FURTHER OBSERVATIONS ON THE PATHOGENESIS OF CONGENITAL GLAUCOMA

BY *A. Edward Maumenee,* M.D.*

THE HISTOPATHOLOGIC FINDINGS on fourteen eyes of eight patients with early congenital glaucoma and on sixty eyes with advanced congenital glaucoma have previously been reported.[1] The abnormalities in the angle of the anterior chamber in these specimens may be summarized as follows.

(1) The most obvious variant from normal is a failure of the iris and ciliary body to separate from the trabecular fibers. The extent to which this occurs is extremely variable. In one case, almost the full extent of the trabecular fibers is covered. In another, the ciliary body may be adherent only to the most posterior end of the trabeculae.

(2) A second finding that occurs with equal consistency is an abnormal insertion of the longitudinal and circular muscle fibers into the corneoscleral portion of the trabeculae. In most instances, the longitudinal fibers extend forward beyond the anterior tip of the scleral spur, even up to the posterior one-fourth of Schlemm's canal.

(3) The scleral spur is frequently difficult to see because of its displacement forward and externally.

(4) The ciliary body is often pulled centrally so that the ciliary processes are central to an imaginary line that passes vertically through the posterior end of Schlemm's canal.

(5) In four eyes that had been recently operated upon, the trabecular meshwork is permeable to red blood cells. These cells are found between all but the outermost layers of the trabecular fibers, 180° from the operative site, even where the iris and ciliary body are extensively adherent to the trabecular fibers.

(6) Schlemm's canal can be identified in most cases of early congenital glaucoma. In the previous report,[1] it was stated that the canal

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was found in all cases of early congenital glaucoma, but in Case 1, where only one slide of one eye was available for study, it was extremely difficult to be certain that there was an endothelial line space that could be identified as Schlemm's canal. On further review of this specimen, Schlemm's canal cannot be positively identified. In other eyes, the canal was collapsed in certain sections, probably due to the anterior external position of the scleral spur. However, a definite endothelial line space could be found in all of the remaining specimens.

(7) In three eyes that had had a recent goniotomy and in one eye with a successfully functioning goniotomy, the base of the iris and ciliary body had been cleaved from the trabecular fibers. The longitudinal muscle of the ciliary body had also been cut free from the trabecular fibers and an artificial scleral spur was created (Figures 8, 20, 22[1]).

(8) As a result of these findings, it was suggested that: (*a*) In congenital glaucoma there is a faulty cleavage of the iris and ciliary body from the trabecular fibers. This, however, did not account for the decreased facility of outflow in these eyes. First, because the adherence of these tissues to the trabecular fibers varied from an attachment to Schwalbe's line to an attachment just forward of the scleral spur. Second, because in eyes that had been recently operated upon (3 goniotomies and 1 sclerectomy with iridectomy) red blood cells passed through the trabecular fibers to the outermost layers adjacent to Schlemm's canal. (*b*) The ciliary processes and ciliary body were pulled centrally, possibly due to a microphakia or relative microphakia. (*c*) An endothelial-lined Schlemm's canal could be found in most specimens of early congenital glaucoma. (*d*) The abnormal insertion of the longitudinal muscles of the ciliary body into the corneo-scleral trabecular fibers forward of the scleral spur is in some way responsible for the decreased facility of outflow. Cleavage of these muscle fibers from the trabecular fibers and the formation of a new artificial scleral spur is the mechanism whereby goniotomy increased the facility of outflow in congenital glaucoma.

NEW MATERIAL

Since this first report, I have had an opportunity to examine histologically eleven eyes from six patients with early congenital glaucoma. Two of these cases have been previously reported. One, by Merrill J. Reeh, in the 1961 *Transactions* of the American Academy of Ophthalmology and Otolaryngology[2] and the second by S. T. Adams, W.

Morton Grant, and T. R. Smith in the 1962 A.M.A. *Archives of Ophthalmology*.[3] Of the remaining eyes, one has been examined through the courtesy of Dr. Parker Heath of Sullivan Harbor, Maine; two through the courtesy of Dr. Lorenz Zimmerman of the Armed Forces Institute of Pathology, Washington, D.C.; two through the courtesy of Dr. Alfred McKinna of Montreal, Canada. The final two eyes were obtained from a patient who died in the Johns Hopkins Hospital.

A brief report of these cases and a histological description of the eyes follows.

CASE 1

Previously reported by Merrill J. Reeh,[2] AVH. Accession No. B46680, Good Samaritan Eye Laboratory. The patient was a colored male who developed photophobia, epiphora, and began rubbing his eyes at four months of age. He was seen by an ophthalmologist two months later, who noted that the corneas were enlarged and cloudy. The tension under general anesthesia was right eye 45 mm. Hg. and left eye 50 mm. Hg. (Schiotz). Goniotomy was performed on the nasal side of each eye. Ten days later the intraocular pressure was right eye 31 mm. Hg. and left eye 60 mm. Hg. A goniotomy was performed on the right eye and a goniotomy and goniopuncture on the left eye. The tension in each eye appeared to be controlled for a period of a month when the child died suddenly of congenital heart disease and pneumonia.

GROSS EXAMINATION. Both eyes measured 20 mm. in the AP diameter and 19 mm. horizontally.

HISTOLOGIC EXAMINATION. Right eye (imbedded in paraffin): The angle of the anterior chamber is slightly different in various sections. In one section the anterior leaf of the iris appears to rise almost from Schwalbe's line. In another section, the iris arises from the middle third of the trabecular fibers. On the opposite side, there is a pectinate ligament or iris process which arises from Schwalbe's line, but posterior to this there is a cleft between the root of the iris and the trabecular fibers. On both sides of the specimen, the longitudinal muscle of the ciliary body terminates well in front of the scleral spur. These fibers insert into the uveal and corneoscleral portion of the trabecular meshwork. The fibers of the trabecular meshwork number about 15 to 17 in front of a well-formed endothelium-lined Schlemm's canal. The canal is present in all sections of the specimen. The trabecular fibers are delicate and separate from one another. Only in one section on one side do the outer trabecular fibers appear slightly more compact than usual. *Red blood cells are found in the trabecular meshwork.* Approximately one-half of the muscular portion of the ciliary body lies in front of a line drawn perpendicular to the globe through

the scleral spur. The lens is kidney-shaped and measures 7 × 2 mm. in a section taken through the pupillary area.

Left eye (imbedded in celloidin): This eye shows essentially the same changes that are found in the right eye. There is an incomplete separation of the iris and ciliary body from the trabecular fibers with the adherence covering approximately two-thirds of the extent of the trabeculae. The sections available for study do not go through the pupillary area, but a line drawn perpendicularly through the scleral spur would pass through the anterior one-third of the muscular portion of the ciliary body. The longitudinal muscle fibers insert into the uveal and corneoscleral trabecular meshwork. The trabecular fibers are normal in length, number, and delicacy, but appear much more compact than those in the other eye. This may be due to the celloidin rather than paraffin imbedding. Schlemm's canal in most sections is either so markedly compressed that it is difficult to identify or it is absent. It can be found in a few sections, however. The size of the lens was not measured because the sections available did not pass through the pupillary area.

