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COMMUNICATIONS

CONGENITAL RETINAL FOLD

BY

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INTRODUCTION.

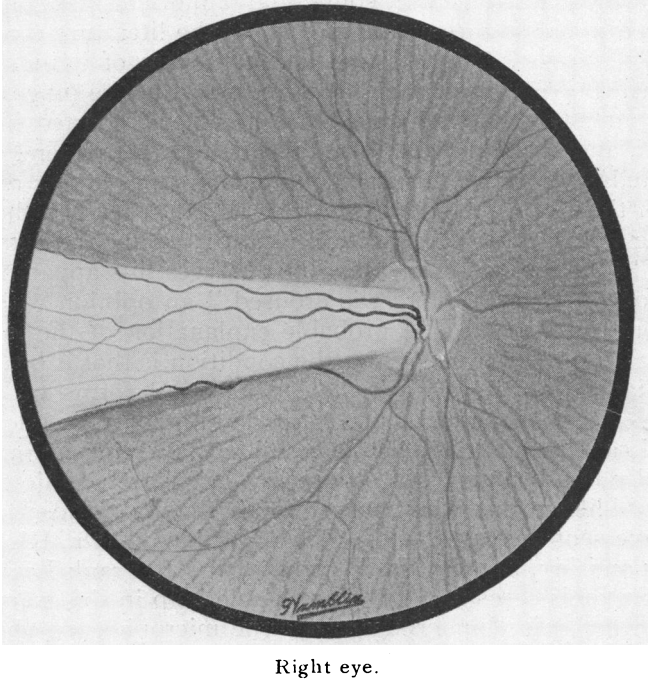
THE curious and striking congenital abnormality about to be described is not so rare as the paucity of the literature concerning it would suggest. Since I first became aware of it in 1928, six cases (eight eyes) have come to my personal notice (one of which I have already published), one case has been reported by Stella Ancona, and at the moment of publication of this paper Professor Weve tells me that he has also collected six cases and is reporting them in the *Arch. f. Augenheilk.* this month. He has shown me his case notes, and the condition is undoubtedly the same. He writes, "It is curious how often one observes this apparently rare condition once one's interest is aroused," an opinion with which I thoroughly agree. The probable explanation of the failure of previous observers to recognize the condition is that it bears some resemblance to persistent hyaloid and other forms of pseudo-glioma. Most of the cases had been diagnosed as pseudo-glioma before I saw them and the eyes which I was able to examine microscopically had been excised on account of suspected glioma.

I would like at this point to express my thanks to those surgeons who have sent me cases,—Mr. Peter Macdonald, Dr. Kirby, Mr. Coulter and Mr. Somerville Martyn—also Mr. Frank Law for the two Moorfields cases and for his valuable help in the examination of the pathological material and for the microphotographs which illustrate this paper.

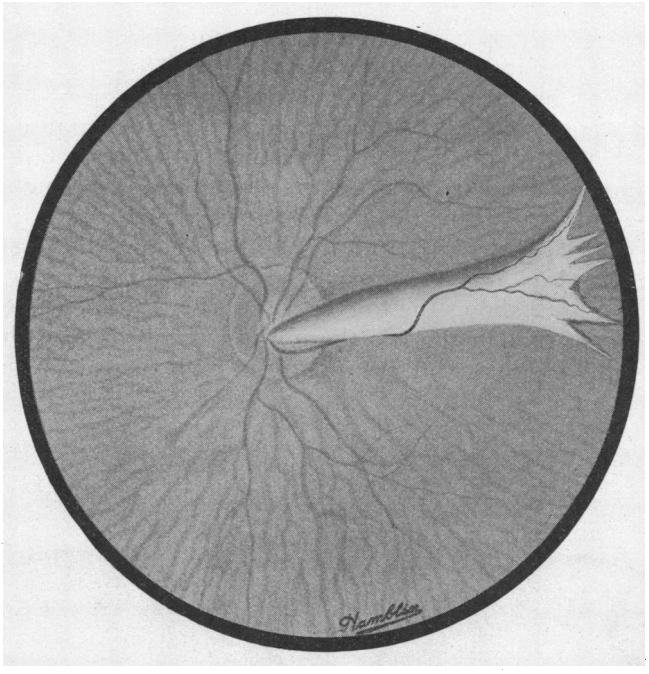
DEFINITION OF THE CONDITION.

The cases belong to a group of defects in the gross structure and differentiation of the inner layer of the optic cup. They arise mostly after the 13 mm. stage (when the cleft is closed) and in most cases the changes do not involve the cleft region and so do not fall into the class of colobomata. In a few the change may begin during the process of closure so that an orientation by means of the cleft is possible, but still the changes are not those of coloboma. All the cases are characterized by the appearance of folds or ridges involving the inner layer of the optic cup and projecting into the vitreous. In some this is shallow, in others high and sharp with a falciform edge. Fine gradations occur and when a series is studied it becomes evident that the deformity links up on the one hand with abnormalities of the cleft region and on the other with a group containing proliferations of the inner layer with rosette and ridge formation and the congenital detachments found in microphthalmic eyes. However, the cases about to be described constitute a definite clinical group to which the term 'congenital retinal fold' should be applied.

Typical cases will now be described from the point of view of ophthalmoscopic appearance, macro- and microscopic appearance and embryology.



Right eye.



Left eye.

FIG. 1.

