CONCERNING CERTAIN PHASES OF THE DEVELOPMENT OF THE VITREOUS

A Demonstration of Lantern Slides*

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THIS contribution takes the form of lantern slides made from unretouched photographs of some of my sections of human fetuses. As most of the illustrations in the textbooks are drawings, and must of necessity express the artist's interpretation, it occurred to me that it would be informative to show these slides as the camera saw them.

SLIDE 1.—Section of a fetus, 10 mm. g. l. The vitreous is in the primary stage, and is a mixture of ectoderm and mesoderm. The section passes through the fetal fissure. The mesoderm is derived from that which accompanies the hyaloid artery, which enters the optic cup through the fetal fissure, and from the surrounding mesoderm, which enters the cup through the space between the anterior rim of the cup and the lens. The ectodermal part is composed of fibrils that grow from the lens and from the inner wall of the optic cup. At this age the lens capsule has not developed.

SLIDE 2.—Section of the same fetus passing through the edge of the fetal fissure and nearer the center of the lens.

SLIDES 3 AND 4.—Sections of the same fetus, with greater magnification. They show the inner wall of the optic cup near the anterior rim and part of the lens. The ectodermal fibrils can be seen arising from cone-shaped projections on the inner wall of the cup and from the surface of the lens. The ectodermal and mesodermal fibrils mingle and fuse.

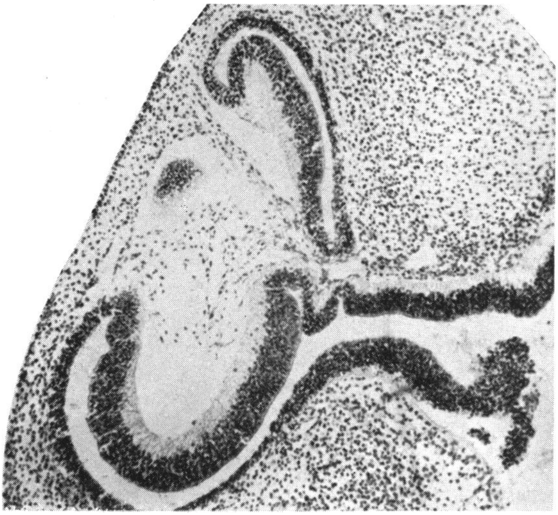
* These slides were exhibited at the 1941 meeting of the American Ophthalmological Society.

SLIDE 5.—Section of a fetus, 20 mm. g. l. The eye is much larger, and the ectodermal portion of the vitreous has grown proportionately. Relatively less mesoderm is seen. The hyaloid artery has approached nearer to the lens, and its branches—the vasa hyaloidea propria—are seen in the vitreous.

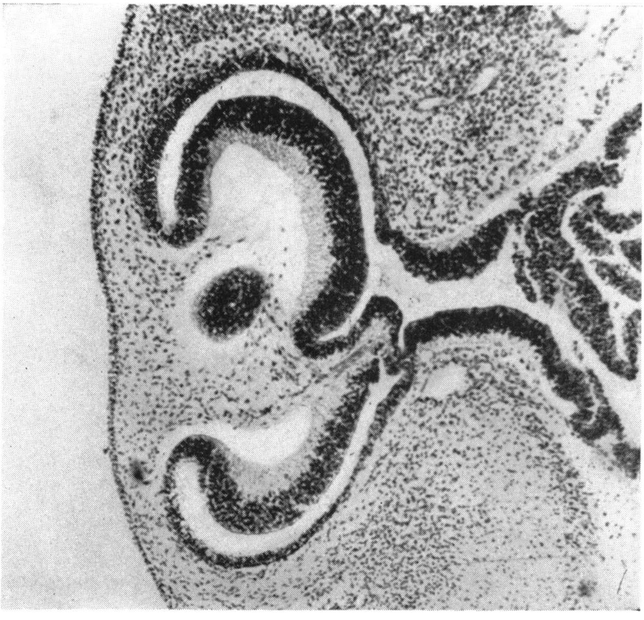
SLIDE 6.—Section of the same fetus, with higher magnification. The capsule of the lens has developed and prevents the lens from contributing to the future growth of the vitreous. This is the early part of the secondary stage of the development of the vitreous. Vasa hyaloidea propria are seen distributed throughout the vitreous, and Müller's fibers, with their expanded bases, are seen forming the internal limiting membrane of the retina.

