ESSENTIAL ATROPHY OF THE IRIS: A HISTOPATHOLOGIC STUDY

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DEFINITION

ESSENTIAL or idiopathic atrophy of the iris is a rare vascular disease, progressive, unilateral, and sporadic, of adult life; females are predominantly affected. Among its characteristics are patchy loss of the entire thickness of the iris, with hole formations, distorted and migrating pupil, and secondary glaucoma. The glaucoma is secondary to outflow obstruction from cuticular membranes and anterior synechiae, and from lost capacities for fluid exchange by the iris.

CLINICAL COURSE

Clinical evolution is remarkably characteristic. The history is free from episodes of injury or primary inflammation. A composite description of the clinical course follows: The onset is gradual, without pain or signs of inflammation. The patient becomes aware of a slight change in the shape or placement of the pupil of one eye. Over a period of two to eighteen years, with an average of about five years, progressive displaced pupil and hole formations develop in the iris. The refractive errors of the cases studied have not materially changed. This indicates that the cornea and lens are not markedly affected in early stages. Visual acuity is disturbed by marked pupil displacement and hole formations, but is seriously impaired by secondary glaucoma. The latter is delayed an average of five or six years, with the shortest period one year, and the longest more than ten. Fundus examinations in early stages return normal findings, apart from the iris changes. Successive biomicroscopic examinations clearly show patchy atrophies of the iris.

* From the Eye Pathology Laboratory of the Massachusetts Eye and Ear Infirmary.
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These are progressive in nature, with the pupil secondarily displaced and marked by incomplete pigment ectropion. By gonioscopic examinations, anterior peripheral synechiae are seen in later stages, beginning on the side of the displaced pupil. A mass of iris tissue is seen, applied to the cornea on the side toward which the pupil is displaced. The synechiae travel from this point around the angle. As the defects in the iris are noted to progress, transillumination shows the patchy or regional loss of substance to be larger in area than is suspected in direct inspection.

Glaucoma gradually appears, ordinarily of a low order at first. The complications of glaucoma develop more rapidly and require earlier treatment in some cases. A distinct subgroup of essential iris atrophy exists, typified by early appearances of glaucoma with corneal edema. As described later, this group is distinguished by cuticular membrane formations.

A variety of surgical and radiation therapies have been employed in this disease. Successful treatment has not been the rule. A few cases have been reported clinically before glaucoma has been established (1, 2).

THEORIES RELATING TO ETIOLOGY

A considerable number of theories have been offered with the various published cases; only a few reports have followed microscopic examinations. Some of the latter follow. Feingold (3; 1918) suggested that the atrophy of the iris was caused by a congenital vascular disturbance of the smaller iris circle, and the glaucoma was caused by irritating effects of degenerating tissue. Licsko (4; 1923) found hyaline degenerations of the iris vessels, as did Feingold. He explained the glaucoma by pigment release from the atrophic iris and by the loss of surface for resorption of intraocular fluid. Bentzen and Leber (5; 1895) reported that the glaucoma caused the iris atrophy. Rochat and Mulder (6) thought that the formation of anterior synechia pulled the iris toward that point, causing tearing and atrophy, progressing to loss of the anterior chamber angle and obstruction with consequent glaucoma. Larson (7; 1920) projected the idea that the iris atrophy was a consequence of some unnamed developmental anomaly, beginning with corectopia. De Schweinitz (8; 1926) related the cause to iris abiotrophy.

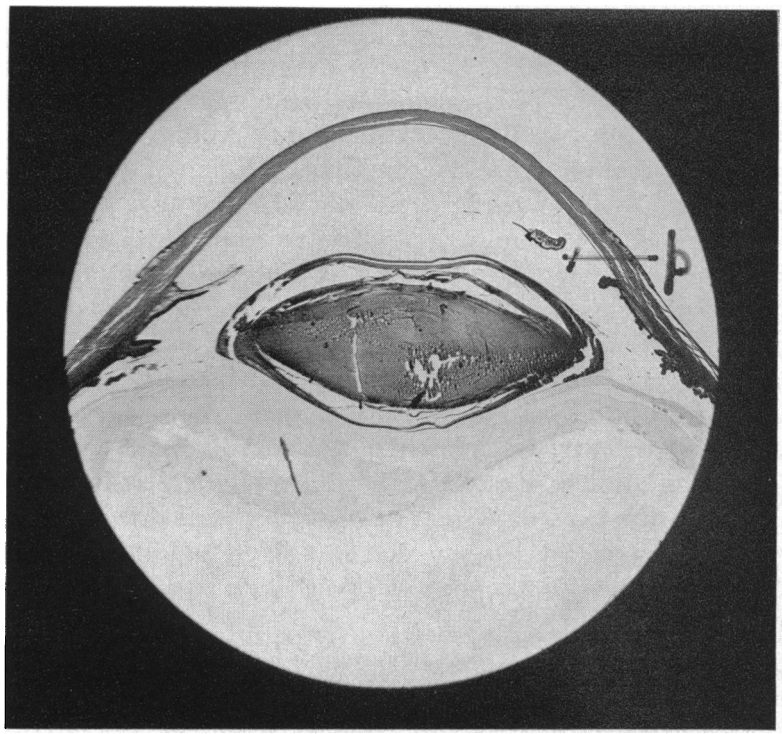

FIGURE 1 (*49-497*). ANTERIOR SEGMENT; LARGE HOLE
(p) Markedly displaced pupil.

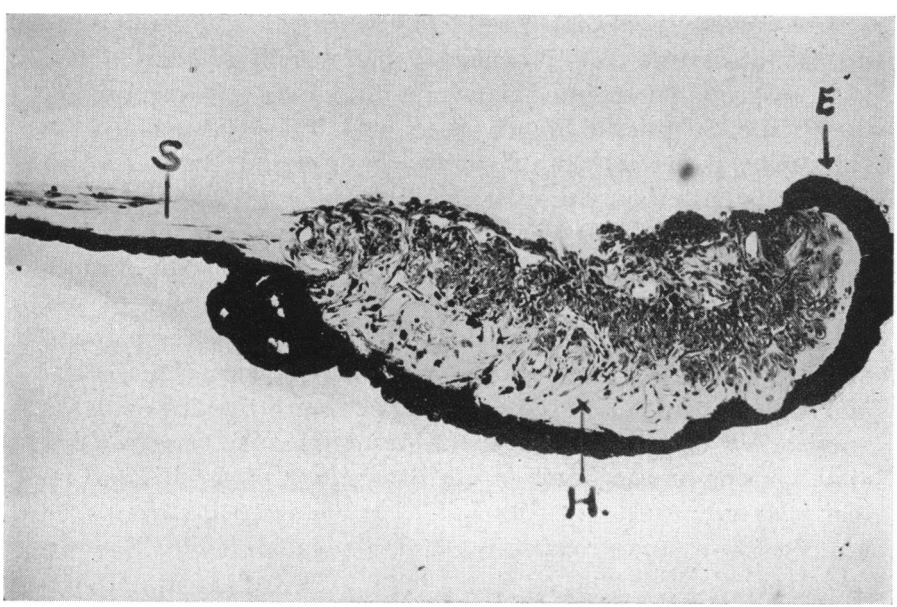

FIGURE 2 (*49-497*). SURVIVING SPHINCTER
E. Ectropion uvei. H. Subsphincter hyaline formation. S. Atrophic stroma.

Kreiker (9; 1928) suggested that the embryonic processes underlying the resorption of the pupillary membrane became active, extended in adult life, and brought about resorption of iris tissue. He reported that the glaucoma rose from occlusion of the chamber angle due to detritus from broken-down iris structures. Waite (10; 1928) ascribed the atrophy of the iris to mechanical stretching, which brought about a narrowing and occlusion of the iridic arteries leading to nutritional loss. Waite postulated that primary changes occurred in the mesodermal portion of the iris, due to a contraction and reduction in size of the lumens of the radial arteries, with loss of nutrition in that segment. As for the elevated intraocular pressure, he believed a likely explanation to be the loss of capillaries in the iris with an atrophy and reduction of resorption capacity. Von Grosz (11; 1936) believed that an hereditary feebleness of the iris was due to a hypothetical neurogenic gene. A group of other reports ascribe the iris atrophy to chronic iridocyclitis.

THE BLOOD SUPPLY OF THE IRIS

Before considering the histopathology found in this series of examples of progressive iris atrophy, some comments will be made on the blood supply of the iris.