IMPRESSION. There is an incomplete opening of the angle of the anterior chamber in both eyes. The longitudinal and circular muscles of the ciliary body and ciliary processes are pulled farther forward to the central portion of the eye than normally. Schlemm's canal is definitely present in one eye, and probably present in the second but is difficult to see. The site of the goniotomy and goniopuncture was not present in any of the sections available for study.

CASE 2

Supplied by Parker Heath.* The patient was a three-week-old white male who had an extensive hemangioma of the face, neck, and trunk. The right cornea was clear. The left was cloudy from birth. There was suggestive pathologic cupping in the right eye. The fundus in the left eye could not be seen. Intraocular pressures were reported to vary between "high normal and definitely elevated." An operation was performed on the right eye. The type of operation and cause of death was not stated in the history available.

GROSS EXAMINATION (as reported by Parker Heath). The right eye measured 19 × 18 × 17 mm. in the anterio-posterior, horizontal, and vertical meridians. Corneal diameter measured 11 × 10.5 mm. horizontally and vertically, respectively. A small perforating wound, 2 mm. from the limbus, was noted at the 9:00 o'clock position. The cornea was hazy. Choroidal thickening was noted in the upper temporal quadrant about 4 mm. from the ora serrata. This was thought to represent a hemangioma of the choroid.

MICROSCOPIC EXAMINATION. The specimen is beautifully imbedded and stained. The lens measures 6 × 2 mm. in a section passing through the pupillary area. There is an incomplete opening of the angle of the anterior

*Presented at the Pathology Club, Washington, D.C., 1959.

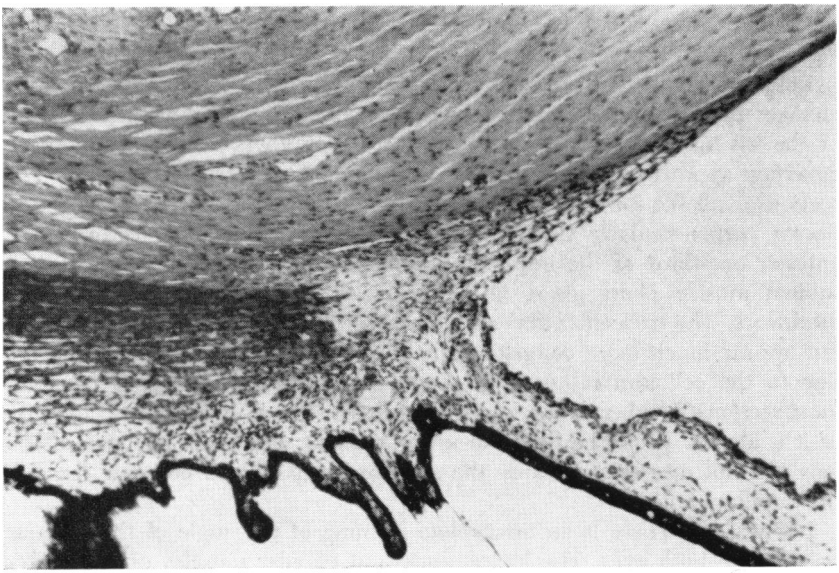

FIGURE 1. CASE 2.

chamber, but the iris is adherent only to the posterior third of the trabecular fibers (Figure 1). A line drawn perpendicularly through the scleral spur passes through the anterior tip (1/20th) of the muscular portion of the ciliary body. The circular muscle is poorly developed. The longitudinal fibers are clearly seen and well developed, and insert into the trabecular fibers in front of the tip of the scleral spur. The trabecular fibers are normal in number, delicacy, and length and do not appear compressed one against another. Schlemm's canal can be easily seen on both sides of the section and is definitely open. *A few red blood cells are enmeshed in the trabecular fibers up to the edge of Schlemm's canal.* There are a number of lymphocytes and plasma cells in the iris stroma and in the trabecular meshwork. The optic nerve does not appear cupped. The hemangioma observed in the choroid by Dr. Heath is not present in the sections available for study. The site of operation (possibly a goniotomy) is not present in the sections available.

IMPRESSION. This is probably a case of Sturge-Weber disease (nevus flammeus) with congenital glaucoma. The trabecular fibers are normal, and there is a slight incomplete cleavage of the angle of the anterior chamber. The scleral spur is compressed forward and externally, and the longitudinal muscle of the ciliary body inserts into the trabecular fibers forward of the tip of the scleral spur. The inner trabecular fibers are probably permeable to aqueous because red blood passed through them to the edge of Schlemm's canal.

CASE 3

FHH (JHH #100 22 14) This white male child was born on June 11, 1961, after a normal gestation. During the first month of life he had frequent loose stools, occasional vomiting, and loss of weight. A diagnosis of malabsorption syndrome, possibly on the basis of abnormal rotation of the intestines, was made. An exploratory laparotomy on August 31, 1961, revealed a normal mesentery and the bowel was thought to be in normal position. The child continued to do poorly. On April 27, 1962, an ocular examination was done under general anesthesia. Four days later he developed an acute intestinal obstruction and died. Autopsy revealed a 360° volvulus of the small intestine, aspiration of the gastric contents, hemorrhagic consolidation of upper right lobe of the lung, and syndactylia of fingers IV and V on both hands.

The ocular history was as follows. The parents thought the child's eyes were large at birth but the mother did not notice photophobia and epiphora until four months of age. In February, 1962, at the age of eight months, the child was seen by an ophthalmologist who made a diagnosis of congenital glaucoma. Examination under intubation fluothane anesthesia on April 27, 1962, revealed tensions in the right eye 18.9 mm. Hg. and in the left eye 14.6 mm. Hg. (Schiotz). The corneas were slightly hazy and edematous. The diameters measured right eye 13.5 and left eye 13 mm. Gonioscopy revealed that the corneoscleral trabecular meshwork appeared to be covered by iris processes. There was definite glaucomatous cupping in both eyes with nasal displacements of the vessels. The facility of outflow in the right eye was 0.17 and the left 0.15.

Both eyes were obtained within two hours after death and profusion studies were done by Dr. Maurice Langham. The complete results of these studies will be reported in greater detail at a later date. The studies on the first eye were completed within three hours and on the second eye within six hours after death. In the left eye the facility of outflow at pressures above 20 mm. of mercury revealed a C of 0.15 at room temperature which would correspond to 0.20 at body temperature. After these studies the needle used to profuse the eye was passed across the anterior chamber and with the aid of an operating gonioscopic lens and Zeiss dissecting microscope a 1-mm. goniotomy was performed. The facility of outflow in this eye immediately increased to 1.0.

A similar procedure was performed on the right eye but the cornea was quite cloudy and it was difficult to see the angle of the anterior chamber. The facility of outflow increased only very slightly, if at all, after the first goniotomy; but, when a second 1-mm. goniotomy was performed, it increased from 0.10 to about 1.0.

GROSS EXAMINATION. The right eye measured 24 × 24 × 24 mm. Cornea measured 12 × 11 mm. The globe was sectioned vertically. The lens measured 9 × 2.5 mm. The left eye measured 24 × 24 × 24 mm.