SLIDE 7.—Section of a fetus, 29 mm. g. l. The hyaloid artery has reached the posterior surface of the lens. The vasa hyaloidea propria are more widely distributed. The membrana limitans interna retinae is quite well developed, and the ectodermal vitreous appears to be in continuity with it. The ectodermal fibrils of the vitreous continue to grow from the surface of the inner wall of the cup after the internal limiting membrane of the retina has formed, for, unlike the capsule of the lens, it is not a glass membrane formed by secretion, but is a portion of the glial framework of the retina. Where the vitreous has been torn away in the process of preparation, the internal limiting membrane may also be seen to have separated from the retina. There is much less mesoderm between the anterior rim of the cup and the lens than there was in the earlier fetuses. The ectodermal fibrils are fused with the mesoderm accompanying the hyaloid artery and its branches.

SLIDE 8.—Section of a fetus, 45 mm. g. l. The eye is much larger, and the ectodermal vitreous is proportionately so. On one side, the vitreous has been torn from its attachment to the retina over a large area, but on the same side it



Slide 1.



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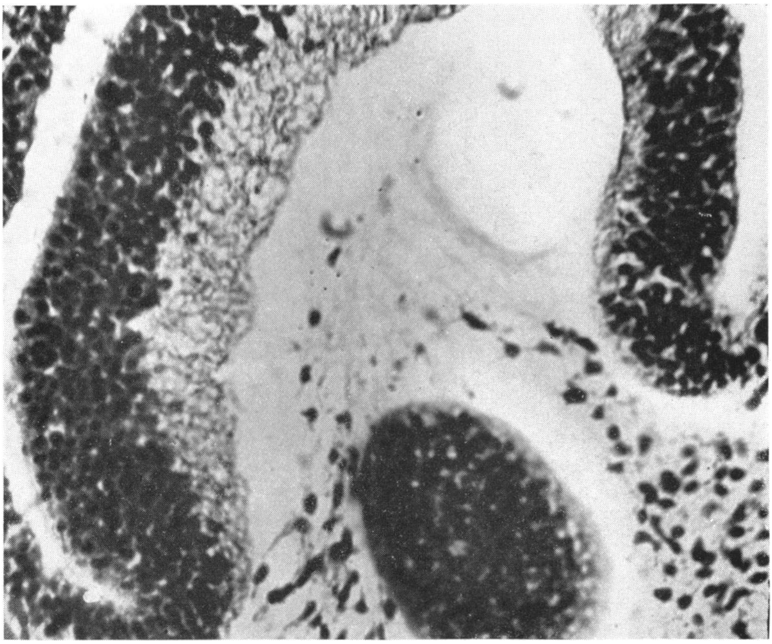
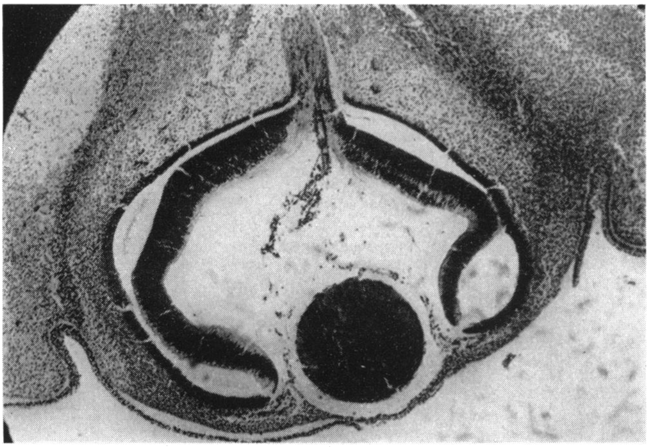
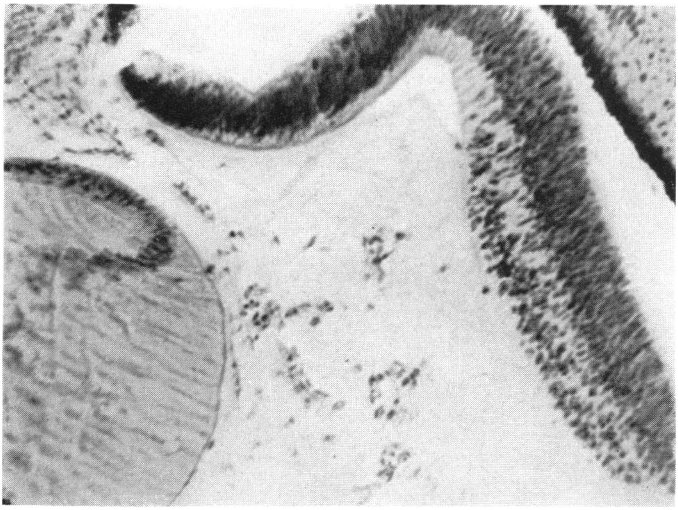


