An outline of the embryology of the eye : with illustrations from original pen-drawings by the author / by Ward A. Holden.

AN OUTLINE

OF THE

EMBRYOLOGY OF THE EYE

WITH ILLUSTRATIONS FROM ORIGINAL
PEN-DRAWINGS BY THE AUTHOR

BY

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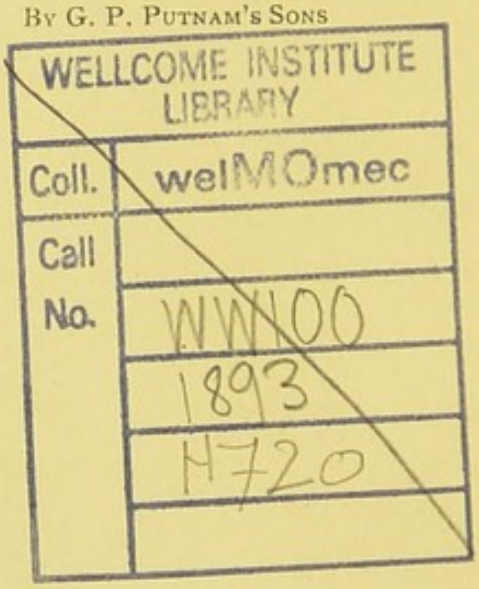

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PREFACE.

THE following study, carried out in the New York Ophthalmic and Aural Institute at Prof. Knapp's suggestion, is based upon the examination of a great number of specimens. The chick-embryos were obtained by incubation, and were hardened in Kleinenberg's or Müller's fluid, and stained with carmine and hematoxylin-eosin. The pig-embryos were obtained fresh and hardened in Müller's fluid, after decalcifying, when necessary, with phloroglucin or hydrochloric acid mixtures, and the sections were stained mostly with hematoxylin-eosin. Some of the breaks in my series were supplied by Dr. B. Alex. Randall of Philadelphia who kindly lent me a number of his specimens, prepared by Dr. Piersol.

W. A. H.

37 WEST 39TH STREET, NEW YORK,
August 15, 1893.

AN OUTLINE OF THE EMBRYOLOGY OF THE EYE.

[The drawings referred to by numbers will be found on the plates at the back of the volume.]

In endeavoring to present a clear and comprehensive description of the development of the eye, it has seemed to me best to give first a brief and purely schematic sketch of the processes which take place, explaining them with diagrams, and next to give an accurate histological description of the various parts of the eye in their successive phases of development, illustrating these descriptions with careful drawings from actual preparations. It will be noticed that the text is not burdened with frequent references to the voluminous literature of the subject. The microscopic descriptions are the unprejudiced interpreta-

tion of what I have myself seen. When some essential point has not been shown in my specimens, an authority that has described it is quoted. In regard to some disputed points the views held by different authorities are given.

The earliest periods up to the formation of the lens-sac have been studied in the embryo-chick, and the later periods, on account of the difficulty in obtaining a complete series of human embryos, have been studied in the fœtal rabbit and pig, the eye of the latter closely resembling that of man.

I.—A Sketch of the Processes Occurring.

At an early stage the ovum consists externally of a layer of closely packed cells having a definite form and arrangement (the epiblast), and beneath or internal to the epiblast of a layer of loosely connected branched cells of irregular form (the mesoblast). As the hypoblast does not take part in the development of the eye, it need not be spoken of here.

Very early in the development of the epi-

blast a linear furrow forms upon its inner surface, and the portion of epiblast surrounding this furrow becomes thickened so as to dip down into the mesoblast and push the furrow before it. At length this furrow closes and, becoming separated from the external epiblastic layer, forms a long narrow tube, the neural canal, which is the beginning of the cerebro-spinal axis (Fig. A).

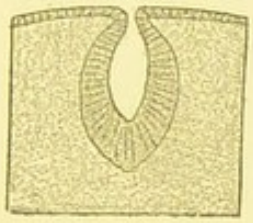


FIG. A.

