PATHOLOGIC CHANGES IN THE ANTERIOR HALF OF THE GLOBE IN OBSTRUCTION IN THE CENTRAL VEIN OF THE RETINA

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Excluding injuries and tumors, there are among elderly persons probably more eyes enucleated for the relief of absolute glaucoma secondary to obstruction in the central vein of the retina than for any other condition. The frequency of the disease increases with advancing years, a fact that is of common experience. Pain and inflammation play an important rôle in this type of glaucoma. A similar type of extremely painful glaucoma may ensue as a complication in cases of complete detachment of the retina. In both conditions operations for the relief of the glaucoma seldom prove successful. After surgical intervention the tension may rise higher than it was before and the pain may be greater. In glaucoma following obstruction in the central vein, an examination will reveal a characteristic picture: an anterior chamber of normal depth, often containing blood, a small pupil, and an iris with new-formed vessels on its surface—all of which are of diagnostic importance. It is usually impossible to see the fundus, not alone because of the smallness of the pupil and the presence of blood in the anterior chamber, but because the vitreous is likely to be clouded by red blood cells coming from the engorged and ruptured veins of the retina.

The history of the case is of aid, since in most instances almost complete blindness comes on somewhat suddenly and the patient is at once aware of it, just as in the case of the abrupt onset of blindness in embolism in the central artery. Once glaucoma is fully developed, the rarer cases in which there

has been noticed a gradually failing vision for some time prior to the advent of blindness are especially difficult to diagnose. Such cases are to be differentiated from those of necrotic sarcomas of the uvea, in which there are blood in the vitreous and aqueous and increased tension. In the hyphemia of a necrotic sarcoma the anterior chamber will be shallow and the pupil will be wide, although in exceptional cases it may be small. In the glaucoma associated with detachment of the retina the pupil is often small, and the anterior chamber may be even deeper than normal. Transillumination is not always reliable, because innumerable phagocytes, having invaded a hemorrhage in the subretinal space, may set free so much pigment in their bodies as to throw a shadow and lead to an erroneous diagnosis of necrotic sarcoma. The pain in glaucoma after obstruction in the central retinal vein and in glaucoma after detachment of the retina differs from that of the ordinary type of glaucoma by its greater severity and its intractability in spite of therapeutic measures, whereas in the common forms of acute glaucoma the pain tends to subside with proper treatment.

In 1924 R. Foster Moore* published a monograph containing an exhaustive clinical study of 62 cases of what he termed "retinal venous thrombosis," which he had followed for many years. In 31 cases the obstruction was in the central vein and in 31 it was in a tributary. In this series glaucoma developed only when the obstruction was in the central vein. In seven cases the average period of time between the occurrence of the obstruction and the onset of the glaucoma was estimated at eighty days. In no case was useful vision preserved. According to Moore, it is the rarest clinical finding that the retina ever becomes free of hemorrhages, even after the lapse of many years, although the obstructed circulation may appear to be adequately compensated by the development of many dilated and tortuous capillaries around the nerve head. Moore not infrequently

* Moore: Brit. J. Ophth., 1924.

found spots of arteriosclerotic retinitis, and white fluffy or woolly-looking areas were frequent in connection with the hemorrhages. Of the series of 62 cases, 41.6 per cent. were known to have developed a gross cerebral vascular lesion. The average length of life after the development of the venous picture was five and eight-tenths years.

In 1907 Verhoeff* reported the anatomic findings in six cases of obstruction in the central vein. He was able to find anatomic descriptions of 39 cases recorded in the literature. Analyzing the findings in these cases and in his own, Verhoeff came to the conclusion that the classic ophthalmoscopic picture of hemorrhagic retinitis after obstruction in the central vein is produced by endophlebitis obliterans and not by thrombosis.

In 1933 Salzmann,† in a monograph, painstakingly recorded the anatomic picture in the region of the nerve head in 65 eyes that were enucleated because of absolute glaucoma. This observer confirmed Verhoeff's deductions in the main, and ascertained that, notwithstanding the fact that an occlusion in the vein frequently causes glaucoma, glaucoma itself often leads to occlusion in the vein by causing its wall to collapse from compression—a fact that, he emphasized, had been underrated.

It is not necessary to include in this text a discussion of the entire literature on the subject. The writings on this subject, especially those of Coats,‡ elucidate mainly the changes and problems presented in the posterior half of the globe. No adequate study of the changes presented in the anterior half of the globe, which are also characteristic, seems ever to have been made. The writer deems it not inopportune to report the results of a systematic inquiry into the pathologic anatomy of the anterior half of the globe, in an endeavor to throw light on the pathogenesis of the peculiar type of

* Verhoeff: Arch. Ophth., 1907, xxxvi, p. 1.

† Salzmann: Glaukom und Netzhautzirculation, S. Karger, Berlin, 1933.

‡ Coats: Roy. Lond. Ophth. Hosp. Rep., 1904, xvi, p. 62.

glaucoma that frequently follows obstruction in the central vein.

Among the theories that have been advanced in explanation of the increase in tension the following come to mind:

1. The theory usually offered in the textbooks, of a general intra-ocular stasis of the blood and lymph, due to blockage in the central vein. This explanation is not satisfactory, since we should expect an increase in the tension immediately after the occlusion, coincident with the greatest amount of pressure in the veins as shown by the edema and hemorrhage present in the papilla and retina; and yet, according to Moore, immediately after the obstruction the globe is softer than normal. Months or years may elapse without signs of ocular trouble other than blindness.

