On the development and abnormalities of the zonule of zinn / by E. Treacher Collins.

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ON THE DEVELOPMENT AND ABNORMALITIES OF THE ZONULE OF ZINN.

By E. Treacher Collins,

Curator of the Museum.

Very little is known as to the development of the suspensory ligament of the lens or zonule of Zinn. Balfour* in his work on Comparative Embryology thus refers to it:—"The development of the zonula of Zinn in mammalia, which ought to throw some light on the nature of the vitreous humour, has not been fully investigated. According to Lieberkühn, this structure appears in half-grown embryos of the sheep and calf. He says, 'At the point where the ciliary processes and the ciliary part of the retina are entirely removed, one sees in the meridian bundles of fine fibres, which correspond to the valleys between the ciliary processes and fill them; also between these bundles there extend, as a thin layer, similar finely striated masses, and these would have been on the top of the ciliary processes.' He further states that these fibres may be traced to the anterior and posterior limb of the lens capsule, and that amongst them are numerous cells. Kölliker confirms Lieberkühn's statements. There can be little doubt that the fibres of the zonule are of the nature of connective tissue; they are stated to be elastic. By Löwe they are believed to be developed out of the substance of the vitreous humour, but this does not appear to me to follow from the observations hitherto made. It seems quite possible that they arise from mesoblast cells which have grown into the cavity of the vitreous humour; solely in connection with their production."

In the tenth edition of Quain's Anatomy,† we find:—"The development of the hyaloid membrane has not been

* Vol. ii, p. 495.

† Vol. i, p. 87.

fully traced out, and the same may be said with regard to the zonule of Zinn. They are probably both formed by part of the same mesoblast as forms the vitreous humour (Lieberkühn, Angelucci)."

All this leaves the matter very indefinite. My attention was first directed to it by the examination of an eyeball which had been enucleated from an infant aged three months, under the supposition that it contained a new growth. Pathological examination, however, revealed that the opaque mass behind the lens which had been taken for the growth was really a collection of cells and fibres into which a persistent hyaloid artery, still patent and carrying blood, passed and broke up. The chief interest of the specimen, however, centred in the fact that it exhibited the fibres of the suspensory ligament in all stages of their development; several of these are shown in Figs. 1 and 2. The fibres of the lens, instead of developing in their normal way, filling and rendering tense the capsule in which they were contained, had undergone retrogressive changes, and left the capsule lax and wrinkled. Whether this was the result of the persistence of the hyaloid artery, or whether it had persisted as the result of changes in the lens, I am unable to determine. Anyhow, as the result of the lax condition of the capsule, the fibres of the suspensory ligament do not appear to have become stretched to their usual extent, and hence we have exhibited all stages of delayed development in them. The full details of this case are given at the end of this paper.

I will now sketch what I find, from the examination of this eye, and from the examination of sections of several human fœtal eyes, to be the course of events in the development of the zonule of Zinn, first briefly stating the steps preparatory to it.

The process of cuticular epiblast, which dips in to form the lens, indents the primary optic vesicle, and at first lies in contact with what becomes the inner layer of the

secondary optic vesicle. Gradually the ingrowing process gets cut off from the surface epiblast, forming thus the primitive lens, which next becomes separated from the inner layer of the secondary optic vesicle at the posterior part, by the formation of the vitreous. It remains, however, for a long time in contact with it at its sides, that is, at that part in which subsequently the ciliary body becomes developed. The lens becomes encircled by what is termed its fibro-vascular sheath, derived in part from the central artery of the vitreous, and in part from vessels growing in between the lens and the cornea. The portion of the inner layer of the secondary optic vesicle still in contact with the lens, that is, the pars ciliaris retinæ, acquires adhesions to this sheath. Then, as the eyeball enlarges, it does so at a greater rate than the lens, so that a portion of the ciliary body which was in contact with the lens grows away from it, and the adhesions which have formed between them become stretched, and the cells forming them much elongated, until only fibres with nuclei lying on them can be distinguished, and ultimately the nuclei also go, leaving only the delicate fibres of the suspensory ligament as we see them in the adult eye.