Cornea measured 13 × 12 mm. The globe was sectioned in a vertical plane. The lens measured 8 × 2.5 mm. The eyes were fixed in formalin and embedded in paraffin.

MICROSCOPIC EXAMINATION. Left eye: The histologic sections are not of the best quality but certain abnormalities can be found in the angles of the anterior chamber. Schlemm's canal is evident on both sides of the globe in 400 microscopic slides. In some sections, Schwalbe's line ends in a prominent knob. The iris root is attached to the trabecular meshwork at about its middle third. The scleral spur is poorly developed and is pushed forward and externally (Figure 2). A tenth of the longitudinal muscle and most of the circular muscle lies forward of a line drawn perpendicular to the globe through the scleral spur. The longitudinal muscle of the ciliary body is continuous with the corneoscleral trabeculae in front of the scleral spur. The corneoscleral trabeculae appear to be compressed more than normally but this might be the result of profusion or imbedding and sectioning of the eye.

Perhaps one of the most interesting aspects of this specimen is the area where the goniotomy was done after death (Figure 3). This incision could be observed histologically through approximately 120 eight micron sections. The angle of the anterior chamber had been completely opened. The iris and base of the ciliary body were separated from the trabecular area and scleral spur. *The uveal portion of the trabecular meshwork was destroyed but the corneoscleral portion was not perforated in any section.* The longi-

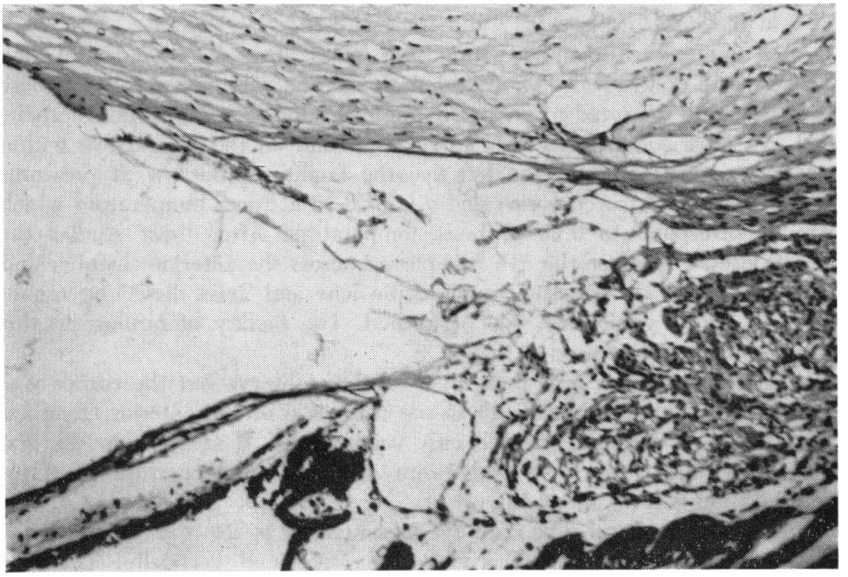

FIGURE 2. CASE 3, LEFT EYE.

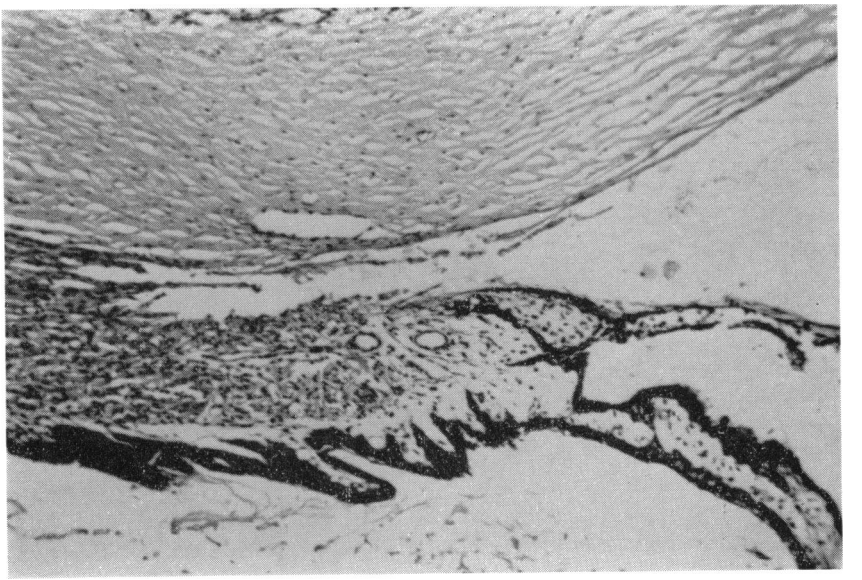

FIGURE 3. CASE 3, LEFT EYE.
Site of successful goniotomy.

tudinal and circular muscles of the ciliary body were detached from the trabecular meshwork and scleral spur. *In other words, this goniotomy was not a trabeculotomy but a cleavage of the iris and ciliary muscle from the trabeculae and scleral spur.*

Right eye: Sections of the right eye were even more distorted than the left. However, certain abnormalities could be detected. The unoperated portions of the angle of the anterior chamber appeared essentially the same as in the left. There is a prominent Schwalbe's line and Schlemm's canal is seen in all sections. The ciliary body and ciliary processes are pulled centrally and the longitudinal muscle of the ciliary body inserts into the corneoscleral trabecular fibers in front of the scleral spur.

In the first, or unsuccessful, postmortem goniotomy the incision was placed slightly too far posteriorly. The root of the iris was severed from the trabecular fibers but the cut separated the circular muscle and part of the longitudinal muscle from the iris and ciliary body. Thus there was a nodule of circular and longitudinal muscle remaining adherent to the corneoscleral trabecular fibers and to the scleral spur (Figure 4). The incision was deep enough so that some of the inner scleral fibers were cut. A well-formed Schlemm's canal was present in the area of the first goniotomy.

In the second, or successful, postmortem goniotomy the incision was quite similar to that in the left eye. The iris and ciliary body were separated from the trabecular fibers and from the scleral spur (Figure 5). In this specimen

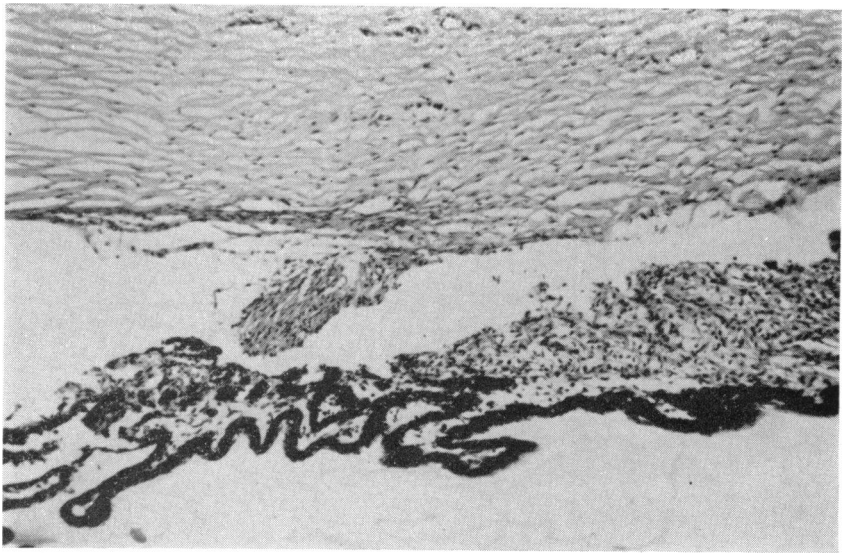

FIGURE 4. CASE 3, RIGHT EYE.
Site of unsuccessful goniotomy.