The right and left eyes (ophthalmoscopic appearance) of a child of 18 months. The left eye shows a high retinal septum stretching from the disc to the temporal side of the equator of the lens. The general level of the fundus is myopic. Retinal vessels pass on to the septum. The lentine end of the septum breaks up into fine branding strands of embryonic tissue attached to the equator of the lens. The right eye shows a symmetrically arranged similar fold which is not so high nor so well marked. This has numerous retinal vessels on its surface.

OPHTHALMOSCOPIC APPEARANCES.

Case 1 (*2 eyes*). Fig. 1 shows the appearance of the eye in a child of 18 months. The general level of the fundus could only be seen with minus lenses and running from the disc outwards in the horizontal meridian towards the temporal edge of the lens was a thick rolled edge visible with a +12·0 D. sphere (with retinal vessels on it) breaking up anteriorly into many strands attached to the ora serrata on the temporal side in the horizontal meridian. This ridge could have no connection with the fissure. The solid appearance of the fold, the septum-like connection with the retina, the presence of branches of the retinal artery on the fold and the attachment anteriorly to the ora serrata, with strands passing to the lens near the equator are characteristic. The vitreous

and lens are clear, the eye of normal size. In all cases strands of persistent embryonic vessels, either the main hyaloid or some of its branches, are adherent to the surface of the fold (not contained within the substance) and may sometimes be seen with the ophthalmoscope, but more often on microscopic examination only.

The situation of the fold is interesting. In most of the cases (Weve and Ancona) it occupied the lower temporal quadrant of the retina, passing from the disc downwards and outwards. In bilateral cases it is symmetrical, but *by no means in all cases does it run downwards and outwards.*

Case 2. Fig. 2 shows the fold in a girl of 9 years. The eye was normal except that in the iris there was a small area of thinning of the stroma down and in, possibly representing a minimal

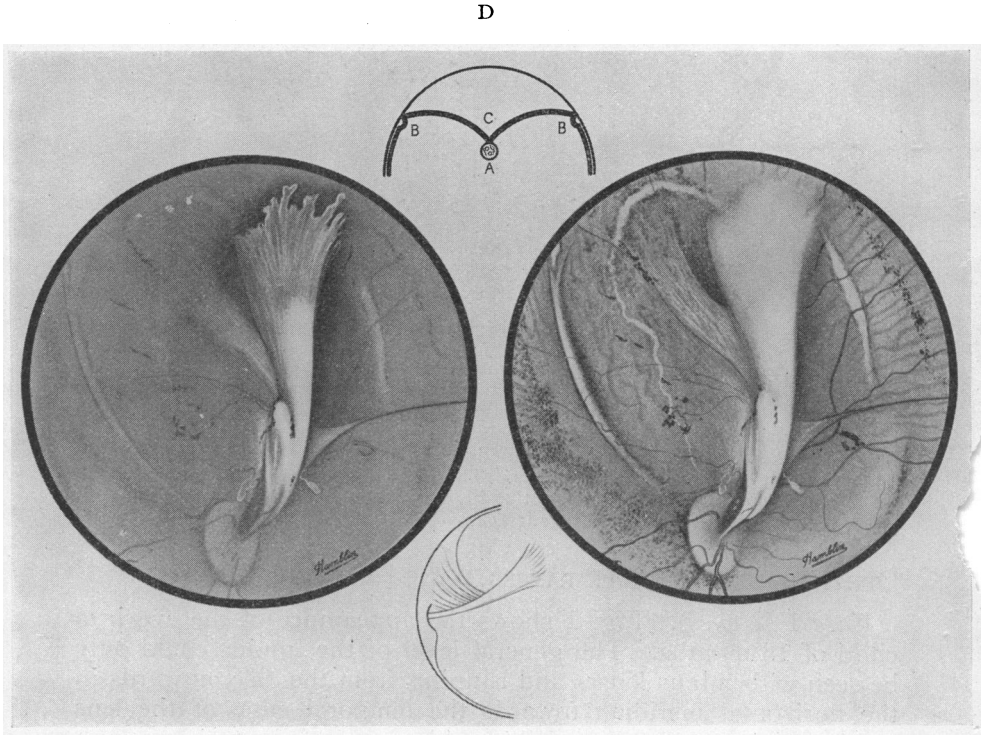


FIG. 2.

Ophthalmoscopic appearance of retinal septum in the left eye of a girl of 9 years. A, as seen with a +12 D. sphere. B, as seen without a lens. C, a diagram showing the vertical disposition of the retinal fold attached to the persistent hyaloid. D, a horizontal section through the fold. (A=the persistent hyaloid in its glial sheath. B=the scar-like adhesion to the pigment epithelium and choroid. C=the tent-like detachment or fold.)

coloboma iridis. (This was present in the right eye also). Ophthalmoscopically a small detachment without a hole and probably congenital was visible in the lower nasal portion of the retina, but the most striking appearances were in the upper part of the eye (thus showing that it had no connection with the fissure). Here a tubular, somewhat cornucopia-like structure ran upwards from the disc opening forwards and disappearing towards the upper edge of the lens. It was white with a little irregular pigment on its surface and became more diaphanous as it passed forwards. It appeared to be a mass formed by proliferation of the glial sheath of the hyaloid. A single vessel left it on the temporal side and disappeared anteriorly. This mass taken alone was typical of a severe persistence of embryonic vessels accompanied by glial overgrowth. The interesting feature, however, was the fact that the retina was adherent to the upper (and posterior) surface of this glial sheath, from the disc upwards for about a third of the distance from the disc to the lens along the abnormal strand. The adherent retina was pulled forward, lines of tension being visible on it, and the base of the localized somewhat tent-like detachment thus formed being marked out by a roughly circular ridge accompanied by pigmentary disturbance, the whole very similar in appearance to those cases of spontaneous limitation of an acquired detachment by formation of a line of scar-like adhesions between retina and pigment epithelium. Fig. 2, A, B, C, and D, show firstly the fundus appearance, with the sharp edge of the retina being pulled forwards by the persistent fibrovascular sheath and secondly, diagrams of hypothetical sections in two planes. In this case therefore the fold passes straight upwards from the disc. The main white mass appears to be formed of the contents of Cloquet's canal, abnormally thickened and attached to the apex of the fold of retina which has been pulled forwards. In this case the hyaloid remnants rather overshadow the fold; in some cases (indeed most) they are small and often invisible except microscopically.

