PERSISTENCE AND HYPERPLASIA OF THE PRIMARY VITREOUS*

[TUNICA VASCULOSA LENTIS OR RETROLENTAL FIBROPLASIA]

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(By invitation)

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This condition, which usually manifests itself as a bilateral congenital lesion of premature infants, has always appeared sporadically but of late there has been an increased incidence, probably stemming from a lower mortality of premature babies. In the past decade or more a number of measures adopted by the pediatricians have contrived to save the lives of many premature babies formerly lost. This seems to be an important reason why the lesion under discussion is encountered more frequently now.

We wish to report on 50 cases which we believe belong to this group, and the following table shows that the incidence of our cases has been higher during the past decade.

YEAR OF BIRTH OF 50 CASES

Year	*Full-term*	*Premature*	*Total*
1930	1	..	1
1931	..	..	..
1932	..	..	..
1933	1	..	1
1934	1	..	1
1935	..	..	..
1936	1	..	1
1937	2	..	2
1938	1	2	3
1939	2	..	2
1940	3	3	6
1941	2	3	5
1942	1	4	5
1943	2	7	9
1944	3	8	11
1945	..	3	3

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The first reference we can find to this condition dates back to 1851 (Howard)[1] and since then many articles have appeared describing various clinical and pathologic aspects of the lesion under various synonyms some of which are the following: Persistent thickened hyaloid artery with secondary changes (Nettleship, 1873),[2] persistent hyaloid canal and artery (Gardiner, 1880),[3] persistence and thickening of the posterior fibrovascular sheath of the lens (Collins, 1892),[4] (Pollock, 1923),[5] atypical development of the anterior part of the vitreous with or without a persistent hyaloid artery (Collins, 1892),[4] congenital membrane behind the lens (Parsons, 1902),[6] persistence of remains of the tunica vasculosa lentis (Bruckner, 1907),[7] persistent posterior fibrovascular sheath of the lens (Lane, 1919),[8] persistence of embryonic fibrovascular sheath of the crystalline lens (Lent and Lyon, 1922),[9] remains of the tunica vasculosa lentis (Gifford and Latta, 1923),[10] (Lloyd, 1931),[11] pseudophakia fibrosa of Czermak (Fuchs, 1923),[12] opaque membrane behind the lens (Collins and Mayou, 1925),[13] shrunken fibrous tissue cataract (Collins and Mayou, 1925),[14] posterior lenticonus (Collins and Mayou, 1925),[15] congenital connective tissue formation in the vitreous chamber (Collins and Mayou, 1925),[16] posterior polar cataract (Mann, 1937),[17] fibrous tissue cataract (Mann, 1937),[18] persistence of the vascular sheath of the lens (Duke-Elder, 1941),[19] fibroblastic overgrowth of persistent tunica vasculosa lentis (Terry, 1942),[20] and retrolental fibroplasia (Terry, 1942).[21] We believe that all of these references refer to various manifestations of the same basic lesion. Terry, in a series of papers[20-24] in which he gave the results of his most thorough study of this subject, chose the term "retrolental fibroplasia." This term is acceptable but we feel "persistence and hyperplasia of the primary vitreous" more accurately designates the lesion.

Terry employed the term "retrolental fibroplasia" to designate primarily a condition occurring bilaterally in premature babies after birth (not earlier than 4 months).

He felt that this is a new acquired condition different from the lesion which is unilateral at the time of birth in full-term infants. From the study of our cases and the literature we do not believe such a distinction is justified but that the same lesion may occur in both premature and full-term babies, may be unilateral or bilateral, and that all are congenital but may not manifest themselves until sometime after birth either because they are not looked for or because the lesion progresses.

Age When Abnormality Was Observed

The age of the patient when the parents or physician first noted any ocular abnormality is stated in 15 of our records.

In 9 patients the lesion was noted during the first week after birth:

Number	*Term*	*Noted*
1 case	Premature	At birth
3 cases	Full-term	At birth
1 case	Full-term	On 2nd day
1 case	Full-term	On 3rd day
1 case	Full-term	On 4th day
1 case	Full-term	Within a week
1 case	Premature	Within a week

In 6 patients the lesion was noted at later dates:

Number	*Term*	*Noted*
1 case	Full-term	On 23rd day
1 case	Full-term	At 4 weeks
1 case	Full-term	At 5 weeks
1 case	Premature	At 10 weeks
1 case	Full-term	At 4 months
1 case	Premature	At 5 months

Of the remaining 35 patients, in some cases the records do not state specifically the time at which the parents observed something abnormal about the infant's eyes; in other cases the parents did not notice anything unusual until the baby was three months or more older although they had sus-

pected for a long time that the baby was not seeing things; however, they did not become seriously concerned until the baby was several months old.

On the basis of the embryology and pathology concerned which will be discussed later, it is difficult to conceive of the tissue being absent at birth and forming subsequently. We know that remains of the hyaloid system and other congenital abnormalities in the structures of the eye are frequent accompaniments of the lesion. Our thesis is that in these cases the primary vitreous, which is a vascularized mesoderm, persists in some or all of its phases at birth and may show regressive or progressive changes. Progressive changes, from the clinical aspect, may be due to actual hyperplasia of this mesoderm or to secondary factors such as hemorrhage, contracture, swelling of the lens, secondary glaucoma, and corneal opacity from contact of the lens and iris with the posterior surface of the cornea. The nature of these secondary changes will be pointed out when the pathology is discussed.

Prematurity.—What constitutes a premature baby is not always clear. For our purposes we have chosen a birth weight of under five pounds or, in instances where the birth weight is lacking (15 of our cases), an infant born before nine months to designate prematurity. With this criterion our 50 cases were as follows:

30 (60 per cent) were premature infants
20 (40 per cent) were full-term infants

Laterality.—Of 30 premature infants: 28 were bilateral; 2 were unilateral. In one of these there was a juxta-papillary area of chorioretinal atrophy in the fellow eye.

Of 20 full-term infants: 7 were bilateral; 13 were unilateral. In one of these hydrophthalmos was present in the fellow eye. Thus, of 50 cases, 35 were bilateral and 15 were unilateral.

Sex and color.—Of 50 cases: 31 were male; 19 were female. All patients were white except 1 case, a negro.

Twins and Triplets.—Three cases were twins; 2 cases were 2 of triplets; the third sibling died at the age of 3 days and the eye status was not known.

Clinical Types

The clinical appearance of this basic condition is varied and depends on several factors: (1) Stage of cessation of the normal involution or disappearance of the primary vitreous including the hyaloid system; (2) amount and character of the hyperplasia of the mesoderm of the primary vitreous; (3) extent and character of the secondary changes (hemorrhage, contracture, glaucoma, swelling of the lens, contact of iris-lens diaphragm with the cornea, etc.).

It is convenient to divide the clinical manifestations into four types as follows:

I. Saucer-shaped whitish opaque tissue conforming to the posterior surface of the lens.

II. An opaque cornea, greatest in the central portion, usually associated with glaucoma, and maybe buphthalmos.

III. Localized area of opaque tissue on the posterior surface of the lens, or at the lens equator, or in the anterior vitreous with or without retinal detachment.

IV. Remains of the hyaloid system.

These four clinical types are not necessarily sharply demarcated but may merge. Type I may change into Type II, or there may be Type I in one eye and Type II in the fellow eye. Otherwise one type cannot go over into another type.

Type I.—This appears as a concave, saucer-shaped whitish opaque tissue against the posterior surface of the lens (Fig. 1). This is the typical and most frequent manifestation of the lesion. The globe is smaller than normal in size, the cornea is clear, and the anterior chamber shallow. The lens is clear but against the convexity of its posterior surface is applied this whitish tissue whose surface is concave to fit the convexity of the lens. Blood vessels of varying size and

number are usually visible in the opaque tissue. The tissue covers the greater part of the posterior surface of the lens but the central portion is densest and there is a gradual thinning toward the periphery of the lens where frequently the fundus reflex, or even some details of the fundus, may be seen. Around the equator of the lens long narrow ciliary processes in one or more sectors can be seen either free or extending into the periphery of the membrane. These processes can usually be seen clinically (Figs. 1 and 10) if looked for, and when present they are pathognomonic of this condition.

From this usual clinical appearance just described there may be some variation which will now be discussed.

The size of the globe was mentioned in the clinical description of 23 cases. Of these, the globes were larger than normal in both eyes of two bilateral cases; the globe was larger than normal in one eye and smaller than normal in the fellow eye in one bilateral case. In all other cases, the eyes appeared to be smaller than normal. Microphthalmos was present in 7 unilateral cases and 12 bilateral cases. It was present in both premature and full-term infants.