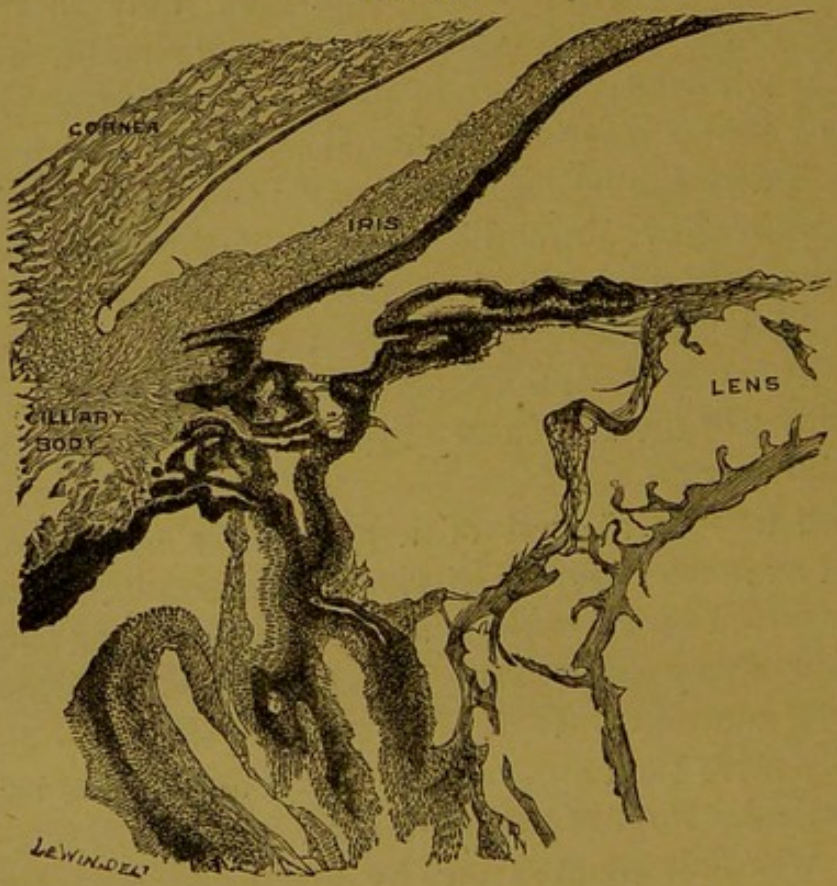
The lens is at first of a globular shape, measuring almost as much antero-posteriorly as laterally. From the drag exerted on its capsule at its peripheral parts, by the growing away from it of the ciliary body, which has acquired adhesions to it, it tends to increase in size laterally more than antero-posteriorly, and hence assumes the lenticular form of the adult lens.

As was first pointed out by Von Ammon, and as has been recently commented on by Mr. Gunn,* in connection with the phenomenon of watered silk retina, rucks are found in the retina of all human fœtal eyes. It would appear that the inner layer of the secondary optic vesicle grows at a greater rate than the outer, and so gets

* Ophth. Hosp. Rep., vol. xi, p. 350.

thrown into the folds, which, as the eyeball afterwards expands, get flattened out. The most pronounced of these folds are, I find, at the ora serrata, which at one time is actually in contact with the posterior and lateral part of the lens capsule. It then acquires adhesions to this latter, and, on the further development of the eye, when the retina has become expanded and flattened out by the enlargement of the globe and the growth of the vitreous, these adhesions become much stretched and elongated, forming thus the hindermost attachment of the suspensory ligament. Figs. 1 and 2 show some of the

