

SOME SUGGESTIONS ON THE EMBRYOLOGY OF CONGENITAL CRESCENTS*

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IN dealing with the question of crescents seen ophthalmoscopically in relation with the optic disc it is justifiable to divide them at the outset into congenital and acquired types. We are not concerned here with the second group, which comprises those crescents (usually on the temporal side of the disc) which accompany myopia and which can often be seen to increase in size and alter in appearance during the period of observation. They are almost certainly due to a slow pathological process in the eye, even though their potentiality may in some cases possibly be present during intra-uterine life.

On the other hand those of the first group, the true congenital crescents, are present at birth and remain stationary throughout life. They are not accompanied by any signs of degenerative change in the eye and the refraction is often hypermetropic. These congenital crescents may occur in any situation around the disc, but Vossius, who examined 111 cases, gives the following figures:—

Below the disc	67	per cent.
Inwards	8.1	„
Down and in	7.3	„
Upwards	4.5	„
Up and out	7.2	„
Down and out	5.4	„

This shows that the inferior position is by far the commonest for a congenital crescent since it occurs in 67 per cent. of cases, whereas the percentage of crescents in all the other possible situations together is only 33 per cent.

These figures contrast strongly with Hertel's for acquired myopic crescents, which are as follows:—

Below	6	per cent.
Up	4	„
Out	79	„
Annular	11	„

Here the enormous preponderance of temporal crescents serves to distinguish this group from the congenital type and seems to point to a very definite connection between the myopic crescent and the posterior staphyloma, which is greater on the temporal side.

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We have then for consideration a group of cases of crescent characterized by the fact that they are congenital, stationary, not necessarily associated with any one error of refraction, and most frequently situated below the disc.

In this group there is apparently some factor which determines the greater proportion of inferior crescents and this factor must be looked for in the normal development of the disc, since an abnormality is more likely to be associated—either as arrest or perversion—with a normally existing embryonic structure than to arise *de novo* as a pure aberrance for which no normally occurring stage can be found to account. The embryonic structure in this case is the choroidal fissure. The presence of congenital crescents in other situations does not detract from the fact that the choroidal fissure is the determining factor in the inferior type. The presence

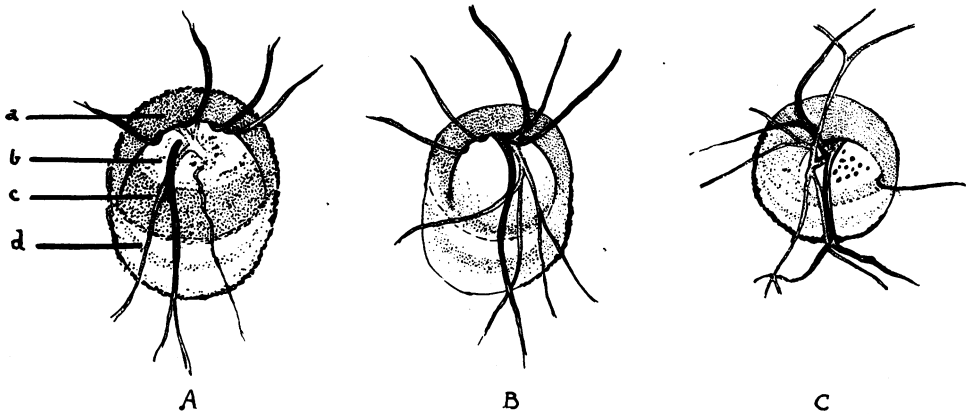


FIG. 1.

of the fissure will merely account for the preponderance of this type, since—as will be shown later—the essential condition for the formation of a crescent is that the pigmented outer layer of the optic cup should not reach quite up to the insertion of the optic stalk; the presence of the fissure merely allows of this occurring more easily below the disc than elsewhere and hence determines the predominance of the inferior type. A somewhat similar condition may, however, result in other situations, as will be explained below, but more rarely, since the chief predisposing factor (the fissure) is absent. Hence the low percentage of congenital crescents other than inferior crescents will be considered in the first place.

The first essential in understanding the formation of an inferior crescent is a detailed study of its ophthalmoscopic and microscopic appearances. The ophthalmoscopic picture is well known and curiously constant. Fig. 1 shows drawings of three typical cases.