It is felt that the enlargement of the globes was due to glaucoma. We found the intra-ocular pressure elevated in several cases of microphthalmos according to the tonometric readings. It is difficult to discuss glaucoma in these cases with confidence due to the fact that the tonometer discs and foot plates are gauged for a normal adult cornea and not for the cornea of an infant or a microcornea. In these cases the determination of the intra-ocular pressure by palpation is perhaps more accurate than by tonometer. Terry stated that "in spite of glaucoma the eyes have not become enlarged." This has been our experience provided we have been accurate in determining the presence of an increased intra-ocular pressure. We have the impression, however, that these eyes are not prone to develop buphthalmos in the presence of what seems to us to be a definitely increased pressure.

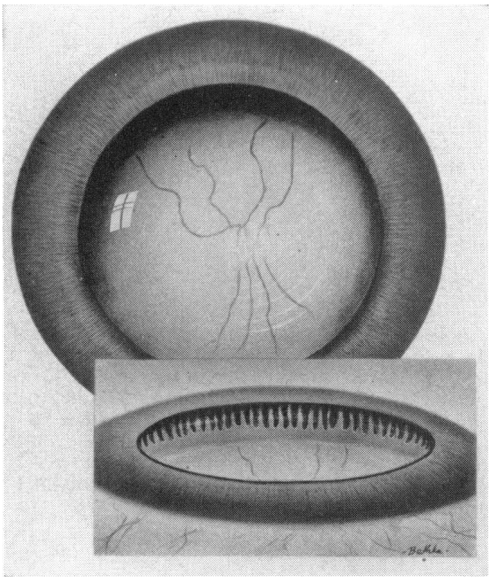

Fig. 1.—Clinical Type I lesion. Above is shown the concave opaque tissue containing blood vessels which radiate from the center. The density of the lesion decreases from the center to the periphery where it is more or less transparent. Below is shown the elongated ciliary processes inserting into the periphery of the retrolental opacity. This is the drawing of the left eye of the twin whose eye is shown in Fig. 14.

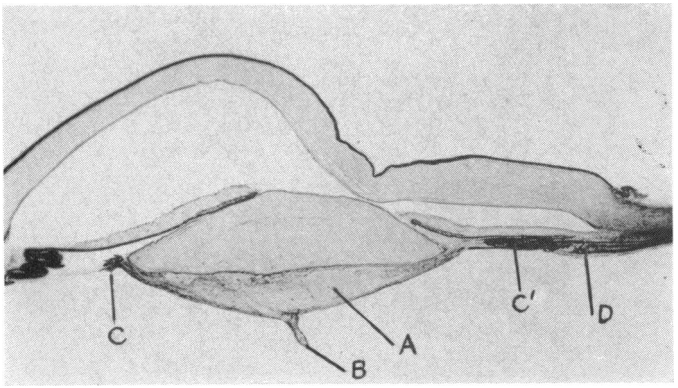

Fig. 2.—A portion of a human eye showing persistence and hyperplasia of the primary vitreous corresponding to clinical Type I. The retrolental fibrous mass is shown at *A* with the hyaloid artery at *B*. The lens is small. Ciliary processes *C* and C^1 extend to the fibrous mass and the retina is seen as far as *D*.

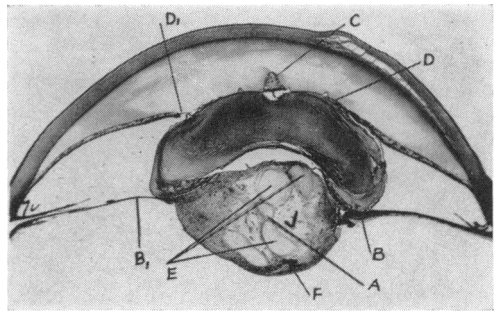

Fig. 3.—A section of a human eye showing persistence and hyperplasia of the primary vitreous corresponding to clinical Type I. The large retrolental mass *A* extends for some distance forward into the lens, giving the lens a kidney shape. At *B* and B_1 rudimentary ciliary processes along with some of the retina extend to the periphery of the mass. An anterior pyramidal cataract is shown at *C*. A pupillary membrane is seen at *D* and D_1. In the retrolental mass are large areas of cartilage, *E*, blood vessels and the tissue at *F* is thought to be smooth muscle. Peripheral synechiae are present.

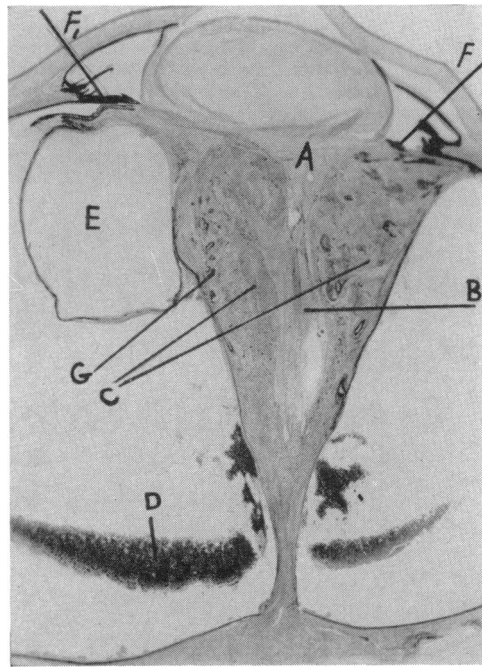

Fig. 4.—A section of a human eye showing persistence and hyperplasia of the primary vitreous corresponding to clinical Type I. The retrolental fibrous tissue at *A* extends down into the funnel *B* of the detached retina *C*. *D* represents subretinal hemorrhage, and *E* a retinal cyst. Elongated ciliary processes *F* and F_1 extend into the retrolental tissue. The retina is composed of undeveloped embryonic tissue with true rosettes at *G* and elsewhere. This represents an instance where the secondary vitreous has failed to form.

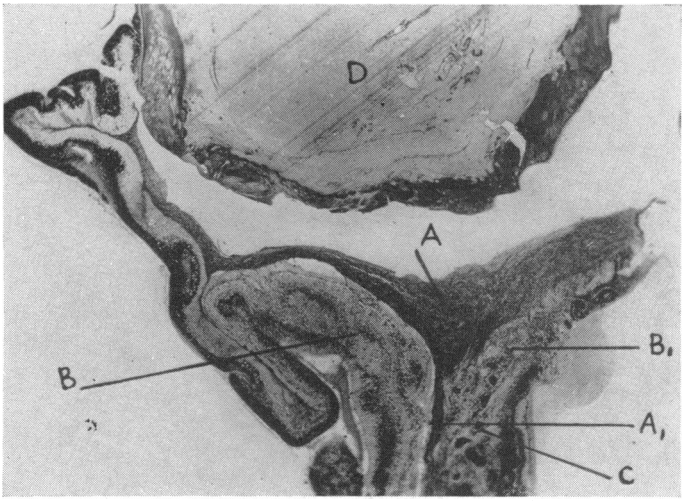

Fig. 5.—A section of a human eye showing persistence of the primary vitreous corresponding to clinical Type I. This is the eye of a three-day-old premature girl obtained at autopsy. The persistent primary vitreous A-A_1 extends down into the funnel of the detached embryonic retina B-B_1 which contains true rosettes C. The separation of the lens D from the retrolental fibrous tissue is an artefact. This represents an instance where the secondary vitreous has failed to form.

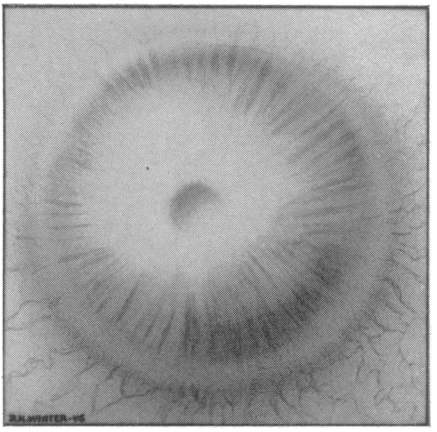

Fig. 6.—Clinical Type II. The opacity of the cornea is greatest in the central portion. There is diminished luster with stippling of the epithelium. The anterior chamber is absent where the lens and iris touch the cornea and is extremely shallow elsewhere.

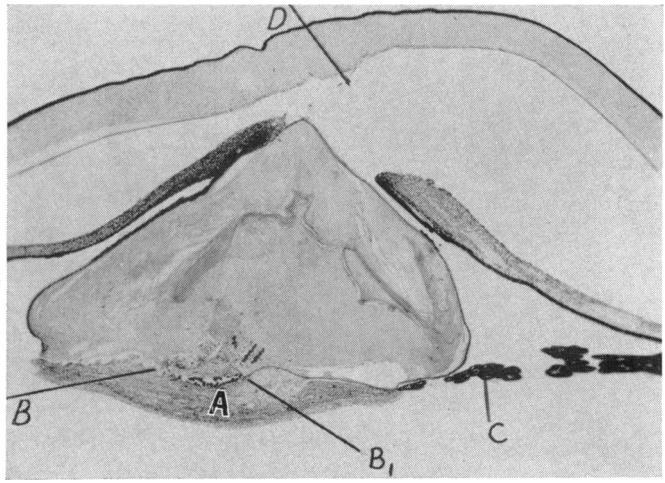

Fig. 7.—A section of a human eye showing persistence and hyperplasia of the primary vitreous corresponding to clinical Type II. The retrolental fibrous mass is shown at *A* and the posterior lens capsule is open from *B* to B_1. A higher magnification of this site is shown in Fig. 8. The ciliary processes *C* extend to the fibrous plaque. The lens is swollen and protrudes forward along with the iris to the cornea. In vivo the apex of the lens, along with the adjacent iris, rested against the cornea at *D* (see Fig. 9).