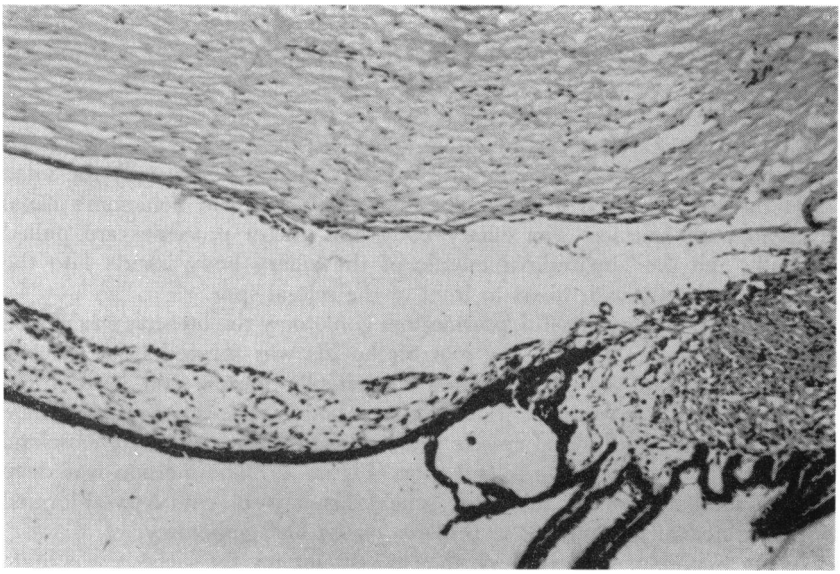

FIGURE 5. CASE 3, RIGHT EYE.
Site of successful goniotomy.

some of the corneoscleral trabecular fibers were removed but at least three to four layers of fibers remained in front of Schlemm's canal in all specimens that were examined. Some of the sections were so distorted that they could not be used for histological examination so it could not be stated that serial sections failed to reveal any evidence of a trabeculotomy.

IMPRESSION. These two eyes show the typical findings of failure of cleavage of the angles, central displacement of the ciliary body and ciliary processes, and abnormal insertion of the longitudinal muscle of the ciliary body into the trabecular fibers. A successful postmortem goniotomy which increased the facility of outflow from 0.15 to 1.0 separates the iris and ciliary body from the trabecular fibers and scleral spur but does not create a trabeculotomy. A goniotomy that did not appreciably increase the facility of outflow separated the iris from the trabecular fibers but was placed deep in the ciliary muscle and allowed part of the ciliary and longitudinal muscles to remain adherent to the posterior portion of the trabecular fibers.

CASE 4

(AFIP accession #904086) RMR white female. The child had cloudy corneas from birth and the eyes appeared larger than normal. A diagnosis of congenital glaucoma was made and the child was placed on pilocarpine. No other ocular history is available.

At five and a half weeks of age, the child died of congestive heart failure. Autopsy revealed a persistent truncus arteriosus, an interventricular septal defect, an anomalous entrance of the left superior vena cava into the left auricle, and a hypertrophy of the right ventricle of the heart.

GROSS EXAMINATION (by Dr. Zimmerman). Right eye: Measurements were 19 $\times$ 18 $\times$ 17 mm. The cornea was opaque and measured 12.5 mm. in diameter. There was a fluffy-white gelatinous material in the anterior chamber in the pupillary area. When the eye was sectioned, a non-pigmented tissue appeared to extend into the angle in the same plane as the anterior portion of the iris.

Left eye: Measured 20 $\times$ 18 $\times$ 18 mm. The cornea was clear and measured 12.5 mm. in diameter. A fluffy-white gelatinous exudate was also present in the anterior chamber in the pupillary zone of this eye.

A note from Dr. Zimmerman states "I could kick myself for not having measured the lens diameter in either eye. We have, however, prepared over fifty sections through the central axis of each eye and in none of these sections does the lens diameter measure more than 5 mm. I still feel that there may well be an absolute microphacia and that this may be at least in part responsible for the malformation of the ciliary body and the anterior chamber angle. It certainly seems as if the zonule is under greater tension and the ciliary processes and the anterior portions of the ciliary muscle appear to be drawn inward and forward by the taut zonule."

MICROSCOPIC EXAMINATION. Right eye: There has been an incomplete cleavage of the angle of the anterior chamber. The ciliary processes and

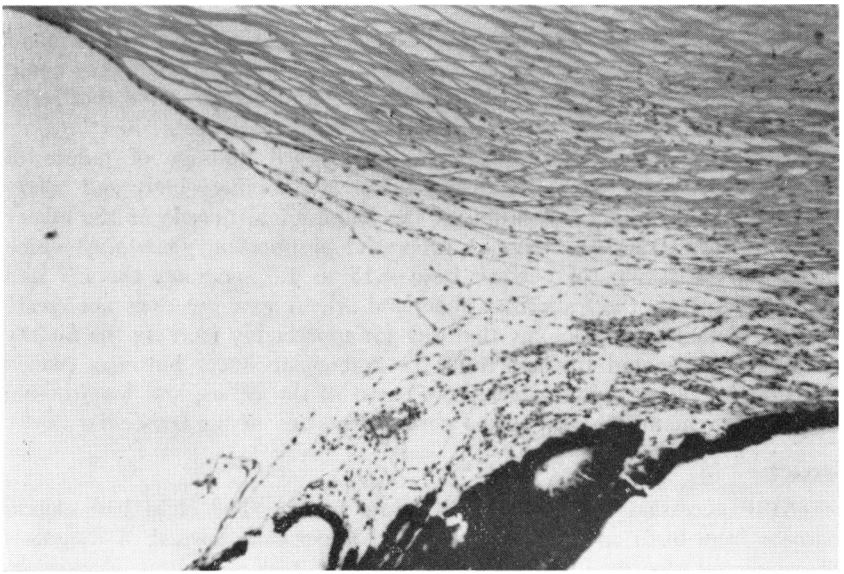

FIGURE 6. CASE 4, RIGHT EYE.
Note absence of Schlemm's canal.

ciliary body are drawn centrally so that a line drawn perpendicularly through the scleral spur passes through the junction of the anterior one-third and posterior two-thirds of the ciliary muscle. The circular muscle is poorly developed. The inner trabeculae that are separated from one another are extremely fine and delicate and appear more like uveal trabecular fibers than corneoscleral fibers. In sections stained with periodic acid Schiff stain, it appears that the corneoscleral trabecular fibers blend in with the sclera. No Schlemm's canal or definite scleral spur can be seen (Figure 6). There are a few endothelial line spaces in the deep sclera that may represent either the deep scleral plexis of blood vessels or collector channels from a non-existent Schlemm's canal.

