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COMMUNICATIONS

ON THE MORPHOLOGY OF CERTAIN DEVELOPMENTAL STRUCTURES ASSOCIATED WITH THE UPPER END OF THE CHOROIDAL FISSURE*

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PART I.

On the morphological value of certain cells found on the optic disc in human embryos.

ON examining sections through the centre of the developing optic disc in human embryos of about the eleventh week the appearances shown in Fig. 1 will be seen. It will be noticed that there is already a fair amount of differentiation of the retinal layers, and that nerve fibres are present. The nerve fibre layer, as it nears the disc, increases in thickness at the expense of the other retinal layers, which become thinner and blend with one another at the edges of the nerve. The nerve fibres, as they pass out of the eye, leave in the centre of the disc a small rather funnel-shaped interval, which is filled in with a cellular tissue, so that there is no real depression below the general surface of the retina here. Indeed, in some human embryos examined this small cone of cells formed even a slight elevation in the centre of the disc. In the figure a

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small blood vessel (a derivative of the intraneural portion of the arteria hyaloidea) can be seen at the apex of the cone. There are

FIG. 1.—Section through the optic disc of a 35mm. human embryo.

FIG. 2.—Section through the whole eye of a young chick embryo.

as yet no retinal blood vessels visible. Branches of the arteria hyaloidea can be seen faintly in the vitreous. It is to the consideration of the origin and morphological value of this small

cone of cells in the centre of the disc that the present paper is devoted.

FIG. 3.—Section through the fused portion of the choroidal fissure in a chick embryo.

FIG. 4.—Section through the primitive pecten in a chick embryo.

There are naturally two possible origins for these cells. First, they may, as has often been upheld, be mesodermal elements carried in along the choroidal fissure with the arteria hyaloidea.

They do not, however, resemble vaso-formative tissue, nor are they continued at all along the vessel in its passage through the vitreous. Secondly, they may be ectodermal in origin and derived from some part of the optic cup. It is, of course, not to be denied that a few mesodermal cells accompany the arteria hyaloidea and take part in the differentiation of its walls, but I think it can be shown that, morphologically at least, the cone of cells in the centre of the disc is primarily ectodermal in origin and is derived from the inner layer of the optic cup.

In order to understand the meaning of this cone of cells it is

FIG. 5.—Section through the upper end of the pecten in a hen's eye.

necessary to consider the development of certain other animals, in which it is seen in a more elaborated form.

In looking at sections through certain early vertebrate embryos, in which invagination of the optic cup has occurred, but before the closure of the choroidal fissure or the appearance of nerve fibres, it will be noticed that the inner (retinal) layer of the cup is separated from the pigment layer and is thrown up into folds, as though it were of greater area than the pigment layer. This appearance of more rapid growth of the inner than the outer layer can be seen to a greater or less extent in most vertebrates, though it is absent altogether in certain primitive forms (e.g., the Ganoid, *Amia*) in which the inner and outer layers of the optic cup are everywhere in perfect apposition. From one point of view, then, developing vertebrate eyes can be divided into two groups, namely, those in which in early stages the inner layer of the optic cup

grows more rapidly than the outer, and those in which it does not. It is with the first only of these two groups that we are concerned. In this group the overgrowth of the inner layer leads to a heaping up and eversion of this unpigmented layer along the choroidal fissure. This is most marked in the upper part of the fissure, since the overgrowth is apparently more active at the posterior pole of the eye than further forward. If the overgrowth is only moderate there will be eversion of the inner layer along the upper part of the choroidal fissure, so that, when fusion takes place between the lips of the fissure here, the actual areas which fuse are derived

FIG. 6.—Section passing through portions of both eyes in a *Calotes* embryo.

from inner layer only and are free from pigment. There will therefore be after closure a linear non-pigmented "scar" on the outside of the cup in the line of the fissure. If, on the other hand, the overgrowth of the inner layer is greater than this, this layer will be thrown up into more marked folds along the edges of the fissure, and when fusion occurs two ridges will be seen in the line of the fissure, both derived from the heaped-up inner layer, one on the outside of the optic cup showing as a well-marked non-pigmented ridge interpolated in the otherwise uniform pigment epithelium and running down from the point of attachment of the optic stalk in the line of the closed fissure; the other a ridge in the same line, but projecting into the interior of the cup. This heaping up of the inner layer in the line of the fissure inside the eye I have called the *crista intraocularis*. This structure is very well marked in birds and its development and fate in the chick will now be considered.