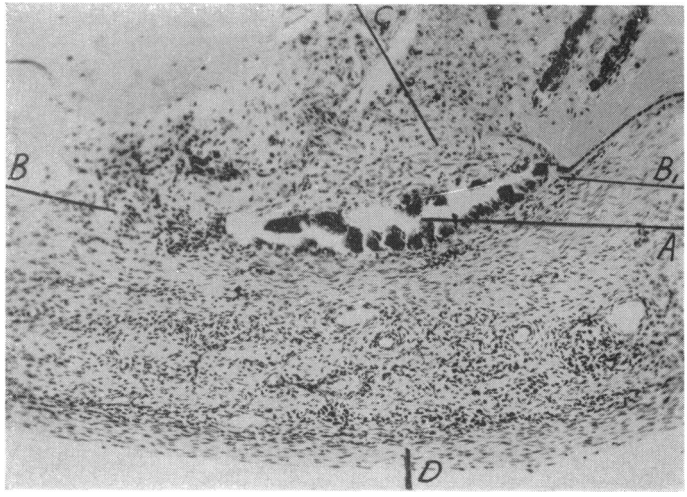

Fig. 8.—A higher magnification of the site from *B* to B_1 in Fig. 7. The opening in the capsule extends from *B* to B_1. The darker areas *A* represent calcium. The region designated *C* is fat, and the layer shown at *D* is smooth muscle. There are a considerable number of vascular channels.

One of the most important factors in the production of glaucoma is the narrowing of the anterior chamber and blocking of the filtration angle due to advancement of the iris-lens diaphragm. This is produced by: (1) Swelling of the lens from an opening in its posterior capsule; (2) contracture of the fibrous membrane back of the lens, pushing the lens and iris forward (suggested by Terry in a personal communication); (3) massive hemorrhage in the vitreous. Another factor is the embryonic filtration angle present in some of these cases.

The clinical appearance does not always remain the same but may present a changing picture. The later occurrence of glaucoma is particularly noted and concurrent with this is usually a decrease or even a disappearance of the anterior chamber, a stippling and opacity of the cornea of varying degree, and cataractous changes.

Hemorrhage may occur from the vessels in the opaque retrolental tissue. We have observed this clinically in three cases.

Typically, the retrolental tissue is concave (Fig. 2) but this tissue may be sufficiently hyperplastic to extend into the lens substance and therefore present a convex surface (Fig. 3). Blood vessels may or may not be seen in the opaque tissue and if present they may disappear in time.

The lens may become cataractous, preventing a view of the retrolental tissue. The cataract develops probably because the posterior lens capsule is opened (Fig. 7).

Type II.—This is characterized by an opacity of the cornea beginning in the central portion and spreading peripherally but always densest centrally (Fig. 6). The anterior chamber is absent or shallow. The corneal epithelium shows stippling, more marked centrally and diminishing peripherally. Glaucoma is present and if of long standing there may be buphthalmos. Type I may develop into Type II. The corneal changes which dominate the clinical picture are due primarily

to an advancement of the iris-lens diaphragm forward so that some of the iris and lens, and particularly the central portion, are in apposition to the posterior surface of the cornea (Figs. 7 and 9). This interferes with the impermeability of the corneal endothelium, permits aqueous to enter the stroma, and produces changes leading to opacification, including pannus formation. The same advancement of the iris-lens diaphragm embarrasses the filtration angle and usually leads to glaucoma. The presence of increased intra-ocular pressure tends to increase the corneal edema. As previously mentioned in discussing glaucoma, the advancement of the iris-lens diaphragm is due to swelling of the lens, contracture of the fibrous sheath back of the lens, and maybe intra-ocular hemorrhage. These factors will be considered further when the pathology is discussed.

The corneal opacity prevents an accurate view of the interior of the eye and frequently the retrolental fibrous tissue is not visible, especially through the central portion of the cornea. The presence of a partially or totally cataractous lens adds to the difficulties. This type may occur in premature or full-term infants and may be unilateral or bilateral. When Type I is present in the fellow eye the diagnosis is easier. This type is easily confused with congenital hydrophthalmos or buphthalmos.

Type III.—This is seen as a localized mass of opaque tissue along the posterior surface (Fig. 10), or the equator of the lens (Fig. 11), or in the region around the base of the vitreous. This tissue may or may not have visible blood vessels and if blood vessels are present they may in time disappear. Hemorrhage may occur in the tissue. If the lesion is located at the equator of the lens, or in the anterior vitreous around the base, it usually is accompanied by a detachment of the retina (Fig. 11) which points toward the lesion; *i.e.*, the elevated retina extends toward or into the tissue and the retina elsewhere may be in good position. A hole in

the retina or a disinsertion may be present. Long ciliary processes point toward the opaque tissue (Fig. 10). Strands or finger-like projections may extend from the mass posteriorly to the surface of the retina (Figs. 12 and 13). One case showed a coloboma of the optic disc.

Type IV.—This comprises instances where the central portion of the hyaloid system, or the greater part of it, remains with little or no retrolental portion (Fig. 15). This group is in contrast to Type III in which a part of the retrolental portion remains but no central hyaloid portion. The hyaloid system is a part of the primary vitreous so that anomalies of the two are associated with maybe the one or the other dominant in an individual case. Just as we can have on the one hand an isolated rest of the primary vitreous on the posterior surface of the lens so we can have on the other hand an isolated remain of the hyaloid artery and all combinations in between the two extremes.

We have, in our series, two particularly interesting cases belonging to this fourth type. The one was a 17-months-old infant who in the right eye had a massive vitreous hemorrhage preventing a view of the interior of the eye. The cause of the hemorrhage could not be determined until complete absorption occurred after several months when a persistent hyaloid artery was found. The other was a similar case of a boy aged 3 years who, on having the left eye bandaged after removal of a foreign body of the cornea, noticed that he could not see with the right eye. Under ether anesthesia, an extensive detachment of the retina was observed and the eye was enucleated with the clinical diagnosis of retinoblastoma. Pathologic examination revealed a vitreous hemorrhage and remains of the hyaloid system; no tumor was present.

In these two cases vitreous hemorrhage occurred from a persistent hyaloid artery and no doubt spontaneously as we know this does happen in other instances where elements of the primary vitreous persist.

The incidence of the four clinical types in our series of cases was as follows:

Type I	*Type II*	*Type III*	*Type IV*
16 bilateral 8 unilateral	9 bilateral 1 unilateral	2 bilateral 1 unilateral	3 unilateral
2 bilateral later progressed to Type II			
4 with Type I in one eye, and... Type II in fellow eye			
2 with Type I in one eye, and		Type III in fellow eye	
1 with Type I in one eye, and			Type IV in fellow eye

DIAGNOSIS

Clinical Type I especially can be confused with retinoblastoma. X-ray studies on 9 cases were negative for calcium. Transillumination of light is good except in those cases with hemorrhage. The most important diagnostic points are: (1) An opaque tissue just back of the lens with a saucer shape or anterior concavity, (2) long ciliary processes extending into the retrolental tissue. Retinoblastoma seldom occurs in a microphthalmic eye. Clinical Type II can be confused with other types of buphthalmos or with corneal changes secondary to intra-ocular inflammation. Clinical Type III can be confused with massive retinal fibrosis of children secondary to intra-ocular hemorrhage at birth.[25] Type IV can be confused with an intra-ocular growth when vitreous hemorrhage occurs.

EMBRYOLOGY

The various phases of this basic lesion consist of arrested development, arrested regression, and hyperplasia of the developing vitreous. A review, therefore, of the development of the vitreous is in order.

First Period (up to the 13 mm. stage).—At the 4.5 mm. stage, mesoderm begins to appear in the space between the lens plate and optic vesicle. This mesoderm is part of the vasoformative cells which will grow in through the fetal fissure to form the hyaloid arterial system.

By the 10 mm. stage large quantities of vascular mesoderm have grown in between the lens vesicle and the inner layer (retina) of the invaginating optic vesicle, forming the hyaloid artery which is entering the eye through the fetal fissure.

At the 12 mm. stage the vitreous is a mass of fibrils derived from the lens (ectodermal) and the retina (ectodermal) and joining up secondarily with fibrils (mesodermal) from the cells of the wall of the hyaloid artery.