Left eye: The angle is essentially the same as the right except that on one side a fairly large endothelial line channel can be noted in the sclera just external to PAS positive scleral fibers that probably should represent the corneoscleral trabeculae (Figure 7). These fibers show about the same degree of compactness as the adjacent sclera.

IMPRESSION. Schlemm's canal could not be found in the right eye. The corneoscleral trabecular fibers were difficult to tell from the scleral tissue in hematoxylin-eosin stains. However, in the periodic acid Schiff stain (PAS stain) the trabecular fibers could be distinguished from the scleral fibers by their more intense staining. In the left eye, an endothelial line channel could be noted in some specimens.

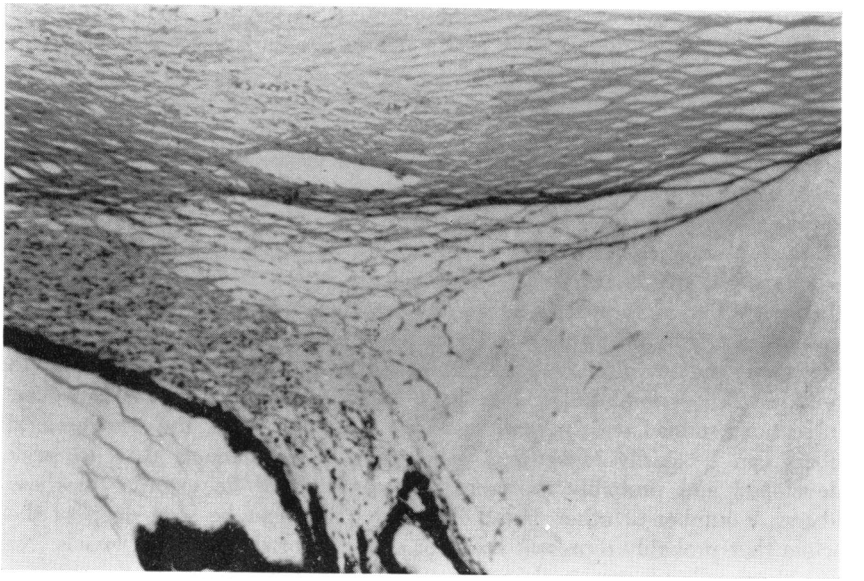

FIGURE 7. CASE 4, LEFT EYE.
Schlemm's canal present.

CASE 5*

#212917 Montreal Childrens' Hospital. DP born on June 6, 1961. Birth weight 4 lbs., 8 ozs. Gestation 33 weeks. White. Male. On general physical examination the child was found to have congenital heart disease, migrognathia, deformity of the chest, cryptorchidism, long fingers with ulna deviation, and a hard mobile enlarged spleen. This was suggestive of Pierre Robin's syndrome.

On July 12 at approximately one month of age an eye examination was done under general anesthesia because of hazy and enlarged corneas. The iris appeared to be deficient in pigment. Tensions measured right eye 2/5.5, 4/7.5 (Schiotz) and left eye 2/5.5, 4/7.5 (Schiotz). On July 27, 1961, bilateral goniopunctures were done under general anesthesia. These were repeated on October 10, that in the right eye being complicated by a marked hyphema. On November 15, 1961, a lavage of the hemorrhage in the right eye was performed and a goniopuncture was repeated on the left side. The child expired twelve hours later. The eyes were removed six hours after death.

GROSS EXAMINATION (Formalin-fixed specimens). The right eye measured 20 × 19 × 19 mm. Cornea measured 12 mm. horizontally and 13 mm. vertically. There was a bubble of air in the anterior chamber and some blood. The globe was sectioned in the horizontal plane. The anterior chamber

*Presented by the kind permission of Dr. Alfred McKinna of Montreal, Canada.

appeared very deep and measured 4.5 mm. at its greatest depth. The lens measured 8 mm. in diameter vertically and horizontally and 2 mm. centrally from the anterior to posterior surface.

The left eye measured 20 × 19 × 20. The cornea measured 12 mm. horizontally and 13 mm. vertically. The anterior chamber was filled with blood. The lens was not seen after the eye was sectioned.

MICROSCOPIC EXAMINATION. (The eye was embedded in paraffin and approximately 600 sections were made of the right eye.) Again the angle of the anterior chamber shows incomplete cleavage. The extent of the adherence of the iris to the trabecular fibers varies in different portions of the eye from an adhesion to approximately the posterior third to the posterior half of the trabecular fibers. The scleral spur is extremely poorly developed and in most hematoxylin-eosin stained sections it is difficult to tell the corneoscleral trabecular fibers from the adjacent sclera. However, in sections stained with periodic acid Schiff (PAS) stain, the corneoscleral fibers can be easily recognized. Endothelial line channels that are well developed and probably represent Schlemm's canal lie external to these fibers. A number of other endothelial line spaces can be seen deep in the sclera that probably represent collector channels or deep scleral vessels. No red blood cells are seen in these vessels. *There is hemorrhage in the anterior chamber and red blood cells lie between the uveal portion of the trabecular meshwork and even between the compressed layers of corneoscleral trabecular meshwork up to the endothelium-lined channels that probably represent Schlemm's canal* (Figure 8). The ciliary processes and ciliary body are pulled forward but as previously mentioned the scleral spur is so poorly developed it is difficult to tell exactly how much of the ciliary muscle lies central to a line drawn perpendicularly through the posterior edge of the corneoscleral trabecular fibers. The circular muscle of the ciliary body is practically non-existent and the longitudinal muscles are not as prominent as they are in other specimens. These longitudinal fibers insert into the uveal portion of the trabecular meshwork. The site of the goniopuncture was not found in the sections examined. Schwalbe's line is represented by a fairly large nodule.

Left eye: The greater part of the globe is filled with hemorrhage. There is a hemorrhagic detachment of the retina and the anterior chamber is filled with organized hemorrhage. The lens has been dislocated into the vitreous. On one side of the eye the iris is necrotic. On the opposite side, there is marked necrosis of the iris but the root can be seen. There is a prominent Schwalbe's line on either side of the globe and extending back from this the corneoscleral trabecular meshwork can be recognized. Red blood cells are enmeshed in these fibers. Endothelial line channels can be seen just external to the corneoscleral trabecular fibers but it is somewhat difficult to determine whether these represent Schlemm's canal or collector channels. It is almost impossible to distinguish the scleral spur or to tell the extent of the iris adhesion to the corneoscleral trabeculae.