Case 3. Fig. 3 shows, not an ophthalmoscopic picture, but the appearance of a macroscopic specimen (lent me by Mr. Law to whom I am also indebted for Case 5). The eye is cut in vertical section and one is looking at the temporal half. A thick septum of retinal tissue with blood vessels on it (branches of the arteria centralis and the hyaloid) runs from the disc forwards. Its free edge passes across the centre of the vitreous to the back of the lens; its line of attachment runs from the ora serrata in the upper temporal quadrant to the disc along a meridian corresponding to 2 o'clock. The line of the fold is therefore up and out from the disc. The lens is clear. The fold is attached to the lens at the extreme equator on the temporal side in the horizontal

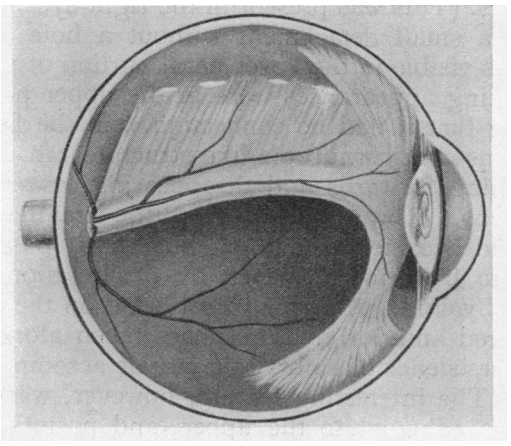


FIG. 3.

Macroscopic appearance of eye containing retinal septum in the upper temporal quadrant. The plane of section is vertical antero-posterior and passes to the nasal side of the disc. The lower expansion is drawn somewhat too far back.

meridian. The fold therefore forms a partition dividing the upper part of the vitreous into unequal temporal and nasal parts. From the anterior end of the fold pass two expansions up and down to be attached to the structures in the region of the ciliary body and back to the walls of the globe as far as the ora serrata. This eye had been excised on suspicion of glioma. The patient was a girl 6 years of age.

Case 4. Fig. 4 shows another macroscopic specimen (sent me by Mr. Peter Macdonald) in which the ridge is not so high nor so sharp as in the preceding case. It runs in this case downwards from the disc along the line of the foetal fissure to the ora serrata, where a small portion of still open fissure can be recognized microscopically, thus placing its line accurately. As in the other cases retinal vessels passed on to the ridge, and a persistent hyaloid (Fig. 10) was adherent to its surface. The portion of retina including the fold showed a shallow detachment. This case I reported in the Transactions of the Ophthalmological Society, 1928.

Case 5 (2 *eyes*). Fig. 5 shows a photograph of another case from the Pathological Department of Moorfields. It is the right eye of a boy of $1\frac{10}{12}$ years. It was excised on a suspicion of glioma. The septum or fold is seen stretching from the disc to be adherent to the lens in the lower temporal quadrant, whence it passes to the ora serrata. Although the other eye of the child was not examined by me there is a note to the effect that there was a greyish band visible ophthalmoscopically on the retina in a similar situation.

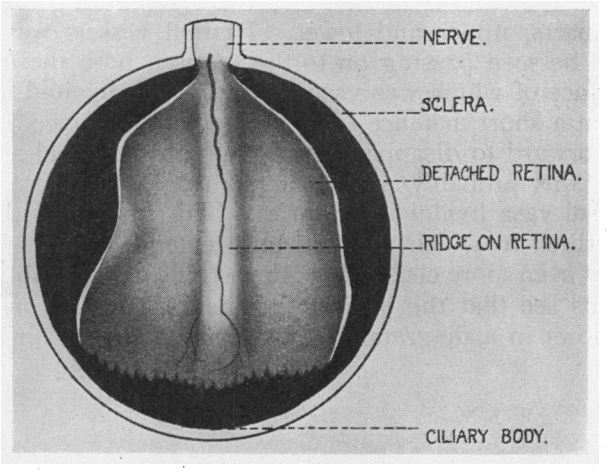


FIG. 4.

Lower half of eye containing retinal fold along the line of the foetal fissure.

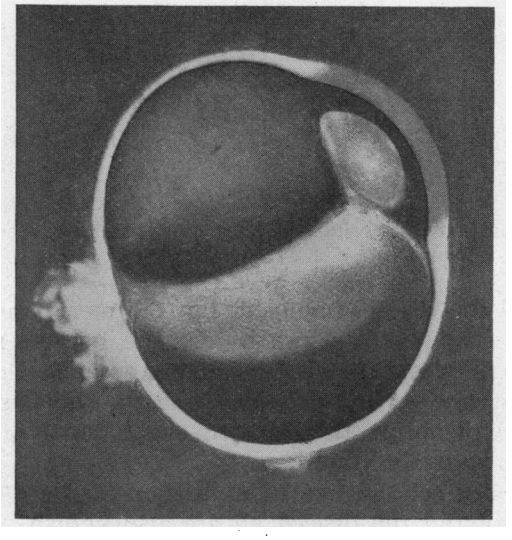


FIG. 5.