This tube becomes dilated at the extremity where the brain is to be formed, and constrictions divide the dilated portion into three parts, called the anterior, middle, and posterior *primary* cerebral vesicles. Later the anterior and the posterior primary vesicles each divide again, forming thus five *secondary* cerebral vesicles.

The first important step to occur in the development of the cerebral system is the bulging out of a small portion of the lateral wall of the anterior primary cerebral vesicle on either side, forming a cavity called the primary optic vesicle (Fig. B). This primary

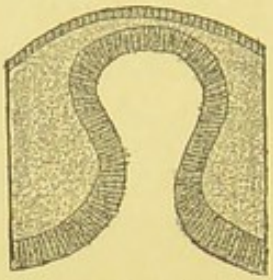


FIG. B.

optic vesicle, which is thus formed from the involuted or neural epiblast, pushes out until it reaches the external epiblast. At the spot where the vesicle is in contact with the external epiblast, the latter becomes thickened and cupped (Fig. C). This cup closes, forming a

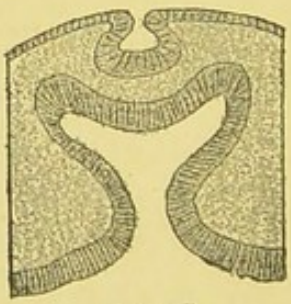


FIG. C.

sac—the lens-sac,—which becomes detached from the external epiblast (Fig. D). The

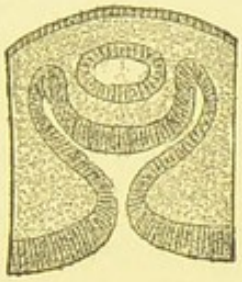


FIG. D.

anterior cells of this sac form the anterior layer of epithelium of the lens, while the cells of the posterior layer of the sac develop into the nucleated fibres which extend forward and make up the substance of the lens.

As the external epiblastic layer becomes cupped to form the lens, the distal wall of the primary vesicle is first depressed, and then, inasmuch as the vesicle continues to grow, it is gradually involuted until it comes to lie in contact with the proximal (posterior) wall. The double-walled cup thus formed is called the secondary optic vesicle (Fig. E).

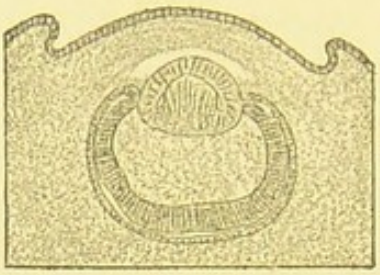


FIG. E.

The cupping of the primary optic vesicle, however, is not confined to its distal wall, but also takes place in its inferior (ventral) wall, so that the secondary optic vesicle has a circular opening distally, occupied by the lens, and a cleft inferiorly, which extends back into the pedicle connecting the optic with the cerebral vesicle. This pedicle, or optic stalk, is the rudiment of the optic nerve (Fig. F).

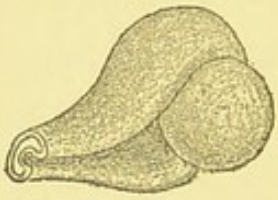


FIG. F.

Later the margins of this cleft unite, and the latter is obliterated. In the mammalia, however, before the cleft closes, mesoblastic

tissue passes through it into the cavity of the secondary vesicle. Previously a small quantity of mesoblastic tissue has been carried in with the lens and takes part in the formation of its vascular sheath, but a greater quantity of mesoblastic tissue passes through the inferior cleft and forms the vitreous, which is an almost structureless substance containing blood-vessels. The vessels entering first at the posterior extremity of the cleft divide into two systems of branches, one of which runs forward in the vitreous near the wall of the cavity, and another runs to the posterior pole of the lens where it breaks up into innumerable twigs which lie in the vascular sheath of the lens.