A and B are from patients seen by the author ; C is taken from Elschnig's paper on the subject and represents the disc during life of a case in which he was able to correlate the ophthalmoscopic and microscopic appearances. It will be seen that in all three the disc can be divided into four areas from above downwards, lettered in the diagram A as *a*, *b*, *c* and *d*.

First, there is a pinkish zone (*a*), resembling the upper part of the normal disc. This appears slightly raised, and the upper branches of the vessels curl over it. It has a sharp crescentic edge

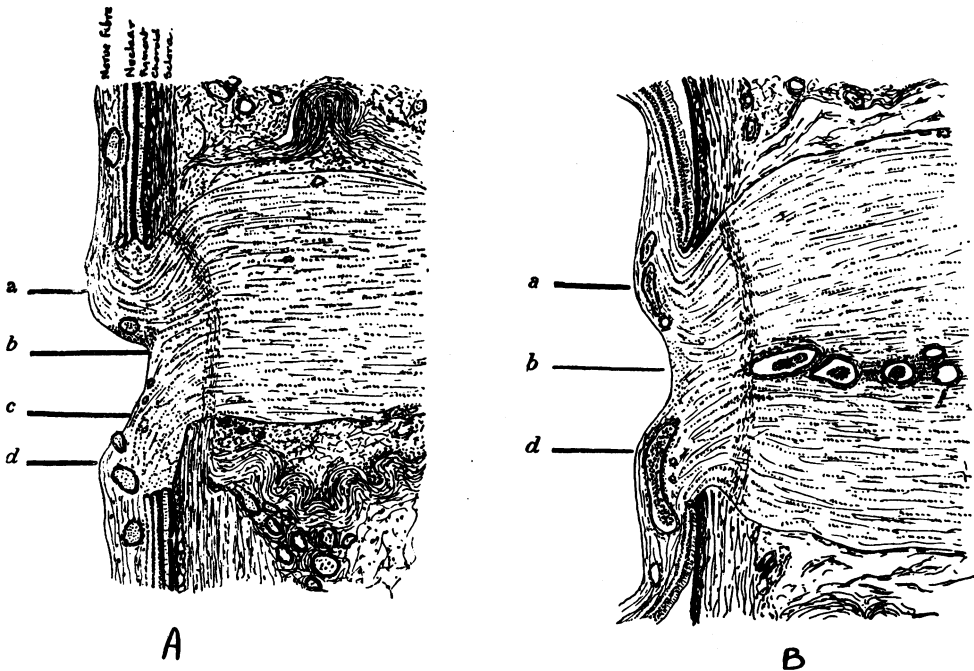


FIG. 2.

below, which separates it from *b*, the pale central zone, which represents the bottom of the physiological cup. This is slightly depressed and the vessels appear from its centre, where the *lamina cribrosa* can sometimes be seen. This zone gradually slopes forwards and passes into the third zone (*c*), which is smooth and pink or greyish like the upper part of the disc and separated by a more or less well-defined edge from *d*, the fourth zone or crescent, which is white or yellow and is often slightly raised. This crescent is frequently divided horizontally by a band of shadow which appears to be due to a small ridge.

Fig. 2A represents a vertical section through an optic disc with an inferior crescent. It is drawn from a slide very kindly

lent me by Mr. Affleck Greeves. It will be seen that the four areas seen ophthalmoscopically can be recognized here. The uppermost pink area is seen at (*a*) as a ridge of nerve fibres. It passes more or less abruptly into the physiological pit, from which the vessels emerge in the area (*b*). This surface slopes forward and so forms the pink zone (*c*) in which are seen some small vessels. The lowest region is again raised almost to the level of (*a*), and shows a definite ridge (*d*) which represents the shadow seen on this lower area ophthalmoscopically. The surface of the disc should be compared with that in Fig. 2B showing a section through the centre of a normal disc. Here it will be seen that there are only three areas (labelled *a*, *b*, and *d*). The upper (*a*) corresponds with (*a*) in Fig. 2A, while (*b*) is the physiological pit (also seen at (*b*) in Fig. 2A). The lower area (*d*) corresponds with (*d*) in 2A, while the smooth slightly forward sloping area seen at (*c*) in Fig. 2A is not represented on the normal disc. The appearance of the discs then in Fig. 1 is due to the interpolation of a smooth area (*c*) between the physiological pit (*b*) and the lower edge of the disc (*d*). It is with the origin and nature of this area (*c*) that we are concerned.