2. One considers the possibility of a swelling of the vitreous body, caused by an imbibition of albuminous substances derived from the hemorrhagic areas in the retina. A swollen vitreous would carry the lens forward, bearing with it the iris and the angle of the anterior chamber. It would press upon the ciliary processes, causing congestion in them and in the iris. One would expect an extremely shallow anterior chamber but on the contrary, the anterior chamber retains its normal depth and the eye may outwardly remain quiescent indefinitely.

3. Glaucoma might conceivably be caused by a coincident congestion in the retina and choroid, as a result of sclerosis of the two vascular systems, but from pathologic experience we know that sclerosis of the retinal system is more likely to be found without sclerosis in the uveal system.

4. Glaucoma could be produced by a change in the fluidity of the aqueous, brought about by the presence of colloidal substances carried forward from the hemorrhages and serum in the vitreous and retina. This theory was promulgated by Coats. However, since in other conditions of extensive and continuing hemorrhage in the retina and vitreous glaucoma does not follow, this theory, as Coats admitted, is assailable.

5. Glaucoma could be caused by a change in the metabolism of the eye produced by toxic substances derived from a disintegration of red blood cells and a degeneration of the retinal tissues and of the stroma of the vitreous. It is conceivable that, once they have reached the aqueous, such toxins would set up an adhesive inflammation leading to peripheral anterior synechiae.

From the standpoint of the last two hypotheses the question of the pathogenesis of glaucoma associated with obstruction in the central vein would seem to be a matter for chemical research, in order to ascertain in what respects the intra-ocular fluids may differ from the normal. The fact that we are unable to decide what these alterations may be should not prevent us from making an anatomic inquiry, since the chemical findings would be of little value unless they could be correlated with a thoroughly investigated pathologic anatomy.

THE ANATOMIC MATERIAL

The present paper is based on a study of microscopic preparations of the anterior segments of 29 globes. In each instance there was a clear record that the obstruction in the vein had preceded the glaucoma.

In regard to the clinical histories, the following information was ascertained:

THE SEX

Women	8
Men	7
Unknown	14
Total	29

THE AGE

Women	*Men*	*Unknown*
32	52	
50	60	
53	60	
60	65	
66	67	
70	70	
73	70	
76		
8	7	14

Total 29

DURATION OF THE OBSTRUCTION

Cases	*Duration*
1	8 days
3	3 to 6 mos.
6	1 to 3 years
1	12 years
18	Unknown

DURATION OF THE GLAUCOMA

Cases	*Duration*
1	Several days
3	A few weeks
7	3 to 6 months
1	1 year
17	Unknown
Total	29

THE TENSION

The tension was frequently mentioned as being extremely high. Tensions of 60, 70, and 80 mm. Hg were noted.

OPERATIONS

There was a record of but two operations having been performed prior to enucleation, which fact was considered to be significant of a general realization of the futility of attempting to operate to save these eyes.

MICROSCOPIC STUDY

The microscopic inquiry was pursued in the following order:

1. A Study of the Vascular Systems of the Retina and Choroid.—The disturbance in the circulation of the retina was often manifested by scattered hemorrhages anterior to the equator and several times free blood was traced almost as far forward as the ora serrata. In the cases of the most extensive retinal hemorrhages there was as complete an absence of evidence of circulatory disturbance in the choroid as there was in those cases in which the retina showed a few or no hemorrhages anterior to the equator. From an anatomic standpoint there is no ground for presuming that an obstruction in the central vein of the retina could have any influence

on the circulation in the uvea except in a narrow zone at the choroidal foramen where an anastomosis of small retinal and choroidal vessels takes place. It is from this source that the dilated loops of veins that serve to re-establish the circulation at the papilla are derived. Furthermore, in confirmation of Moore's clinical observation that a disturbance of the pigment epithelium of the choroid is never seen clinically except at the fovea, the study revealed no special changes in the pigmented layer or in the choriocapillaris. In no case could a marked sclerosis in the choroidal system of vessels be distinguished.

2. A Study of the Vitreous Body.—There were four cases that spoke definitely against the theory that a swelling of the vitreous, by compression of the ciliary body, had caused stasis. In these cases the vitreous was largely broken down and was detached posteriorly, being separated from the retina by an albuminous fluid. We are prone to associate a detached and broken-down vitreous with low tension. There was blood in the vitreous in nine cases, in two of which it was extensive. In 11 cases the vitreous appeared to be normal, showing that it is possible for glaucoma to occur after obstruction in the central vein without blood in the vitreous.

3. A Study of the Ciliary Body.—In 14 cases the ciliary body was atrophic, but the atrophy was most evident in the ciliary muscle as it is seen in glaucomatous eyes and in those of aged persons. In a striking way, in case after case, the ciliary body showed only such evidences of circulatory disturbance as could be attributed to the high tension. With few exceptions the ciliary body was remarkably free from signs of inflammation.