The cleft in the optic stalk closes about these mesoblastic vessels and they come to lie in the centre of the optic papilla, the branches which run in the vitreous being obliterated before birth.

As soon as the secondary optic vesicle is formed, its two layers begin to differentiate,

the internal or distal layer becoming thicker to form the retina, and the external or proximal layer diminishing to a single stratum of cells, which become pigmented and form the pigment-epithelium.

While this differentiation is taking place, the mesoblastic tissue just about the vesicle becomes denser and many blood-vessels appear in it, forming the rudiment of the choroid.

Mesoblastic tissue also pushes out just behind the external epiblastic layer and forms the rudimentary cornea, the external epiblastic layer forming the epithelium. A single layer of unbranched mesoblastic cells covering the primitive cornea posteriorly becomes the corneal endothelium, and this secretes Descemet's membrane.

In the meantime the secondary vesicle grows much faster than the lens, and the folded margins of the vesicle-wall which remain in contact with the lens are drawn inward, thus beginning the formation of the iris. A sheet from the surrounding mesoblast passes out

over the margin of the vesicle-wall and becomes continuous with the anterior portion of the vascular sheath of the lens, forming the pupillary membrane. The epiblastic vesicle-wall and mesoblastic sheet develop simultaneously to form the iris. The pupillary membrane together with the remainder of the vascular sheath of the lens is absorbed before birth.

As the vesicle-wall grows, it is thrown into a fold near the equator of the lens, and this fold becoming filled with mesoblastic tissue forms the ciliary body. Further growth of the vesicle in an equatorial direction produces a number of meridional folds, which form the ciliary processes.

At this time the distal wall of the vesicle, which in its posterior portion thickens to form the retina, thins down in its anterior portion to a single layer of cells. This layer is called the pars ciliaris retinæ in that portion which covers the ciliary body, and becomes pigmented and forms a portion of the uveal layer where it covers the posterior surface of the iris.

The lids are formed by folds of epiblast thrown out above and below, into which mesoblastic tissue pushes. These folds as they develop cover the cornea and finally meet. The epithelium of either lid margin proliferates and joins with that of its fellow, thus connecting the lids securely together and forming a closed sac, the conjunctival sac. This sac is lined by the epiblastic layer, which remains as the epithelium of the conjunctiva. The connective-tissue portions of the lid are derived from the mesoblast.

The lachrymal duct is formed from the lachrymal furrow (Fig. 19, A and B), a groove lined with epiblast, extending from the eye to the olfactory opening. This groove forms a canal and becomes separated from the external epiblast.

To return and trace the development of the cerebral vesicles. Their walls, as we have seen, consist of a layer of involuted epiblast or neural epiblast. The first marked change to occur is that the posterior portion of the wall

of the anterior primary vesicle—which subsequently becomes the second secondary cerebral vesicle—bulges out to form the primary optic vesicle. From the primary optic vesicle develop the pigment-epithelium and the retina proper, which latter may be divided into, 1st, the cerebral layer (nerve-fibres, ganglion-cells, etc.), conducting elements, and, 2d, the layer of modified neural or sensory epithelium (outer nuclear layer, rods and cones), which makes up the percipient elements of the organ of vision. The lens and conjunctiva originate in the external epiblast, and the remaining structures of the eye arise from the mesoblast.

Soon after the formation of the optic vesicle, the auditory vesicle appears near the fifth secondary cerebral vesicle. The auditory vesicle, however, is not formed by a bulging of the neural epiblast composing the cerebral vesicle wall, but by an indipping of the external epiblast, forming a closed sac and afterwards becoming separated from the external epiblast. This sac becomes the epithelial

lining of the labyrinth—the modified sensory epithelium forming the percipient elements of the organ of hearing. The auditory nerve pushes out to it from the brain at a later period.