At the 13 mm. stage the hyaline capsule surrounding the lens has completely formed. The lens no longer, therefore, contributes to the formation of vitreous. Vitreous fibrils, remaining adherent to the lens capsule, condense to form a thin fibrous envelope surrounding the lens and containing in its meshes the vessels of the vascular capsule. This fibrous capsule is the capsula perilenticularis fibrosa and originated from the lental part of the primary vitreous.

Development of vessels in the first period: At the 6 to 7 mm. stage the terminal part of the hyaloid artery ends near the posterior surface of the lens plate; it sends capillary branches into the meshes of the capsula perilenticularis fibrosa, forming a vascular net over the posterior surface of the lens. This is the beginning of the tunica vasculosa lentis, and is seen at the 8 to 9 mm. stage.

By the 10 mm. stage these vessels have extended anteriorly to form the lateral (equatorial), or capsulo-pupillary, portion of the tunica vasculosa lentis.

The vitreous as it now exists is known as the primary vitreous. It consists of ectoderm derived from the lens and retina, and of mesodermal vasoformative tissue which has formed the hyaloid artery, the posterior and lateral portions of the tunica vasculosa lentis (enmeshed in the capsula

perilenticularis fibrosa). The formation of the hyaloid capsule at the 13 mm. stage marks the end of the period of development of the primary vitreous.

Second Period (12 to 65 mm. stage).—By the 16 mm. stage arterial branches arising from the hyaloid have begun to project into the freshly forming vitreous and are termed the vasa hyaloidea propria.

By the 25 mm. stage the anterior, or pupillary, portion of the tunica vasculosa lentis has formed.

Up to 40 mm. the vitreous (ectodermal and mesodermal) is still full of vessels as far as the periphery, *i.e.*, to the internal limiting membrane. The vasa hyaloidea propria have reached their maximum development.

After the 40 mm. stage the smaller vessels in the vitreous begin to atrophy, the portions nearest to the lens remaining visible the longest, with the result that the region nearest the retina becomes free of vessels. This avascular portion is known as the secondary vitreous. Its appearance is due to: (1) Atrophy of the proximal ends of the vasa hyaloidea propria and (2) further formation of additional vitreous from the retina as the eye enlarges.

There is a cessation of growth of the primary vitreous, and a continued increase in the amount of secondary vitreous filling the eye as it enlarges, thus giving a relative, but not an absolute, decrease in the size of the primary vitreous.

The condensation line between the primary vitreous and the secondary vitreous forms the "wall" of Cloquet's canal. In the canal passes the hyaloid artery from the optic disc to the posterior surface of the lens.

The primary vitreous is funnel-shaped, narrow at the disc, and wide at the lens (Fig. 16).

Fate of the posterior portion of the tunica vasculosa lentis and the vitreous vessels.—After the 20 mm. stage, the caliber of the vessels decreases. At the 60 mm. stage, the vasa hyaloidea propria are the first to show signs of regression; they shrink in caliber first at their proximal ends (at their origin from

the hyaloid artery), losing connection with the hyaloid artery. Their distal ends remain attached to the vessels on the posterior surface of the lens and tend to curl up.

By 8½ months, all vessels except the main trunk have atrophied completely.

During the eighth month the main trunk of the hyaloid artery becomes impervious in its central part; atrophy proceeds more rapidly in its proximal portion, so it loses connection with the disc, and floats freely in Cloquet's canal from the posterior surface of the lens; it also tends to curl up. This portion atrophies during the first few years of life.

Pathology

We have available 17 eyes which contribute to the study of the pathologic processes concerned in the condition under discussion.

I

13 Eyes from 13 Different Cases of Persistent Primary Vitreous

The retrolental fibrous sheath.—Each eye had a fibrous sheath of varied thickness and shape behind the lens (Figs. 2, 3, 4, 5, 7, 9 and 12). In most instances this sheath conformed to the contour of the posterior surface of the lens but occasionally the sheath was flat and rarely protruded inward, presenting an anterior convexity instead of an anterior concavity. The sheath was composed mostly of fibrous tissue rather rich in blood vessels. In 7 of the eyes there was, along the posterior surface of the sheath, a definite layer which histologically resembled smooth muscle (Fig. 8D). This was thickest at the central area where it merged with the remains of the hyaloid system when present (Fig. 3F). The staining reaction of this tissue with hematoxylin and eosin was consistent with that of smooth muscle but with the trichrome stain it took more of a bluish color than adult smooth muscle but less than connective tissue. In 3 of the eyes the sheath contained fat (Fig. 8C), in 1 large areas of cartilage (Fig. 3E),

and in 1 an area of tissue interpreted as undifferentiated mesenchyme. Remains of the hyaloid system were noted in 4 eyes. This consisted of a patent vessel extending from the disc to the posterior central portion of the fibrous sheath. Very long, slender ciliary processes extended to the periphery of the sheath in all eyes. These processes were enmeshed in the periphery of the retrolental fibrous tissue either on one or both sides of the sections, and in 5 eyes the retina also. In 1 eye (Figs. 12 and 13) a fibrous strand coursed from the fibrous sheath across the vitreous cavity to the surface of the retina where traction probably from contracture caused a detachment of the internal limiting layer of the retina (Fig. 13D). In 2 eyes there was evidence that the membrane had grown; in the one it had extended along the anterior hyaloid membrane for a short distance and in the other it had extended into the lens substance as papillary ingrowths.

The lens.—The posterior lens capsule was open in 7 eyes (Figs. 7 and 8). In 2 eyes in which this was not seen, the capsule was thrown into wrinkles or folds apparently from the contracture of the fibrous sheath along its posterior surface. This may explain the mechanism by which the capsule is broken. The subcapsular epithelium extended under the posterior capsule in multiple layers in 5 eyes and in 1 eye around the region of the broken capsule this epithelium had proliferated. Apparently from the opening in the posterior capsule the cortical area of the lens was cataractous in 7 eyes (Fig. 7) and in 1 eye (Fig. 3C) there was an anterior polar cataract seen as a pyramidal shaped extension due to proliferation of the subcapsular epithelium. In the cararactous cortical material large lens cells were present in 2 eyes. Other changes consequent to the opening in the posterior capsule were swelling of the lens and mild inflammatory reaction in the fibrous sheath adjacent to the opening, including some phagocytes containing soft lens matter. The lens in 6 of the eyes was definitely smaller than normal (Fig. 2) and 3 of these were kidney-shaped with the concavity

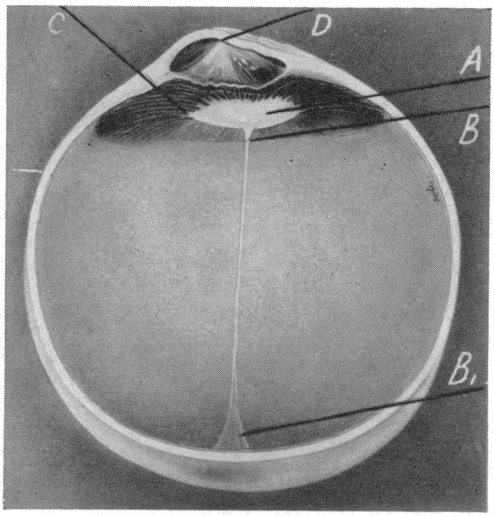

Fig. 9.—The gross appearance of the eye shown in Figs. 7 and 8. One side of the globe has been removed. The retrolental fibrous tissue is seen at *A* with the hyaloid artery *B* to B_1 coursing from the posterior surface to the disc. The zone of long ciliary processes extending into the retrolental mass is seen at *C*. The lens and iris extend forward to touch the cornea at *D*.

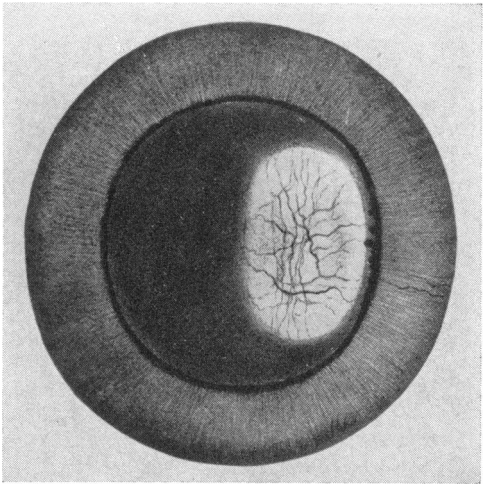

Fig. 10.—Clinical Type III lesion without retinal detachment at two days of age (noted by father who is a doctor). At two months of age a hemorrhage was noted over the surface of the lesion and in the course of several weeks this hemorrhage absorbed. After one and one-half to two years the blood vessels disappeared and now at the age of five years the lesion is the same size, somewhat less dense, avascular, and with a small localized almost chalky-white area interpreted as a focus of calcium deposit. The above illustration was made when the patient was nine days old and shows a vertically oval, whitish opaque, vascularized lesion located on the posterior surface of the lens. Elongated ciliary processes are seen extending toward the lesion. (Case of Dr. M. Uribe Troncoso.)