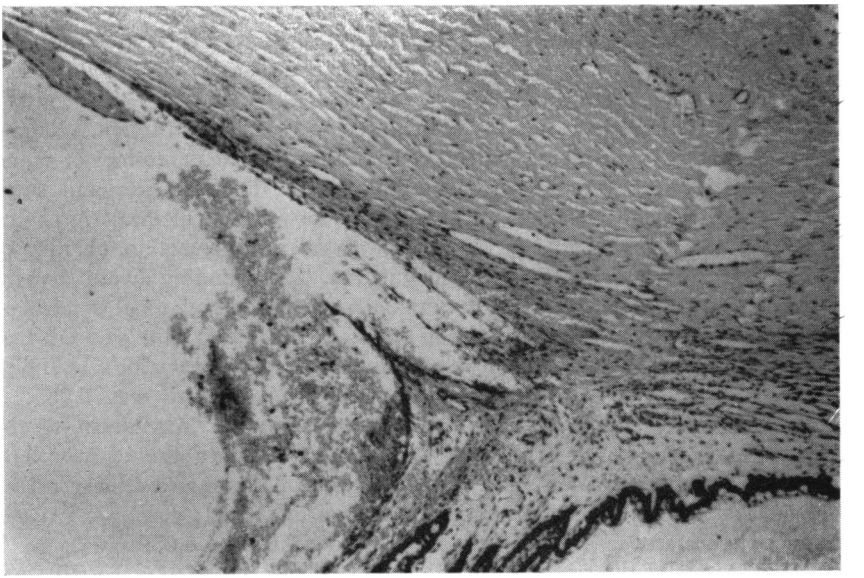

FIGURE 8. CASE 5, RIGHT EYE.
Note red blood cells between trabecular fibers.

IMPRESSION. In the right eye, the corneoscleral trabecular meshwork appeared to be unusually compact. Whether this was an actual fact *in vivo* or whether this was due to fixation in sectioning is impossible to state. Nevertheless, red blood cells were able to pass through these compressed fibers up to the inner wall of Schlemm's canal. The ciliary body and ciliary processes were pulled towards the central portion of the eye and the longitudinal muscle of the ciliary body inserted into the corneoscleral trabecular fibers in front of the scleral spur.

In the left eye, there appeared to be a Schlemm's canal on either side of the globe but the specimen had been so damaged from operative procedures and hemorrhage that it was difficult to interpret the changes in the angle of the anterior chamber.

CASE 6*[3]

A 6-lb. female infant was born in the thirty-eighth week of pregnancy. Her eyes had an unusual bluish haze at birth and the pupils were dilated. The corneas measured 12 mm. in diameter and were cloudy, more centrally than peripherally. The pupil measured 7.25 mm. in diameter and did not react to light, nor did it constrict to diisopropyl fluoro-phosphate; ectropion uveae was marked. Intraocular pressures on the fourth day of life measured

*Published A.M.A. *Archives of Ophthalmology*, 68:191, 1962. The eyes were examined through the kind permission of Dr. Samuel T. Adams.

right eye 35 mm. Hg. and 27 mm. Hg. (Schiotz). The left eye measured 30 mm. Hg. and 23 mm. Hg. with 7.5 and 10 gram weights respectively. The child developed an intestinal obstruction and died on the forty-fifth day of life.

General pathological examination showed intestinal obstruction, bilateral renal calcification involving collecting tubules, multiple micro-foci of metastatic calcifications in the cardiac muscle of the left ventricle and small arteries of the left ventricle, micro-foci of metastatic calcification of the white matter and thalamus of the brain with microglial reaction, changes of the ossification of the costochondral junction. These findings were thought to be compatible with Lowe's syndrome or oculocerebral renal syndrome.

Profusion studies were done on the eye by Dr. Morton Grant who felt that the patient had an aniridia and adhesion of the iris to Schwalbe's line. The facility of outflow in the right eye at room temperature was 0.035. A goniotomy designed to separate the abnormal anterior attachment of the iris from the angle wall but not designed to cut into the corneoscleral trabecular meshwork in an area of about 1 to 1½ hours increased the facility of outflow to only 0.064. A similar procedure in the left eye over 2½ to 3 hours circumference increased the facility from 0.037 to 0.053.

In a section of the right eye where the globe measures 16 × 15 mm. and the corneal diameter 10 mm., the lens measures 3.75 mm. × 3 mm. It is round, rather than kidney-shaped, as seen in most specimens of congenital glaucoma.

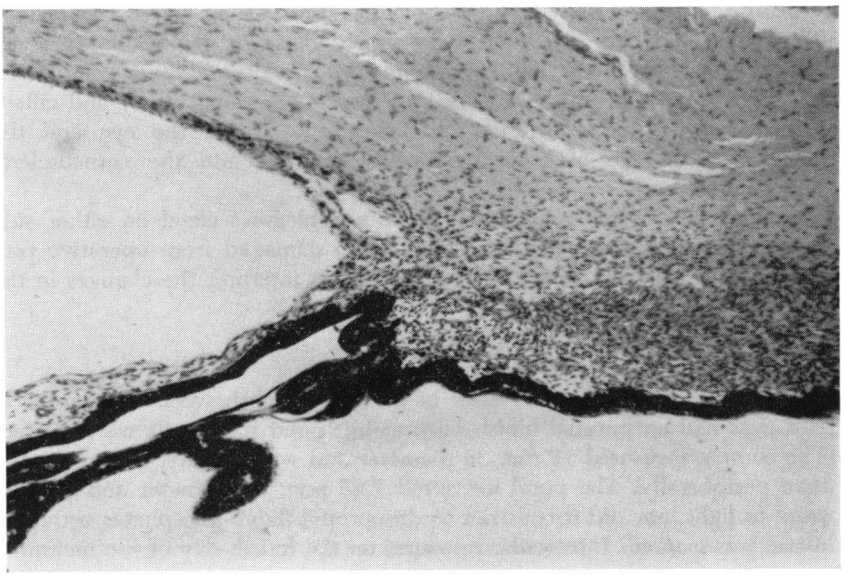

FIGURE 9. CASE 6.

MICROSCOPIC EXAMINATION. Very little can be added to the excellent description of the microscopic appearance of this eye and the microphotographs which have been published. However, it might be noted that the angle has an extremely fetal appearance. There is practically no separation of the iris and ciliary body from the trabecular fibers and it is even difficult to tell which cells might have become trabecular fibers and which might have belonged to the iris and ciliary body (Figure 9). This appearance is similar to that seen in embryos of less than 150 mm. in length. The ciliary processes and ciliary body are drawn quite markedly centrally. The scleral spur is non-existent but if one guesses at the posterior aspect of the trabecular fibers approximately one-third of the ciliary muscle lies forward to a line drawn perpendicularly through this point. As previously reported, Schlemm's canal cannot be found in the specimens available for study.

IMPRESSION. This is the most fetal type of angle that I have seen in any case of early congenital glaucoma. Schlemm's canal appears to be absent and even the collector channels are not evident in the deep sclera. In the postmortem goniotomy, the iris and the longitudinal and circular muscles were separated from the trabecular meshwork. This, however, did not appreciably increase the facility of outflow.

DISCUSSION

Examination of 11 eyes of six patients in this study has confirmed in part previous observations on 14 eyes of 11 patients with early congenital glaucoma. Thus, in Cases 1, 2, 3, and 5 there appeared to be an adequate Schlemm's canal. Iris processes to Schwalbe's line were frequently observed. Also there were varying degrees of adherence of the iris and ciliary body to the corneoscleral trabecular fibers. However, it did not appear that these adhesions were sufficient to prevent aqueous from leaving the anterior chamber for in three eyes that had been operated upon shortly before death red blood cells permeated the trabecular fibers up to the inner wall of Schlemm's canal (Case 1, RE; Case 2; Case 5, RE).