The next point of note in Fig. 2A is the arrangement of the retina at the upper and lower margins of the disc. At the *upper edge* the nuclear and pigment layers end by blending with each other at the margin of the disc. The nerve fibre layer becomes thicker and the nerve fibres curve backwards round the edge formed by the sharp ending of the nuclear layers. The pigment layer and the choroid extend farthest towards the nerve and form a sharp spur which indents the nerve. A similar condition is seen at both edges of the normal disc (Fig. 2B) and the constriction thus formed is the narrowest part of the nerve. (The exact arrangement of the nuclear layers where the retina ends is subject to individual variations in normal discs.) The sclera does not extend quite so far as the pigment layer and the *lamina cribrosa* is seen continuous with the sclera a short distance behind the point of maximum constriction of the nerve, and stretches across the nerve just where it begins to widen out again.

At the *lower edge* of the disc in Fig. 2A the nuclear layers of the retina do not extend so far as at the upper edge. They end by blending with each other, but the pigment layer ends on a level with the other layers and does not extend as a spur. The sclerotic is continued beyond the pigment layer and so comes to lie immediately deep to the nerve fibre layer, separated from it by a rapidly thinning continuation of the choroid. The sclera runs up to the edge of the nerve and its fibres are continuous with those of the *lamina cribrosa* here as they are above. The appearance of indentation or constriction of the nerve at its exit from the eye thus

is absent below, since this indentation is normally caused by the pigment epithelium which here has fallen short of the edge of the nerve. Hence the essential difference between the upper and lower margins of the disc (normal and abnormal parts) is that, while at the upper edge the pigment layer indents the nerve, at the lower margin it fails to reach the nerve altogether and so there is an area just below the disc (turned towards the vitreous) in which the nerve fibre layer is alone present. It is to be noted that in Fig. 2A, there is no sign of atrophy of this nerve fibre layer in the crescent, the ridge (*d*) being practically the same height as the ridge (*a*) at the upper margin of the disc, so that there is nothing to suggest that the condition is due to stretching, as has sometimes been suggested.

These facts can also be expressed in another way, thus: if a series of sections approximately through the centre of normal discs be examined it will be found that the distance between the upper and lower endings of the pigment layer is always the narrowest part of the nerve, and that this distance is always less than the diameter of the nerve at the centre of the *lamina cribrosa*. In eyes presenting inferior crescents, however, the distance between the upper and lower ending of the pigment layer is always equal to or more than the diameter of the nerve at the *lamina cribrosa*. This shows that there is an actual anomaly of development of the edge of the disc and not merely an oblique insertion of the nerve. That this anomaly involves the lower portion of the disc and adjacent retina only is indicated by the fact that the *lamina cribrosa* is normal in structure and position and that the nerve behind it is normal.

Figs. 3 and 4 are taken from Elschnig's paper on "Conus nach unten", and show a similar condition. Fig. 4 is not a typical case since there is atrophy of the nerve fibres in the crescent, which is not seen in Figs. 2A and 3. Fig. 3 represents the microscopic appearance of the case seen in Fig. 1C.

We have then to account for a condition in which the retinal pigment epithelium and also the nuclear layers have failed to reach the lower edge of the nerve, so that a small area devoid of every layer except nerve fibres is interpolated between the lower edge of the disc and the true lower edge of the nerve.

A study of the normal development of the upper end of the choroidal fissure shows us, as I pointed out in a communication to the Anatomical Society in 1920, that normally there is an eversion of the unpigmented inner layer of the optic cup along the edges of the cleft in its upper part. This eversion is not so well marked in the human eye as in other forms, but that it does occur is shown by Fig. 5A. This is a drawing of a section through the eye of a 15mm. human embryo just below the insertion of the optic stalk. It shows the choroidal fissure open, with the as yet undifferentiated inner layer everted in the fissure. Fig. 5B is a section through the same

eye a little lower down, shewing that fusion has occurred between the lips of the fissure, and a little mass of unpigmented inner layer cells has been left in continuity with the pigment layer, though they have here lost their original connection with the inner layer.



