of the variability of the reaction, this is a difficult point to study. Lastly, the question of removal of only a portion of the muscles on the chance of producing the reaction, as in a Hummelsheim-type procedure, is left unanswered because of the variability of reaction. If the reaction could be produced in a standard fashion on both eyes of the same animal, such a study would be more feasible.

SUMMARY

Anterior segment ischemic changes can occur without detachment of any muscles. The most common cause of such ischemic changes of the anterior segment is the removal of too many rectus muscles in one operation.

Twenty dog eyes and eight monkey eyes were subjected to the disinsertion and detachment of various combinations of extraocular muscles. The dogs were sacrificed at intervals from 30 to 90 days. During the observation period, they were observed for gross and slit-lamp changes. The enucleated eyes were studied microscopically for signs of ischemic and necrotic changes.

Two patients who were studied, observed, and treated for anterior segment ischemia following muscle surgery are described. The changes which occur after extraocular muscle surgery are extensive and include corneal edema, cataract, chemosis, corneal changes, decreases in intraocular pressure, decreases in outflow or glaucoma, and frank necrosis. The variables which lead to this reaction are described in detail. Also, some unanswered queries, such as the duration of the reaction and the time interval of the reaction after multiple muscle operations are discussed.

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DISCUSSION

DR KENNETH C. SWAN. Dr Hiatt's report adds to the growing evidence that in some patients the anterior segment of the eye is vulnerable to ischemic reactions, even when only a part of its arterial circulation is disrupted. As long ago as 1943, Linder called attention to the risk involved when three or more rectus muscles were severed at the same operation. Dr Hiatt's descriptions of ischemic reactions following tenotomy of three recti muscles in two patients and a series of dogs and monkeys add support to Linder's warning. No ischemic reactions occurred in the eyes of monkeys when only two horizontally acting rectus muscles were detached. Dr Hiatt has noted that there are considerable individual differences in tissue reactions to the severing of the anterior ciliary arteries. These differences may be due to factors other than anatomical variations in the distribution of the vessels. Knox has noted ischemic reactions involving the anterior segment in some patients with sclerotic diseases affecting the carotid system. Increased coagulability and viscosity of the blood, such as may occur in leukemia, also have been identified as predisposing factors. Anterior ischemic reactions recently have been reported in a patient with giant cell arteritis. The development of ischemic responses in the anterior segment following the experimental obstruction of the vortex veins indicates that alterations in the venous system also may contribute to the ischemic reaction. These and other predisposing conditions merit consideration before surgery is undertaken on more than one extraocular muscle at the same procedure.

In the presentation of his patients, Dr Hiatt decribed the characteristic clinical picture of severe acute arterial insufficiency. When the microscopic picture is

reviewed, the violence of the clinical signs and symptoms is understandable. This slide, which illustrates the end results of an ischemic reaction, was provided to Dr Leonard Christensen by Dr A. Ray Irvine, Jr, and Warren Wilson, Los Angeles. [SLIDE] In this low-power microphotograph, the ischemic reaction can be seen to be limited at the site of the globe where diathermy was applied in the treatment of retinal detachment. The long posterior ciliary artery apparently was occluded. As seen in higher magnification, the ciliary muscle largely has been replaced by cicatricial tissues. The epithelium of the ciliary body, as well as the entire iris stroma, are atrophic and disorganized with extensive proliferation of pigment. The violence of the reaction led to seclusion of the pupil, with resultant iris bombé formation on the untreated side. There are degenerative changes, but the basic architecture of the iris and ciliary body appears intact. [SLIDE] This microscopic section documents that the primary damage in anterior ischemia is to the uvea, and that despite the seemingly good anastomosis between the anterior ciliary and the long posterior ciliary arteries, segmental ischemic reactions do occur.

In the eye just shown, damage to the long posterior ciliary artery occurred during surgery to correct retinal detachment, but this artery also is vulnerable in strabismus surgery. [SLIDE] Textbooks describe the long posterior ciliary artery as penetrating the sclera a few millimeters from the optic nerve and then running forward with a nerve into the suprachoroidal space where it would be protected by the full thickness of the sclera; however, surgical explorations and studies of enucleated eyes show that in some eyes, the longer posterior ciliary artery penetrates the sclera further forward and may still be quite superficial in the equatorial region, as shown in this gross specimen. [SLIDE] Viewed from the inside, the artery and nerve can be seen to lie directly against thin sclera. C. S. O'Brien was aware of this possibility and more than 40 years ago began to teach that in recession operation, the scleral sutures should be placed above and below the horizontal meridian to avoid damage to the artery and nerve.