Slide 3.

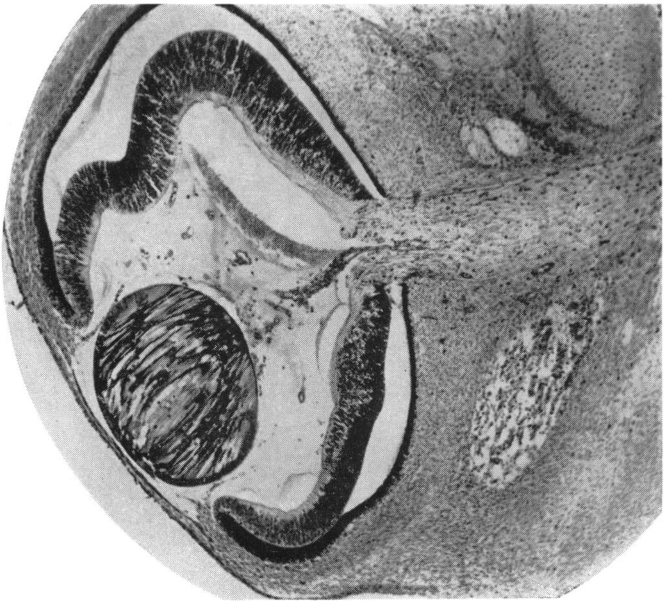
Slide 4.



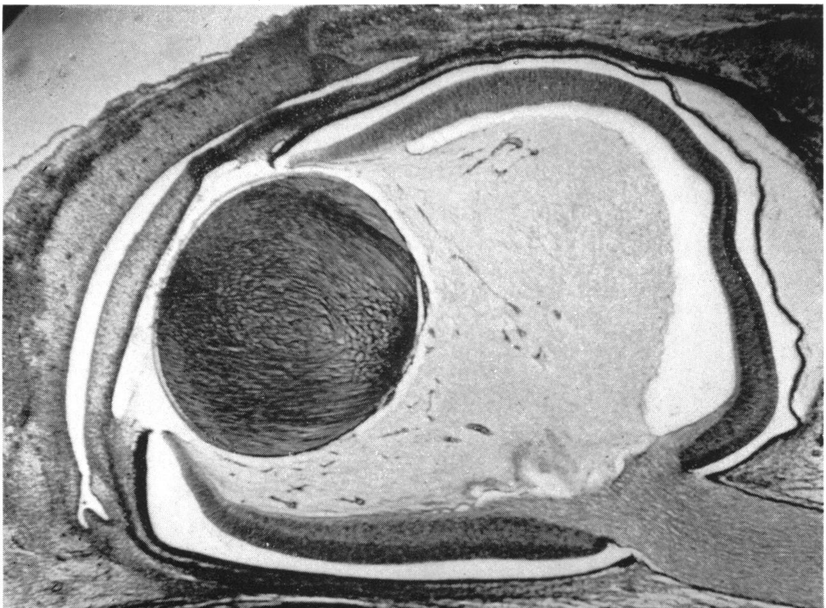
Slide 5: Anterior.



Slide 6.



Slide 7.



Slide 8.

is firmly attached near the anterior rim of the cup. This attachment is called the vitreous base. After the anterior rim has grown forward and the ciliary body and iris are formed, this place will be the ora serrata. In post-natal life, the vitreous will still be firmly attached here in a ring, said to be 1.5 mm. in diameter. In the posterior part of the eye, in the region of the optic nerve, the vitreous is seen to be firmly attached. This arrangement also continues throughout adult life. The tunica vasculosa lentis has formed, as has also the capsula perilenticularis. The greater portion of the vitreous is now ectodermal. It is the secondary vitreous, or permanent vitreous. A triangular area of coarser meshwork is seen in the central part of the vitreous, behind the lens. This is the remains of the primary vitreous.