FIG. 3.



FIG. 4.

This eversion of the inner layer occurs in a large number of vertebrate eyes (e.g., mouse, pig, chick, terrapin, dogfish), and in some the connection of the everted portion with the inner layer is lost after fusion of the edges of the fissure, while in others it persists. If it persists, nerve fibres are able to grow into the everted portion, since it is structurally continuous with the inner, fibre-bearing

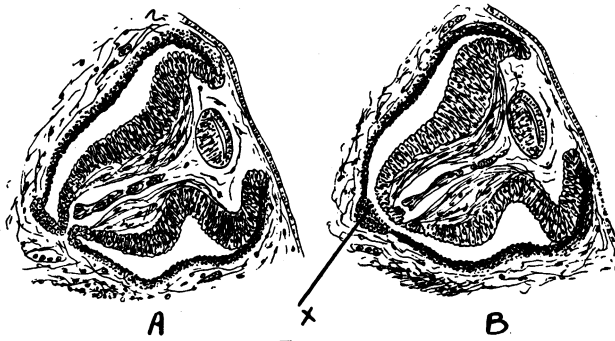


FIG. 5.

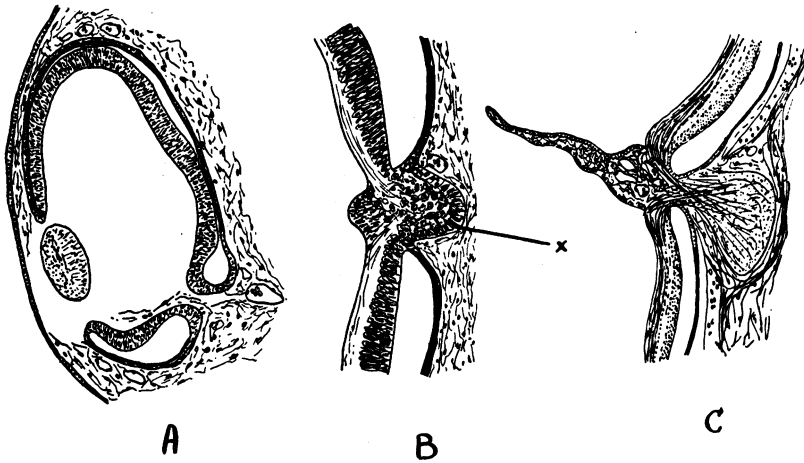


FIG. 6.

layer of the optic cup. Thus nerve fibres may leave the eye not only at the extreme upper end of the cleft where the inner layer of the cup is continuous with the ventral layer of the optic stalk, but also along a varying portion of the cleft below this. This condition of things is seen in its most highly elaborated form in the chick, in which the everted lips of the fissure with nerve fibres growing into them show as a pigment-free ridge on the back of the embryonic eye below the nerve, and later, in the adult, these nerve fibres form

the *cauda* of the nerve. Fig 6 shews three stages in the development of the *cauda* of the hen. A shows the whole eye of a three days' chick with the fissure still open and the edges everted. B shows the region of the fissure after closure, the unpigmented mass of cells (x) being comparable to the mass (x) in Fig. 5B, with the difference that in the chick it has retained its connection with the inner layer. C shows the developing *cauda* in an older chick where the cells of the projection have been obliterated by the nerve fibres.

Fig 7 shows the back view of a reconstructed model of a chick's eye (A) and a human (B) (13 mm.), showing the non-pigmented area below the disc. In the human embryo this unpigmented area has quite disappeared in the 18 mm. stage, while in the chick it persists.

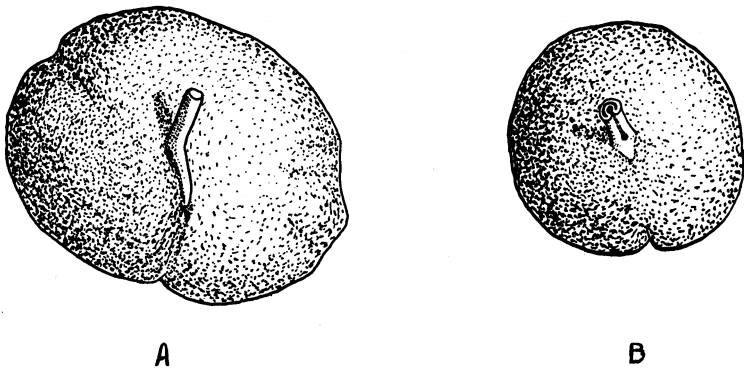


FIG. 7.