In closing, I thank Dr Hiatt for sharing his clinical experiences and results of experimental surgery with us, thereby focusing our attention on the important subject of anterior segment ischemia.

DR WARREN WILSON. Doctor Harrington, ladies and gentlemen. Since I was the clinician involved with one of these patients I thought I would give a brief review of that case.

This was an 80-year-old gentleman who came to the office the day he developed his first symptoms. There was a very large tear on the temporal side of the retina in the right eye. He was admitted immediately to the hospital. This was approximately twenty-five years ago and at that time we allowed a day or two in bed for the retina to flatten before proceeding with surgery. The technique used employed the Walker-Pischel pins and although we avoided the midline area, and hopefully that of the route of the long posterior ciliary artery, it was undoubtedly burned by the diathermy current which would spread further than the tip of the pins or the surface applicators. Removal of the lateral rectus muscle may have been a contributing factor as well.

Had he lived in the present era with the use of cryotherapy it is quite possible this eye might have been saved.

DR JOHN WOODWORTH HENDERSON. Mr President, members and guests. I feel that I should mention to you the fact that I still believe the Jensen procedure is a very good one. We have now done over 50 of these in our department and we have had no problems of this type. This includes every case with 25 diopters of deviation or more employing a medial rectus recession as part of the procedure.

I would like to relate one other case to you and also to ask the question about what is the proper interval. I had a small girl brought to me a number of years ago with a very marked head turn with the left eye turned out so badly that her head was almost turned around. She, unfortunately, had a deep amblyopic eye on the other side which failed to respond to any form of amblyopia treatment. Because of the deviation we decided that we would start with a lateral rectus exploration procedure and found a fibrous band in the lateral rectus location and released the band. This did very little for her head turn, so we went back again, re-explored her lateral area and again found fibrous tissue with no circulation. We released the bands more. We then explored the medial rectus and found no medial rectus. It was absent entirely. So, we had a patient with only a superior and inferior rectus and then questioned what is the interval between operations you select when there is only one seeing eye. We decided to transpose the superior and inferior recti medially. We did one muscle and waited six months before transposing the second muscle. She was in the office recently after an interval of about ten years. She still has a small amount of head turn but it is quite cosmetically acceptable. So the question basically is, "Is there any way one can settle this question without knowing whether recanalization of the anterior ciliary vessels occur?" I believe this needs to be answered for us.

I enjoyed Dr Hiatt's paper very much.

DR ROGER HIATT. I would like to thank Doctor Swan and the others for their comments. Since Doctor von Norrden called our attention to this reaction he had with a Jensen procedure, we have begun to look at these muscles under the microscope and begin to doubt what's written in the textbooks about the way the vessels run. They reportedly lie along the border of each muscle with the lateral rectus only having one on the inferior border. We began to question if this is true and that meant further study. Secondly, Doctor William Scott in that report I told you was given at ARVO last month down in Sarasota stated that it was his opinion that if you took off the inferior rectus and the lateral rectus you would tend to get more reaction than from taking off the inferior and medial. That's interesting because of the difference in the medial and lateral rectus muscles. The third point is, yes to the question that was asked, we never got the reaction if we did less than three muscles. The fourth point is, how long to wait. Following our study we've gone up to 90 days, but what are you going to do about McNeer's patient who had a reaction ten years later, and that really comes to the

point that Doctor Henderson raised. What really needs to be studied is what happens to the blood supply if you take off the four muscles, whether you do them in stages or all at once, and does the blood supply return to normal again.

Thank you very much.

Dr Harrington, members of the Society and guests. I would like to congratulate Dr Hiatt on his excellent presentation. He has emphasized some important factors. With reference to the experimental surgery on monkeys which I performed some years ago, I would point out that these were young animals. The approximate age of these animals was determined radiologically by checking the maturation of the hand bones and was found to be comparable to a 13- or 14-year-old child. As Dr Hiatt has indicated there is less likelihood of ischemia of the anterior segment in younger individuals.

The most important question relates to the time interval between the performance of the two stages of surgery. It would seem that a minimum interval of three or four months should be allowed before proceeding to the tendon transplants involving the vertical recti. Again, this interval should probably be longer in older patients than in adolescents. I would be most interested in Dr Hiatt's comments.