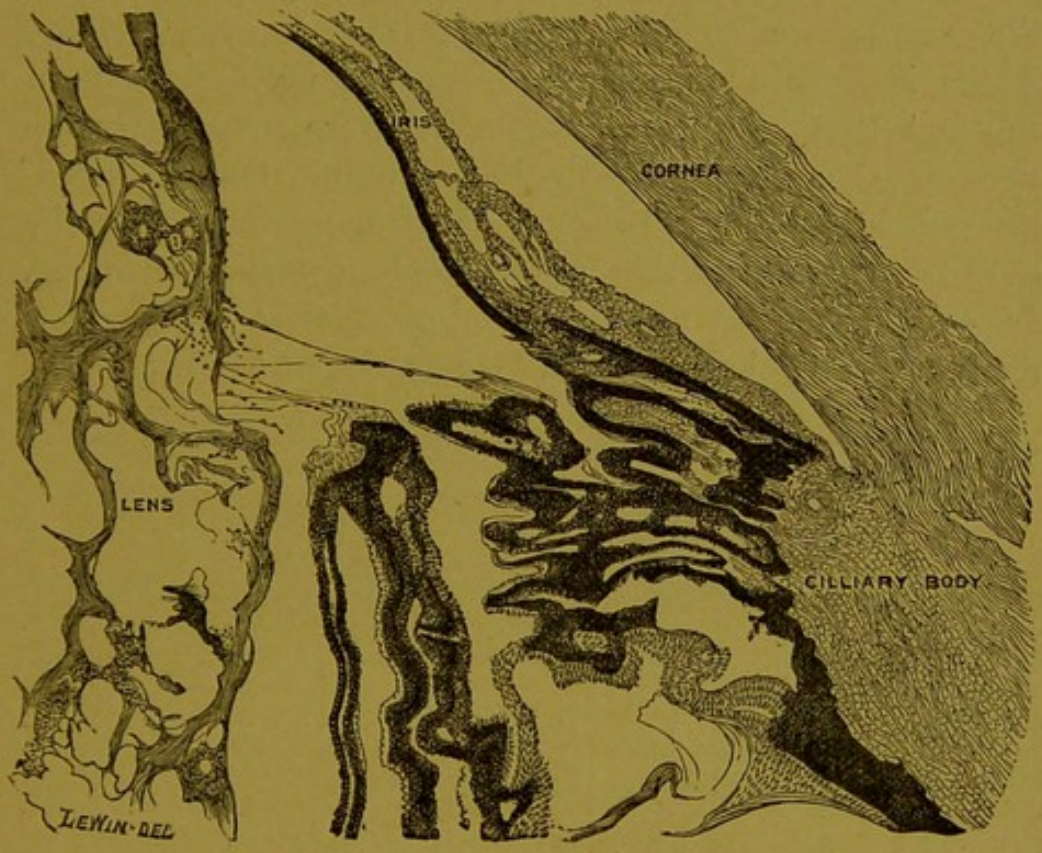
Fig. 1.



stages in the development of a fibre of the suspensory ligament. In Fig. 1 an adhesion, passing from a ciliary process to the capsule of the lens, composed entirely of spindle-shaped cells is represented. In Fig. 2 several fibres are seen exactly like those found in the normal adult eye, with the exception that every here and there

they have nuclei on them, clearly indicating their cellular origin.

Fig. 2.



I have been unable to determine definitely whether the cells from which these fibres develop are derived from the fibro-vascular sheath of the lens, or from the cells of the inner layer of the secondary optic vesicle which form the pars ciliaris retinæ, or in part from one and in part from the other. The fact that they belong to the connective tissue class would lead one to expect, that they are more likely mesoblastic in origin, and therefore derived from the fibro-vascular sheath, than epiblastic, and derived from the pars ciliaris retinæ.

In a series of human fœtal eyes which I have of various ages, from 4 months up to the 9th month, the gradual separation of the ciliary processes and of the fold of the retina at the ora serrata from the sides of the lens with which at first they are in contact, is well shown.

The following table shows the gradual relative altera-

tion in size of the diameters of the eyeball, and of the lens, throughout fœtal life. Though the number of eyes I have had the opportunity of measuring is small, I think the results are sufficiently accurate for my purpose. There is a possible source of error in my figures, from the fact that all the measurements were made after the eyes had been hardened in Müller's fluid. On account of there being necessarily some delay in my obtaining the eyes after removal, this was the only course open to me. In every case an antero-posterior vertical section was made of the eyeball, and the lens measured *in situ*:—

Age.	No. of eyes examined.	Diameters of eyeball.			Diameters of lens.	
		Antero-posterior.	Lateral.	Vertical.	Antero-posterior.	Transverse.
4th month	3	8·1 mm.	7·8 mm.	7·5 mm.	2·8 mm.	3·3 mm.
5th month	1	11·75 mm.	11·5 mm.	10·5 mm.	3·5 mm.	4 mm.
6th month	4	12·5 mm.	12 mm.	11·1 mm.	3·8 mm.	4·5 mm.
7th month	8	14·3 mm.	13·2 mm.	12·6 mm.	4 mm.	5 mm.
9th month	3	16·75 mm.	16 mm.	15·3 mm.	4·3 mm.	5·75 mm.
Adult....	Merkel	24·3 mm.	23·6 mm.	23·4 mm.	3·7 mm.	9 mm.