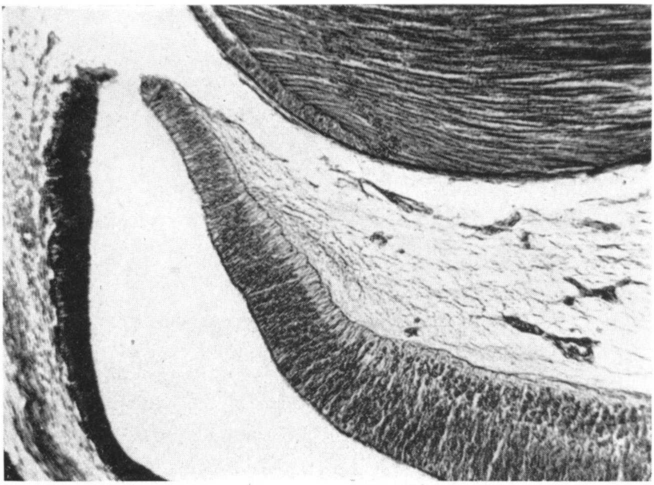
SLIDE 9.—This is a greater magnification of the last section. It shows the retina near the anterior rim of the cup and part of the lens. The membrana limitans extends nearly to the rim. Müller's fibers and the internal limiting membrane are clearly discerned, and it can be seen that the vitreous is a continuation of the internal limiting membrane, therefore no other membrane could be between the vitreous and the retina, so that there can be no posterior hyaloid membrane. When a so-called subhyaloid hemorrhage occurs, the blood lies under the internal limiting membrane.

SLIDE 10.—The same section nearer to the center of the retina.

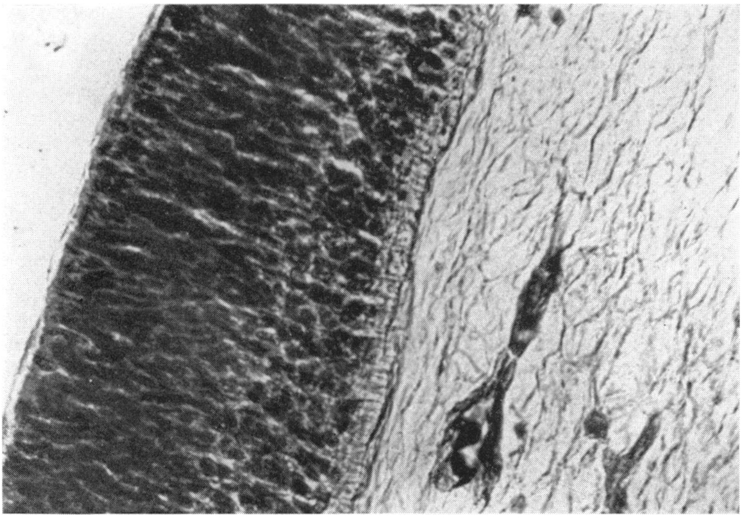
SLIDE 11.—Section of a fetus, 110 mm. g. l. This slide shows the region back of the lens. The section is very thin, and the lens was lost, but the capsule remains *in situ*, so that the relations of the parts are correct. The dark line is the lens capsule. Immediately posterior to it are seen sections of vessels of the tunica vasculosa lentis, and then a line that is partly interrupted. This line is the capsula perilenticularis, sometimes called the anterior hyaloid membrane. Immediately posterior to this is a triangular area of vitreous, the base of the triangle being toward the lens capsule, which is of coarser mesh than the surrounding vitreous, and separated from it by a fine darker line. This area is the primary vitreous, or the anterior end of the canal of Cloquet, at the apex of which a part of the hyaloid artery may be seen. The dark line between the primary and secondary vitreous is what has been called the wall of the canal of Cloquet. It is not a membrane, but is a condensation of the vitreous fibrils. It is continuous with the capsula perilenticularis anteriorly, and is therefore a continuation of what is called the anterior hyaloid membrane. Later the capsula perilenticularis behind the lens atrophies and the anterior end of Cloquet's canal is open. Toward the end of fetal life very little of the primary vitreous remains. Sometimes, however, this primary vitreous fails to absorb and the mesodermal part develops into fibrous connective tissue, and a firm, triangular, opaque mass is formed behind the lens. Ophthalmoscopically, this mass has been diagnosed as glioma of the retina.