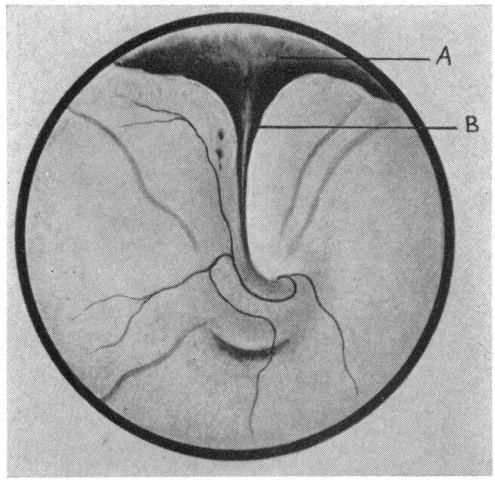

Fig. 11.—Clinical Type III lesion with retinal detachment. The fibrous plaque of tissue located at the posterior equatorial region of the lens is seen at *A* and from it a fibrous extension *B* courses backward to the retina which is detached. There was a partial coloboma of the optic disc. This patient who has a similar lesion in the fellow eye was one of triplets one of whom died and the other had persistence and hyperplasia of the primary vitreous clinical Type I in one eye and clinical Type II in the fellow eye.

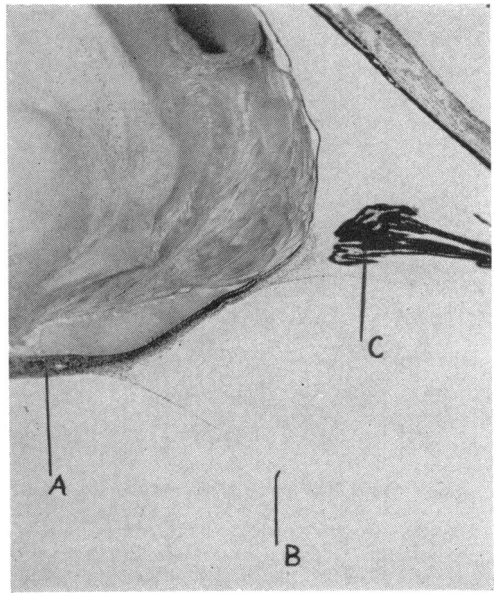

Fig. 12.—A section of a human eye showing persistence and hyperplasia of the primary vitreous corresponding to clinical Type III. From the retrolental fibrous plaque *A* a strand of tissue *B* crosses the vitreous to attach to the retina (see Fig. 13). Long ciliary processes *C* extend to the periphery of the retrolental tissue.

directed posteriorly (Fig. 3). In 4 eyes a portion of both the lens and iris were in contact with the posterior surface of the cornea (Figs. 7 and 9), causing corneal changes consisting of edema, some infiltration by leukocytes, and early pannus formation. In 1 of these eyes the lens was dislocated into the anterior chamber and in another a swollen cataractous pyramidal shaped lens protruded through the pupillary area to the cornea.

The retina.—In 8 of the eyes the retina was in place, appeared to have all of its elements, and no reason could be noted organically why it should not be capable of functioning. In 1 eye the retina although in place was definitely malformed as evidenced by a deficiency in the nuclear elements, rods, and cones. In 5 of the above-mentioned 9 eyes the retina proper extended together with the ciliary processes into the periphery of the retrolental fibrous sheath (Figs. 2 and 3). By contracture of the sheath the processes and retina seemed to have been drawn more and more toward the sheath. In only 1 eye had this process led to a slight detachment of the retina. This was only a small slit separation in the periphery on one side. In most instances the ciliary processes and retina were enmeshed in the sheath only on one side which was usually the nasal side. In 3 of the 9 eyes the ora serrata of the retina extended to the base of the iris or to the ciliary processes on one side.

There were 5 eyes in which the retina was completely detached funnel-fashion with the retrolental fibrous tissue occupying the base and extending varying distances into the funnel (Figs. 4 and 5). These 5 globes had identical pathologic changes and constitute a distinct group. They are characterized by embryonic retina as a solid mass of tissue just back of the retrolental fibrous sheath. In this retinal tissue true rosettes were seen in 4 of the eyes and calcium deposit in 3. Four of the eyes showed subretinal hemorrhage which was of a massive nature in 2. Four of the eyes showed malformed and embryonic filtration angle, ciliary body, and iris.

One of these cases was a 3-day-old premature girl weighing 2460 Gms. whose eyes were obtained at autopsy. The right eye was of normal size and microscopically showed persistence of the tunica vasculosa lentis and some primary vitreous, persistence of the hyaloid artery, coloboma of the iris, pupillary membrane, retinal folds, and ciliary processes on the posterior surface of the iris. The left eye (Fig. 5) microscopically showed microphthalmos, persistence of the primary vitreous, embryonic detached retina with rosettes and calcium deposition, coloboma of the iris, pupillary membrane, and ciliary processes on the posterior surface of the iris. The autopsy findings were prematurity, congenital abnormalities of the heart (atrophy and stenosis of the pulmonary artery, hypertrophy of the ductus arteriosus, partial defect of ventricular septum, right transposition of aorta, and congenital dilatation and hypertrophy of the right side of the heart), congenital absence of the right hypogastic artery, congenital fracture of the right parietal bone, craniotabes, congenital emphysema, congenital abnormality of the eyes, papilloma of the tongue, partial cleft palate, acute omphalitis, polydactylism of the right hand and both feet, physiologic jaundice, Meckel's diverticulum, accessory lobe of spleen, accessory lobe of liver, uric acid infarcts of kidneys, bicornate uterus, and bilateral club feet.

These 5 eyes seem to represent instances in which the secondary vitreous failed to form. To summarize, therefore, this is a subgroup of Type I characterized by a persistence of the primary vitreous and failure of the secondary vitreous to form, detached embryonic retina, later maybe subretinal hemorrhage, and frequently glaucoma. It may be that hemorrhage of the primary vitreous with organization and contracture also plays a part.

The iris and ciliary body.—Some degree of pupillary membrane was noted in 6 of the eyes (Fig. 3). Both the iris and the ciliary body were rudimentary or underdeveloped in 7 eyes and to a lesser extent in several others. As previously

stated, the iris along with the lens was in apposition to the posterior surface of the cornea either in part or totally in 4 eyes. Peripheral synechiae were present in 5 eyes. The filtration angle was embryonic or underdeveloped in 5 eyes.

Glaucoma.—There was histologic evidence of glaucoma in 6 eyes—peripheral synechiae in 5, cupping of the disc in 1, and hydrophthalmos in 3.

II

Two Eyes from One Case of Persistent Primary Vitreous Indicating the Relationship to Hemangioma

Of twins born three months prematurely the one lived and no abnormalities were noted except of the eyes. Clinically both eyes showed the following (Fig. 1)—the anterior chambers were almost absent and back of each lens there was a vascular, white, saucer-shaped sheath and long ciliary processes were visible around the periphery. The diagnosis of persistent primary vitreous of each eye was made.

The other twin, who weighed one pound ten ounces at birth, showed, when several weeks old, an exophthalmos of the right eye and examination of the interior of this eye showed a detachment of the retina above with impaired transillumination over the detached area. Examination of the left eye was negative. After many attacks of cyanosis with cessation of respiration the infant died and an autopsy was performed.

The autopsy findings were as follows—prematurity; hemangiomata of the pharynx, carotid body on the right side, orbit on the right side, both retinae and adjacent vitreous, and choroidal plexus of the fourth ventricle; extramedullary blood formation in the spleen, liver, adrenals, kidneys, and lymph nodes; splenomegaly; jaundice; lobular pneumonia of the right lower lobe; accidental involution of the thymus gland; accessory adrenal gland attached to the fallopian tube; and patent foramen ovale.

Microscopic examination of the eyes shows: *Right eye* (Fig. 14): The retina is detached over one-half of the globe and there is a tear at the ora serrata which may be an artefact. Over the surface of the retina, and particularly that portion detached, there are many blood vessels without much supporting tissue extending from the nerve head to a point just behind the ora serrata. These vessels and their supporting tissue are attached to the inner surface of the retina. There is some vitreous hemorrhage which apparently came from the epiretinal vessels. The hemorrhage has partially organized and the contracture of this, perhaps together with the supporting fibrous tissue of the vascular layer along the retinal surface, has led to detachment of the retina. At no point can excessive blood channels be seen in the fiber layer of the retina. The filtration angle is embryonic in type.

Behind the globe there is a large non-encapsulated hemangioma (Fig. 14D) containing large blood-filled sinuses surrounded by hyperplastic endothelial cells.