4. A Study of the Iris.—(*a*) *The Stroma.*—In contradistinction to the ciliary body and choroid, the iris in these cases presented a number of pathologic changes. In 18 cases the stroma was atrophic. The word atrophy is here employed as E. Fuchs used the term to describe the appearance of the iris after inflammation. In glaucoma, due to a disappearance

of its elements, the stroma is thinner, but in inflammation of low grade the normal thickness may be retained, although the original normal loose and delicate stroma is replaced by a more cellular and compact one. It was this latter type of atrophy that characterized the majority of the irides of this series. The cellular elements were diffusely distributed, and lymphocytic foci were absent. It was remarkable that in many cases the normal thick-walled vascular system of the iris was replaced by a system of atypical thin-walled vessels such as are familiarly seen under the microscope in atrophy of the iris of inflammatory origin. There were no hemorrhages in the irides, so that it could be said that no division of the uveal tract showed any unusual congestion. In several cases the stroma presented necrotic areas in the pupillary zone. In one instance the necrosis in the iris was associated with a necrosis of the ciliary processes. Such necrotic areas are not infrequent in glaucomatous globes. In a number of specimens the stroma of the iris appeared to be normal.

(*b*) *The Posterior Surface.*—In 20 globes the pigment epithelium was entirely unaffected. In five cases there was a simple posterior synechia at the pupil. In four cases the pupillary margin of the iris was drawn into a membrane that stretched across the lens.

(*c*) *The Anterior Surface.*—In nearly every case a membrane was encountered lying on the anterior surface of the iris. The majority of the membranes were in the pupillary zone. In four instances these membranes consisted largely of endothelial cells. In eight specimens the membranes were composed almost entirely of capillaries. The greater number of membranes were made up of a mixture of endothelial cells, fibroblastic cells, and blood vessels, the last usually predominating. The membranes were thin, and the walls of the vessels were extremely delicate. In two instances the membranes were thick and presented the characteristics of granulation tissue. The first of these was in the globe of a woman, aged fifty years. The eye had been inflamed for a period of

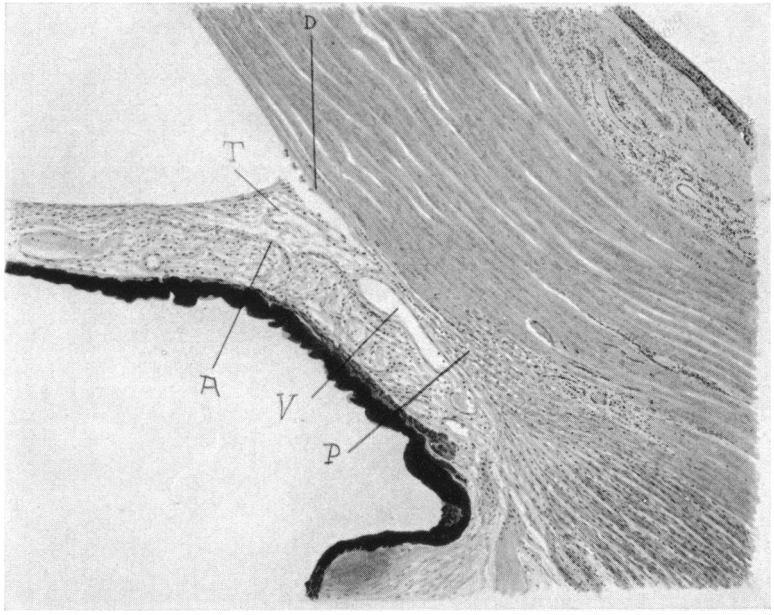

Fig. 1.—(*A* and *T*) Triangular-shaped tissue situated between the margin of Descemet's membrane (*D*) and the anterior limiting layer of the iris. The triangular formation lies with a broad base on the iris and with its apex on Descemet's membrane. By means of this tissue the iris is fixed to the pectinate ligament and the periphery of the cornea. The spaces between the layers of the pectinate ligament (*P*) are less wide than normal. Schlemm's canal is obliterated. Between the pectinate ligament and the iris an empty vessel (*V*) is visible.