The condition in the adult fowl is worth studying. Fig. 8 shows a longitudinal section through the optic disc of a hen. Apart from the presence of a pecten, which we are not concerned with here, the following points are of note. It will be seen at once that the nerve is as it were drawn down as it enters the eye and so forms a long tail-like prolongation below, inside the sclerotic, known as the *cauda* of the nerve. From this it is obvious that the optic disc seen ophthalmoscopically is a long vertical oval and not a circle. The appearances seen in Fig. 8 bear comparison with those of the inferior crescent seen in Fig. 2A. In the first place the upper margin of the hen's disc shows the sclera (which in birds is cartilaginous) ending at the nerve, which is here slightly indented by the pigment layer. The constriction of the nerve, is not so marked as in the human eye in Fig. 2A.

Below, the cartilaginous sclerotic comes up to the lower edge of the nerve and the nerve fibres here turn round with a much gentler curve than they show at the upper margin. The pigment layer and choroid indent the nerve above, but below they fall a long way short

of the lower border of the nerve, so that over a certain area (*c*) all the layers of the retina are absent except the nerve fibre layer, which is in contact with the sclera, only separated from it in part by a large vein. This area therefore resembles the area (*c*) in Fig. 2A in that it represents an area below the nerve on the vitreous surface of the eye over which only nerve fibres are present. It

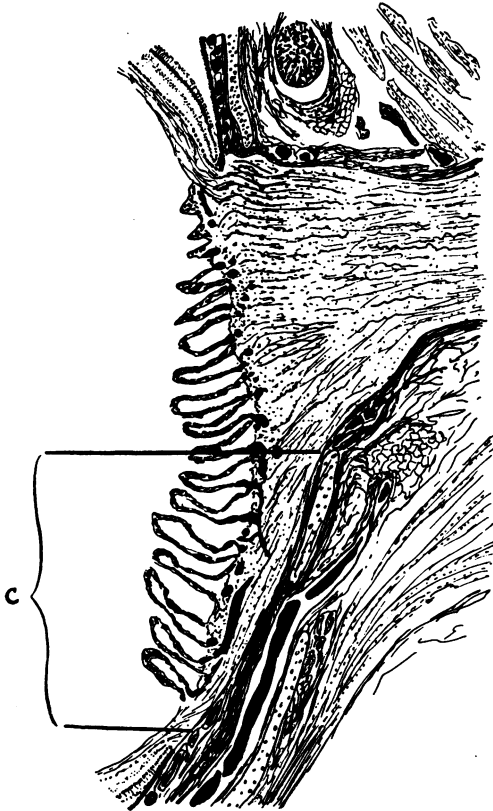


FIG. 8.

lies wholly within the sclerotic in both cases and does not affect the nerve except as regards the curve made by the lower bundle of nerve fibres as they enter the nerve. In Fig. 8 this area appears in a more exaggerated form than in Fig. 2A. Fig. 9 is a scheme showing the essential similarity of the condition in the hen and the human inferior crescent, together with a normal human disc shown in the same way. In birds the *lamina cribrosa* is not marked though there is a certain amount of thickening of the connective tissue

between the bundles of nerve fibres in the upper part of the nerve which probably represents it.

Thus we see that the persistence of the unpigmented everted projection seen below the nerve in many vertebrate embryos, including man, may give rise by its normal persistence (in the bird) to a condition resembling anatomically an exaggerated inferior crescent. Is it not likely, therefore, that the occasional inferior crescent in man is formed in the same way by the persistence of the continuity of the inner layer of the optic cup with the everted portion and the subsequent growth of nerve fibres into it? The