A finding that had not been previously recognized on histological examination of early specimens of congenital glaucoma was found in Case 6. In this specimen there was a very prominent Schwalbe's line and an almost complete failure of the development of the angle of the anterior chamber. The cells and fibers in the iris and ciliary body were almost impossible to differentiate from those in the trabecular fibers and there was a total failure of separation of the tissues beginning at Schwalbe's line. Schlemm's canal appeared to be totally absent. This specimen had the appearance of an angle of the anterior chamber of a 140-mm. embryo. After reviewing the material in the previous

report, it would appear that Case 1 also did not possess a Schlemm's canal.

Case 4 in this presentation is most unusual. In one eye, there appeared to be an endothelial line channel that probably represented Schlemm's canal. In the other eye, however, Schlemm's canal could not be found. In these two specimens the angle of the anterior chamber was considerably better developed than in Case 6 and there was a cleavage of the iris and ciliary body from the trabecular fibers to about half the normal extent.

There was another finding that was difficult to evaluate and interpret. In Cases 3, 4, and 5, the corneoscleral portion of the trabecular meshwork appeared to be unusually compact. In some sections it was difficult to tell the trabecular meshwork from the scleral fibers. However, in one of these specimens (Case 5, RE), red blood cells passed from the anterior chamber through the trabecular fibers up to the inner wall of Schlemm's canal. In Case 3 the compact corneoscleral trabecular fibers did not prevent fluid from flowing out of the eye. This was shown by profusing the enucleated eye and producing an increase of facility of outflow from 0.10 to 1.0 by a goniotomy that did not incise the corneoscleral trabecular fibers.

In eight of these 11 eyes, as in 13 of the previous 14 eyes with congenital glaucoma, the longitudinal muscle of the ciliary body attached to the corneoscleral trabecular fibers anterior to the scleral spur. The consistency of this finding in eyes with early congenital glaucoma suggests that it plays a part in producing a decrease of facility of outflow in these eyes. This is substantiated by the histological finding that goniotomy severs the longitudinal muscle from the trabecular fibers and produces a new attachment for the longitudinal muscle or an artificial scleral spur (Case 2, LE; Case 5, RE; and Case 8, RE & LE of previous report[1]) (Case 3, LE of this report).

The exact mechanism whereby the anterior insertion of the longitudinal muscle of the ciliary body into the corneoscleral trabecular fibers produces a decrease in facility of outflow, however, is not known. It was hoped that pharmacologic studies *in vivo* might be helpful in demonstrating that there was an abnormal pull of the longitudinal muscle on the trabecular fibers. However, neither pilocarpine, diisopropyl fluoro-phosphate (DPF), 10% neosynephrine, nor atropine had any appreciable effect on the intraocular pressure or facility of outflow in patients with congenital glaucoma. The patients so studied were not those cited in this report.

The profusion studies done on Cases 3 and 6 are of particular interest. In Case 6 there was a very low facility of outflow of 0.035 in the right eye and 0.037 in the left eye at room temperature. Goniotomy increased this only to 0.076 in the right eye and 0.053 in the left eye at room temperature. This was compatible with an absence of Schlemm's canal in this case. In Case 3 the facility of outflow as determined by profusion studies was 0.10 in the left eye. This was approximately that found by tonography *in vivo*. A goniotomy in the left eye detached the iris and ciliary body from the corneoscleral trabecular fibers and severed the longitudinal muscle from the corneoscleral trabecular fibers. The corneoscleral trabecular fibers, however, were not incised. In spite of this, the facility of outflow in this eye increased to 1.0 when approximately a 1 to 1.5 mm. goniotomy was done. Serial sections through the area of the goniotomy showed that a trabeculotomy had not been done in any section. In the right eye a misplaced goniotomy that cut into the cilary muscle failed to increase the facility of outflow (Figure 4). However, a second goniotomy that severed the longitudinal muscle from the trabecular fibers did increase the facility of outflow from approximately 0.10 to 1.0.

These histologic studies would indicate that there are at least two congenital abnormalities that may produce a decrease in the facility of outflow of aqueous and congenital glaucoma. One of these is an absence of Schlemm's canal. The other is an incomplete cleavage of the angle of the anterior chamber with an abnormal insertion of the longitudinal muscle of the ciliary body into the corneoscleral trabecular fibers. The degree to which the iris and ciliary body adhere to the trabecular fibers is extremely variable. However, the insertion of the longitudinal muscle anterior to the scleral spur into the corneoscleral trabecular meshwork is extremely constant. Profusion studies on four eyes are of great interest. On two of these studied by Adams, Grant, and Smith[3] a goniotomy failed to appreciably increase the facility of outflow. In two other eyes (Case 3), studied by Langham and myself, a goniotomy markedly increased the facility of outflow. In the first two eyes there was no Schlemm's canal and in the second two Schlemm's canal could be easily seen. It is obvious that a great number of eyes with congenital glaucoma need be studied with the profusion technique and examined histologically before any definite conclusions can be made. However, it is very tempting to suggest that a cause of failure in a correctly performed goniotomy in some cases is due to an absence of Schlemm's canal.

There are two other findings in these eyes that should be noted. The first is an unusually prominent Schwalbe's line. This is particularly true in Cases 3, 5, and 6. The significance of this and the failure of the development of the angle of the anterior chamber is not known but it should be pointed out that in Axenfeld's syndrome or mesodermal dysplasia of the iris this is a constant finding.[4]

The other finding is the apparent inward pull on the ciliary processes and ciliary body by the zonular fibers. It has been mentioned in the previous report that this may be due to a microphakia or at least a relative microphakia in these eyes. This inward pull on the ciliary processes and body was again found in all 11 specimens studied. Since a similar change can be found in eyes with persistent hyperplastic vitreous, it suggests that the maldevelopment of the lens holds the ciliary body forward and prevents normal cleavage of the angle of the anterior chamber.

In a previous report, eight normal eyes of stillborn fetuses between the ages of six and seven months, 13 eyes of fetuses of eight months' gestation, 15 eyes of fetuses of nine months' gestation, all showed normal angles of the anterior chamber except for a few iris processes. The longitudinal muscle of the ciliary body inserted into the scleral spur in all cases. A similar finding was observed in 24 eyes from patients of one year of age or less.

Case 2 was a patient who had a nevus flammeus and hemangioma of the choroid. The abnormality of the angle of the anterior chamber in this patient was similar to those of other cases of congenital glaucoma of unknown origin.

The multiple congenital abnormalities found in these patients lends weight to the previous observation that congenital glaucoma may be associated with other congenital abnormalities.[5,6]

SUMMARY

Eleven eyes of six patients with congenital glaucoma have been studied. In three of these eyes there was an absence of Schlemm's canal. In the other eight eyes, Schlemm's canal was present. Profusion studies by Adams, Grant and Smith in two eyes without a Schlemm's canal showed no increase in facility of outflow after goniotomy. Profusion studies in two eyes with a Schlemm's canal showed a marked increase in facility of outflow after goniotomy in this study. The inward pull on the ciliary processes and ciliary body by the zonular fibers of the lens has been striking in all specimens studied of congeni-

tal glaucoma. The possibility that a microphakia might contribute to the failure of the development of the angle of the anterior chamber is suggested.