The points which this table shows, bearing upon my subject, are:—First, that the diameters of the globe at the 9th month are just double what they are at the 4th month, and in the adult treble the size; that the transverse diameter of the lens is likewise double in the 9th month, and treble in the adult what it was at the 4th month. So supposing, as is the case, that the ciliary body touches the sides of the lens at the 4th month—in that the eyeball is much larger than the lens to begin with, and both increase to double and treble their size—then, unless the thickness of the coats of the eyeball also become double or treble what they were—which they do not—there must be a gradual

growing away of the ciliary body from the sides of the lens.

Secondly, that the transverse diameter of the lens, which at the 4th month is only a little more than the antero-posterior diameter, in the adult lens is nearly three times as much. This globular form of the fœtal lens has been pointed out by Otto Becker and others.

Thirdly, it would appear that the lens in adult life measures somewhat less antero-posteriorly than what it does in fœtal life. I do not think the number of eyes I have examined are sufficient to make this certain, still the explanation I have given of the development of the suspensory ligament renders it likely. It would be only natural that, when the tension caused by the stretching of the fibres of the ligament due to the enlargement of the globe became felt, some flattening from before backwards of the soft lens matter and bowing of its fibres should occur.

The above description of the way in which the zonule of Zinn develops not only throws light on some of the congenital abnormalities met with in connection with the lens, but also receives considerable support from its mode of explaining them.

Taking first the condition known as *coloboma lentis*, an excellent *résumé* of the literature of which malformation, together with two new cases, has been published by Dr. Heyl,* I cannot do better than quote the passage in which he sums up:—"From the preceding, it may then be seen that coloboma of the lens is a condition which presents at the place of defect an edge, not rounded as in the normal condition, but either straight in the horizontal direction or incurved; that the amount of deficiency varies from a slight indentation to about one-quarter of the lens substance, the centre of the lens, its poles, and the lens substance in the immediate vicinity being uninvolved;

* Trans. of 5th Internat. Ophth. Congress, p. 16.

that the lens sometimes, in addition to the defect, is imperfectly developed in all its meridians; that the deficiency is always in the inferior half, and, almost without exception, entirely so; and, finally, that coloboma of the other ocular structures frequently co-exists, but very frequently no trace of it can be found."

Now, supposing the pars ciliaris retinæ failed to acquire adhesions to the lens capsule in one part of its circumference, it follows that the suspensory ligament would be absent in that position; and that as the eyeball enlarged, that portion of the capsule to which no suspensory ligament was attached would not be held taut, and made to expand, like the remainder. Consequently there would be a depression in the lens in that situation. The amount and shape of the deficiency would depend on the extent of the defect in the suspensory ligament. There would not, of course, be any alteration in the nucleus or poles of the lens, for these are formed before the influence of the suspensory ligament comes into play. The most likely cause for the non-adhesion, and so for the defect in the suspensory ligament, would be the absence of the ciliary body or pars ciliaris retinæ, in fact, a coloboma of the ciliary body. And Dr. Heyl says this condition does frequently co-exist with a defect in the lens, the defect being at the situation of the fœtal cleft.

Mr. Gunn,* regarding the condition of coloboma lentis from the clinical side, has arrived at a similar conclusion as to its mode of formation; thus, he says:—"The notch in the lower border of the lens may be accounted for by the imperfect development of the ciliary processes and suspensory ligament, so that the soft lens is not here drawn outwards into its normal comparatively sharp curve at its equator."

The same observer† has recently pictured and described a case of a congenitally misplaced and notched

* Ophthalmic Review, vol. viii, p. 234.

† Trans. Ophth. Soc., vol. ix, p. 166.

lens, in which a distinct gap in the suspensory ligament was visible, corresponding to the notch.

Ectopia lentis or congenital displacement of the lens has been attributed by Becker to irregular development of the suspensory ligament. And I think the explanation I have given of the mode of formation of the latter helps us to understand how this comes about.

The literature of the subject has been carefully worked up by Dr. D'Œnch,* and he ends his article with the following conclusions:—

"1. Ectopia of the lens is a malformation, the causes of which, thus far, remain unknown.

"2. It always affects both eyes, generally in a symmetrical manner.