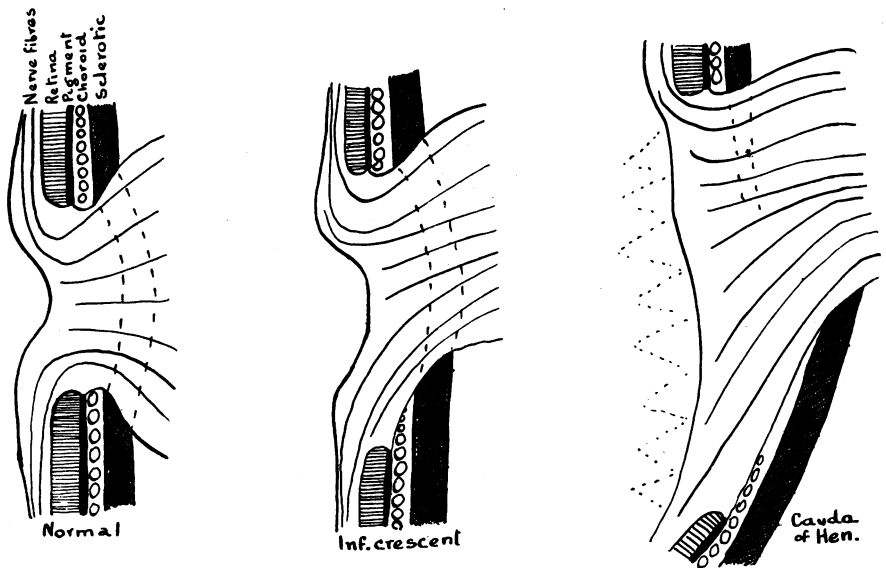


FIG. 9.

inferior crescent, then, can be looked on as an attempt at the formation of a *cauda* to the optic nerve similar to but much less than that normal in birds.

To argue from the normal hen to the abnormal man may seem to err in the direction of speculation, even though a definite point of similarity can be found embryonically. It is, therefore, advisable to examine other forms with a view to seeing if any connecting link can be obtained. It is among the Reptilia, in the rôle of common ancestors, that it will be as well to look. The embryo lizard is suggestive. Compare Fig. 10, which is a transverse section through the lower part of the optic disc of a *Calotes* embryo, with Fig. 6C, and the similarity is striking. The apparent *cauda* in the lizard is not very long, however, and at this stage a vertical section through the disc much resembles an inferior crescent. Fig 11 shows three

reconstructions of vertical sections through the optic discs of lizard embryos. A and B are from Calotes embryos, and C from a West African lizard. The line a b shows the plane of the section seen in Fig. 10. It will be seen in all of them that the nerve enters obliquely and is slightly drawn down, so that, whereas at the upper margin of the disc the pigment epithelium forms a fairly sharp edge round which the nerve fibres turn with an acute bend, at the lower margin the curve of the nerve fibres is much gentler. Also, as was pointed out for inferior crescents in man, the distance



FIG. 10.

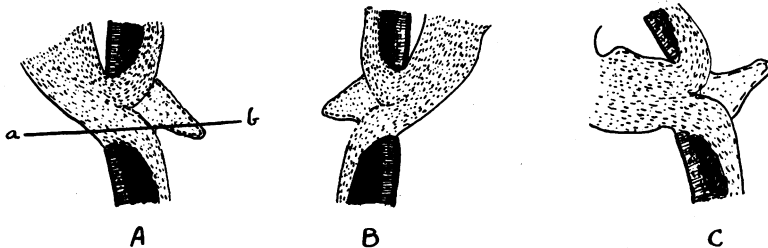


FIG. 11.

between the upper and lower limits of the pigment epithelium is greater than the diameter of the narrowest part of the nerve. The embryo lizard thus shows a condition extremely resembling an inferior crescent, which has been elaborated by birds into the well-marked *cauda*.

Fig. 12 shows as a point of interest the possibility that the process in man may go even farther. Fig. 12A is a transverse section through the *cauda* of a hen and Fig. 12B is taken from Elschnig's paper and shows a curious case in which the nerve appeared to run obliquely at the back of the eye. The similarity

in all essential points between the two figures is striking; unfortunately Elschnig does not give full enough details of his case to enable us to stress the analogy further.

The question of the occurrence of congenital crescents in man in situations where they could not have been associated with the choroidal fissure is of more difficulty. There are, however, a few suggestive facts to be considered.