The earliest vessels of the iris to form are part of the pupillary membrane derived from branches of the long ciliary arteries. The anterior group enters into the large arcade vessels of the pupillary membrane, the middle branch passes into the iris stroma, and the third turns posteriorly into the ciliary body region. By the seventh prenatal month the most anterior set of vessels, arteries and veins, forms the net and vascular arcades of the pupillary membrane. Longer coursing vessels within the stroma create a plexus of capillaries to supply the sphincter of the pupil. A subsphincter plexus, mostly of capillaries, lies in front of the myoid and the pigment layers, and supplies them and the subsphincter zone. The central and second arcades of pupillary vessels become atrophied up to the anterior leaf of the zigzag line by full-term time. The surviving first anastomosing arcade becomes the lesser circle of the iris and remains an arteriovenous channel. This minor vascular circle of the iris contributes some vessels to the stroma in adult life. The pat-

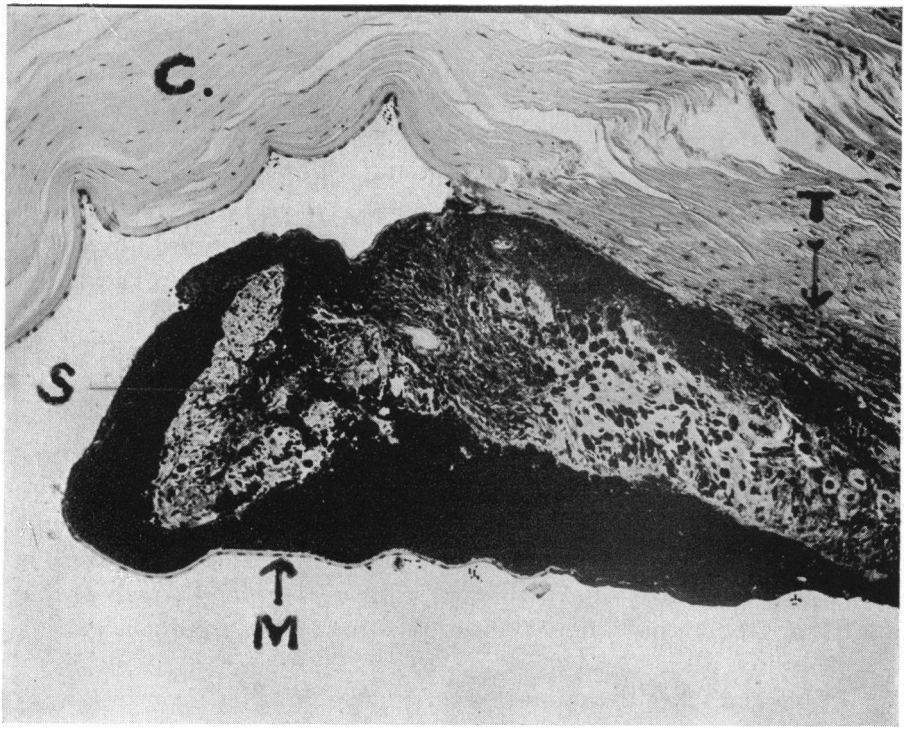

FIGURE 3 (*49-170*). COLLAPSED, FOLDED IRIS; PRIMARY SYNECHIA
C. Cornea. T. Trabeculum. S. Sphincter. M. Membrane.

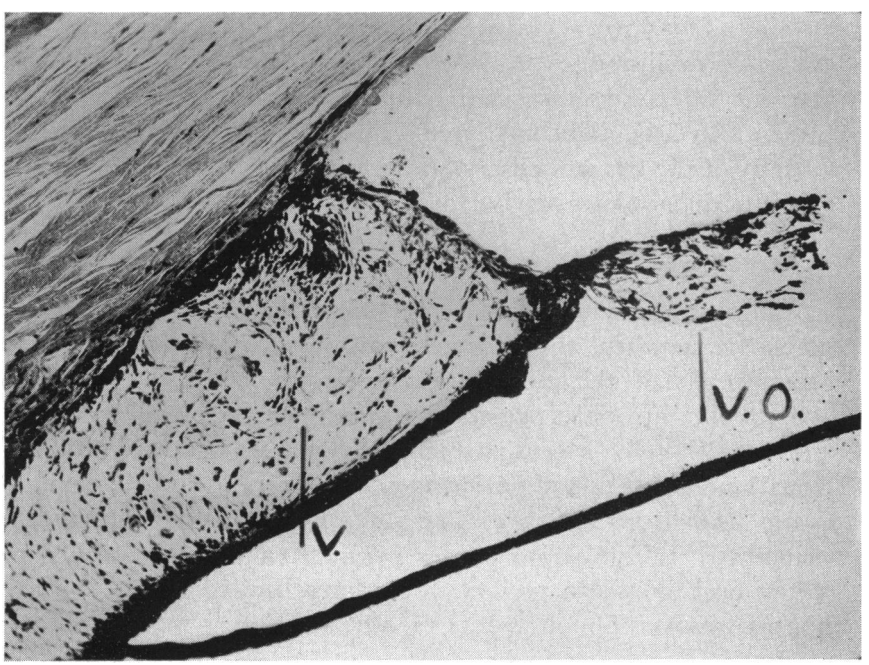

FIGURE 4 (*52-61*). SURVIVING IRIS; SYNECHIA
V. Vessels nearly occluded and functioning. VO. Occluded vessels, iris lost.

tern is brought out clearly in early stages of iritis when the congested blood columns and the contributions from the minor circle again become obvious. In irises with scanty pigment, at this time two or three layers of vessels can be seen running toward the pupillary margin, the superficial ones supplying the stroma and anastomosing with the lesser circle.

That the iris is richly supplied with blood vessels and capillaries is best appreciated when many sections are cut in various planes. The collections of blood vessels are loosely bound together by various thicknesses of supportive fibrous tissue. The loose structural design of the iris permits rapid motility. Sustained thickening during dilatation and thinning during contraction must have some effects upon the efficiency of the blood vessels. It is possible that the normally thick, stiffened walls of the blood vessels of the iris are functionally important in resisting kinking and mechanical occlusion.

Reactions from traumatic and surgical injuries, from retained foreign bodies and cysts, and from glaucoma give us a considerable insight into the panorama of vascular disease of the iris. We can learn that occlusions in a group of vessels cause but very limited atrophy. The normal elaborate anastomosis apparently limits the effects of occlusion. Also, in the iris much fibrosis of repair is atypical unless lens substance, extensive hemorrhage, or both are present. In late glaucoma, free from inflammation, an over-all atrophy of the iris and ciliary body is seen, but the pigment layers and intrinsic muscles survive to the last.

THE SECONDARY IRIS ATROPHIES

Among the many causes of secondary atrophy of the iris are glaucoma, senility, and recurrent inflammation. They resemble only superficially the essential progressive type.

Secondary atrophies are characterized by signs of inflammation and repair—cells, extensive pigment displacements or proliferations, hemorrhages, and new-formed blood vessels. Cuticular membrane formations are rare. The secondary types of atrophy are principally referrable to causes other than vascular occlusion. When occlusions are present, these have limited effects and are nonprogressive. The atrophies present a different pattern. In the