SLIDE 12.—Section of a fetus of unknown length. Age, approximately four and one-half months. The section shows the space between the lens and the ciliary region. In it are fibrils which originate from the ciliary epithelium and course toward the lens. These fibrils are part of the tertiary vitreous or suspensory ligament of the lens. Just posterior to them may be seen a dark curved band composed of condensed vitreous fibrils; this occupies the position of the lateral part of the anterior hyaloid membrane, separating the tertiary from the secondary vitreous. It touches the lens at the site of Egger's line.

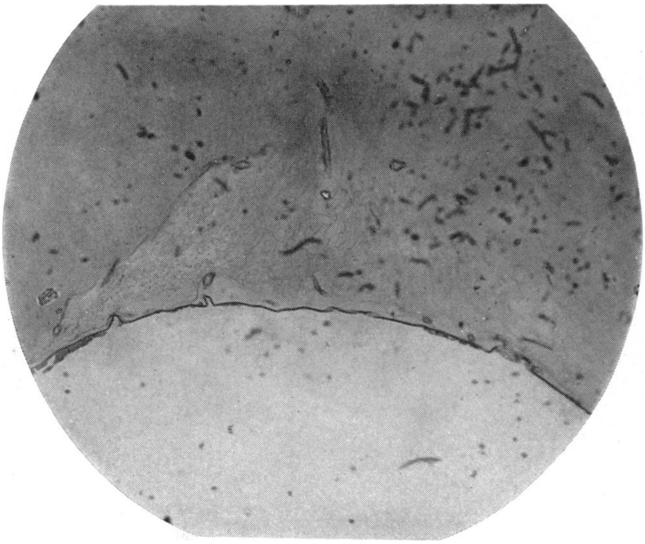
SLIDE 13.—A cross section through the lens and ciliary processes of a fetus, 350 mm., g. l. Numerous fibrils may be seen extending from the ciliary epithelium to and attached to the capsule of the lens. They are the fibrils of the tertiary vitreous, which become the suspensory ligament of the lens. The tertiary vitreous is ectodermal in origin, and grows from



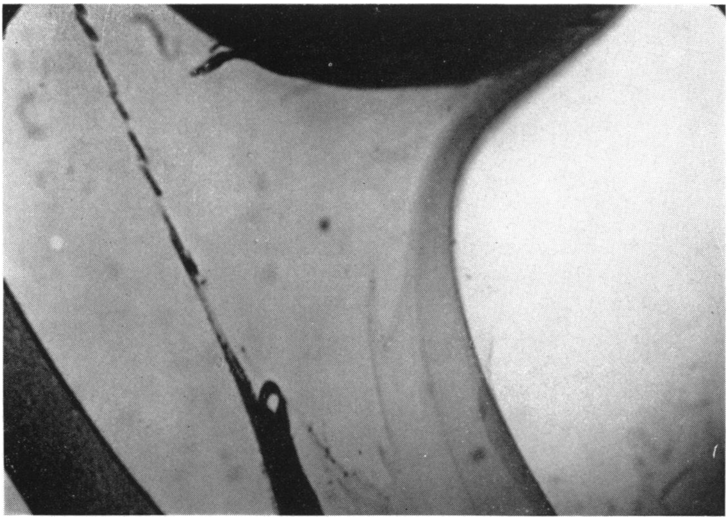
Slide 9.

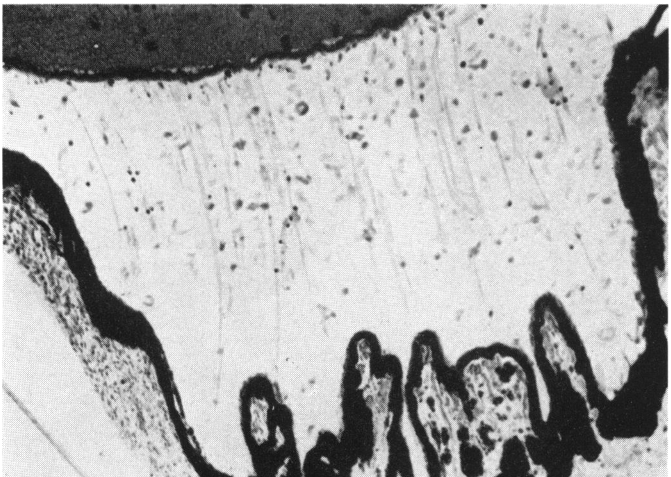


Slide 10.