Few congenital crescents occurring in anomalous situations have been investigated microscopically and I have not been able to

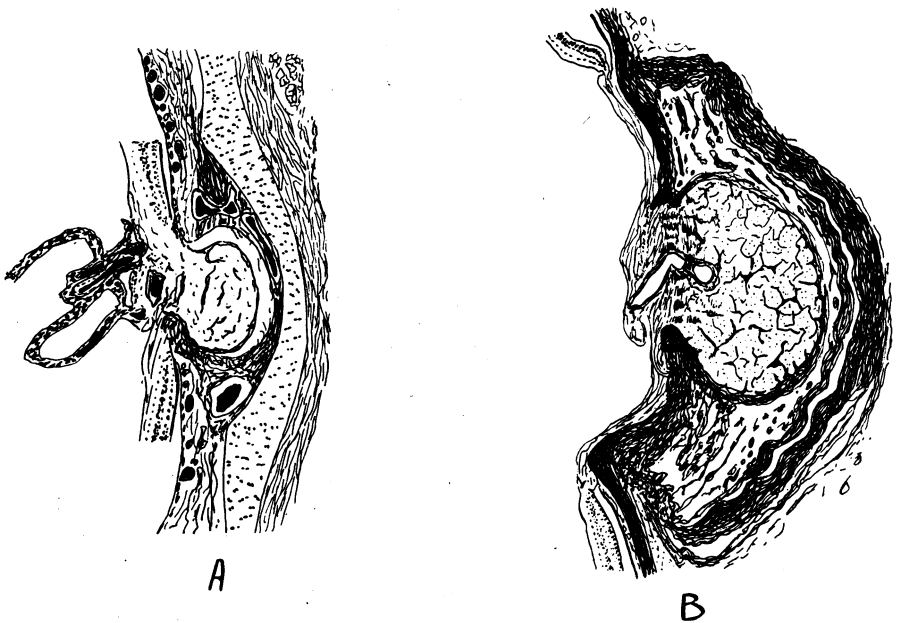


FIG. 12.

obtain a specimen. It appears, however, from the work of Elschnig and others that the condition presents a resemblance to an inferior crescent, the same main feature, namely, a failure of the pigment epithelium and choroid to reach the edge of the nerve, being present. In some cases, of crescents inferior and otherwise, stress is laid on the atrophic condition of the sclera in the crescent area, though this does not appear to be uniformly present. A point of great constancy, however, is the failure of the choroid in the crescent. In most cases the choroid proper is only continued a very short distance beyond the edge of the pigment epithelium, though it can often be traced as a very atrophic membrane as far as the edge of the optic nerve proper. All congenital crescents have, then, in common the failure of the pigment epithelium to

reach the edge of the nerve and the failure of the choroid just beyond the edge of the pigment.

How can one explain the falling short of the pigment epithelium in regions remote from the fissure? Normally in man neither the dorsal nor the invaginated ventral wall of the optic stalk shows any signs of pigmentation during development, the pigment always stopping short exactly where the stalk joins the globe of the eye. This is not necessarily true in other animals and may vary in abnormal cases in man. Pigmentation of the optic stalk occurs normally in bat embryos.

It seems likely from the work of Coats, Monthus and Opin, and others that a certain class of congenital anomalies of the eye may be due to the aberrant differentiation of one part of the optic cup into tissue resembling that normally derived from another part. For example the ventral layer of the optic stalk may give rise to a patch of rudimentary retina in the nerve. In the same way the usual sharp differentiation between pigmented epithelium and unpigmented optic stalk at their junction might fail in one direction or another; either the pigment might extend on to the stalk or the unpigmented stalk might appear to encroach on the globe. This failure of pigmentation in the outer layer of the optic cup might conceivably occur in regions far away from the insertion of the nerve and indeed has been shown to do so. It is still more likely to occur in situations where pigmented normally joins unpigmented epithelium, namely round the disc.

This aberrant differentiation was well shown in a case of Mr. Frank Juler's, which I had the opportunity of examining and which has since been published. Here the pigment epithelium was continued directly along the optic nerve for some distance. The same case also showed the converse condition, namely a failure of pigmentation in the outer layer of the cup. There were, above the disc but not in connection with it, some small oval areas of cells exactly resembling cells of the pigment epithelium and continuous with them, but containing, some no trace of pigment and others a few brown granules only.