Left eye: The retina is in position but along its entire surface there are small blood vessels either as a thin layer or as localized clumps with relatively little supporting tissue. These same vessels are also seen anterior to the nerve head. In places these vessels over the retina lie along the surface of the internal limiting membrane while elsewhere they appear in the nerve fiber layer. Some vessels parallel the surface while others course obliquely or perpendicularly to the surface.

The angles are embryonic and the iris stroma appears more vascular than usual. The surface markings of the iris are obscured by a vascular tissue.

Pathologic diagnoses of eyes and adnexa were hemangioma of the right orbit; detachment of the retina of the right eye due to vitreous hemorrhage, organization and contracture from an hemangioma of the primary vitreous and vascular layer of the retina; and hemangioma of the primary vitreous and vascular layer of the retina of the left eye.

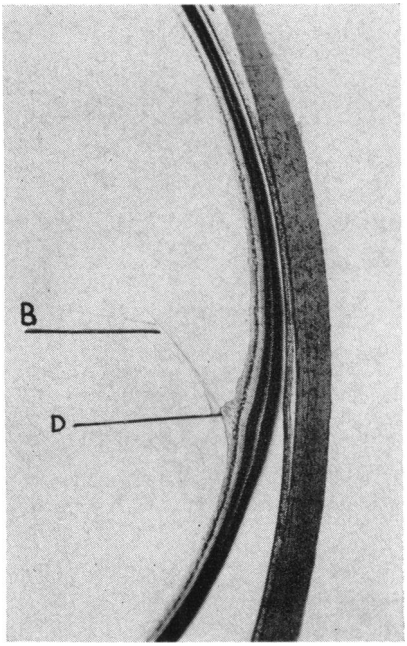

Fig. 13.—The fibrous strand shown in Fig. 12 at *B* is seen here *B* attaching to the inner surface of the retina which it is detaching by its pull at *D*.

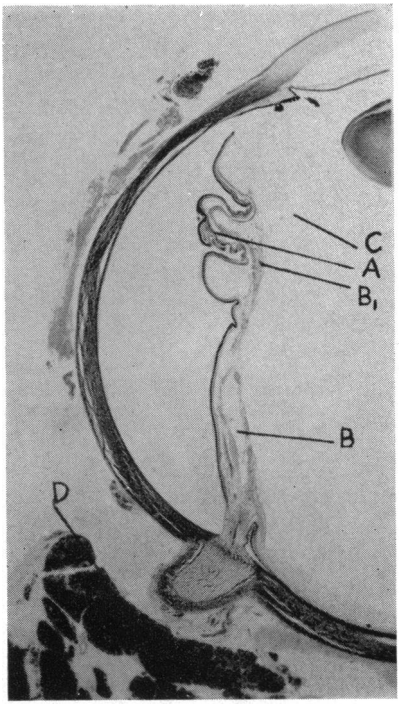

Fig. 14.—The section of an eye of a three-month-old premature baby girl obtained at autopsy. The lesion corresponds to clinical Type III. The twin of the patient lived and has typical clinical Type I lesions in each eye (see Fig. 1). Over the surface of the detached retina *A* is hemangiomatous tissue *B* and B_1 in which is some hemorrhage. Contracture has detached the retina and thrown it into folds. A strand of fibrous tissue *C* extends from the hemangiomatous tissue to the posterior surface of the lens. *D* shows a portion of a typical hemangioma of the orbit which produced proptosis. The fellow eye showed a layer of flat, hemangiomatous tissue along the surface of the retina. (See autopsy findings in text.)

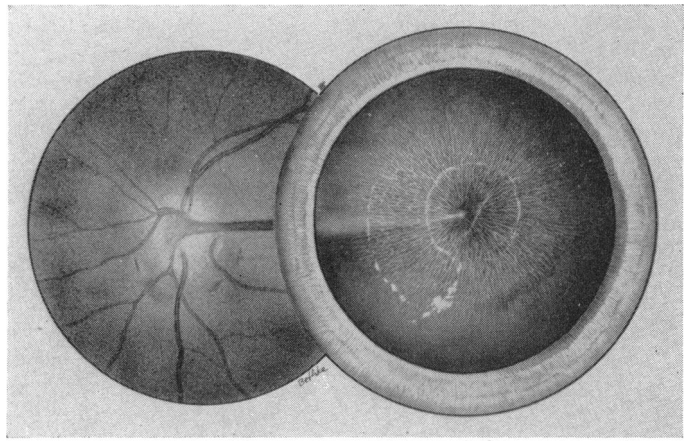

Fig. 15.—The clinical appearance of a case in which the features of clinical Type IV dominate those of clinical Type I. The patent hyaloid artery containing blood is seen extending from the disc to the posterior surface of the lens while along the posterior surface of the lens there is a fine lacelike pattern of fibrous tissue which might be interpreted as some persistence of the primary vitreous without hyperplasia. This is in contrast to clinical Type I in which the persistence of the hyaloid system plays a secondary role. Clinical Type IV in its most typical form is persistence of the hyaloid system without the retrolental lesion just as clinical Type I is the retrolental lesion without the hyaloid system. (Case of Dr. Charles A. Perera.)

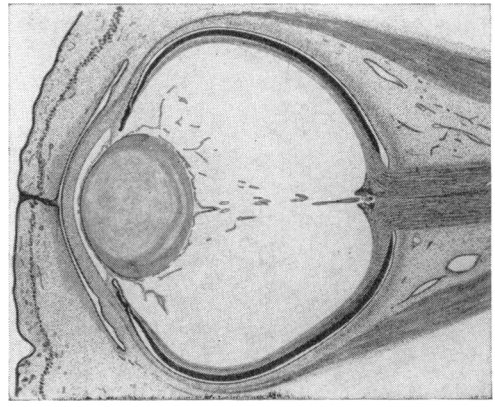

Fig. 16.—The primary and secondary vitreous of a 130 mm. fetus as depicted on Tafel XXII in the Atlas zur Entwicklungsgeschichte des Menschlichen Auges, 1911, Bach und Seefelder. The hyaloid system, together with the primary vitreous, forms a vascularized, funnel-shaped zone of mesoderm extending from the retrolental region to the disc.

III

One Eye with a Persistent Hyaloid Artery from which a Spontaneous Vitreous Hemorrhage Occurred

This is the globe removed from the boy aged 3 years described on page 171.

IV

One Eye of a Red Setter Puppy showing Persistence and Hyperplasia of the Primary Vitreous

A white reflex was seen through the pupil and the eye was enucleated with the idea that the lesion might represent a retinoblastoma. Microscopic examination showed the typical lesion representing clinical Type I.

Etiology

We feel that the lesion represents the congenital remains or persistence of embryonic tissue and, therefore, is not essentially an acquired one. Sixty per cent of our cases occurred in premature infants. We are inclined to believe that the same factor which precipitates early birth may also cause the eye lesions. Infection as the cause of congenital defects is receiving special attention now due to the accepted connection between maternal rubella during pregnancy and congenital anomalies of the offspring. Also, toxoplasmosis may occur apparently in a subclinical form in the pregnant woman and produce congenital eye defects as well as choroiditis in the offspring which may be born prematurely. One of our cases was a premature boy whose right eye showed persistence and hyperplasia of the primary vitreous (clinical Type I). The left eye, which was of normal size, showed an area of juxtapapillary choroiditis not unlike that caused by the toxoplasma.

We do not have convincing evidence indicating that the lesion occurs as the result of maternal infection. We obtained in 12 of the mothers a history of uterine bleeding ranging

from the second to the eighth months. The duration varied from a day to several months. Three of the mothers with uterine bleeding also had upper respiratory infections with temperatures and two mothers without uterine bleeding also had what was thought to be upper respiratory infections.

TREATMENT

Surgery has been necessary for glaucoma 12 times. Iridencleisis, cyclodialysis, trephining, and iridectomy with sclerectomy have been tried and iridencleisis seems to be the most effective. The iris is usually friable and a keratome section must be placed accurately because of the shallow anterior chamber. Because accurate examination, including tonometric readings, is not possible without general anesthesia, valid results of the glaucoma surgery cannot be given.

On the premise that the retina seems capable of functioning, judging by the microscopic examination of these eyes, an effort has been made to salvage vision in six eyes of six patients. The object has been to remove the lens substance by repeated discissions and finally to make a vertical cut in the retrolental fibrous tissue with de Wecker's scissors. When the discission is done the lens substance tends not to become opaque, swell, protrude into the anterior chamber, and absorb. Very little seems to happen when the lens capsule is opened. The capsule opening, therefore, can be very extensive without fear of undue swelling. After it was thought that the lens substance had been dissipated for the most part then a central vertical incision was made through the remaining tissue with De Wecker's scissors. This maneuver was followed by hemorrhage which filled the anterior chamber but absorption took place in due time. In one instance three discissions and two incisions with De Wecker's scissors were necessary. In two of the six cases the mother states that the baby can pick up objects and believes this vision comes from the operated eye. These procedures have never left

the pupillary area completely clear and leave a lot to be desired.