Slide 11: Anterior.


Slide 12.


Slide 13.

the cells of the anterior surface of the optic cup, but not from the limiting membrane, as there are no Müller's fibers in this portion.

DISCUSSION

DR. F. H. VERHOEFF, Boston, Mass.: Dr. Haden has given a beautiful photographic demonstration of the generally accepted theories regarding the embryonic formation of the vitreous. I agree with practically everything he said in this regard. However, there is one statement with which I do not agree. He asserted that there is an internal limiting membrane of the retina, but not a posterior hyaloid membrane. There are many who agree with him on this point. I believe that there is definitely a posterior hyaloid membrane, but there is a doubt as to whether we should speak of an internal limiting membrane. Sections of an adult human eye stained in Mallory's connective-tissue stain show a definite hyaloid membrane stained blue in contrast to the contiguous retina, which is stained red. One of the embryonic specimens, similarly stained, which Dr. Haden presented on the screen, showed such a membrane. When there is a subhyaloid hemorrhage, it occurs beneath this membrane, and when the vitreous separates from the retina this membrane comes off with it. If it is not a membrane, then what should it be called? The fact that it is a condensation of the vitreous does not prevent it from being a membrane. I shall not discuss the question of artefacts—any objections along this line would weigh equally against both of us, since we employed fixed tissues in our studies.

DR. E. V. L. BROWN, Chicago, Ill.: Dr. Haden's specimens show definitely that the primary vitreous develops in part from the lens and, so far as I know, this has not heretofore been demonstrated.

DR. THEODORE L. TERRY, Boston, Mass. (by invitation): Dr. Haden has considerable courage in investigating this problem in embryology because there are so many points of lively dispute. I am glad to hear that he has taken a definite stand on some of these questions. The stand which Dr. Haden has taken concerning the development of zonular fibers from the tertiary vitreous is interesting in its relation to an understanding of zonular fiber involvement in exfoliation of the lens capsule. If his contention is correct,—and there are many observers who do agree with it fully,—then the zonular fibers are of entirely different type material from the lens capsule, and we would not expect the zonular fibers to exfoliate actively as the anterior capsule of the lens does. If that is the case, then these small particles of exfoliated material often seen enmeshed in the zonular fibers must not have originated there.

The problems related to the development and fate of the blood vessels of prenatal vitreous are extremely interesting. Perhaps considerable information—and doubtless some misinformation—may be gained from the study of embryonic specimens of various animals. For instance, only in the rat and in rodents as a class do the vasa hyaloidea propria approach close to the retina to form the membrana vasculosa, which persists as a preretinal vascular layer, the retina itself remaining avascular; whereas in man the vasa hyaloidea propria do not extend near to the retina. An understanding of the vessel-attracting property in the rodent retina and the vessel-repelling property in the retina of man would probably be of great value.

Blood vessels of the prenatal vitreous are of further clinical interest because of the occasional discovery, after birth, of a persistence of the tunica vasculosa lentis, or even a persistence of the vascular system of the primary vitreous *in toto.* This lantern slide shows just such a vascularized mass behind the lens. Dr. Haden has studied this section, which is one of an eye removed from an infant nine days after birth because of a clinical diagnosis of retinoblastoma. The connective-tissue elements appear to be mesenchyme in which collagenous fibers are developing. The mass is of larger size than that ever attained by the tunica vasculosa lentis, and perhaps even by the primary vitreous itself. It is attached firmly to the ciliary processes and even to the retina. This mass could not be removed surgically without removing the tips of the ciliary processes and a part of the retina as well.

These other slides show similar but less extensive collagenous mesenchyme containing blood vessels just behind the lens, and similarly these membranes are intimately attached to the ciliary processes and to the retina, which is normally very far forward because of the narrow pars plana of the ciliary body at this stage of development. This condition may be concealed by secondary cataractous changes. In one such instance the lens was largely eradicated by discission. During the second discission, the dense membrane could not be cut by the knife-needle. A so-called cataract extraction was performed, and the mass was removed. The surgeon did not realize the real nature of the condition until microscopic study of the sections of the material removed showed the presence of typical mesenchyme containing much collagen and many blood vessels. Attached to this mass were several small bits of ciliary body and retina.