The neural epiblast undergoes a thickening in its entire extent and forms the brain and cord, the cavity remaining as the cerebral ventricles and the spinal canal. The first vesicle forms the cerebral hemispheres, the corpus callosum, lateral ventricles, etc.; the second (thalamencephalon) gives rise to the retina and optic nerves by means of its prolongation, the optic vesicle, while its lateral walls thicken to form the optic thalami, its roof to form the pineal gland, its floor to form the pituitary body, and the cavity remains as the third ventricle. The early embryonic relations undergo a considerable change, however, and the optic tracts later connect the eye with the third cerebral vesicle (mesencephalon), from which arise the corpora quadrigemina. The fourth vesicle gives rise to the cerebellum and pons, and the fifth to the medulla oblongata.

II.—Histological.

1. *Primary optic vesicle.*—The wall of the primary optic vesicle is the direct continuation of the neural epiblastic layer forming the wall of the cerebral vesicles (Fig. 1, A). For a considerable time its histological structure does not change. It consists of cells, somewhat similar to ordinary epithelial cells, in a layer from three to five cells deep, more or less regularly superimposed in a radial direction, the limits of the cell-bodies being mostly indistinct. The external and the internal margins of the layer are sharp and regular.

Outside the cerebral vesicles lies the mesoblast composed of branched cells not closely packed, and containing many thin-walled blood-vessels, which lie for the most part near the wall of the vesicles. Covering the whole is the external epiblast, a homogeneous layer of protoplasm with a single row of granular nuclei.

In birds the primary optic vesicle reaches the external epiblast, there being no mesoblastic cells between the two. In mammals,

however, it has been questioned whether there is not a continuous thin layer of mesoblastic tissue separating them.

2. *Secondary optic vesicle.*—The first step toward the development of the secondary optic vesicle is the thickening of the external epiblast to form the lens. This thickening takes place at the point where the primary optic vesicle is in contact with the external epiblast. As this thickening increases, the adjacent wall of the primary vesicle is pushed in. This is shown in Fig. 2, in which the section is excentric so that the beginning lens-sac is cut through its periphery and hence appears simply as a thickening and not as a cupping, which is shown in Fig. 3. In Fig. 2 the section also passes outside the pedicle of the vesicle, and the latter appears therefore as a closed sac.

With its further growth the outer or distal wall of the primary vesicle becomes still further involuted (Fig. 3), although for a time the two walls are not in contact in their entire

extent and the cavity of the primary vesicle is not entirely obliterated. Eventually the two walls come to lie in apposition (Fig. 6) and form respectively the inner and outer layers of the wall of the secondary vesicle. In birds the lens occupies but a small portion of the cavity (Fig. 6); in mammals, however, for a time the lens almost completely fills the cavity (Fig. 4).

As is shown in the diagram, Fig. F, the ventral or inferior wall of the primary vesicle also becomes cupped, and thus a cleft is formed inferiorly in the secondary vesicle. If a sagittal section is made passing through this cleft we see the superior or dorsal wall of the vesicle only, while inferiorly the lens is in contact with the mesoblast (Fig. 4).

The pedicle or stalk of the primary vesicle has at first a wide lumen, but while the secondary vesicle is being formed, this lumen becomes narrower. The cupping of the inferior wall of the secondary optic vesicle extends back into the optic pedicle, and, more-

over, the pedicle for a short distance backward is furrowed so that its inferior wall lies in contact with the superior (Fig. F).

The histological changes which occur while the secondary optic vesicle is being formed, are as follows : As soon as the cupping commences the anterior or distal wall increases in thickness without materially changing its structure, except for the fact that the radial arrangement of the cells becomes more regular. In place of being 3–4 cells deep, it gradually increases in thickness until it is from 6–9 cells deep. The posterior or proximal wall on the contrary steadily decreases in thickness until it comes to be a single stratum of cells in its entire extent (Figs. 3, 4, 6, and 7). These are rather large cells, columnar in the anterior segment of the vesicle, and becoming gradually cuboidal in the posterior segment. After a time small pigment granules appear in the internal portion of each cell. The pigment is deposited earlier and more densely in the anterior segment (Fig. 7).