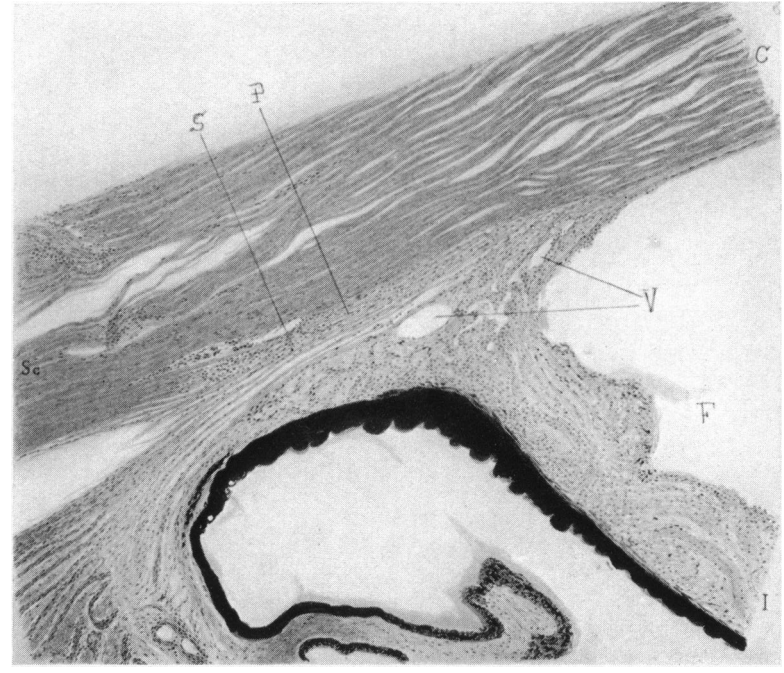

Fig. 2.—The root of the iris lies against the pectinate ligament (*P*), which is sclerosed. Schlemm's canal (*S*) is open and is filled with blood. The stroma of the iris is but little changed and is fixed by a vascular tissue to the periphery of the cornea, forming a pseudo-angle. The anterior chamber is filled with an albuminous fluid (*F*). In the area of the pseudo-angle are several thin-walled dilated blood vessels (*V*).

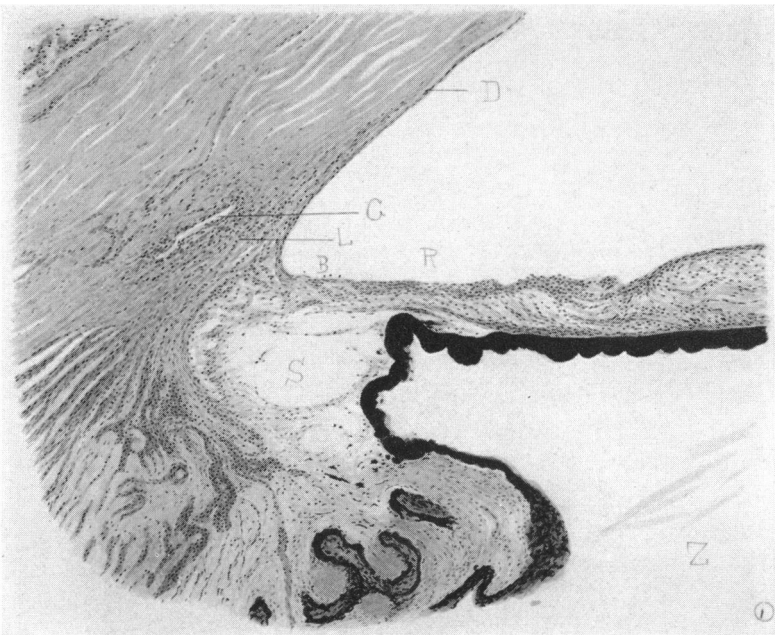

Fig. 3.—The root of the iris (*R*) is drawn by a tissue (*B*) toward the pectinate ligament, forming a bridge which separates the space (*S*) from the anterior chamber. The pectinate ligament (*L*) is sclerosed, the lamellae lying close together. Zonular fibers (*Z*). Periphery of Descemet's membrane (*D*). Schlemm's canal (*G*).

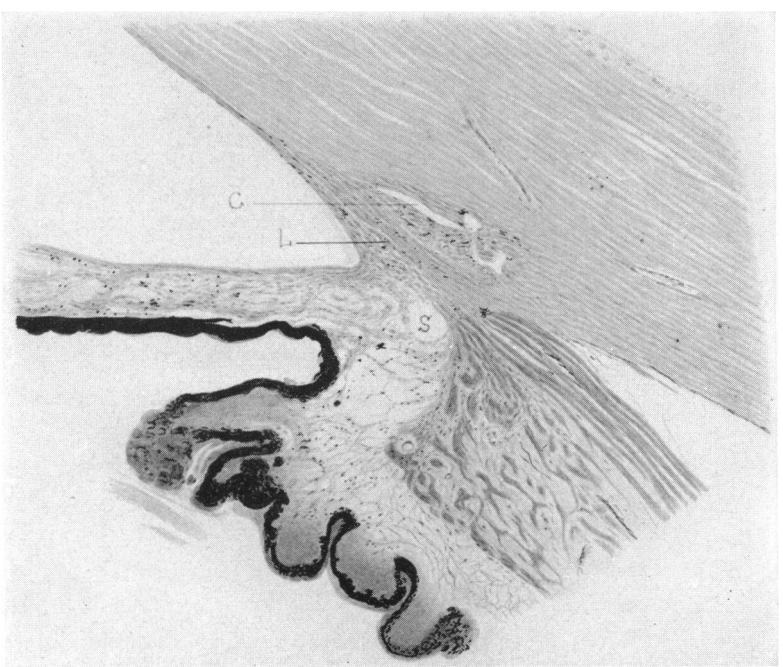

Fig. 4.—Here is shown the filtration angle in the same case as in figure 3, but on the opposite side. The iris root is attached to the pectinate ligament and is drawn toward it, bridging over a small tunnel-shaped space (*S*) which in the section appears to be round. The trabeculae of the pectinate ligament (*L*) are still open, as is Schlemm's canal (*G*).

three months, and the tension was said to have been extremely high. Granulation tissue entirely surrounded and overlapped the pupil. This tissue was made up of cells chiefly of the epithelioid type, containing a little pigment, and was suggestive of tissue of a tuberculous nature. We know that tuberculous periphlebitis in the retina may involve the central vein and cause it to become occluded. It is possible that the thrombosis mentioned in the history may have been of tuberculous origin. The second case was that of a woman, aged thirty-two years. In young persons obstruction in the central vein is usually atypical. In this instance thrombosis in the central vein was recorded as having taken place five years before enucleation. In addition to granulation tissue at the pupillary border, endothelial plaques were present elsewhere on the surface.