Lower half of eye containing retinal septum in the lower temporal quadrant.

Case 6. The sixth case rests on notes sent me by Mr. Somerville Martyn. In this case there was a persistent hyaloid artery attached to a membranous fold or septum which stretched

from the disc to the nasal side of the eye separating the vitreous into two parts, upper and lower. Retinal vessels were present and could be seen passing on to the septum, both the upper and lower surface of which was vascularized. The hyaloid artery left the septum a short distance from the posterior surface of the lens and ran forward to disappear from view on the nasal side of the lens. (It was probably not the main trunk, therefore, but one of the nasal vasa hyaloidea propria). This resembles the second case described in which the fold only extended part of the way and shows even more clearly how these folds are probably formed.

We thus see that the position of the septum is not constant. Fig. 6 shows in a diagram the positions of the fold in these six

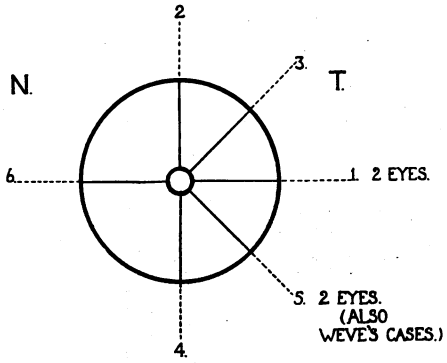


FIG. 6.

Diagram showing position of retinal septum in cases recorded.

cases. In all the disc is involved, but the meridians vary. The temporal side, however, shows by far the greater number. Of my six cases (8 eyes) five were in the temporal half of the retina, one upwards, one downwards and one on the nasal side. In seeking an explanation therefore, a cause capable of acting in any meridian must be found.

Other cases of septum-like reduplication of the retina in situations not involving the disc at all are also known. These again are associated with abnormal adhesion of embryonic vitreous vessels to the inner layer of the optic cup. Fig. 7 shows a microphthalmic eye in which the fold is at the ora serrata and projects equatorially inwards behind the lens. This case does not come strictly within the scope of the present paper but is included to lend force to the contention that retinal reduplications can occur in almost any situation.

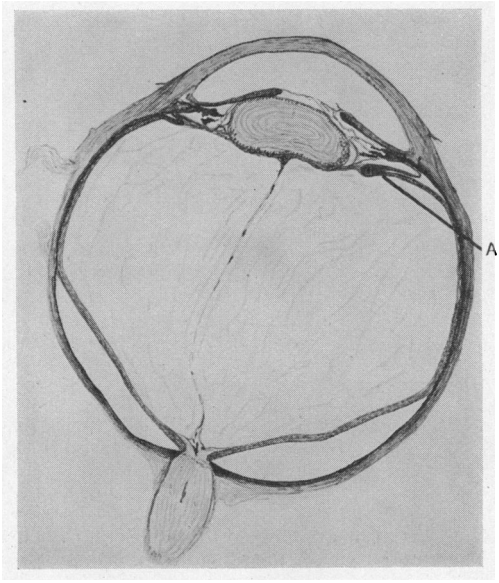


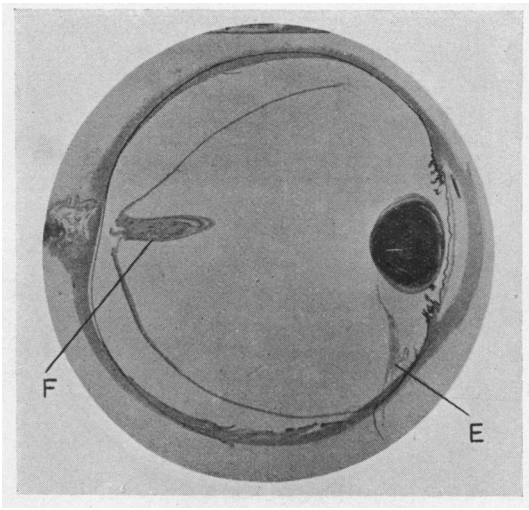
FIG. 7.

Section of microphthalmic eye with retinal fold at the ora serrata (seen at A). The top of the fold is adherent to the vascular capsule of the lens.

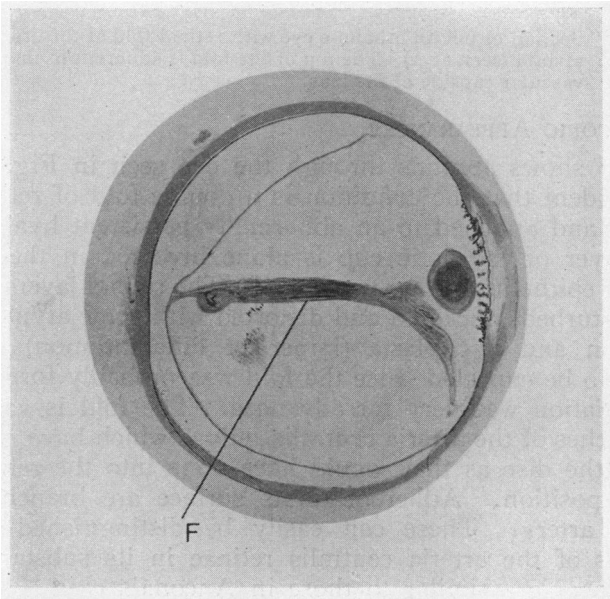
MICROSCOPIC APPEARANCES.