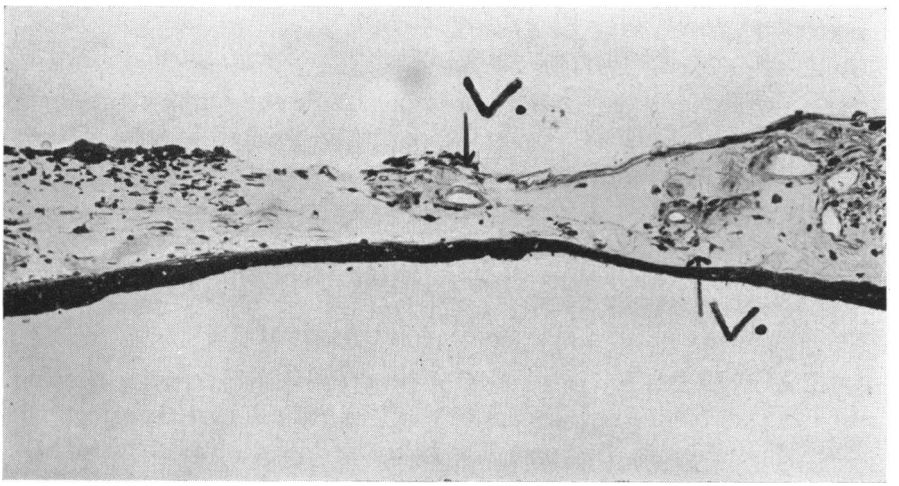

FIGURE 5 *(49-170)*. V. SURVIVING ISLAND OF IRIS STROMA WITH PATULOUS VESSEL

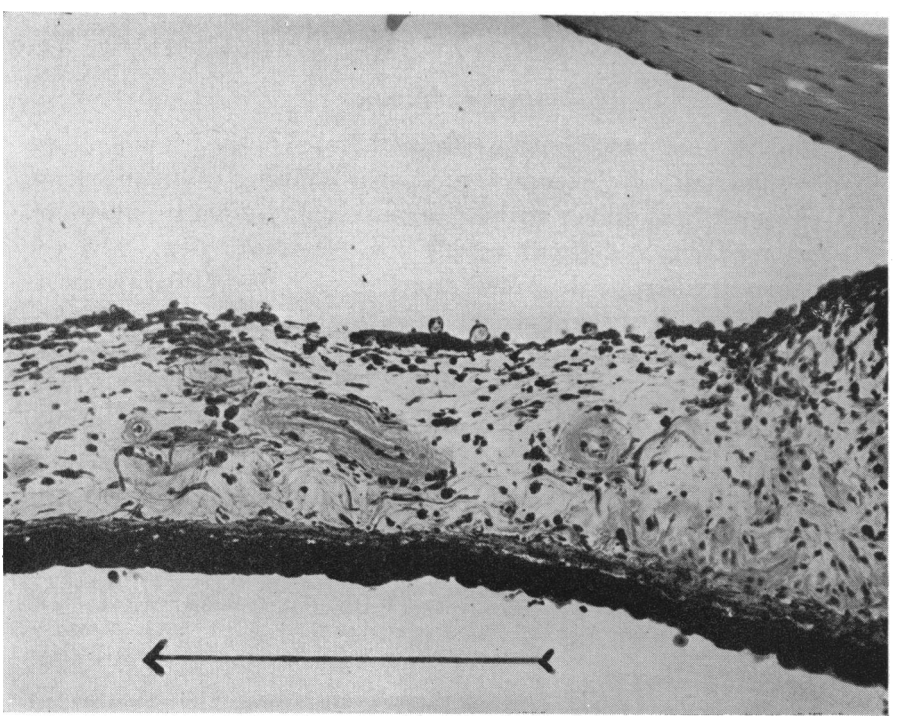

FIGURE 6 *(49-170)*. LUMENS OF IRIS VESSELS DECREASING TO COMPLETE OCCLUSION IN ZONE OF ATROPHY

zones principally affected, some blood vessels survive. The sphincter is often lost; especially is this true with the senile secondary atrophies accompanied by glaucoma. The limited extent of the atrophy or its over-allness in either case may show a distorted pupil opening, but rarely a migration. And ectropion uveae, while common in secondary atrophies of the iris, is due to anterior membranes and is usually completely around the pupil border.

THE MATERIALS FOR THIS STUDY

The materials for this study of progressive iris atrophy consist of the eyes from five patients in the Eye Pathology Laboratory of the Massachusetts Eye and Ear Infirmary[1] and clinical histories. Correlations were made with the histopathology found in five examples of this disease from the Armed Forces Institute of Pathology.[2] Serial sections were made in some; in many, various planes were cut. Routine and special stains, with and without depigmentations, were employed. The iris of a latex-injected stillborn infant was also studied.

HISTOPATHOLOGY

The histopathology is primarily distributed to the iris and ciliary body, and follows the complicated anastomosing vascular system. This engenders a spotty atrophy because anastomoses supply blood when medium and small vessels are closed off. But when the changes about to be described attack a main vessel like the great arterial circle, a net of capillaries, or a group of communicating blood vessels, then the region supplied becomes atrophic since no round-about channels are available to supply blood.

The smaller arteries and capillaries showed marked reduction in lumen diameters with hyaline thickening of the walls. Various degrees of closure up to complete obliteration were common; the latter was seen at the borders of atrophic zones (Figure 9). The arteriovenous channel, or lesser circle, was regionally closed, and

[1] Massachusetts Eye and Ear Infirmary, Eye Pathology Laboratory, 6-10, 021; 9-12, 531; E-49-170; E-49-497; E-52-61. The writer is grateful to Dr. Louis Goman of Saginaw, who supplied two specimens, and to Dr. P. Jewett of Worcester, Massachusetts, who supplied one.

[2] From the Armed Forces Institute of Pathology the following cases were studied, due to the kindness of General deCoursey, Director, and Mrs. Wilder, Pathologist: 57865; 27355; 66298; 84236; 162225.

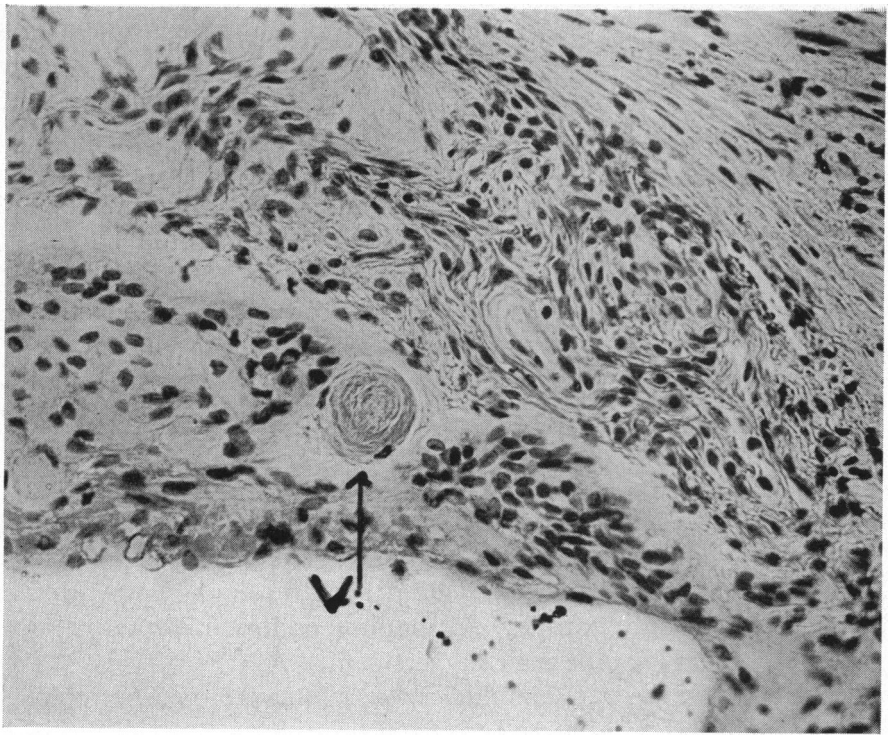

FIGURE 7 (*49-170*). BLEACHED; COMPLETE OCCLUSIONS OF VESSEL (V) SUPPLYING DILATOR

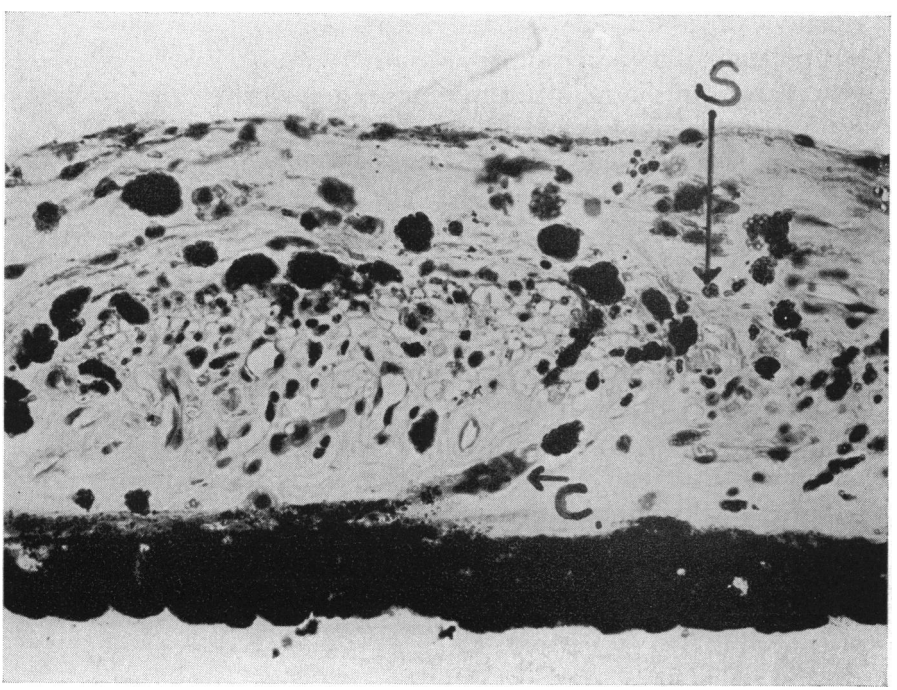

FIGURE 8 (*49-170*). C, SPHINCTER CAPILLARY AT POINT OF ENDOTHELIAL PROLIFERATION AND OCCLUSION; S, ATROPHIC SPHINCTER

in other places showed subintimal hyaline thickening with collections of fatty cells. In one specimen the great arterial circle in the head of the ciliary body was occluded completely and replaced by hyalin (Figure 10). Usually, surviving iris tissue could be correlated with apparently functioning vessels.