Fig. 2 shows a section through the eye of a young chick embryo. The section passes through the choroidal fissure just below the insertion of the optic stalk. It will be seen that the pigment layer is only one cell thick and that the inner (retinal) layer is already several cells thick, and is separated from the pigment layer. At the fissure the heaping up and eversion of the inner layer is very apparent, especially at the upper edge, the inner layer becoming continuous with pigment layer at X, some distance from the fissure and outside the eye. The heaping up which, after fusion, will form the internal ridge (*crista intraocularis*), is seen at Y. A filmy

FIG. 7.—Section through the whole eye of an *Acanthias* embryo.

strand of mesoderm containing blood corpuscles passes in at the fissure and stretches across the lower part of the cup at this stage. Fig. 3 shows a section through the upper (just closed) part of the fissure of an older chick. It will be seen that the two ridges derived from the heaped up inner layer are well marked. On the outside of the eye the everted portions of the inner layer have fused, forming a non-pigmented projection continuous with the pigment layer at X, which corresponds with the point X in Fig. 2. The *crista intraocularis* projects as a definite papilla into the vitreous. The continuity between and similarity of the cells of the inner layer of the cup and the cells of the *crista intraocularis* can be seen at this stage, when very little differentiation has occurred in either. The cells of the external everted projection can also be seen to resemble those of the inner layer and show a definite epithelial arrangement,

which entirely differentiates them from the surrounding mesoderm outside the cup. There are no blood vessels or corpuscles visible in either of the two projections at this stage, and I think it is quite obvious that both of them are in continuity with and derived from the walls of the optic cup and are not mesodermal in nature. In this section nerve fibres are just beginning to appear on the surface of the retina, and are running towards the site of the fissure, along the line of which in its upper part they leave the eye. In doing this they do not grow over the vitreous surface of the *crista intraocularis*, but pass through deeply at its base, running obliquely

FIG. 8.—Section through the optic disc in a young dogfish.

and thus cutting off the central cells of the *crista intraocularis* from the rest of the inner layer, though the original continuity can long be traced through scattered nuclei lying among the nerve fibres and connecting the base of the *crista intraocularis* with the end of the inner layer. Thus the *crista intraocularis* becomes apparent as a wedge of cells projecting into the vitreous between the converging bundles of nerve fibres, and at this stage corresponds with the cone of cells seen in the human embryo in Fig. 1, although in the chick the crista is linear and not circular. Bergmeister has described this wedge of cells in the chick but does not, as far as I am aware, trace their subsequent fate. Ucke, following up Bergmeister's work, again maintains their ectodermal origin and further shows the existence of similar ectodermal cells on the disc in certain fish and amphibians and in the sheep. He also mentions

that in certain low forms (*Ammocoetes*) the nerve fibre layer is not the most internal in the definitive retina, but is covered by a double layer of epithelial cells, and he suggests that the cone of cells seen in the chick's eye represents all that is left in higher forms of this internal epithelial layer. However that may be in *phylogeny*, the fact remains that *ontogenetically* the *crista intraocularis* is composed of cells cut off from the inner layer of the optic cup by issuing nerve fibres.

As the cleft closes (in the chick) the small strand of vascular mesoderm which was seen entering the eye through the fissure in

FIG. 9.—Section through the whole eye of a pig embryo.