Fig. 8 shows sections through the eye seen in Fig. 3. It is quite evident that the condition is a double fold of retina pulled inwards and attached to an abnormally persistent hyaloid. The inner layer of the optic cup is alone involved in the fold, the pigment epithelium being unaffected. The retinal layers are somewhat disturbed, puckered and distorted with some atypical rosette formation and hypoplasia (imperfect differentiation) of layers. This is to be expected since the fold was probably formed before differentiation was very far advanced. The fold is vascularized by branches of the arteria centralis retinae which have grown into it from the disc as they would have done into the retina in the normal position. Adherent to its surface are branches of the hyaloid artery. These can easily be distinguished from the branches of the arteria centralis retinae in its substance. The appearances are similar to those in Ancona's case (Fig. 9) and the condition falls into the same category except that in her case the ridge occupied the line of the fissure as in my fourth case.

Fig. 10 shows a section of the ridge in Fig. 4. Again the ridge is composed of retinal tissue with the hyaloid artery adherent to its vitreous surface. Fig. 11 shows a section of the case seen in Fig. 5. The appearances are similar to those in Fig. 8.

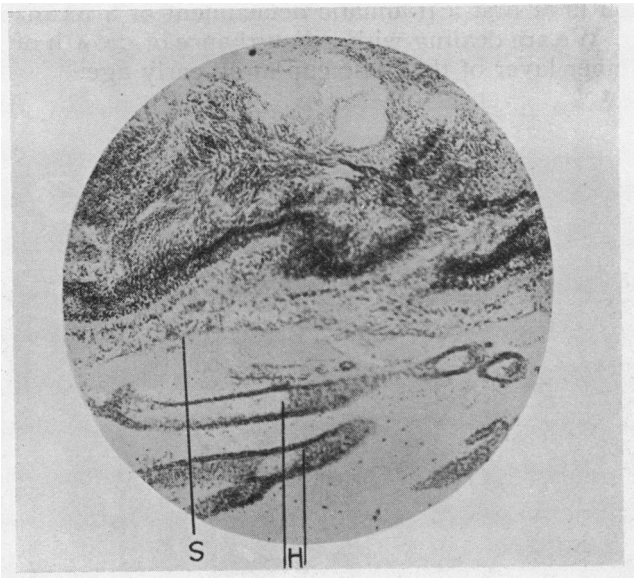


The fold cut at its attachment to the disc. F. The fold.
E. The anterior end of the attachment to the ora serrata.

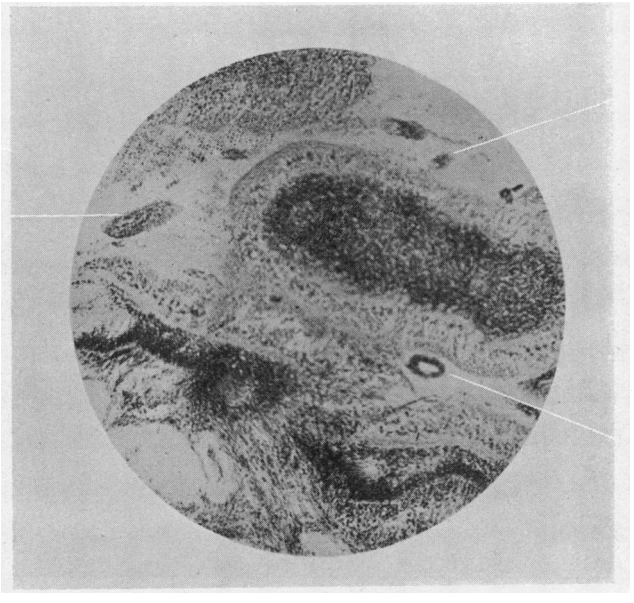


The fold cut along its whole length. F. The fold.

In all the cases which have been examined microscopically the whole of the retina (not only that in the fold) shows imperfect differentiation. This puts out of count any suggestion that the



The hyaloid artery on the surface of the fold. S. Vitreous surface of the fold. H. The hyaloid artery.



H, branches of the hyaloid among puckerings on the fold.

FIG. 8.

Microphotographs of sections of the eye in Fig. 3.

condition is at first a traumatic detachment or a localized inflammation. We are dealing with a disturbance of growth of the whole of the inner layer of the optic cup at an early age.