We intend to try irradiation on some of the selected cases as soon as the patients are older.

Discussion

We have deduced from the clinical and pathologic findings that the basic lesion is a persistence in part or *in toto* of the primary vitreous (Fig. 16) with or without hyperplasia and with or without secondary changes consequent to hemorrhage, opening of the lens capsule, and glaucoma. As the primary vitreous is mesenchyme it is not surprising that the various tissues into which the mesenchyme can develop are seen in the hyperplastic retrolental tissue, to wit: fat, cartilage, smooth muscle, blood vessels, and connective tissue. Haden[26] in his description of the embryology of the vitreous, states, "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."

There is a tendency for hemorrhage to occur in the persistent primary vitreous and this may lead to organization, contracture, and their attendant sequelae. There is also frequently an opening in the posterior capsule of the lens and this leads to cataract with lens swelling and maybe some inflammatory changes. The corneal changes seen in clinical Type II are due primarily to the entrance of aqueous into the stroma caused by the contact of a portion of the lens and iris with the posterior surface of the cornea but augmented by the presence of glaucoma.

There seems to be evidence to indicate that the formation of the secondary vitreous plays a role in some of the pathologic findings. If fibrous strands of the primary vitreous remain adherent to the inner surface of the retina then, when

the secondary vitreous forms, the retina may be detached. All degrees of this process may be seen, even to the point where the primary vitreous is adherent to the entire inner surface of the retina and the secondary vitreous either fails to form or forms sparingly with complete detachment of the retina.

There seems to be some relationship of the lesion under discussion to hemangioma. The primary vitreous is for the most part angioblastic mesoderm and in some areas of microscopic sections studied, the retrolental tissue showed highly vascularized areas not unlike hemangiomatous tissue. Most hemangiomas encountered over the body are viewed as having their origin from congenital rests of angioblastic mesoderm. Basically, therefore, the relationship exists and this is borne out by both our clinical and pathologic findings. We noted hemangiomatous lesions of the skin of the face, scalp, body, or extremities in seven of our cases. We also had a case with the clinical Type I lesion associated with microphthalmos on one side and on the other side hydrophthalmos due, we thought, to hemangioma of the choroid together with a hemangioma of the skin of the upper lid. Furthermore, in describing our pathologic material we cited the autopsy findings of a case with hemangioma of one orbit, both retinae and adjacent vitreous, and elsewhere over the body whose premature twin had typical clinical Type I lesions of both eyes. The fact that the basic lesion in both the persistence of the primary vitreous and in hemangioma consists of congenital remains of angioblastic mesoderm makes the two conditions fundamentally related.

We wish to express our thanks to Drs. R. Franklin, D. B. Kirby, J. H. Dunnington, C. A. Perera, R. G. Ingalls, R. C. Castroviejo, Olga Sitchevska, R. T. Paton, H. S. McKeown, E. L. Goar, T. H. Johnson, M. Uribe Troncoso, F. Barber, R. B. Thomas, and R. N. Berke for their kindness in allowing us to see their cases and to incorporate them in our work.

We are indebted to Miss Lily Kneiske for her assistance.

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DISCUSSION

PROF. IDA MANN, Oxford, England: I wish first to congratulate Drs. Reese and Payne on this interesting presentation of a very careful piece of work. These cases have been recognized since the middle of the nineteenth century and a great variety have been described as it is doubtful whether any two cases are completely identical. The present collection and classification brings out very well the part played in their production by the primary vitreous and also their association with other developmental anomalies. These cases are all good examples of the general principle of the production of developmental anomalies through arrest at a definite stage of intra- or extra-uterine life followed by aberrant growth. This aberrant growth may lead to excess normal tissue or, by atypical differentiation of pluripotential cells, to the appearance of tissue abnormal in that situation; *e.g.*, cartilage and unstriped muscle in the posterior vascular capsule. That prematurity is often

a feature of these cases is not surprising since the interference with development seen in the eye may be part of a general aberration manifesting itself both as prematurity and in various associated malformations (*e. g.*, of heart, lungs, palate and extremities as described by Doctor Reese). The primary cause of the whole clinical picture is likely to be a maternal upset probably nonspecific in nature but specific in time. That this can happen has been shown by many experimental embryologists, and is now known to occur in man; *e. g.*, in rubella cataract and in the maldeveloped retinae of foetuses X-rayed *in utero*. I would therefore like to suggest to Dr. Reese that it would be more helpful if he would consider classifying his cases, not on clinical findings alone, but into groups based on the probable stage in development at which the initial arrest occurred. Judging the cases from a purely embryologic standpoint I should say his subgroup of Type I begins earliest, probably at about the 15 mm. stage and certainly before the end of the organogenetic period. May I also urge in the description of this group the use of the term "failure of coaptation of the retina" in place of "detachment"?

His Type III is also early, beginning certainly before the third month and is allied to congenital retinal septum which can also be explained as a localized linear failure of secondary vitreous.

Type II probably begins between the fifth and sixth months as there seems to be an accompanying arrest of formation of the angle of the anterior chamber while those cases of Type I which subsequently develop glaucoma arise possibly only a little later. Type IV is obviously related to an arrest at the very end of foetal life only (during the eighth month).

This classification could be checked and amplified if very accurate data could be obtained of the time of the maternal upset as evidenced by the occurrence of bleeding and of respiratory infections noted in 14 of the mothers. The cases would then probably be seen as a continuous series rather than as sharply differentiated types.

DR. F. H. VERHOEFF, Boston, Mass.: I think this is a very interesting and instructive demonstration. In specimens sent me for examination by the Army Medical Museum I have seen all of the conditions described by Dr. Reese. I was particularly interested in his finding of cartilage in the tissue. In the Army Medical Museum a recent specimen, which I had believed to be unique, showed this even better than the one he demonstrated on the screen.

Dr. Reese spoke of hemorrhages occurring in some of these eyes

I should like to ask him if he has ever seen hemorrhage extending from the retrolental tissue into the lens. I have seen this in at least one case.

I think his classification is a most useful one, and in the future will prove of great assistance in the description of such cases. To follow Prof. Mann's suggestion, all he will need to do is to assign certain embryonic periods to the stages he has mentioned.

DR. HENRY HADEN, Houston, Tex.: Dr. Reese and Dr. Payne are to be congratulated upon this comprehensive study.

I agree with them that the term persistence and hyperplasia of the primary vitreous is appropriate for the congenital abnormalities under discussion. The primary vitreous is composed of mesoderm which flows in between the rim of the optic cup and the lens, the mesoderm that accompanies the hyaloid artery as it passes through the foetal fissure into the optic cup, and ectodermal fibers derived from the lens and inner wall of the optic cup.

Toward the end of foetal life the mesodermal part of the vitreous disappears and the permanent vitreous is exclusively ectodermal in origin. Under certain circumstances a portion of the mesodermal tissue is not absorbed and a variety of lesions such as Dr. Reese and Dr. Payne have described are the result. The size, position, and style of the lesion is influenced by the foetal age at which the normal recession of the primary vitreous ceased.

I do not see why one should look farther for the nature of these congenital anomalies. A glance at a few sections of the developing vitreous should make this clear.

DR. T. L. TERRY, Boston, Mass.: That Drs. Reese and Payne hold certain views in disagreement with mine is encouraging. What stimulates search for an unknown truth more than theories that are at variance! I am sure that we shall find mutual pleasure and satisfaction in working out an agreement as full understanding of the process is attained.

Their belief that the abnormal development occurs before birth is the most outstanding difference. The evidence is based on one instance in which the infant weighing 3 lbs. 5 ozs. was observed on the day of birth to have the disease process well developed. Warkany has proved that the young born of rats in an extreme stage of vitamin A deficiency develop abnormal eyes early in gestation. We have confirmed his findings. Chief among these abnormalities is the growth of mesodermal tissue in the meshwork of the tunica vasculosa lentis behind the lens. Although such extreme

depletion of vitamin A is not likely in the human, it could cause such a sequence of events. It may account for the lesion on which Drs. Reese and Payne base their conclusion of intrauterine development of the process in their most dramatic case.

The process can and does develop during intrauterine life. It has been observed in full-term infants at time of birth. I agree with Reese and Payne that this is probably a process identical with that seen in the premature infants, but I do not believe we have proof yet that they are identical. The frequency of the disease is greater, the more premature the infant. The lantern slide shows graphically the increase of frequency of the process the more prematurely the infants are born. The causes of prematurity in infants with and without the ocular malady are not greatly dissimilar, and in many instances the cause is unknown. In some of the instances of spontaneous prematurity the mother had no illness and no known disability before the premature birth. I would expect the ocular defect to manifest itself at birth or very soon thereafter in premature infants nearing term, whereas in the infants weighing three pounds or less, it would not appear for weeks or even months. It is to be regretted that Reese and Payne did not indicate the stage of prematurity of each of their cases.