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DISCUSSION

DR. LORENZ ZIMMERMAN. Thank you for the privilege of allowing me to attend this meeting and of opening the discussion of Dr. Maumenee's paper.

I have been following Dr. Maumenee's work for quite a long while with considerable interest. One of the first projects going on that I learned about when I first started working in ophthalmic pathology, not quite nine years ago, was Dr. Maumenee's efforts to collect material of the type he has shown us this morning. This represents a lot of work, to collect twenty-five eyes of early congenital glaucoma. No single laboratory receives very many specimens, and I think Dr. Maumenee deserves a lot of credit for having pursued this with such vigor over such a long time.

[Slide] Dr. Maumenee, in his American Ophthalmological Society thesis, called to our attention something that apparently had been overlooked. Many of us had been impressed by the fact that in the eyes with congenital glaucoma the ciliary processes come off farther forward, and some of the ciliary muscles, particularly the circular muscles, are farther forward.

But what he pointed out was that the longitudinal muscles, instead of inserting into the scleral spur, frequently continue for varying distances into the trabecular area anterior to the scleral spur.

One of the things that impresses anyone who studies a number of eyes with congenital glaucoma is the variation that is encountered. In some instances—and I am sure you noticed this in the slides Dr. Maumenee showed—this covering of the trabecular area goes almost all the way up to Schwalbe's line. In other cases the degree of malformation is very much less. I am sure this must account, in part at least, for the variable results that are obtained surgically.

Another thing that one is impressed by is the variation in the amount of longitudinal muscle that is inserted anterior to the scleral spur. This was brought out rather vividly at the recent meeting of the Ophthalmic Pathology Club when Dr. Maumenee circulated some of his slides. Some members who were studying the slides said, "This slide shows that this doesn't always occur," and yet other people said, "I see it in my slide." In other words, even within a given eye multiple sections will show different relationships in different planes of sections; again I think this might be responsible for some of the variations obtained surgically.

[Slide] Here is a more advanced example. Here is the scleral spur. You see the most of the functional part of the trabecular meshwork is covered by the uncleaved iris tissue.

[Slide] Here again, as Dr. Maumenee pointed out, in most of the eyes he has collected the canal of Schlemm is open, but it is separated from the chamber angle, which we see down at the lower right, by this adherent, uncleaved iris root.

I would like to show you another example of congenital glaucoma that was not included in Dr. Maumenee's series, nor was it listed among the malformations in Dr. Scheie's series. We have received several eyes from children whose eyes were malformed at birth—that is, they had cloudy corneas—and after histologic examination they were found to have a retinopathy that looked strikingly similar to the retinopathy of prematurity (retrolental fibroplasia) although these were not markedly premature babies.

[Slide] This is one of those cases. This child was born after 33 weeks' gestation and weighed 5½ pounds. The child died after 2½ hours as a result of a malformation of the brain. Both corneas were cloudy at birth.

[Slide] Of interest was the fact that this child had retinal lesions that looked indistinguishable from those of retrolental fibroplasia.

[Slide] The child died after 2½ hours, so oxygen toxicity was not a factor here.

[Slide] You see the large dilated, thrombosed retinal vessels back in the region of the nerve head.

[Slide] The angle showed an interesting uncleaved iris root, with vascularization of the anterior surface of the iris.

[Slide] The forward insertion of the longitudinal muscle that Dr. Maumenee described is not shown in this case. There is incomplete cleavage, and the iris root is adherent to the trabecular meshwork and there is neovascularization, all of this having taken place *in utero*. Here is another example of a chamber angle malformation that we have seen in at least half a dozen cases of congenital glaucoma.

DR. HERMANN M. BURIAN. I was exceedingly glad to learn from Dr. Maumenee's interesting presentation that he now agrees that there are cases of congenital glaucoma in which there is an absence of Schlemm's canal.

We have maintained this for a number of years, only to be told that this

absence was secondary. There are, as we have shown, in fact two groups of developmental glaucoma. In the first there is an absence of Schlemm's canal and there are severe abnormalities in the architectonic structure of the trabecular meshwork. In the second the canal of Schlemm and the trabecular meshwork are relatively normal in appearance, but the access of the aqueous to the outflow channels is barred by mesodermal structures, owing to a failure of the chamber angle to open fully by cleavage.

I have also pointed out that in the first form goniotomies are useless and other forms of operations must be employed. I found it, therefore, particularly interesting that Dr. Maumenee was able to give us direct evidence for this by showing on enucleated eyes that goniotomy can produce an increase in outflow in the cases in which there is a canal of Schlemm, whereas in the others it cannot.

As for the importance of the forward insertion of the longitudinal fibers of the ciliary muscle, emphasized by Dr. Maumenee, I have this to say. One should be careful in stating that the longitudinal muscle fibers normally end in the scleral spur. This might imply that the muscle fibers and their tendons stop at that level. Our own investigation and the excellent work of Rohen have clearly demonstrated to us that in normal, non-glaucomatous eyes the tendinous connective tissue from the muscle fibers goes through and around the scleral spur and is continuous with the trabecular fibers of the outer portion of the uveal meshwork. These trabecular fibers then become actually, in a manner of speaking, the tendons of the longitudinal muscle fibers.

DR. MAUMENEE. I wish to thank Dr. Zimmerman and Dr. Burian, Dr. Zimmerman for showing such beautiful illustrations confirming the pathological findings that have been observed, and also for pointing out that there is still another type of anomaly that can occur in the angle in these children who have this very unusual type of retinopathy.

I was impressed in his slide with the new-formed vessels on the surface of the iris that almost looked like rubeosis of the iris; but he tells me this is not present in all sections of the specimen.

Dr. Burian brought up two interesting points. One was the question of normal controls. Whereas I did not mention normal controls today, I did examine some sixty infant eyes from children less than one year old, from about 7-month stillborns to one year of life, and I did not find that anomaly of the longitudinal muscle bypassing the scleral spur and flattening the scleral spur as shown in these specimens.

Dr. Burian is perfectly right. Some fibers of the ciliary muscle do insert into the uveal portion of the trabecular meshwork, and I agree with him entirely that with special stains one can see the tendons of the longitudinal muscle passing through the scleral spur and up into the trabecular meshwork; but the anomaly I have shown here I have not seen in a normal eye previously.

I might mention that my first thought about this anomaly was that the muscle had pulled in such a way that it would close off Schlemm's canal, and I tried to prove this pharmacologically by giving children DFP or very intensive miotic therapy, hoping that this would close off the angle and make the pressure go up. It did not. I then gave them atropine to see if I could reduce the pressure. At first I was rather hopeful and thought that this was reducing the pressure, but as we kept the children on atropine the pressure then went back up again; so I have to say that neither miotics nor mydriatics have any effect on lowering or raising the intraocular pressure in these cases.

I think from our physiology studies on the eyes that have been enucleated it appears that this defect is somewhere in the outer wall of the trabecular meshwork, fairly near Schlemm's canal but not right exactly in Schlemm's canal. Following a goniotomy the trabecular fibers do remain.