Another rarely found capillary change consisted of a collection or knot of endothelial cells apparently occluding the lumen, beyond which the slightly thickened and otherwise normal wall collapsed (Figure 8).

A relative absence of hemorrhage indicated that arteries and the arterial side of capillaries were closed, with resultant anemic infarction. A slow evolution of necrosis would be expected in the richly vascularized anastomosing system. When a large vessel—the large circle—becomes occluded, the result no doubt is to speed the progress of the atrophy. A complete occlusion of the major circle was found in only one case (Figure 6).

Considering the histopathologic material in a group, the atrophy was distributed to parts and to the entire thickness of the iris in zones, and regionally dependent upon the duration of the process and the collective effect of multiple occlusions. The sphincter usually escaped until the last and often it stood out, surviving with a supplying artery and capillary plexus (Figure 2). Fatty degenerative changes in the sphincter were related to closures and hyalinization of the supplying capillary plexus. The dilator myoid, especially, suffered from anemic infarctions, following spotty hyalinization up to the point of complete closure of the supplying capillaries. Varying degrees of fragmentation up to complete loss were noted (Figures 5, 6, 7).

One would expect the blood vessels of the ciliary body to display similar occlusions and secondary atrophies in some cases; in other words, the process in the iris probably extends outside to closely related ciliary vessels. This has occurred (Figures 14, 15). The vessels affected are the branches from the long ciliary arteries which turn into the ciliary body. These branches are mainly distributed to the anterior and middle thirds of the ciliary muscle wedge. The fractional losses of the ciliary body resemble those of the iris, except that evidences of fibrous repair can be found in later stages.

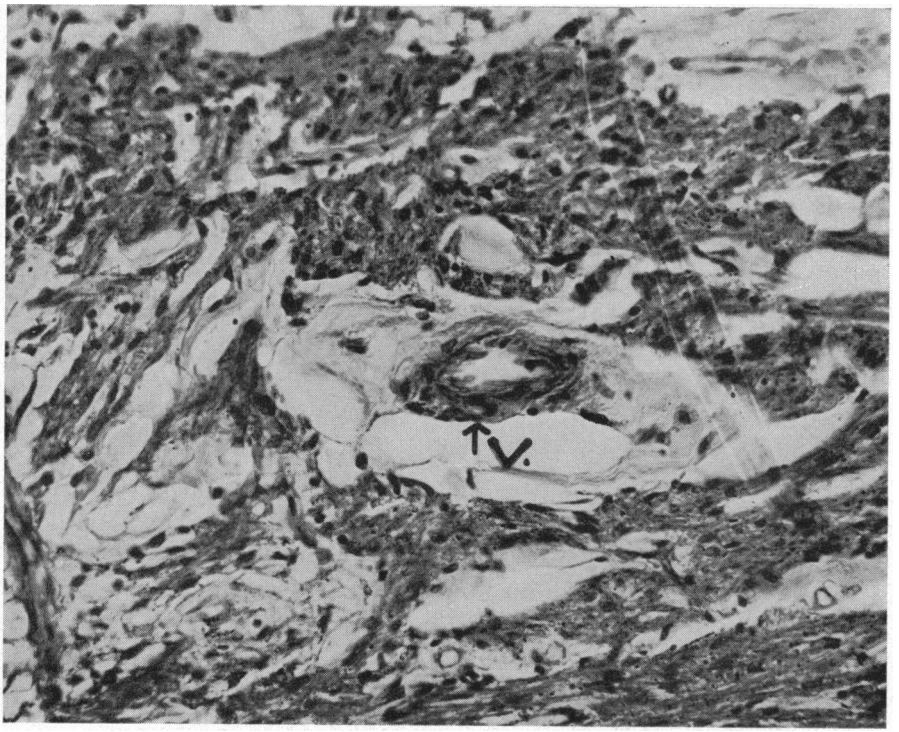

FIGURE 9 (52-61). V, SUBINTIMAL THICKENING, MAJOR VASCULAR CIRCLE OF IRIS

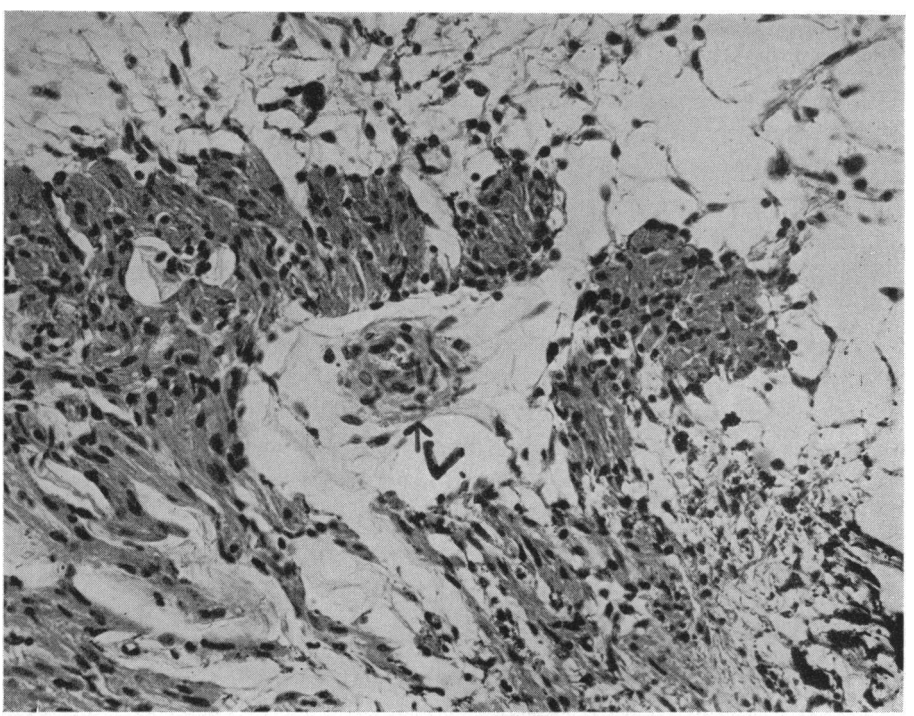

FIGURE 10 (52-61). V, COMPLETE OCCLUSION OF MAJOR VASCULAR CIRCLE OF IRIS

In general, the distribution of occlusions, hyaline thickenings, and exaggeratedly reduced calibres of the vessels was found to be spotty. One would expect necrosis to be slow in evolving because of the hyaline nature of the changes in the vessel walls, the scattered distribution, and the rich anastomosis normally present in the iris blood supply. An attempt was made to trace the vascular patterns of the iris in an infant. A stillborn fetus was injected with latex. The injection mass collected unevenly with an elaborate regional distribution in small vessels and capillaries, while some of the larger vessels were relatively free (Figure 16). This illustrates somewhat the pattern made by the vascular disease of progressive atrophy.

Where the supplying arteries and capillaries have survived in the progressive atrophy specimens, the iris stroma and muscles have survived (Figure 4). In one case, the pigment layer of the iris displays intraepithelial cysts (Figure 13) in regions of still functioning vessels. In zones where the pigment epithelium is lost and in points of partial loss, the bordering capillary plexuses are mostly or completely occluded. When the supplying vessels are partially affected, and with very small lumens, the pigmented epithelium shows vacuolization. Close correlation is consistently noted between survival of various iridic tissues and patency of what are thought to be supplying arteries and capillaries. The absence of hemorrhage and signs of cellular inflammation is noteworthy, and to be expected in anemic infarction.

When the progressive occlusions have been distributed chiefly to one sector or half of the iris, the pupil is distorted and the sphincter is usually pulled away from this side. Thus, the initial bunching-up of tissues is found on the least affected side. Here the iris is folded somewhat and forms a substantial mass of tissue in contact with the cornea. Anterior synechiae are begun from this point. Where the distribution of the atrophy is in quadrants, the pupils may assume a square shape and remain relatively centrally placed.