A routine study of the eyes of premature infants, followed from day of birth to a time when all danger of retrolental fibroplasia development has passed, has shown me that this disease process can and does become manifest in some premature infants after birth. Dr. Stewart Clifford, who follows closely the premature infants after their incubation, has referred a case to me in which the retrolental tissue was a small opaque spot in the back of the lens resembling a giant Mittendorf's dot. In one week this opaque area had increased so that it covered perhaps half of the back of the lens, and the anterior chamber was becoming shallow. At the end of the second week the chamber was becoming more shallow. The opaque tissue covered the entire posterior lens surface. I have seen two other such cases. Clifford and I have seen other cases jointly in which the eyes looked normal at birth, but after discharge from the hospital the opaque retrolental tissue developed and the anterior chamber became obliterated, although we did not see these patients while the fibroplasia was developing. Clifford and I have not been able to determine during their incubation which premature infants will develop retrolental fibroplasia, but Clifford has shown that some 12 per cent, or one out of eight, will develop it some weeks or months after birth.

When the true nature of this condition is fully understood, there will be a satisfactory explanation for isolated observations which now seem in conflict. As has been said often, full-term birth, indeed, is only an incident in life, but in extremely premature birth there is a tremendous revolution of physiologic processes. The organs of digestion, respiration, temperature regulation, internal secretion and even the eyes are called upon to function. An abnormal process can be instituted by this precocious function sufficient to cause such an aberration of ocular development. Why both eyes or the eyes of both twins are not uniformly involved is another puzzling finding in the present state of our ignorance. The view that there is an external exciting cause for this abnormal development and that the most common single factor in many of the individuals who develop it is extremely premature birth produced by a variety of causes, leads to a definite experimental and investigative approach.

According to Clifford, the only associated defect is in lack of mental development present in some of these infants. The occurrence of angioma I first noted in a patient from Havana, one whom Reese may also have seen. Since then I have found angioma in 16 additional cases. I have not found any statistics showing the frequency of angiomata in infants as a whole, although I am told it is high.

A less important difference in our views is that of terminology. The disease, I believe, represents a growth of embryonic connective tissue in the mesh of the closed tunica vasculosa lentis, which in part, concurrently, or later reopens before its lumen has become impervious. I say "reopen" because the vessels of the tunica vasculosa lentis system had previously been observed when the eyes of extremely premature infants were first examined and had become invisible when they stopped carrying blood. It is not a persistence of the vascular tunic in its embryonic and early fetal state in a region where no such solid tissue is ever encountered during normal development. Thus, I object to the "persistence" used in the title, which the essayists suggest. I consider primary vitreous to be the total mass of mesodermal and ectodermal syncytium between the lens and the retina up to the 40 mm. stage. That blood vessels are a part of it, I do not agree, although blood vessels for a time pass through it and perhaps contribute to its early growth. When the blood vessels disappear, I do not visualize the primary vitreous changing over to secondary vitreous, but it persists throughout life as the less viscous material filling the so-called retrolental space and Cloquet's canal. In this view, Professor

Ida Mann told me she was in agreement. If it is correct to consider the hyaloid artery and tunica vasculosa lentis to be an integral part of primary vitreous, then the name "Hyperplasia of the Primary Vitreous" loses much of its objection to me. Primary vitreous reaches its full growth at the 40 mm. stage. Were the vitreous a perfect sphere instead of part of a sphere, its total volume would be less than .420 cmm. The volume of the adult vitreous approximates 4,300.00 cmm. If the retrolental fibrous proliferation represents a hyperplasia of the primary vitreous, even though it does not permeate the entire vitreous of these small eyes, it would represent a very great hyperplasia indeed. Exception might be taken to the length of the name suggested by Reese and Payne. Of all the terms formerly used, "fibrovascular sheath" is perhaps the least objectionable, but it does not locate the disease process in any one organ of the body or in any position in the eye, as does "retrolental fibroplasia."

That a name like "retrolental fibroplasia" is needed is shown by the frequent repetition of some such terms as retrolental "fibrous mass . . . fibrous membrane back of the lens . . . retrolental tissue . . ." occurring sometimes more than once to a page in the essay of Reese and Payne.

Because of the slow manner in which the lens material is absorbed following discissions, probably the result of reduced production and accumulation of aqueous humor in the eye, I have been eradicating the lens by a linear extraction associated with an iridectomy above and an iridotomy below in an attempt to prevent blocking of the pupil. I have used this operation only when the anterior chamber is absent, lento-corneal synechiae are present, and central corneal opacities are developing. An injection of normal saline solution into the anterior chamber demonstrated the presence of these conditions. Careful suturing of the wound permits the retention of injected air in an attempt to prevent recurrence of the anterior synechiae. Following the operation an adequate anterior chamber is usually present.

The suggestion of radiation to close the blood vessels in the fibroplastic tissue is a sound one which I shall try.

The essay of Reese and Payne indeed contains a great deal with which I fully concur. The quality of their illustrations deserves the highest praise.

DR. REESE (closing): We stated that our classification was purely a clinical one and adopted for conveniency. I think Professor Mann's idea to make the classification include the stage at which the mal-

development in the embryo occurs is well worth while. I agree with her that the term "detachment of the retina" employed with respect to our subgroup of Type I might more accurately be replaced by the term "failure of primary coaptation of the retina."

We appreciate very much Dr. Haden's beautiful sections showing the embryology of the primary vitreous and the manner in which it undergoes involution.

Dr. Verhoeff mentioned the relationship to hemangioma. I stated that our conception of a hemangioma is that it represents a congenital rest of angioblastic mesoderm which later begins to grow into a neoplasm. It does not behave like a true neoplasm clinically because angiomas do not have as a rule the capacity for unlimited growth. I tried to point out the fundamental relation of hemangiomas and this lesion and to give what evidence we have that the two may be associated.

We tried to point out what evidence we had of the relationship of the lesion under discussion and infection. We do not believe that this evidence is convincing.

We have never noted hemorrhage extending from the retrolental tissue into the lens as Dr. Verhoeff has.

We believe this lesion is congenital irrespective of whether it occurs in premature or in full-term infants. The matrix of the lesion is present at birth with varying degrees of hyperplasia subsequently. This interpretation is not based solely upon one case as stated by Dr. Terry but upon several factors: (1) In premature infants the lesion was observed at birth in one case and less than one week of age in one case; in full-term infants the lesion was noted at birth in three cases and less than one week of age in four cases. The clinical and pathologic features appear identical in both groups. (2) The hyaloid artery, if absent at birth, never develops later; rather, if it is observed later it was necessarily present at birth. In other words, the hyaloid artery is always a congenital manifestation. The hyaloid artery is frequently associated with the condition under discussion. (3) The various tissues (connective tissue, blood vessels, fat, cartilage, and smooth muscle) seen in these lesions take origin from mesoderm. Mesoderm does not form after birth.

Dr. Terry disagrees somewhat with our conception of the primary vitreous. It seems to me our views in this regard are the ones generally advanced by the embryologists. Irrespective of names there certainly occurs in embryonic life an angioblastic mesoderm inside the eye and normally this disappears. When it persists and becomes hyperplastic we believe it gives rise to the various lesions described in this general group.

Dr. Terry refers to a case in which he observed an increase in an island of retrolental tissue resembling a giant Mittendorf dot. One of our cases (Fig. 10) was perhaps similar when first observed a few days after birth. After four years our case showed no increase in size and the blood vessels disappeared.

Dr. Terry's case in which he observed the development of this lesion from birth is difficult to explain on the basis of our conception of the lesion. I imagine it can be explained on the ground that there was a small area of that retrolental tissue present and this showed an unusual degree of rapid hyperplasia.

If anyone plans to study this basic lesion experimentally we think the dog might be a good medium. We base this on the fact that we have seen a typical Type I lesion in a red setter puppy. This puppy had a white reflex in the pupil, and because of the possibility of retinoblastoma an enucleation was done. Sections showed typical retrolental fibrous tissue with a hyaloid artery.

THE EXPOSING AND FIXING OF THE EYE IN THE EARLY DAYS OF CATARACT EXTRACTION

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Ophthalmology, which might be likened to a highly specialized organ in the "body medical," has been characterized by an unfailing tendency to absorb into itself with imperious force whatever good might come within its grasp, while rejecting from its constitution all empiric elements which might have affected its vitality and, so to speak, metabolically, hinder the development of a creature which has, in time, influenced all medicine and led to the happiness of the world. It should be profitable for us, at this fiftieth century since the earliest recordings, to remind ourselves that that development has been but slowly progressive and that the hidden forces within the body were derived usually from single inventions or observations.

Today the tyro is inclined to accept the present status as he finds it, oblivious of how laboriously the science has