"3. The direction of the displacement is almost always either upward, upward and inward, or upward and outward.

"4. The lenses are generally transparent; sometimes their size is below the mean.

"5. The suspensory ligament is sometimes found, sometimes not.

"6. In about one-fourth of all cases there is myopia.

"7. The position of the lenses may remain unchanged throughout life, but spontaneous dislocation may also result.

"8. Heredity has been proven."

Supposing the adhesion, which takes place between the capsule of the lens and pars ciliaris retinæ to form the fibres of the suspensory ligament, be absent over a large area, then on the expansion of the globe there would be no counteracting force on one side to hold the lens in position, and it would be drawn towards that side on which the adhesions had formed. The determining cause as to whether a coloboma of the lens be formed, or an ectopia, would depend on the extent of the deficiency in the suspensory ligament. In some cases, as would be

* Archives of Ophthalmology, vol. x, p. 89.

expected, both are present. When the deficiency is very great indeed the lens would be mobile, and might become dislocated.

Abnormal density or frailty of the adhesions in part of the circumference would also be likely causes of displacement of the lens, and would account for those cases in which some of the fibres of the suspensory ligament can be seen passing (in a case of displacement upwards), from the lower margin of the lens to the ciliary body.

Delay in the closure of the fœtal cleft, though it did not lead to a permanent coloboma of the ciliary body, could yet lead to ectopia of the lens; for the eye might have expanded to such an extent, that the lens would have been drawn away from the lower portion of the globe, before the ciliary process had sufficiently developed to have acquired adhesions to its capsule.

Mr. Nettleship,* in his text-book on diseases of the eye, says :—"Congenital dislocation of the lens is often accompanied by other defects of development, such as coloboma."

It is noteworthy that the lens is almost invariably displaced upwards, either directly or with some inclination inwards or outwards, that is to say, it is almost always displaced in the opposite direction to the fœtal cleft, which we know is generally downwards or downwards with either a slight inclination inwards or outwards.

The second case, of which I give the details at the end of this paper, resembles in several points the first. Both were diagnosed as cases of glioma of the retina, and the eyeball accordingly enucleated. In both the central hyaloid artery was persistent and patent, and in both it terminated anteriorly in a mass of cells and fibres at the posterior surface of the lens. The lens, however, in the two cases was different, for in the second case it was well formed and the capsule tense, though more globular than usual, and with some irregularity of its cells and fibres at the

* Diseases of the Eye, 5th Ed., p. 181.

posterior part. The relation of the ciliary processes in the second case was also peculiar, for on one side of the sections they all passed behind the lens, being adherent to the mass on its posterior surface; while on the opposite side they were arranged in their usual way, some in front and some behind. The lens thus appeared displaced forwards, somewhat on one side. Nassaux* has figured and described a case very similar to mine, in which all the ciliary processes were behind the lens, adherent to the mass in which the hyaloid artery terminated.

Grolman† records a case of microphthalmos with a congenital vascular cataract and persistent hyaloid artery, in which he pictures the ciliary processes as having adhesions to the fibro-vascular sheath of the lens.

In a microphthalmic eye examined by Hess‡ there was a persistent hyaloid artery, dividing into branches in a membrane behind the lens, which latter was small and displaced upwards, there being a coloboma of the iris downwards. The iris and ciliary processes above were adherent to the anterior face of the lens; below they turned backwards along the lower surface of a bundle of fibres, which was prolonged forwards through the coloboma from the membrane behind the lens.

It would seem that when the central artery of the vitreous remains persistent and patent, the fibro-vascular sheath behind the lens also persists and becomes much thickened, and that the relation of the ciliary processes to the lens in some of these cases becomes altered, the latter being displaced forwards in front of them, between them and the iris. As the result of this they form adhesions entirely to the posterior part of the fibro-vascular sheath, and not any to its sides or anterior part. Consequently, as the globe expands, no lateral traction is exerted on the lens capsule, and the cells in the region of

* Archives d'Opht., T. 3, p. 502.

† Archiv für Ophth., B. xxxv, Ab. ii, p. 187..

‡ Archiv für Ophth., B. xxxiv, Ab. iii, p. 148

the nucleated zone, instead of flattening out into fibres at the sides of the lens, spread round its posterior capsule, line it, and afterwards swell up into cells resembling epithelial cells of a large type. These are represented diagrammatically, and, of course, out of proportion to the rest of the structures, in Fig. 4. The lens thus comes to have a shape more globular than normal.