5. A Study of the Angle of the Anterior Chamber.—In the investigation of the formation of the synechiae at the angle of the anterior chamber the specimens were separated into those representing:

(*a*) *The Formation of Membranes.*—The specimens from one globe showed a thin vascular membrane that lined the pectinate ligament and the root of the iris. The angle was of normal contour. It is conceivable that in time this membrane would have become thicker and denser and by contraction would have drawn the movable root of the iris forward to become adherent to the immovable pectinate ligament and cornea. Specimens of other globes revealed the sulcus lined by several layers of endothelial cells loosely disposed.

(*b*) *The Formation of Bridge Synechiae.*—In two cases there were so-called bridge synechiae, in which a narrow zone of the iris near its periphery was found adherent to the middle of the pectinate ligament. In this way the root proper of the iris and the external one-third of the ligament retained their normal relationship, forming the walls of an open space separated from the rest of the anterior chamber

by the adhesion. Bridge synechiae are familiar in cases of iritis.

(*c*) *The Formation of Fully Developed Synechiae.*—Broad adhesions—much broader than those commonly encountered in ordinary glaucoma—characterized the specimens from most of the globes. They were often so broad that they covered, in addition to the entire ligament, the periphery of Descemet's membrane. The synechiae were generally not very compact. Usually a compressed vascular membrane would be traced between the surfaces of the iris and the ligament. Notwithstanding the breadth of the adhesions, Schlemm's canal was seldom compressed, as is the rule in ordinary glaucoma.

The Pseudo-Filtration Angle.—In coming away from its insertion on the cornea the iris usually made a sharp bend of from 30 to 40 degrees, forming what was termed the pseudo-filtration angle, which, being located on the cornea, caused the pseudo-root of the iris to be at a much higher level than the free pupillary border in contact with the lens. The adherent portion of the iris never showed so great an atrophy as was to be expected with such broad adhesions.

Vascular Tissue in the Pseudo-Angle.—In almost every case an extraordinary finding was the presence of a triangularly shaped vascular formation in the pseudo-angle. The base of the triangle rested on the anterior limiting layer of the iris and the apex was directed toward the cornea. In some cases the loops of capillaries were so numerous and so dilated that the structure assumed the form of a cavernous tissue. From the triangular formation a thin vascular membrane usually spread out over the adjoining surface of the iris. There was but one case—and that was of long duration—of a pathologic ectropion of the uvea. Perhaps the vascular nature of the membranes rendered them less contractile than more cellular membranes would have been.

In spite of its great breadth, in a number of the globes, the union between the iris and the pectinate ligament was in-

terrupted. In explanation of this it was observed that the iris was attached to the ligament by means of an extremely vascular membrane which was easily torn away. In ordinary glaucoma, on the other hand, the union is a direct cellular one in which the cells of the atrophic iris intermingle with those of the sclerosed ligament. That the adhesion may readily be separated in life was shown in three cases in which extensive hemorrhages had taken place into the anterior chamber. That the separation in these cases was not an artificial one was proved by the presence of a plug of blood in the slit formed by the separation.

6. Contents of the Anterior Chamber.—Hyphemia was present in the preparations from 17 globes. In six cases the space was filled with a clear albuminous coagulum indicative of active inflammation. In one case a fibrinous exudate was seen. Pigment-granules were encountered several times. In one case a few lymphocytes were observed, but in no instance were there definite deposits on Descemet's membrane.

Comparison of the Findings at the Angle of the Anterior Chamber with Those at the Nerve Head.—Taking the series as a whole, the glaucomatous excavations were not nearly so deep as one would have expected, having regard to the broad extent of the peripheral anterior synechiae. There were 16 cases of pathologic excavation. In four of these the recession was extremely slight. In four cases there was no excavation. In these last mentioned cases the atrophy of the nerve fibers in the trunk seemed to be as complete as in those cases in which an excavation was observed. It is possible that the sudden congestion of the blood vessels due to the obstruction in the vein may have caused an inflammatory reaction in the cribrosa, stimulating the connective tissue and glial cells to proliferation. In this way the perforations once occupied by frail nerve fibers could have been made smaller by the swelling, and at the same time would be filled with a firm tissue capable of withstanding an increase in the intraocular tension.

INTERPRETATION OF THE ANATOMIC FACTS

Having described the pathologic anatomy, it remains to discuss the problem of the pathogenesis of the membranes on the anterior surface of the iris and on the chamber surface of the pectinate ligament, which, by forming a barrier to the outflow of the aqueous, gave rise to the glaucoma. If one can discover what agency had excited the tissues to produce the membranes, then the problem of the causation of the glaucoma is also solved.