Cuticular membranes, well endowed with endothelial cells, were clearly demonstrated in five cases of the ten. These membranes were found to extend from the cornea over the sclerocorneal trabeculum, and over the synechiae, when present (Figure 11). The membrane took a modified Hotchkiss stain (Figure 12). The loca-

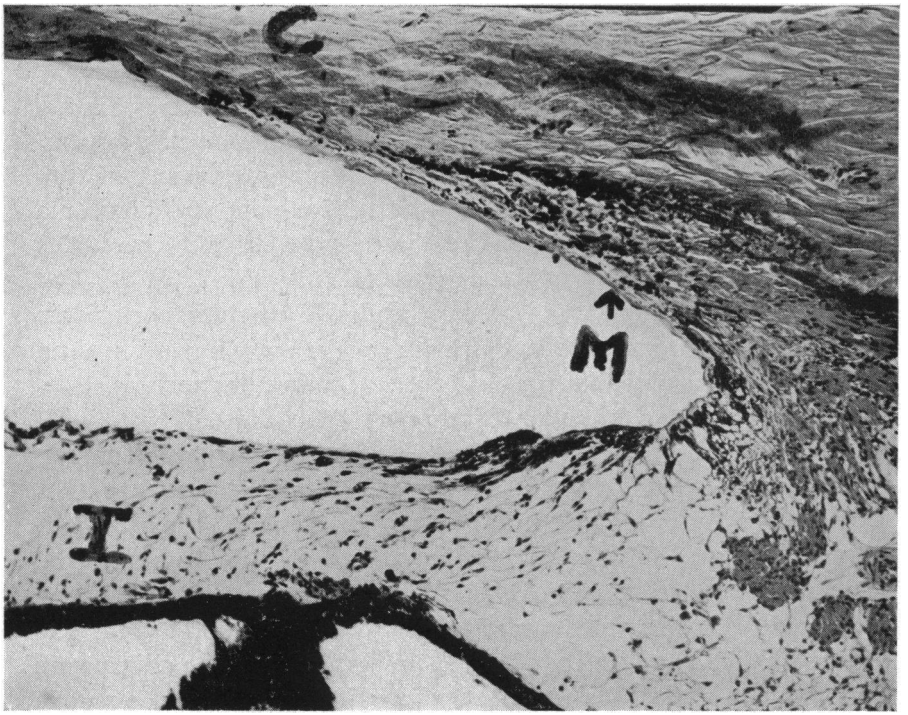

FIGURE 11 (52-61). M, ENDOTHELIALIZED CUTICULAR MEMBRANE LYING OVER SCLEROCORNEAL TRABECULUM; C, CORNEA; I, IRIS

Early glaucoma; nerve head not cupped, and retina and ganglion cells intact.

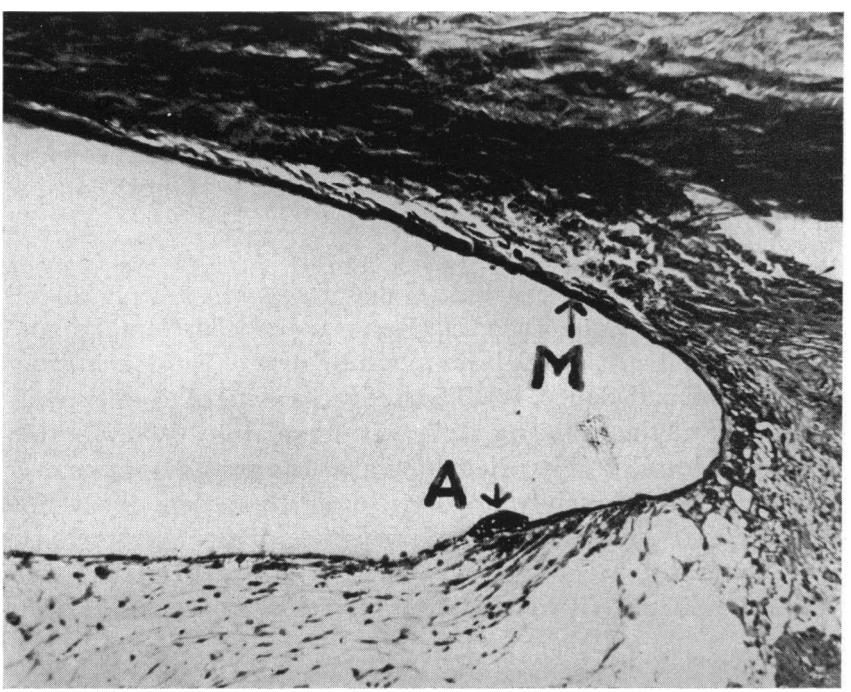

FIGURE 12 (52-61). M, CUTICULAR MEMBRANE AFTER HOTCHKISS STAIN; A, THICKENED GROWING HEAD OF MEMBRANE

tion of the membranes clearly suggested cause for an early appearance of glaucoma. It is possible that the clinical variety of progressive iris atrophy which shows corneal edema and glaucoma in early stages is a cuticular membrane type. Judging from this series, about one third of the patients fall into this category. The cuticular membrane type displays multiple vascular occlusions; and whatever formulates vascular endothelial activity and hyaline collections may equally stimulate corneal trabecular and iris endothelial growth and cuticular membranes.

Other parts of the eyes showed secondary participation in the glaucomatous part of the disease. In the retinas of late stages, loss of ganglion cells was the rule, but these were well represented in the early cases. The optic nerve head also escaped cupping in the early cases. Occlusive vascular disease was not notable in the choroid or in the short ciliary vessels. Careful study of many sections of the vena vorticosa showed no atypicality. The ciliary ring in the late stages of the disease showed advanced glaucomatous atrophy. Segmental atrophies related to vascular occlusive disease were found affecting the middle layers of the muscle ring in the early cases.

The corneas showed a tendency to collapse and undulate, and otherwise were affected by the secondary glaucoma. The endothelium was not found to be especially disturbed except as described—by contributing toward cuticular membrane formations. One case had a small onyx in the cornea. The anterior chambers proved to have irregular depths, due partly to corneal collapse and partly to synechiae.

THE SHIFT OF THE PUPIL

The dilator myoid has an aggregate power considerably more than the sphincter, as has been found by tests of isolated strips of each (Heath and Geiter, 12). The linear efficiency of the dilator exceeds that of the sphincter. Whereas the dilator myoid is a thin sheet, it is broad, and its orientation gives it a great advantage over the sphincter. The sphincter covers linear distance by contracting *pi* times per linear unit. The regulating dilator can cover an equivalent distance by contracting or relaxing only one unit. Thus the dilator has an advantage for linear movement over the