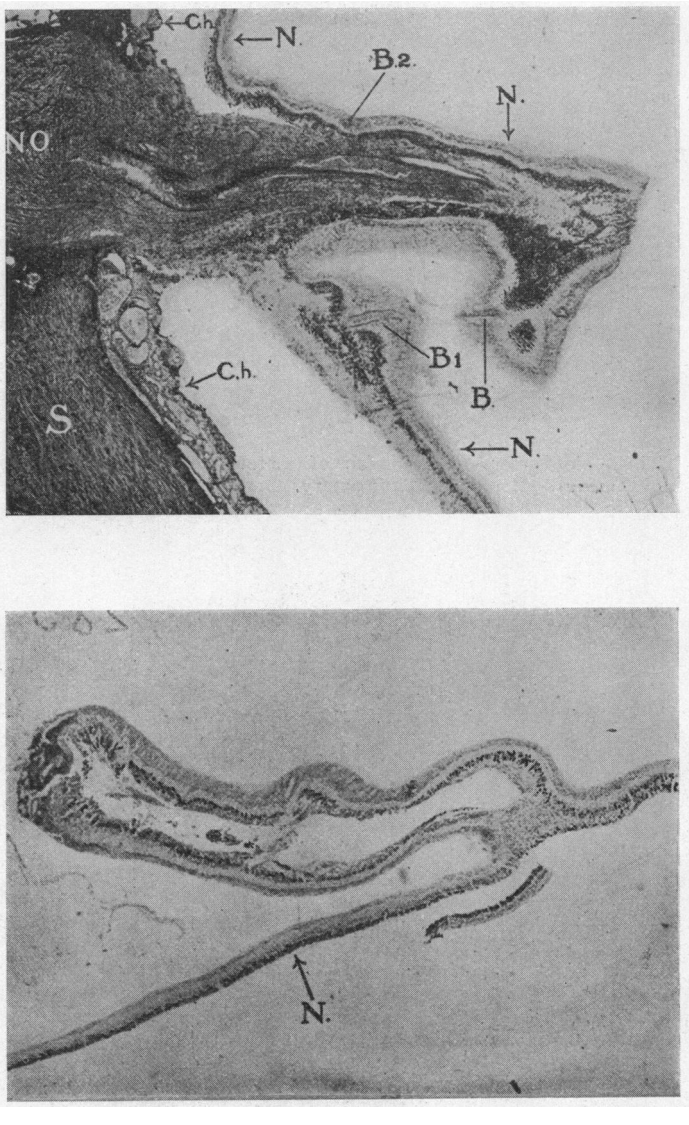


FIG. 9.

Two sections (from Stella Ancona's paper, Nederl. Tijdschrift voor Geneeskunde, Vol. LXXIX, ii. p. 135, 1935) showing the fold near the disc (A) and further out (B)—compare with Fig. 8.

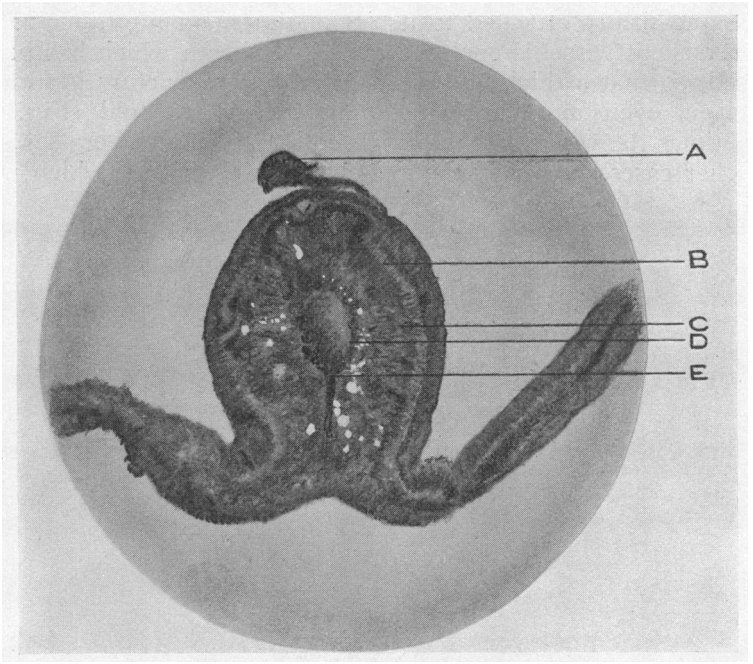


FIG. 10.

Section through the ridge seen in Fig. 4. A, the hyaloid. B, the inner molecular layer. C, D and E, imperfectly differentiated retinal layers.

EMBRYOLOGICAL CONSIDERATIONS.

The main points of embryological importance to be considered are, (1) the nature of the tissue composing the fold, (2) the relation of the fold to the hyaloid artery, and (3) the position of the fold.

1. *The nature of the tissue in the fold.* This is, in all cases which have been examined microscopically, composed of a reduplication of the retina (internal limiting membrane to rods and cones inclusive) without involvement of the hexagonal pigment epithelium. The retinal structure is somewhat disturbed, the layers imperfectly differentiated and rosettes are often present. There can be no doubt whatever in any of the cases that the fold is formed wholly from the inner layer of the optic cup.

2. *The relation of the fold to the hyaloid artery* In all the cases examined microscopically and in many of those seen clinically there is evidence of attachment of the hyaloid artery or one of its branches to the apex of the fold. In some cases this is a single fine strand only. Fig. 10 shows the vessel connected with the top of the ridge in the fourth case by a fine strand of tissue. In Fig. 9, however, the vessel is almost embedded in the

ridge and firmly attached to it. Sometimes, on the other hand, the persistent vessel is enclosed in a glial sheath which has proliferated, so that a thick and imposing tubular structure is formed which is even more arresting than the retinal fold (Fig. 2). Sometimes the vessel and the ridge both extend to the ora serrata. In other cases, however, the vessel leaves the ridge (which may