Case 1.—Edgar D., aged 3 months, was brought to Mr. Couper, at the Moorfields Hospital, on March 7th, 1890, by his mother, who stated that she had noticed from his birth that his left eye was different to his right. At first, she said, there were two small white specks on it; which gradually became larger and covered the sight. There had not been any discharge from the eyes, and they had not been inflamed. It was her sixth child. Two of the others had died of convulsions while teething. There was no history of any eye affections or tumours in either the mother's or father's family.

On examination of the left eye the cornea was seen to be clear. The iris was in close contact with its posterior surface, there being no anterior chamber. The pupil was blocked by a greyish opacity. The right eye was apparently normal.

A new growth in the left eye was suspected, and it was enucleated on March 11th, 1890.

Pathological Examination.—The tension of the eye was full. The antero-posterior diameter measured 15·5 mm. and the vertical 14 mm. The cornea, which was slightly hazy, measured 9 mm. across. On section of the eyeball, the iris was found in contact with the cornea throughout its whole extent. The lens was in contact with the posterior surface of the iris; it presented a very irregular appearance. It was shrunken and irregularly mottled, and on its posterior surface was an opaque white mass. The ciliary processes on each side passed vertically inwards, and appeared long and narrow. The vitreous was of good consistency. Passing through its centre from the optic disc to the posterior surface of the lens was a delicate grey band, the unobliterated hyaloid artery. The retina had several little puckers in it. Anteriorly in the entire circumference there was a large fold, which touched the posterior surface of the lens at its periphery.

Microscopical Examination.—The iris has attached to its anterior surface at its pupillary margin on one side a process composed of cells and a loose fibrous network, the other extremity of which floats free in the anterior chamber in the pupil. It is evidently a remnant of the pupillary membrane. The two layers of pigment on the posterior surface of the iris have become somewhat separated towards the pupillary margin, and on one side there seems to have been some slight adhesion of the iris to the anterior capsule of the lens.

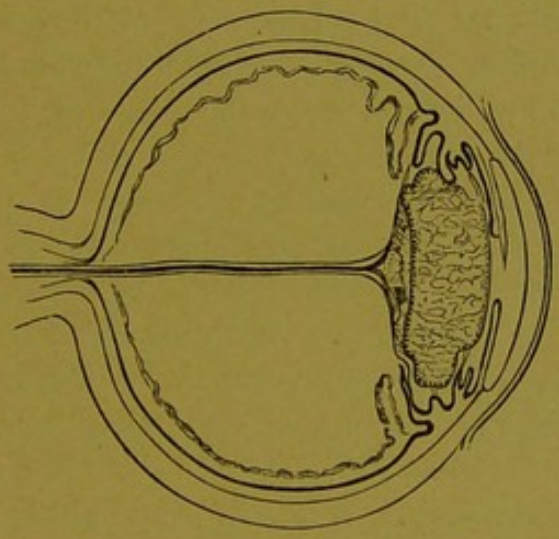


Fig. 3.—Represents a diagrammatic section of the eyeball in Case 1.

The lens is composed in greater part of a network of hyaline substance with large irregular spaces in it. Its capsule is wrinkled, and has cells lining it throughout its entire circumference. In the anterior part of the lens in some of the sections there is a mass of nucleated cells. Behind the posterior capsule of the lens, and intimately in contact with it, is a collection of fibres and cells, some round and some spindle-shaped. This collection is thickest in the centre, and tapers off on each side, where some of the ciliary processes are adherent to it. The hyaloid artery passes into it, and breaks up there into branches.

The ciliary processes are narrow; in some places they lie in contact with the lens capsule. The foremost ones have, stretching between them and the lens capsule, fibres like the fibres of the suspensory ligament, with every here and there nuclei lying on them. (See Figs. 1 and 2.)

These fibres as they approach their insertion into the ciliary processes become thicker, and in some places composed of several layers of elongated cells, which gradually become merged into the layer of unpigmented cells covering the ciliary processes. The hindermost ciliary processes have passing out from them processes composed of spindle-shaped cells, which are connected with the mass of cells behind the posterior capsule.

In some cases a direct adhesion between the lens capsule and a ciliary process is seen by means of elongated cells.