The final lantern slide shows the appearance of a bilateral vascularized membrane behind the lens of an infant born prematurely, and weighing only about two pounds at birth. Dr. Paul Chandler had a similar case and Dr. Charles Perera, of New York, has three such cases, all in infants weighing less than three pounds at birth. Is there any reason why prematurity should give rise to a persistence of these embryonic structures, or are they rare and coincidental occurrences?

DR. J. S. FRIEDENWALD, Baltimore, Md.: I must disagree with Dr. Haden as to the question of the hyaloid membrane. A number of years ago I devised a technique by which the retina can be stained postmortem and examined on the flat, without sectioning. This technique consists of introducing the histologic stains only on the anterior surface of the retina, and allowing them to penetrate through the anterior layers only, so that the deeper nuclear layers do not become deeply stained; the retina is sufficiently transparent to enable one to examine it very well with quite high power histologically through the anterior surface. Dr. Maumenee, who was at that time working in my laboratory, made some studies with this technique, and discovered that on the surface of the retina there is a layer of cells with which he had not previously been familiar. If one examines a preparation of this kind, one sees the ganglion cells of the retina in regular pattern under the retinal surface, and anterior to these cells is seen a layer of cells with elongated nuclei which are distributed in a fairly regular pattern over the surface. These cells, once they are recognized, can also occasionally be seen in ordinary histologic sections, where one sees cross sections of these cells as an exceedingly flat, endothelium-like cell lying anterior to the internal hyaloid membrane. Dr. Maumenee never published this observation, because he found that these cells had been described fifty years ago by His, and were known to Parsons forty years ago. The fact that this layer has been lost sight of in current work on the embryology of the vitreous makes me suggest that it might be worth while to allow me to include a photomicrograph of one of Dr. Maumenee's preparations in the discussion of this paper.

DR. HENRY C. HADEN, closing: Naturally, I hesitate to differ in any way from Dr. Verhoeff, because his knowledge of such things is so much greater than mine, but I cannot change my opinion. This is a high-power picture (slide No. 9) of the one Dr. Verhoeff spoke about. There would be no doubt if you could see the section under the microscope. There is no question but that these are Müller's fibers, and that connected with Müller's fibers is what is known as the internal limiting membrane of the retina; moreover, there is no doubt about the fact that the ectodermal vitreous is growing from it. Slide No. 10 shows the same section farther back in the eye and shows the same line (internal limiting membrane). It is just an academic question, probably, whether the internal limiting membrane of the retina is the hyaloid membrane or whether the hyaloid membrane is the internal limiting membrane, but I do not believe that there is any other membrane between the vitreous and the retina than the internal limiting membrane. That which Dr. Verhoeff pointed to in slide No. 8 is a portion of the vitreous torn loose and colored blue; when seen under the microscope it shows the internal limiting membrane attached to it—at least that is my interpretation of it.

In regard to Dr. Brown's question as to the origin of the ectodermal vitreous from the lens: When the optic vesicle branches off from the anterior cerebral vesicle it comes into contact with the surface ectoderm. After a time the optic vesicle invaginates, leaving the surface ectoderm. As it turns in to form the optic cup it brings with it fibrils from the surface ectoderm. This part of the surface ectoderm invaginates and forms the lens cup, so that there is a continuation of ectodermal fibrils from its posterior surface to the anterior surface of the inner layer of the optic cup. These fibrils continue to grow after the lens vesicle is formed; they remain in continuity with those of the anterior surface of the inner layer of the optic cup and help to form the ectodermal vitreous.

Dr. Friedenwald, I am very much obliged to you for telling me this, and some time I hope you will let me see your slides.

Dr. Terry, I do not know anything about the blood supply of the rat.

Slide No. 11: This section shows how the hyaloid canal is not a canal, but is simply the primary vitreous. This has mesodermal tissue in it, which sometimes is not absorbed and goes on to the formation of a connective-tissue mass back of the lens. I believe that this accounts for the appearance, in Dr. Terry's slide, of a mass in the vitreous behind the lens.