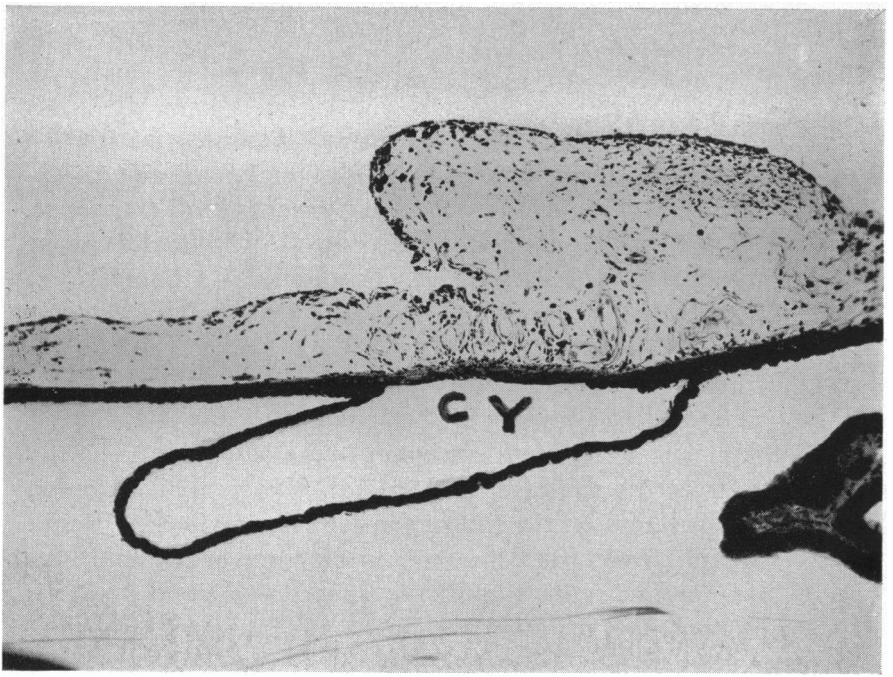

FIGURE 13 (52-61). CY, INTRAEPITHELIAL CYST, FED BY A GROUP OF FUNCTIONING VESSELS

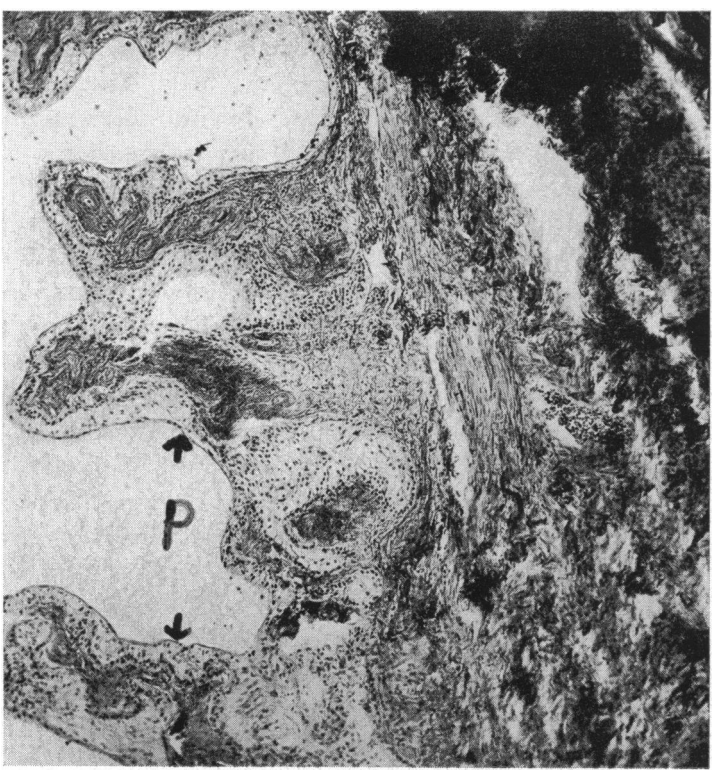

FIGURE 14. CILIARY BODY BLEACHED; THE CENTRAL MUSCULAR ZONE IS ATROPHIC BECAUSE SUPPLIED BY OCCLUDED VESSELS

The processes (P) are relatively normal, supplied by unaffected vessels.

sphincter of 3.1416 to 1. Consequently, with substantial atrophy of the stroma and the dilator on one side, the functioning or opposite side shifts the pupillary sphincter towards itself (Figure 1). A study of the holes in the iris correlates well with the shift of the pupil toward the functioning side. The result is a bunching of iris tissue at the base of this side (Figure 3).

ECTROPION UVEAE

Incomplete ectropion uveae is often noted clinically and is found in sections. The incomplete ectropion uveae is explained by the joint effects of the sphincter and dilator. The partial ectropion of the uvea is found on the side of the defective dilator. No doubt the ectropion results from the mechanical force of the sphincter where unopposed by the dilator; the unanchored pupil border is pulled forward with the uvea. This maneuver is assisted by hyaline formations under the sphincter (Figure 2).

SECONDARY GLAUCOMA

The joint occlusive activities of cuticular membranes and of synechiae would seem to make glaucoma inevitable, even in the presence of a limited atrophy in the ciliary body. The shifted and bunched iris becomes a mass of tissue, which of necessity projects anteriorly and makes corneal contact. Thus the anterior synechial pattern is begun. Another source of glaucoma is related to the iris itself. The iris is capable of picking up a high percentage of particulate matter from the anterior chamber. Wandering cells carrying phagocytized material migrate into the iris with great ease and travel actively or passively within the perivascular membrane about the vessels. An iris undergoing destruction by autolysis after anemic infarction supplies a considerable amount of material which must go somewhere or be collected in depots. Its usual channels of exit through the iris are destroyed. This detritus is unable to escape through the trabeculum of the angle. It accumulates, some in cells, some loose and amorphous. From this accumulation are created additional blockades of outflow.

Cuticular membranes, endowed with endothelial nuclei, are clearly seen in the sections made from moderately advanced cases of progressive atrophy. They occupy the inner sclerocorneal tra-

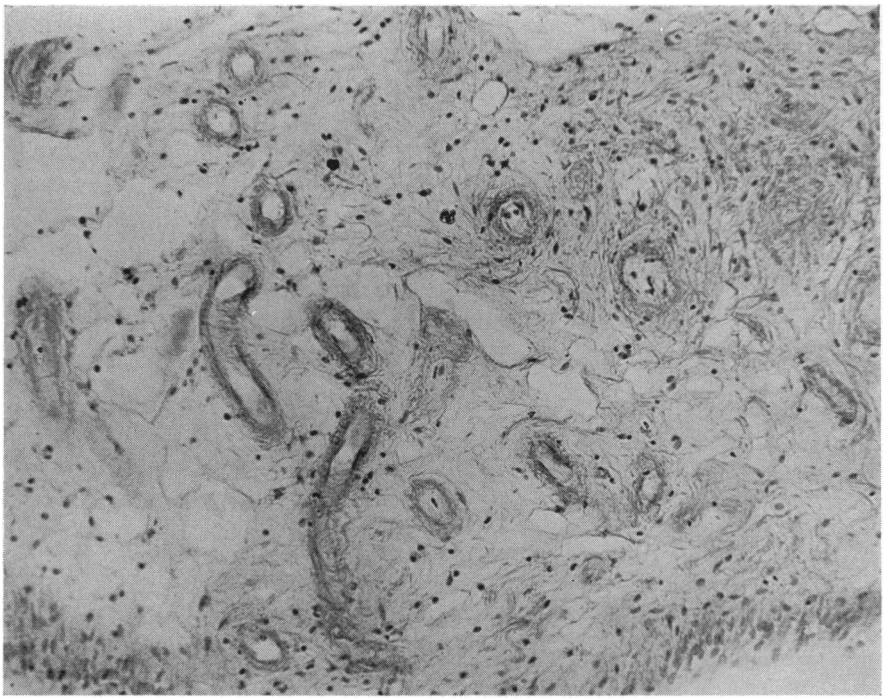

FIGURE 15. BLEACHED CILIARY BODY; SURVIVING HYALINIZED VESSELS, DESTINED FOR A FUNCTIONING ZONE, PASSING THROUGH AN ATROPHIC REGION, THE LATTER SUPPLIED BY OCCLUDED VESSELS
Numerous fatty lipophages are present.

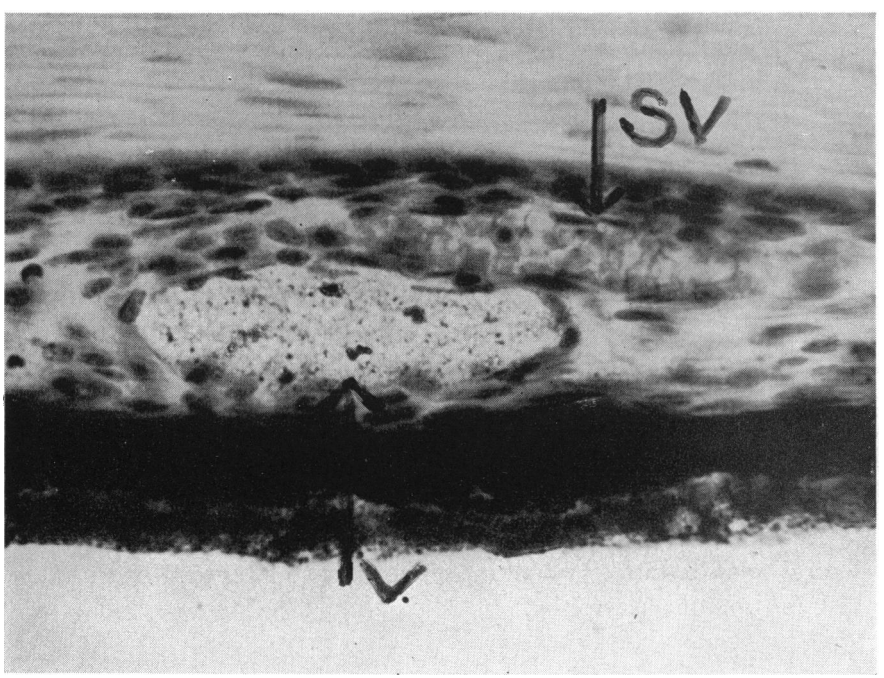

FIGURE 16 (*49-92*). V, LATEX-INJECTED IRIS VESSEL SUPPLYING DILATOR AND STROMA. SV, VESSEL RUNNING PARALLEL AT THIS POINT WITH DIFFERENT ORIGIN, PROBABLY DESTINED FOR THE SPHINCTER REGION, IS FREE FROM INJECTION MASS

beculum, the iris remnants, or run over the synechia and on the back of the cornea, with different degrees of participation in each. In one case a cuticular membrane separated the trabeculum from a synechia. The physiological function of the iris in removing crystalloids, plasmoids, and particulate matter is progressively lost by atrophy, and this in turn contributes toward glaucoma.

The glaucoma in this series is represented by various stages, early and late, and its role as a complication is clearly demarcated. In relation to the glaucoma, the corneal, retinal, and optic nerve changes, and possibly the cataract formations, are all secondary complications. Disseminations of pigment from the iris are too often found in laboratory material unrelated to glaucoma to be considered important in progressive idiopathic atrophy of the iris as a cause of glaucoma.