Fig. 2 gets pushed more and more distally. It eventually disappears, and birds do not possess a definite *arteria hyaloidea*. From its proximal end in the eye, however, branches pass into the lower end of the *crista intraocularis* and vascularize it from below upwards. The *crista intraocularis* then grows out into the vitreous as a thin wedge of very vascular tissue, and forms the primitive pecten. This continues to grow and becomes many times folded upon itself. Later, pigment is developed in it, but long after pigmentation of the other structures in the eye is complete. Fig. 4 shows a section through the eye of an older chick. It will be seen that the *crista intraocularis* is now entirely cut off from the rest of the inner layer and that it is extremely vascular and is beginning to show signs of folding. Fig. 5 shows a section through the extreme upper end of the pecten in an adult hen's eye. It will be

seen that its position corresponds with that of the *crista intraocularis* in the embryonic chick's eye. The pecten is thus primarily an ectodermal structure derived from the inner layer of the optic cup, and is secondarily vascularized by (mesodermal) vessels growing into it from its lower end, these being derived from the proximal end of the strand of mesoderm which enters the open part of the choroidal fissure at an early stage and disappears without forming a definite hyaloid artery.

The vascular supply of the pecten is separate from that of the choroid, as can be shown both by a study of its development and

FIG. 10.—Section through the whole eye of a 15mm. human embryo.

by experiments such as those of Mihalkovics, who found that, on injecting the choroidal vessels, no fluid passed into the pecten. He denied the truth of the opinion of Gegenbaur and Leydig who looked on the pecten as an intraocular portion of the choroid, but he considers it as developed from mesoderm caught between the lips of the closing fissure. This view is also upheld by Slonaker, who has studied the development of the sparrow. It is, I think, certain that the pecten is primarily an ectodermal structure, since a definitive *crista intraocularis*, continuous with the inner layer of the optic cup, can be seen before there is any sign of vascularisation. In the adult condition, it is true, the mesodermal elements dominate the picture; the ectodermal remnants only remain as a neuroglial network supporting the capillaries, and continuous with the neuroglial septa in the optic nerve. This view is held by

Denissenko, who, however, gives no definite account of the development, and by Franz, who arrived at the conclusion of the nervous origin of the pecten from a study of the adult organ only.

Fig. 6 represents the developing pecten in the lizard *Calotes*. The optic discs of both eyes are shown. The condition is exactly similar to that seen in the chick (Fig. 3) and again there is as yet no vascularization of the *crista intraocularis*, which shows here a very definite epithelial arrangement of its surface cells. In *Calotes*, as in the chick, a vessel enters the vitreous through the open part of the fissure below the *crista intraocularis*.

FIG. 11.—Section through the whole eye of a 33mm. human embryo.

The final elaboration of the *crista intraocularis* is therefore the pecten of lizards and birds. We will now turn to other forms in which a definitive pecten is never developed. Among fishes the dogfish, *Acanthias*, will serve as an example. Fig. 7 shows a section through the open choroidal fissure in an *Acanthias* embryo. It will be seen that the overgrowth of the inner layer is not so marked as in the chick, but that there is definite separation between the layers and heaping up of the inner layer in the lips of the fissure. Fig. 8 shows a section through the optic disc of a much older dogfish, in which some cells of the inner layer have been cut off by the issuing nerve fibres, and remain in the centre of the disc as a cone-shaped plug. Nuclei can still be seen scattered among the nerve fibres and connecting this plug with the inner layer, of which it is part. Since the nerve fibres only leave the eye at the upper end of the choroidal fissure in the dogfish, this plug of cells (the analogue of the *crista intraocularis*) is circular

and not linear, and since the vascular mesoderm entering the fissure in Fig. 7 entirely disappears and does not send branches to these cells, the cone does not grow out into the vitreous or undergo any further development at all.

Among mammals the same condition of overgrowth of the inner layer of the optic cup is found. In some (e.g., mouse) it is only great enough to produce eversion and the appearance of non-pigmented cells on the outside of the cup, while in others (pig and man) an elevation (*crista intraocularis*) is formed inside the eye as well. Fig. 9 shows a section through the eye of a young pig

FIG. 12.—Diagram after Versari to show the development of the arteria centralis retinae.