The portion of retina between the ora serrata and the hindermost ciliary process is exceedingly short. Fibres with nuclei on them pass from it to the mass of cells at the back of the lens. At the ora serrata the retina is folded inwards. The layers of the retina present their normal appearance. The choroid has fewer vessels and more cells in it than usual; scarcely any of these are pigmented. The central artery of the vitreous can be traced as a continuation of the central artery of the retina, from the very centre of the optic disc to the posterior surface of the lens, where it divides and is surrounded by the mass of cells as above mentioned. Red blood corpuscles are seen in the artery. While in the vitreous it lies in a canal lined by cells.

Case 2.—Rosa S., aged 4½ months, was admitted as an in-patient, under Mr. Hulke, at the Moorfields Hospital, on September 30th, 1887. Her mother stated that the child was born with the lids of her right eye discoloured, like a "black eye." This discoloration lasted for about a fortnight. The eye itself was not blood-shot, and there was no discharge from it. She always thought the right eye to be rather larger than the left. Two months ago she first noticed a white speck on the patient's right eye, which had increased in size. The child was born at full time; no instruments were used. It is her fifth child; three of the others are living; one died of bronchitis.

On examination the right eye was found to have hardly any anterior chamber; pupil inactive; tension full. A yellowish reflex was seen from behind the lens. The left eye was healthy. A new growth was suspected, and the right eye enucleated.

Pathological Examination (made by Mr. Lawford, who has kindly permitted me to make use of his notes).—The eyeball was small; there was no puckering of the sclerotic. The cornea was clear. The iris was pushed forwards into contact with its posterior surface, and looked very convex anteriorly. The iris was adherent to the anterior capsule of the lens. The lens was clear and nearly globular in shape, and in contact with the posterior surface of the iris. A persistent hyaloid artery passed through the vitreous from the optic disc to the posterior surface of the lens, where there was an opaque membrane stretching across the globe. The ciliary processes were thin and elongated, and attached to this membrane. The retina and choroid appeared healthy.

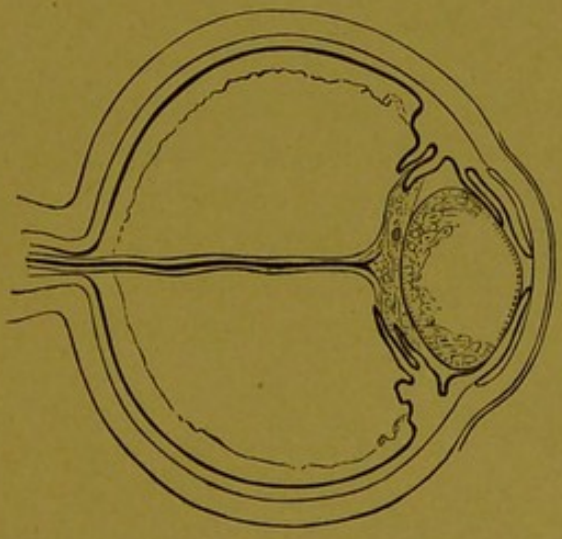


Fig. 4.—Represents a diagrammatic section of the eyeball in Case 2.

Microscopical Examination.—The iris is much bent forwards. The lens is in contact with its posterior surface. The relation of the ciliary processes to the latter is different on the two sides. On one they all pass behind it, and are very narrow and long. On the other, some pass in front and some behind, and they are shorter and broader. All those passing behind are connected by fibres with a mass of cells, some round and some fusiform, on the posterior surface of the posterior capsule of the lens, into which the persistent hyaloid artery passes and divides. Fibres are also seen passing from this mass of cells to the portion of retina between the ora serrata and the ciliary

processes, which is shorter than in the normal eye. The lens has cells lining not only its anterior but its posterior capsule also. No definite nucleated zone can be made out in the lens. There are a large number of nucleated cells like swollen epithelial cells about its posterior and lateral parts. Its posterior capsule has some wrinkles in it. The retina appears normal. The optic papilla is thicker on one side than the other. The hyaloid artery does not pass into the vitreous directly from its centre, but from the side where the thickening is. The artery has its usual coats, and is surrounded by a thick sheath, composed of cells and fibres. Red blood corpuscles can be seen in the artery. The choroid is less vascular than normal, and its cells have scarcely any pigment in them.

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