This serves to show that a localised failure of the pigment epithelium may occur. It is conceivable that such an area arising in association with the insertion of the optic stalk might give rise to one type of congenital crescent.

With regard to the failure of the choroid in the region of the crescent the following facts are of importance. The development of the choroid appears to occur *pari passu* with that of the pigment epithelium, and they seem to exercise some reciprocal action. Mesoderm which is in contact with the pigment epithelium develops into choroid, but mesoderm in contact with the inner layer of the optic cup does not. This applies both to the mesoderm which

passes into the eye through the fissure and to the mesoderm in contact with the normally everted fold of inner layer along the fissure or with abnormally everted inner layer in an inferior crescent or a coloboma. The interdependence of the pigment and the choroid is also shown by Juler's case mentioned above. Here the pigment epithelium was abnormally continued along the nerve and was accompanied by choroid which thus extended beyond its normal limits to follow the pigment epithelium. The failure of choroid to develop except where mesoderm is in contact with pigment epithelium can be seen in the chick, in which the choroid stops short at

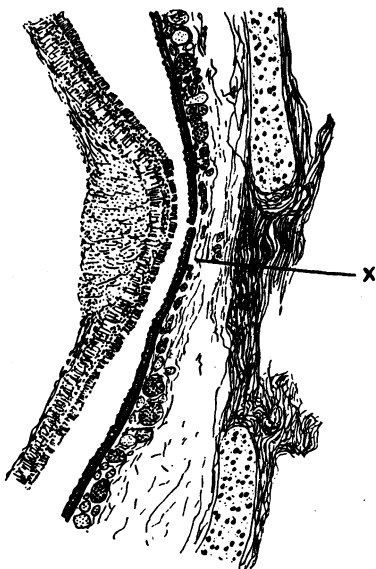


FIG. 13.

the edges of the developing *cauda*, and in the mouse, in which for a little time there is a lagging behind of the choroid just below the nerve where the eversion occurred during closure of the fissure.

In some animals the result of the inhibiting action of the fissure on the development of the choroid remains more or less permanent, so that even after the fissure has become completely obliterated and the pigment epithelium has coalesced across it an area of relative atrophy of the choroid remains to mark the site. This is the case in the alligator, as is seen in Fig. 13 at (x). The same absence of choroid where mesoderm comes in contact with inner layer has been shown experimentally by Koyanagi. He examined the eyes of embryo rabbits bred from a buck with congenital coloboma, and showed that in the developing coloboma there was often excessive

eversion of the inner layer and absence of the choroid, so that the floor of the coloboma was formed by the duplicated retina in contact with the sclerotic. It therefore seems probable that the absence of pigmented epithelium in a congenital crescent is enough to account for the failure of the choroid also.

With regard to the occasional atrophy of the sclerotic seen in the crescents it is to be mentioned that, to a certain extent, the appearance of the sclerotic condensation in the embryo chick is related to the presence of the choroid. This is shown by the fact that the sclerotic condensation first appears round the equator of the eye and spreads towards the posterior pole, showing at one time a very definite thin area behind the *cauda*. The condensation of mesoderm is succeeded by a cartilaginous change and this is also distinctly delayed along the *cauda*, the sclera remaining fibrous here for some time but finally becoming cartilaginous like the rest. In the alligator, however, the cartilaginous change never occurs in the region of the choroidal thinning described below the nerve, and in Fig. 13 it can be easily seen that there is a gap filled by fibrous tissue in this situation. Sometimes then the sclera is permanently inhibited and sometimes only retarded. This is comparable to the varying condition of the sclera found in the floor of congenital crescents.

To sum up therefore, we may say in the first place, that congenital crescents in any situation are due to the failure of the pigment epithelium to reach the site of implantation of the optic stalk.

This failure may occur anywhere, since aberrant differentiation of any of the various parts of the secondary optic vesicle is known to occur. It is, however, much more likely to occur below the disc than elsewhere, since it is normal here at one stage of development in man. Hence the greater frequency of inferior crescents, which can be looked on as developmentally homologous with the *cauda* of birds: the architectural basis of the *cauda* being present though small in the normal human embryo.

This failure of the choroid is directly correlated with the absence of pigmented epithelium and the occasional failure of the sclera has its parallel in the retardation of condensation along the fissure during development.

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