embryo just below the optic stalk. The fissure is open, and it will be seen that the inner layer is markedly everted and also slightly heaped up inside the eye. When fusion occurs, and nerve fibres appear, a few of the cells of the inner layer are cut off and remain as a cone-shaped plug in the centre of the disc. In man a similar condition is seen. Fig. 10 shows the eye of a human embryo of the sixth week. It will be seen that eversion of the inner layer is well marked in the fissure; the internal heaping up is not so well marked. The hyaloid artery is seen entering the fissure. When fusion occurs and nerve fibres appear a few of the inner layer cells are cut off just as in other animals and remain as a cone-shaped plug on the disc. In addition, however, in man (and pig also) the vessel entering the eye remains as the very definite arteria hyaloidea. Fig. 11 shows the condition in a nine weeks human

embryo. The optic nerve is forming and a definite nerve fibre layer is apparent. In the centre of the disc the arteria hyaloidea is seen entering the vitreous at the bottom of a little depression. On either side of this depression are a few very definite cells, the representatives of the *crista intraocularis*, namely, cells cut off from the inner layer of the optic cup by the issuing nerve fibres. In this section the connection of these cells with the retina rather than with the vessel is very clearly shown, since they are separated from the vessel by a definite space, but are continuous with the nerve fibre layer and with scattered cells in this which appear to be derived from the other layers of the retina.

The subsequent fate of this cone of cells in man is of interest. It has been worked out in detail by Versari. Briefly it is as follows. A bulb-shaped swelling appears in the arteria hyaloidea as it passes through the centre of this cone, and from this bulb branches appear which vascularize the cone. This is analogous to the vascularization of the *crista intraocularis* in the chick by derivatives of the vascular mesoderm entering the vitreous at its lower end. The cone does not, however, grow outwards into the vitreous in man, but the vessels in it insinuate themselves among the nerve fibres and, spreading over the whole retina in the substance of the nerve fibre layer, form the arteria centralis retinae and its branches. Fig. 12 from Versari shows the vascularization of the cone. This occurs in the pig similarly. In the mouse, where there is no cutting off of the cells of the inner layer to form a cone, the intra-ocular blood supply is formed quite differently, namely, by a laying down on the retina of the most peripheral of the vitreous branches of the arteria hyaloidea, so that in these animals the branches of the arteria centralis retinae are always superficial to the nerve fibres and not embedded in them as in man.

It is thus evident that the cells found on the optic disc in human embryos are ectodermal cells of the inner layer of the optic cup, which have become cut off from their fellows by issuing nerve fibres. They are the representatives of the cells of the *crista intraocularis* in birds, and their function both in man and in birds is to form a nidus for the proximal branches of the vessel from which the definitive intraocular blood supply is developed. In birds the cells of the *crista* are more definitely cut off from the rest of the inner layer, and so, when it becomes vascularized, it grows out into the vitreous, while in man and some other mammals (e.g., pig) the cells are more scattered among nerve fibres, so that when vascularization takes place the small vessels grow in amongst the nerve fibres and penetrate in this layer all over the retina. In animals in which there is no intra-retinal blood supply (e.g., *Acanthias*) the cone of cells may still be present but the arteria hyaloidea disappears without vascularizing it.

PART II.

On the morphological value of certain non-pigmented cells found below the insertion of the optic stalk in the 15mm. human embryo.

FIG. 1 represents a section through the optic cup of a 15mm. (sixth week) human embryo just below the insertion of the optic stalk. The inner layer of the cup is everywhere separate from the outer layer, and the cells of the outer layer show dense pigment deposited in them, except at the posterior pole, where it is to be seen that

FIG. 1.—Section through the whole eye of a 15 mm. human embryo.

a small mass of unpigmented cells interrupts the pigment layer. This mass marks the situation of the upper end of the closed part of the choroidal fissure, the only open part of this upper end being at its extremity for the passage of the hyaloid artery. The development of this unpigmented mass of cells is straightforward enough and it is easy to see the ontogenetic reason for their presence. Their morphological associations are, however, interesting.

As I pointed out in the first part of this communication, there is in certain vertebrate eyes a more rapid growth of the inner layer of the optic cup (at the posterior pole) than of the outer. If this occurs before closure of the choroidal fissure, it leads to eversion of the inner layer in the lips of the fissure, most marked in its upper part, so that, when closure of the fissure occurs, fusion takes place between unpigmented (inner) layers only. Thus it comes about

that there is an unpigmented "scar" (everted inner layer) visible on the outside of the pigmented optic cup for some little time after

FIG. 2.—Section through the eye of a 15 mm. human embryo just above that shown in Fig. 1.