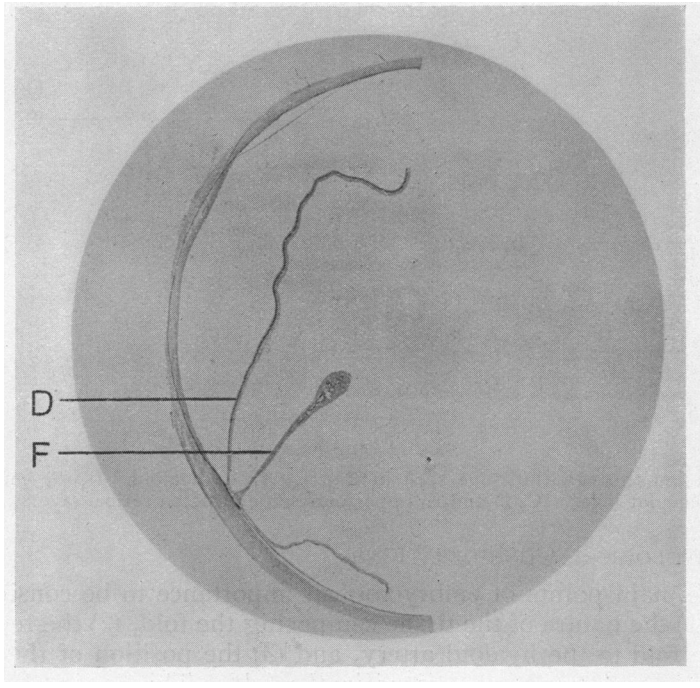


FIG. 11.

Microphotograph of the retinal ridge in Fig. 5. D, detached retina. F, fold composed of two layers of retina.

then flatten down) and runs on alone as a single or a branching strand, to the lens (Cases 2 and 6). In all cases the vessel was displaced somewhat from the centre of the eye and was not attached to the posterior pole of the lens, but to some point near its equator. This makes it possible that the vessel which persists is not the main trunk but is one of the vasa hyaloidea propria. On the other hand, however, it is quite possible that it is the main trunk which has become displaced and separated from the lens because of its adhesion to the fold. It may or may not be impervious to blood. Blood is seen in it in Fig. 8.

3. *The position of the fold.* This is variable. It cannot have primary connection with the foetal fissure though, as we have seen, it can sometimes occupy the position of this. It can apparently occur in any meridian, but according to Weve's cases and some of mine there is a marked predilection for the lower temporal quadrant, external to the line of the fissure. No structure exists here normally capable of determining this position, nor are the embryonic vitreous vessels larger here. At present no reason can be given.

SUGGESTED MECHANISM OF PRODUCTION OF THE DEFORMITY.

It is apparent that embryologically speaking the defect consists of the adhesion of the primary vitreous and its contents to one portion of the inner layer of the optic cup, the secondary vitreous which should normally separate them being absent along the line

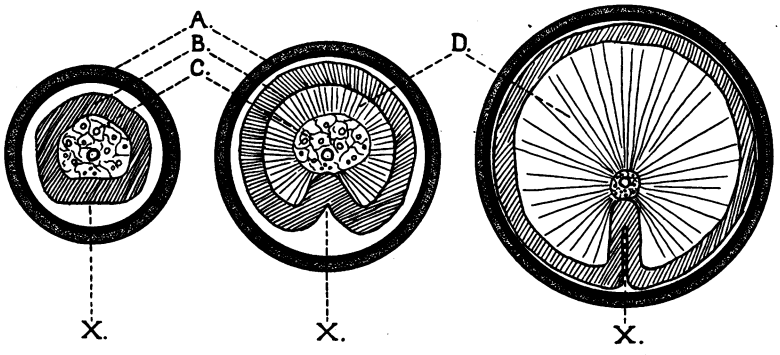


FIG. 12.

Diagram showing formation of a retinal fold. 1. Equatorial section of eye at 13 mm. stage. A = choroid and pigment epithelium. B = inner layer of optic cup. C = primary vitreous. X = point of adhesion between primary vitreous and inner layer of optic cup. 2. Equatorial section at beginning of formatlon of secondary vitreous D. This is absent at the point of adhesion X. 3. The fully formed fold in the adult.

of adhesion. Secondarily to this adhesion both the structures involved become displaced, the inner layer of the cup being detached (or rather prevented from coapting with the outer layer) and raised up into a ridge, and the contents of the primary vitreous becoming displaced from the optic axis towards the side of the adhesion. We can represent what happens in a series of diagrams (Fig. 12). In the first diagram we see an equatorial section of an eye at the 13 mm. stage. A represents the choroid and pigment epithelium. B is the inner (retinal) layer of the optic cup not yet in contact with the outer layer, and C is the primary vitreous,

richly vascular, which fills the whole eye at this stage. Let us postulate an abnormal adhesion of one or more vessels to the retina at the point X at this stage.

The second diagram shows the same eye at about the 48 mm. stage. Secondary (avascular) vitreous has formed from the inner layer of the optic cup and as the eye has increased in size we get the apparent compression of the primary vitreous in the centre of the eye where it forms Cloquet's canal. If the adhesion is still present at the point X the secondary vitreous will have been pre-

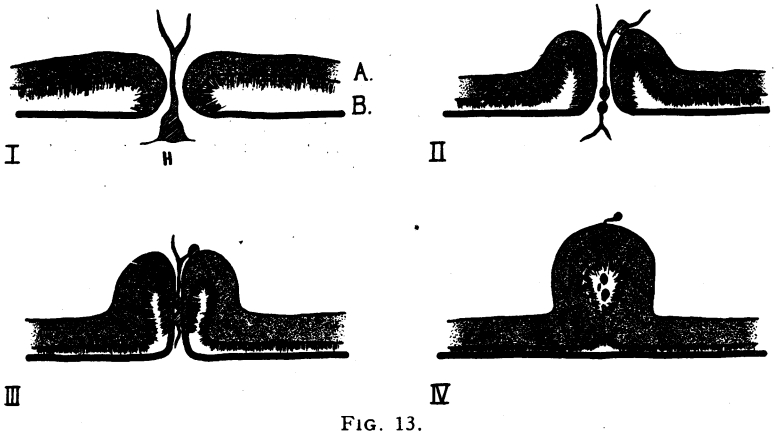


FIG. 13.