SUMMARIZING DISCUSSION

The histopathology found in the relatively early stages of progressive iris atrophy, before destructive effects from late glaucoma have occurred, indicates that the mechanism for the atrophy lies in multiple anemic infarctions, following segmental vascular occlusions. The cause or causes of the localized vascular changes remain unknown. The occlusions were somewhat randomly arranged in the several systems of iris vessels, arising from the long ciliary artery, and extended inwards so that successively more stroma and iris tissues were lost. The occlusive phenomena were seen in all sizes of arteries and capillaries. Furthermore, the overall narrowing of the lumens of the arterioles found in surviving portions of the iris reduced the amount of blood allowed to pass through and apparently stepped up the velocity of atrophy. However, the surviving portions of the iris show vessels numerous enough to keep the tissue viable. Where the atrophy is most marked and but few fibrous strands remain, the blood vessels have disappeared or have become completely hyalinized. Where blood vessels are functioning, and only where patulous, some evidence of overactivity is suggested by separation of the posterior pigment layers into intraepithelial cysts. The clinical course and pathological manifestations seen in sections correlate well with the distribution of the atrophy.

The shift of the pupil occurs toward the functioning meridian when in the opposite meridian the dilator is atrophic or lost. This also is identifiable clinically by zones of atrophy or holes, as seen by transillumination. The shift of the pupil ring is in the plane of action of the surviving dilator because of the latter's greater overall efficiency in making linear movement. A bunching-up of iris tissue at the base of the surviving side subsequently makes contact with the cornea and forms anterior peripheral synechiae. The frequency of demonstrable cuticular membranes found in more than a third of the cases suggests that this is an important factor in glaucoma and explains the early manifestations of glaucoma in some cases. These have been called the "cuticular-membrane types." Endothelial cells are viable and well represented over the membranes.

Incomplete ectropion uveae is explainable by the rolling-out effect of the sphincter where unopposed by the dilator. It is usually present in late stages.

Two features of the disease cannot be explained, namely, predominance in adult females and unilaterality. Among the clinically reported exceptions is a bilateral case in a five-year-old boy (Fine and Barken, 13).

The glaucoma phase of the problem is recognizable as a complication of the primary iris disease. The increased intraocular pressure can be due to cuticular membrane, synechiae, cellular detritus, and trabecular block, or a combination of these. A further possibility exists that the glaucoma is related to reduced capacity for absorption by the iris because this tissue is largely lost. The unilaterality is not explained. The fact that females are chiefly afflicted suggests that some endocrine mechanism plays a part in the primary occlusions of the iris arteries and capillaries.

CONCLUSIONS

These studies were made from the histopathology found in ten cases, exhibiting early and late stages of the disease. As in previous studies, females predominated. This disease of adults is unilateral, of spontaneous origin, and exhibits glaucoma as a complication of a primary progressive disease. Secondary glaucoma may appear in early stages which are characterized clinically by corneal edemas

and increased intraocular pressure before advanced atrophy of the iris occurs. This type of progressive atrophy is characterized histologically by cuticular membrane formations.

Idiopathic progressive iris atrophy (essential) is caused by readily demonstrated multiple vascular occlusions, which progressively create anemic infarctions and loss of iris tissue in all layers. The ciliary body is similarly, but regionally, affected in some cases. The cause or causes of the local changes in the blood vessels remain unknown. Vascular closures are demonstrable in both iris arteries, capillaries, and in the lesser and greater circles of the iris. These sporadic manifestations are somewhat like those seen in the spleen. Subintimal hyaline thickening and lipid-cell accumulations were commonly found. Occlusions of capillaries occurred from endothelial cell plugs and the iris is especially vulnerable to nutritional impairment from the reduced size of lumens because of already existing thickened walls.

The glaucoma of progressive essential atrophy of the iris is explainable on four grounds, principally involving decreased facility of outflow: (1) partial coverage of the sclerocorneal trabeculum by cuticular membranes; (2) peripheral anterior synechia; (3) loss of the resorption capacity of the iris from actual loss of iris tissue; (4) the blockading effect over the angle from iris debris and detritus.

The absence of inflammatory cell changes is explainable, as is the clinical course, by anemic infarctions. Close correlations are noted between clinical course and the histopathological findings.

No genetic patterns were found in the cases studied.

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DISCUSSION

DR. JOHN S. MCGAVIC. As Dr. Heath pointed out, no one knows very much about this rare condition. I am glad, therefore, that I was asked to discuss the paper, and not the disease itself. It is a beautifully written paper, as you will all see when the *Transactions* appear. It stands out as a splendid literary work, Dr. Heath having great facility with words on paper, leaving us with a clear understanding of what he is trying to say via a very pleasant verbal route. The correlation of all the clinical findings with the histopathologic findings is done down to the last detail. The illustrations are splendid, and the latex-injected specimen is particularly interesting. It was a good idea for him to review for us the blood supply of the iris and ciliary body, somewhat as Dr. Vail did a few years ago for the optic nerve.

Although in the literature there are five to ten cases reported as bilateral, each of them has something to make one feel it is of the secondary type of glaucoma. One was in a child of five, and showed no proliferative changes in the iris. Another had posterior synechiae, and one had very little atrophy which sounded like simple atrophy secondary to increased intraocular pressure. Still another lacked holes in the iris.

One of the most interesting and most difficult things to explain is the unilaterality of this disease. A second puzzle is its occurrence in relatively young people. The endothelial proliferative changes seem to play a very prominent part, both in regard to the lining of the blood vessels and to the endothelium on the anterior surface of the iris, and, of course, this endothelium gives rise to the glass membrane which is on the anterior surface, and, as you saw in one of the specimens, on the posterior surface of the iris.

In spite of the fact that the dilator is seen to have more aggregate power than the sphincter, most of us are inclined to think of the sphincter as the stronger muscle. I believe there is another explanation for the immobility of the pupil. Two factors enter in: one, fatty degeneration present in the sphincter muscle, and the other the fact

that the sphincter muscle is incapacitated by ectropion uveae in most cases. Then the pupils no longer dilate or contract. This is not peculiar to essential atrophy of the iris, but is present in atrophy with replacement by connective tissue in any type of glaucoma, so that here we have a sphincter which cannot act well because of fatty degeneration and because the iris is surrounded by a cuticular membrane due to the endothelial proliferation, and so the dilator can act unopposed except by the deformity of the iris itself.

Dr. Heath has shown the vascular occlusions very conclusively. Most vascular diseases, if not hereditary, tend to run in families. To the best of my knowledge, this disease does not tend to run in families. If the vascular disease were the primary cause, it would seem it would be bilateral, and it probably would not be quite so selective in the iris and, to a lesser extent, in the ciliary body. We therefore must look for some cause for the vascular occlusion, and so far as I know, no such cause has been brought forward. A neurogenic hypothesis was suggested in 1936 by von Grosz as "a hypothetical neurogenic gene." This is the only suggestion of a neurogenic origin. The unilaterality, the rarity, the inevitable progression of the disease, and the vascular occlusions might be laid to a neurogenic cause, and as long as we do not ask for the cause of the neurogenic disturbance we are all right! It is possible a neurogenic factor might affect the trophic supply to the iris and produce atrophy. It was a pleasure to read and to discuss this fine paper by Dr. Heath.

DR. F. H. VERHOEFF. This is undoubtedly the most complete and best histologic study of this disease that has ever been made. One of the most interesting things (and Dr. Heath did not emphasize it) was his discovery of a cuticular membrane over the ligament—an adequate explanation of the glaucoma in many cases. His explanation of the iris atrophy being caused by obstruction of the blood vessels at first glance seems to be very good and it would be difficult for anyone to disprove, but it seems to me he has not excluded the possibility that the atrophy comes first and the change in the blood vessels is secondary, or that both occur together. I think abiotrophy has not been mentioned here. For some reason it is a very popular term, and I think it might be used in connection with essential atrophy of the iris. It is generally assumed to mean premature senility, but abiotrophy often differs from ordinary senility. Senile atrophy of the iris does not produce the picture of essential atrophy. It seems to me, in spite of the fact that essential atrophy of the iris has not yet been shown to be hereditary, that it is a genetic disease and ultimately will be found to be hereditary. But what I wish to call attention to particularly is the similarity of this iris atrophy to a choroidal condition incorrectly called choroideremia. Troncosa in the first edition of his book says that this should be called

essential atrophy of the choroid. Bedell and McCullough call this condition choroideremia. This term was originally used to mean congenital absence of the choroid, just as aniridia was used for congenital absence of the iris. Does anybody ever call essential atrophy of the iris aniridia? Why should we call this essential atrophy of the choroid choroideremia? Bedell and McCullough have each done a beautiful piece of work, and McCullough was the first to determine the hereditary aspects of the condition and to examine it microscopically. They have really shown that nobody has yet seen a case of choroideremia. What they call choroideremia is a progressive disease. If we get a real case of choroideremia, what are we going to call it if we have adopted the term for something else? I have talked with Dr. Bedell about this, and he says he is willing to admit his mistake. Essential atrophy of the iris and essential atrophy of the choroid are very similar histologically, and in both conditions the question arises as to whether the obliteration of the vessels is primary or secondary. The fact that iris vessels are so different from vessels elsewhere in the body tends to support Dr. Heath's contention. While the two conditions are remarkably similar, they differ in two important respects. Essential atrophy of the choroid is bilateral and is definitely hereditary, while essential atrophy of the iris is unilateral, and has not been shown to be hereditary.