EVIDENCE IN FAVOR OF THE THEORY THAT TOXINS CAUSE THE FORMATION OF MEMBRANES

It was a striking fact that the membranes in so many cases were located in the pupillary zone. We are accustomed to associate membranes in this zone with toxins, just as we see them form there in ulcus serpens of the cornea when toxins reach this surface from in front by diffusing through the aqueous. The membranes are present also in necrotic sarcomas when toxins are carried forward by fluid through the pupil. Again we see them when toxins reach the aqueous from the stagnant fluid dammed up in the subretinal space of old detached retinas. The toxins that are assumed to be generated after occlusion in the vein reach the pupillary zone of the iris first as they enter the chamber. The anterior limiting layer of the iris is more delicate in this area than in the ciliary zone, and besides, the circulation, being at this point farthest removed from the greater arterial circle, may be sluggish. These are the factors, it would seem, that render the pupillary zone of the iris especially vulnerable to irritant substances in the aqueous, and cause it to react by the formation of membranes on its anterior surface. As its root is approached the iris again becomes thin, so that the blood vessels that radiate from the greater arterial circle are exposed to the aqueous as they lie in the crypts, over which the anterior limiting layer is absent. The proliferation

Fig. 5.—The root of the iris is separated by blood from the pectinate ligament (*P*), but evidently it was adherent to the cornea previous to the occurrence of the hemorrhage. The pectinate ligament is sclerosed. The parenchyma of the iris is very dense, but it retains its normal thickness. *T*, triangular tissue. *S*, space caused by hemorrhage.

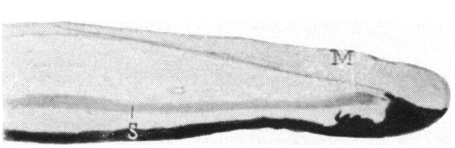

Fig. 6.—A new-formed membrane (*M*) is lying upon the pupillary area of the iris. The pigmented layers at the pupillary border appear as if they were pushed backward. The sphincter muscle (*S*) is normal.

of the endothelium so often seen in the sulcus has been considered an expression of irritation resulting from an accumulation of toxins there. To account for the overwhelmingly vascular element in most of the membranes it was believed that the walls of the exposed blood vessels at the root of the iris received a stimulus from the toxins, in response to which they formed capillaries. This may be likened to the condition in which the blood vessels lying in contact with the limitans interna of the retina are seen at times to react to toxins by sending capillaries forward into the vitreous body.

EVIDENCE AGAINST THE THEORY THAT TOXINS GIVE RISE TO THE FORMATION OF MEMBRANES

In diffusing forward, the toxins before they reached the anterior surface of the iris doubtless came into contact with the pigmented epithelial layers of the ciliary body and of the iris, so that one would expect to find membranes on these surfaces and yet there were none present. The epithelial layers are probably more resistant to the toxins than is the endothelial lining of the anterior chamber. In this way the vascular layer of the ciliary body as well as the posterior layers of the stroma of the iris were protected from toxins.

MANNER OF THE FORMATION OF THE MEMBRANES AND EXPLANATION OF THEIR VASCULARITY

The membranes appeared to be formed directly from a proliferation of the endothelial cells and from a simultaneous sprouting of capillaries from the radiating branches at the root of the iris. It was clear that they did not represent an organization of an exudate because the anterior chamber was singularly free from cellular débris. Whenever blood was present it was plain that the membranes were preexistent. Being delicate and vascular, the membranes were always sharply delimited from the underlying dense, pigmented anterior limiting layer of the iris. No direct communication could be traced between the blood vessels in the

vascular loops in the pseudo-angle and in the membranes with the vessels in the stroma. In both systems the blood vessels were traced to a common origin in the radiating branches, as the latter were given off from the greater arterial circle in the vascular layer of the ciliary body. The typical blood vessels in the stroma replacing the original thick-walled ones, which were possibly out of place in an altered parenchyma, remained in the stroma, whereas the others sprang forward and mounted over the anterior limiting layer to supply the membranes of endothelial origin. The facts that the membranes were traversed by so many dilated and tortuous capillaries and that the pseudo-angle was so frequently occupied by large distended loops of capillaries were attributed to a disturbance in the circulation caused by the synechiae, which, in growing more compact, interfered with the return flow of the blood from the membranes.

ORIGIN AND NATURE OF THE TOXINS THAT PRODUCED THE MEMBRANES

The toxins must have had their source in the disintegration of constantly recurring hemorrhages and exudates in the retina. They could not have been virulent, otherwise they would have caused cyclitic membranes to form on the internal surface of the ciliary body and the posterior surface of the iris, as do the toxins coming from bacteria that are introduced into the vitreous. Time is required for the toxins to gain force enough so that their action can be felt. It is possible that other forms of recurrent hemorrhages may produce just as many toxins, but in these cases the posterior efferent pathway of the lymph at the papilla is open so that the poisons are carried off and not diffused forward. In the cases in this series it was the combination of hemorrhage and blockage that seemed to decide the development of the glaucoma.

It is most likely that a similar combination produces the glaucoma in old complete detachments of the retina in which the posterior efferent pathway of the lymph is sealed by

membranes that form on the nerve head. In cases of ordinary glaucoma the anterior pathway is first affected, and the posterior pathway only gradually becomes blocked as the excavation increases and the condensation of the lamina cribrosa progresses. The reason that membranes do not form on the iris and that glaucoma does not ensue in other types of long-continued recurrent hemorrhages in the retina may be understood by the fact that in these cases the posterior efferent pathway of the lymph remains open, whereas in obstruction in the central vein the closure of this pathway may possibly be almost coincident with the obstruction in the vein. It therefore appears that in determining glaucoma following occlusion in the central vein three anatomic factors are to be borne in mind: (1) A disturbance in the blood outflow caused by an obstruction in the central vein; (2) a disturbance in the lymph outflow caused by a blockage in the efferent pathway, the result of congestion and edema at the nerve head; and (3) a disturbance in the aqueous outflow caused by membranes and adhesions forming at the angle of the anterior chamber. That glaucoma does not occur in every case of obstruction in the central vein may be due to the rapidity or slowness of the onset of the obstruction, which in some cases gives more time and in others shorter time for the establishment of a collateral circulation at the nerve head.