Diagram showing how inversion of the lips of the fissure may be produced by adhesion of a vessel (or of the primary vitreous) before closure is complete. I. The normal open fissure. A = inner, B = outer layer of optic cup. H = hyaloid artery. II. Commencing inversion. III and IV. Further and final stages of abnormal closure.

vented from forming here and the inner layer of the cup will have been pulled up into a narrow tent-like detachment. If this continues as the eye grows the condition in the third diagram will occur, which is almost identical with that found in the actual sections.

If the adhesion happens to occur along the line of the cleft while this is first closing at the 13 mm. stage, a slightly different mechanism may occur. Both edges of the cleft may be pulled inwards and a condition of abnormal *inversion* of the inner layer (the opposite of the abnormal *eversion* which precedes the formation of a coloboma) may occur. This is shown diagrammatically in Fig. 13, and is what I presumed had occurred when I first reported Case 4, in 1928. I, shows the open fissure with the hyaloid passing through it. II, shows inversion with adhesion of branches of the hyaloid to the edge. III, is a further stage, and IV is the final stage after fusion. In this case the interior of

the fold was occupied by some aberrant vessels which had become included as closure occurred and by some hyaline material derived probably from abnormal rods and cones.

A somewhat similar scheme might explain Ancona's case, in which there was a curious aberrant strand of nerve fibres on the deep surface of the inner layer in the fold. Fig. 14 shows a possible explanation, though Ancona's own, that the condition was due to the persistence of the connecting portion of von Szily's primitive epithelial papilla is also possible. 1, shows the fissure

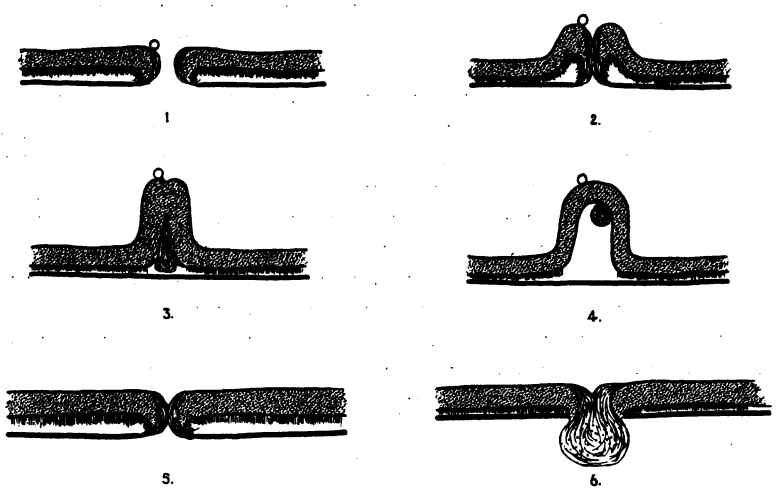


FIG. 14.

Scheme to explain the presence of abnormally placed nerve fibres in cases in which the fissure is involved. 1. Aberrant nerve fibres passing out of fissure. 2. The fissure closing and including the nerve fibres. 3 and 4. Two forms of closure with abnormally placed nerve fibres. 5 and 6. Normal development of the cauda in birds.

closing with the vessel adherent to one of its lips and aberrant nerve fibres passing out along its margins. 2, shows the beginning of the fold and the nerve fibres included in the inner layer. 3 and 4, show possible further stages with formation of an aberrant bundle of nerve fibres. This is in accordance with von Szily's experimental work on abnormal closures of the fissure. He showed that such aberrant bundles of nerve fibres were common in the malformed eyes of the embryos of the colobomatous stock he used. It would be quite reasonable to suppose that they might occur in other abnormalities of closure of the fissure also. The condition has its parallel in the normal development of birds in which the cauda of the optic nerve is formed by just such an outgrowth of nerve fibres through the closing fissure. This is seen in 5 and 6 (Fig. 14).

These modifications of the process seen in Fig. 12 are merely dependent on the vessel happening to adhere to the inner layer of the cup in the cleft region.

This theory, that the condition consists essentially of abnormal adhesion of the primary vitreous to the inner wall of the optic cup with hindrance of formation of secondary vitreous in that situation appears to be consistent with the clinical findings. It explains the presence of embryonic vitreous vessels on the free edge of the fold and is consistent with all the three types of case described, namely those in which the fold extends all the way from the disc to the ora serrata, those in which it only extends part of the way but the vessels go on, and those in which the cleft region is involved.

The cause of the adhesion is obscure. There are no signs of inflammatory change, but haemorrhage at an early stage could not be excluded. Professor Weve tells me that in many of his cases there is a familial and hereditary factor and that in bilateral cases the appearance is symmetrical, both facts against any theory of foetal inflammation or fortuitous haemorrhage. The small number of cases available makes it impossible to say anything definite as to the commonest situation, but sufficient different positions have already been seen to warrant the assumption that it can occur in situations other than temporal, and even not in connection with the disc at all.

Conclusions

This paper deals with a little known condition which can be described as "congenital retinal fold." Cases are described, all showing a falciform fold projecting into the vitreous, composed of a double layer of retina supplied by branches of the retina centralis retinae and having adherent to its surface remains of embryonic vitreous vessels. The fold has been found in many situations.

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