DR. RAMON CASTROVIEJO. This is a most interesting paper, and I was particularly interested that Dr. Heath mentioned the fact that the ciliary processes are not affected. That will explain the glaucoma in part. The channels of excretion are much affected, the production of aqueous humor is maintained, and therefore the balance of tension is broken.

Dr. Heath has not mentioned anything about treatment, but his findings may lead to some valid conclusions. If the channels of excretion are damaged, it would be difficult to succeed in getting a cure by the ordinary filtration operation, and therefore other ways of balancing the tension should be found. I recall two cases of essential atrophy of the iris, one in the Vanderbilt Clinic in a boy four or five years old. One eye had advanced atrophy and advanced glaucoma and this eye had to be enucleated. In the other eye we did a filtering operation of the Elliot type. This child was kept under observation at the Vanderbilt Clinic until a year ago, and I was able to observe him. In the eye that was preserved there was good balance of tension and good function.

The other case was a young woman of twenty years of age with essential atrophy of the iris in both eyes, one advanced, and the other moderately advanced, who had been given up because miotics did not work and we did not feel any operation would prove successful. Five years ago I visited Dr. Franceschetti at Geneva, and he spoke to me

about cyclodiathermy and showed me two cases recently operated upon. After that I talked about this operation and thought I would use it. The case of this young woman appeared to me an excellent one for cyclodiathermy, and I did 16 electrocoagulations all around the limbus in the two eyes. The tension has remained balanced for three years. I think this operation would seem to be indicated in such cases, in that balance of secretion with excretion can be established.

I am very glad I have been able to acknowledge the contribution of Dr. Franceschetti, who suggested to me this surgery of glaucoma, and I wish to congratulate Dr. Heath again for this wonderful histologic paper.

DR. ARTHUR J. BEDELL. I rise to tell you I am going to disappoint you by not opening a discussion on choroideremia; the verdict has been rendered.

Four photographs will illustrate Dr. Heath's subject.

The first is an essential atrophy of the iris in a male with a pale temporal section and localized decrease in the thickness of the iris. The second, taken four years later, shows the increase in the atrophy with a rise in the intraocular tension.

The third is of a woman who came at a stage of advanced iris atrophy, and the last portrays the changes after two and a half years when her glaucoma had increased and an overwhelming hemorrhage almost filled the anterior chamber, making enucleation necessary.

I was thrilled at hearing Dr. Heath's paper and I am sure all of us will go home with a better understanding of essential iris atrophy.

DR. J. S. FRIEDENWALD. Dr. Verhoeff has emphasized the difficulty in deciding whether the vascular occlusions in these cases are primary to the disease or secondary, as is seen in many atrophic tissues in which the blood vessels undergo obliteration. This has been a primary problem in the interpretation of the disease for many years, and I am eager to hear what Dr. Heath has to say further on this subject, since I realize his presentation was cut short. There are, I believe, some arguments as the discussion now stands, which I am sure Dr. Heath will be able to clear up, which lend weight to the opposite interpretation to that which he has given.

In the first place, for instance, in extensive tears of the iris root where a great many of the iris blood vessels are deprived of blood supply, one does not see patchy atrophy similar to that seen in essential atrophy. On the contrary, the damaged part of the iris undergoes some fibrosis, but there is no appreciable tissue loss. Again in Dr. Heath's own pictures he shows some regions where surviving blood vessels cross an atrophic area, and in those areas the atrophy can hardly be consequent on the loss of the blood vessel which is the sole remainder.

It has been my good fortune recently to see a disease in mice which I believe is an example of the same condition we see in human beings. These mice occurred in a strain at Oak Ridge, and are now being studied very extensively. They show, as they grow older, an essential atrophy of the iris which looks clinically exactly like the human disease, except that it is bilateral in these animals. A few eyes so far have been studied by Walter Benedict, and I was privileged to look at some of the sections. Dr. Verhoeff will be interested to know that some of these animals have essential atrophy of the choroid as well as essential atrophy of the iris. Since this disease develops slowly in the course of the lifetime of a mouse, one can get as many specimens as one wants at different ages, and it may be possible to see whether the vascular obliteration precedes or follows the atrophic process.

DR. HAROLD F. FALLS. The question of differential diagnosis warrants short consideration. In this respect I should like to suggest that Dr. Fine's previously reported case of bilateral essential atrophy of the iris in a young child is possibly a case of Axenfeld's syndrome. This syndrome is characterized by persistence of postendothelial tissue in the anterior ocular segment at birth and displays a tremendous range of pathological aberration. The neuroectodermal leaf of the iris may occasionally be fairly well developed, but in general presents extensive maldevelopment, such as absence of the sphincter, polycoria, pseudopolycoria, iridotasis, iridoschisis, and so forth. The mesodermal leaf of the iris is generally underdeveloped, exhibiting peripheral synechiae, "embryotoxon," slit pupil, corectopia, dyscoria, ectropion uveae, and so forth. Glaucoma eventually ensues and is frequently diagnosed as "juvenile glaucoma." Axenfeld's syndrome is usually inherited as an autosomal dominant with wide variance in expressivity but good penetrance. The mere presence of unilaterality in essential atrophy need not exclude the consideration of a genetic etiology. Romberg's syndrome, or facial hemiatrophy, is unilateral, yet is considered to be genetically determined. Status Bonnevie-Ullrich may exhibit a tremendous amount of widespread anomaly, chiefly unilateral, and is most likely the result of a noxious gene action.

Lastly, to support Dr. Verhoeff's contention of abiotrophy, I should like to recall Dr. Sorsby's conclusion that choroidal sclerosis (choroidal atrophy) is an involutional change in the choroidal vasculature leading to extensive secondary retinal alteration. The latter, characterized by atrophic areas possessing scallop-like borders, are in my opinion clinically pathognomic of choroidal abiotrophy. In this respect please recall the early appearance of "choroideremia" and gyrate atrophy.

Sorsby's choroidal sclerosis, or abiotrophy, is most likely a recessive gene trait with the early stages appearing in mid-adult life and extending into late senescence. The term "choroideremia" in my opinion no

longer is acceptable, since the incipient stages of this choroidal abiotrophy in the male were not seen or recognized by the early workers in this field.

A few of the abiotrophic diseases certainly simulate very closely the embryological involutional stages in ocular development. Essential atrophy of the iris may well be such an abiotrophic disease.

DR. PARKER HEATH. The first thing I would like to do is to thank the discussers for the way in which they have enriched the paper.

I have not time to try to particularize, but one point I would like to speak about, and that is this: we made special studies of the atrophies related to senile changes in the iris—those due to glaucoma, to trauma, and those related to some kind of inflammation. We found that iris changes from these causes were quite different from those of essential atrophy. The atrophies of the nonprogressive type do not correlate with complete regional capillary bed loss and occlusions. The reason the atrophy is not progressive in the ordinary case is that collateral circulation is so extensive and so rich in the iris that any ordinary occluded zone is supplied by blood from other sources. The extraordinary thing about these patients is the over-allness of the occlusive factor. I have been unable, however, to identify specifically the changes in the vessels, or to dissociate them completely from those found in senile processes.

The strain of mice which Dr. Friedenwald spoke about is new to me, and I think that it will be very interesting to work out the possible relationships to humans. Regarding surviving vessels in an atrophic zone, see Figure 15.

The glaucoma of essential iris atrophy is obviously secondary and often due to cuticular membrane. What causes the primary arterial, arteriolar, and capillary disease I have no conclusive ideas, any more than I have of what causes the lesion in senile states.

Genetically, none of these 10 cases had a known characteristic pedigree. I can see the suggestion of some sex-linked form of heredity. The interesting facial hemiatrophies have genetic manifestations and spotty iris atrophies. Possibly someone will turn up a pedigree in due time applicable to progressive iris atrophy, classifying it among the abiotrophies.