COMMENT

1. Two conditions seemingly combine to produce the intractable pain—glaucoma and the inflammatory reaction following the formation of toxins, the latter persisting and increasing.

2. It is probable that in many cases the progress of the glaucoma is divided into three stages: (1) The early stage, in which there may be no hyphemia, but in which the tension is slightly elevated and the slit-lamp would reveal the beginning of capillary formation on the iris. (2) The stage

in which hyphemia is present and the eyeball is hard and painful. (3) The advanced hemorrhagic stage, in which there is massive hemorrhage in the anterior chamber, the globe being of stony hardness and the pain becoming unbearable. In this latter stage it is probable that many of the capillary loops have burst at the pseudo-angle, and that with the pouring out of blood, the anterior chamber has become deeper than it was, thus mechanically producing complete laceration of the pseudofiltration angle.

3. The pathologic anatomy explains why it is that after operation these globes may be even harder and more painful than they were before. The thin walls of the engorged vessels in the membranes, unable to withstand the sudden reduction in the intra-ocular tension as a result of the opening of the globe, rupture and set free so much blood that the end-result is a superimposition of hemorrhagic glaucoma on hemorrhagic glaucoma.

DISCUSSION

DR. F. H. VERHOEFF, Boston: This is an extremely interesting piece of work, and I concur in what Dr. Samuels has said. I have studied such cases microscopically for a number of years since the first report referred to was published, and I have made serial cross-sections of the optic nerves in all cases of primary or hemorrhagic glaucoma. It do not believe that Dr. Samuels has done this in any of his cases, but that he simply accepted the clinical diagnosis of obstruction of the central vein. I have examined between 200 and 300 eyes, and I have found the changes that Dr. Samuels has described. Confirming my first observations, I have never seen any evidence of thrombosis of the central vein, but proliferative endophlebitis has always been present. I believe that thrombosis does occasionally occur in clinical cases, but when it does, glaucoma does not often ensue and there may be recovery of vision. Obstruction of the central vein due to endophlebitis may take place very slowly or quite rapidly. Sometimes it is associated with obstruction of the central artery. In a great many of these eyes it is not possible to determine whether the obstruction of the vein or the glaucoma was primary, because, as I demonstrated years ago, glaucoma itself may cause obstruction of the central vessels—

and it may cause exactly the same kind of obstruction that we find as a primary disease of the vessels.

In regard to the glaucoma, I believe that Dr. Samuels' explanation is almost certainly correct for most cases, but we do have patients in whom the glaucoma comes on early. In the first case I reported the glaucoma came on rapidly, and I have observed a similar case every now and then.

In the early stages of obstruction of the central vein, as a rule, the tension, instead of being high, is slightly below normal. I have had cases which indicated that when the glaucoma occurs early it means an eye that is extremely susceptible to the disease, and that the glaucoma is produced in a different way than when it occurs late. When the circulation of the retina is cut off, substances are probably given off that may irritate the interior of the eye. As a rule, when these eyes are brought to our attention, the glaucoma has existed for a long time; so that we are led to conclude that these toxins must act in a very low-grade way. They produce the changes in the filtration angle before the onset of the glaucoma, and when we find severe symptoms of iritis are present it means that the toxins have been active for a long time.

This subject is extremely interesting, but as in most cases the eyes must practically always be removed, it does not seem to be of great importance clinically.

DR. ALLEN GREENWOOD, Boston: There are two observations I wish to make—one in regard to a patient whom I saw three weeks ago. Ten days after a complete closure of the vein an acute iritis developed, followed in forty-eight hours by an acute glaucoma. The acute glaucoma was materially relieved temporarily by eserin, and four days after the onset of the glaucoma the eye was removed because of pain. The specimen is at present in Dr. Verhoeff's care. In this patient the iritis preceded the glaucoma, and it is the only case that I have ever seen in which a glaucoma came on within two weeks of the time of a complete obstruction.

The other observation I desire to bring to your attention is that, so far in my cases of closure of the central vein, I have never seen glaucoma develop in the other eye. Perhaps I have been peculiarly fortunate, but I am going to ask Dr. Samuels if in all these cases the other eye eventually develops a glaucoma. In my experience, I have not seen a single case of glaucoma develop in the opposite eye after one eye had been removed for a glaucoma following closure of the central vein.