FIG. 3A.—Section through the whole eye of a mouse embryo.

closure of the fissure. This is the case in man in the upper portion of the fissure. Fig. 2 shows a section through the same eye as Fig. 1, very slightly higher up, namely through the still open

upper end of the choroidal fissure. It will be seen that the inner layer of the cup, which is still undifferentiated, is separated from

FIG. 3B.—Section through the whole eye of a mouse embryo.

FIG. 4A.—Section through the whole eye of a pig embryo.

the pigment layer and is thrown up into folds and is also pushed out considerably in the lips of the fissure. It is obvious that fusion will occur between these everted non-pigmented areas and

that, when subsequent separation into outer and inner layers takes place in the region of this fusion, a portion of the inner layer will be left in continuity with the pigment layer.

The eversion of the inner layer in the lips of the fissure is even more marked in some other mammals. Fig. 3A shows a section through the eye of a mouse, in the upper part of the fissure. The eversion is well marked. There are no nerve fibres in the retina, but pigment is already developed in the outer layer. Fig. 3B shows the same eye at a lower level, through the closed peripheral portion of the fissure. The line of the fissure is still evident as a

FIG. 4B.—Section through the whole eye of a pig embryo.

slight groove on the outside and ridge on the inside of the cup, and the unpigmented everted portion of the inner layer is very obvious. It is in direct continuity with the pigment layer and has lost all connection with the rest of the inner layer.

Figs. 4A and B show exactly similar sections through an embryonic pig's eye. The eversion is even more marked, and, in this case also, the connection of the unpigmented cells with the inner layer is rapidly lost.

A similar condition is found in the Sauropsidans. Fig. 5A shows a section through the whole eye of a *Chrysemys* embryo (terrapin). It will be seen to resemble closely the eye of the young chick figured in Part I (Fig. 2, Pt. I). There is marked eversion in the fissure. Fig. 5B shows an older *Chrysemys* after fusion has occurred along the whole length of the fissure. Its site, however,

is clearly marked by the small mass of unpigmented cells in the outer layer in the lower part of the eye.

FIG. 5A.—Section through the eye of a *Chrysemys* embryo.

FIG. 5B.—Section through the eye of a *Chrysemys* embryo.

In the chick the condition is further specialised and elaborated. As was pointed out in Part I the overgrowth of the inner layer produces not only eversion along the fissure, but also the heaping

up of a "*crista intraocularis*" inside the eye. After closure of the fissure, therefore, two ridges are apparent in its line, one pro-

FIG. 6.—Section through the eye of a young chick embryo.

FIG. 7.—Section through the primitive pecten in a chick embryo.

jecting into the eye (*crista intraocularis*) and the other unpigmented, on the outside. In this bird the outer ridge does not lose its connection with the rest of the inner layer as it does in the other

animals considered, with the result that when nerve fibres develop in the retina (which they do in the chick very soon after fusion has begun) they pass into this everted projection as they leave the eye, since it is in origin directly continuous with the inner (fibre-bearing) layer of the cup. The nerve fibres, then, leave the eye in the line of the upper part of the closed fissure. They enter the everted projection and run up in the substance of this on the back of the eye in order to pass into the trunk of the nerve at the level of the upper end of the choroidal fissure. These bundles of fibres running up on the back of the eye constitute the "cauda" of the adult hen's nerve. Fig. 6 shows the site of the fissure in a chick's eye just when nerve fibres are appearing. They are seen to be passing into the everted non-pigmented portion, cutting off, as they do so, the inner ridge (*crista intraocularis*) which will later form the pecten. Fig. 7 shows a later stage, when the cauda appears as a bundle of nerve fibres, the original inner layer cells having disappeared, and the pecten is growing out into the vitreous.

Thus we see that the little mass of unpigmented cells seen on the outside of the human embryo's eye at about six weeks, is the remains of that portion of the inner layer which became everted in the lips of the fissure before closure. In the chick this occurs over a large area and nerve fibres growing into it form what is known as the "cauda" of the nerve, but in mammals (including man) the eversion only takes place at the upper end of the cleft, no nerve fibres grow into it, and the little mass of cells merely represents for a short time an abortive potential cauda. Under normal conditions it disappears rapidly and completely.

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