DR. E. V. L. BROWN, Chicago: I wish to discuss the freedom of the ciliary body and the involvement of the iris in this process. Ernst Fuchs made the observation that in detached retina we eventually find a low-grade cyclo-iritis, often followed by a secondary cataract, because the fluid which accumulates behind the retina eventually becomes highly toxic and diffuses through the retina into the vitreous and then over the ciliary body and through the pupil to produce an iritis. It does not involve the ciliary body and processes because of the fact that we have two layers of epithelial cells covering over the ciliary processes and the back of the iris, whereas the front of the iris is especially rarefied. In one theory of the disposition of the aqueous it is held that it goes through the anterior layers of the iris and is absorbed by the iris veins into the general circulation. This would account for the absence of cyclitis, and the eventual development of iritis with many new-formed vessels on the surface of the iris. Perhaps this same general theory will help to explain the entire freedom of the ciliary body which Dr. Samuels noticed in the cases reported —ciliary body free and the iris eventually developing vessels.

DR. E. A. SHUMWAY, Philadelphia: I believe that a case which I have had the opportunity of studying for fully five years may explain perhaps some of the features to which Dr. Samuels and Dr. Verhoeff have referred. The patient is a man about sixty years of age, with a somewhat high blood-pressure, and a slight kidney involvement. He is an extremely nervous individual, who developed in his left eye a blocking of the central vein, or at least of one of its branches. In this case there were very extensive retinal hemorrhages. I presumed that the vision in the eye would be lost. However, after thorough investigation by the medical staff of the Lankenau Hospital, the patient was treated from the general standpoint. Six months later a complete obstruction of the central vein in the other eye developed. In this eye the symptoms were followed, within a very short time, by a typical iritis, which went on to a secondary glaucoma with intense pain. As the other eye had been involved, I deemed it best to operate. An operation was performed and the result was, as usual, unsuccessful. I did not do an inclusion operation, which might have helped. However, the eye became intensely painful and had to be removed. Pathologic examination of the eye showed occlusion of the central vein. The interesting feature in this case is that the other eye, evidently, had an occlusion of only a branch of the central vein, and the patient retained a vision of 5/15 and is able

to perform important work as secretary of a large building and loan association. There is no evidence of glaucoma. The field shows a defect corresponding to the position of the blocked branch, but at no time has there been cupping of the nerve. In this case I think we can assume, at least so far as the clinical evidence shows, that the patient manifested no tendency to the development of glaucoma; otherwise he would, in the five years I have observed him, have shown some evidence of the disease in the eye first affected. The other eye had complete occlusion, and perhaps, as Dr. Samuels suggests, there was more reason for the development of a toxin which caused the acute iritis and probably membrane formation and acute secondary glaucoma.

DR. WILLIAM H. WILMER, Washington, D. C.: Like my colleagues, I have also encountered these troublesome cases, and I have had a large share of unsatisfactory results. However, I have occasionally been gratified by securing a happy termination from cyclodialysis in glaucoma following obstruction of the central retinal vein. Of course, the surgical procedure was followed by rest in bed and the appropriate general and local treatment.

DR. JOHN W. BURKE, Washington, D. C.: I would like to call attention, from the clinical standpoint, to Dr. Samuels' statement that peripheral adhesions are very lightly held. Recently I had to do an extraction, following a trephine operation performed by me in 1912. This patient returned with an acute glaucoma, with peripheral adhesions, so far as I could see, completely around the periphery of the base of the iris. After I did the extraction, the iris fell back completely to its normal plane.

DR. BERNARD SAMUELS, closing: In regard to Dr. Verhoeff's discussion, I am glad that he agrees in general with the conclusions I have reached.

Replying to Dr. Greenwood, it was von Graefe who, soon after the invention of the ophthalmoscope, was the first one to describe the picture of obstruction in the central vein, and he pointed out the tendency of such an eye to develop glaucoma. As the years went by it became evident that it was only in rare cases that the fellow-eye suffered a similar lesion. In Moore's report on the clinical findings in 62 cases there was only one instance of bilateral involvement, which corresponds to Dr. Greenwood's experience.

I wish to thank Dr. Brown for the explanation he has given of the frequent absence of inflammation in the ciliary body.

Dr. Shumway's case is interesting in that it brings out the

rule that glaucoma develops as a result of occlusion in the main vein and never as a result of occlusion in a branch.

Dr. Wilmer's and Dr. Burke's observations on the operative aspect of these cases are interesting. It may be that Dr. Wilmer's success was due to the fact that in the operation of cyclodialysis the adhesions are easily broken up, thus permitting a free discharge of the toxic aqueous.

TUBERCULOUS AND STREPTOCOCCIC RETINAL HEMORRHAGES*

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As the cases that gave rise to the question underlying this discussion do not conform in detail to a given classification, the title of the paper may seem to be somewhat broad, in so far at least as the use of the terms "tuberculous" and "streptococcic" apparently imply or assume the cause. That in the instances to be cited there is a definite relation between retinal hemorrhages, on the one hand, and tuberculous and streptococcic infection, on the other, the evidence would seem to show, and it is the purpose of this article to set this evidence forth. The writer realizes fully and appreciates the position of those who maintain that in a specific case it is far from easy to show, beyond reasonable doubt, that the streptococcus was the cause of the retinal hemorrhage. As a justifiable hypothesis, however, and merely for the sake of argument, it may be premised that streptococcic focal infections exist in certain persons suffering from ocular disorders; in the event that those foci are removed and recovery follows in due time, it is at least tenable that a definite cause and effect relationship may exist. That there are valid objections to this conclusion, even when the clinical experiment has been successful, no one will deny.

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