3. *Contents of cavity of secondary vesicle.*— The changes which take place in the vesicle-wall up to this point may be clearly followed. With the contents of the vesicle it is not so simple. The questions as to the origin of the lens-capsule and the lining membrane of the vesicle cavity, the structure of the vitreous and the zonula, and the arrangement of the vessels of the vitreous and retina, have been subjects of endless controversy, and still there are many points which it seems impossible to settle absolutely.

a. Vascular sheath and capsule of lens. In birds the primary optic vesicle extends to the external epiblast, there being no mesoblastic layer intervening. When the lens-sac is developed and the distal wall of the primary vesicle becomes cupped to form the secondary vesicle, no mesoblastic tissue is carried in with it and no vascular sheath of the lens is formed (Fig. 6). In mammals, the earlier writers (Kölliker, Lieberkühn, etc.) supposed a mesoblastic layer to exist between the primary

vesicle and the external epiblast, which layer, being pushed into the cavity of the secondary optic vesicle, formed the posterior portion of the vascular sheath of the lens. Some later investigators (Kessler and others) have supposed that no continuous layer of mesoblastic tissue lies between the primary vesicle and the external epiblast. The latter view would seem to me the more probable, as the posterior sheath of the lens at an early stage is incomplete.

If we examine a lens carefully at an early stage (Fig. 4, rabbit); while the vascular sheath is still incomplete both posteriorly and anteriorly, we find that the sharp margin which borders every embryonic epithelial layer has become thicker and already represents the beginning of the lens-capsule. In eyes slightly older (Fig. 5) we see a well marked capsule which is readily detached.

At the stage shown in Fig. 4 the internal layer of the secondary vesicle is bounded on either side by a thin membrane, which becomes

respectively the limitans interna and externa retinæ. The lamina vitrea, commonly regarded as part of the choroid, develops just external to the outer layer of the secondary vesicle, and all these membranes, including the lens-capsule, may be regarded as cuticular structures formed from epithelial cells.

The earlier writers supposed the lens-capsule to be of mesoblastic origin, formed by the cells of the vascular sheath of the lens. As we have seen, however, the lens-capsule begins to form in mammals before the sheath is completed, and in birds the capsule is formed as in mammals, but no vascular sheath exists at any time.

Many embryonic questions have had light thrown upon them by the study of pathological processes. It has been found in man that if from any cause the epithelium of the lens be displaced, the epithelium secretes a homogeneous membrane in its new position (Schirmer). Furthermore the sheath of the lens is a vascular structure and not a fibrous one. In ex-

centric sections through the lens in fœtal eyes of various ages, we see only a system of branching capillaries running in a meridional direction about the lens. In the early stages fusiform cells are seen here and there external to the capillaries (Fig. 5), but in all probability at least some of the cells lying apparently free in the vitreous are simply portions of a capillary wall. At a late stage when the capsule has already attained a considerable thickness, some leucocytes are found among the vessels. On the whole, however, the sheath of the lens is at no period a cellular tissue, and the designation *fibro*-vascular sheath is not so proper as Kölliker's original name "tunica vasculosa lentis."

The only rational explanation of the lens-capsule, both anterior and posterior, is to my mind that of its being a product of the epiblastic cells making up the lens-sac.

b. Vitreous. While the secondary vesicle is being formed the lens-sac occupies nearly the entire cavity in mammals, but when the

two layers of the vesicle-wall are in apposition a free space appears between vesicle-wall and lens (Fig. 4). With the further development the vesicle enlarges relatively faster than the lens and the free space becomes gradually larger. Vascular mesoblastic tissue pushes through the inferior cleft into this space. At this time (Fig. 4) the cavity of the secondary vesicle is filled with a fluid similar to that filling the rudimentary anterior chamber. At a slightly later stage, when the lens is fully formed, we find this space filled with a gelatinous mass containing blood-vessels (Fig. 5), some of which run on the surface of the lens, others on the inner surface of the vesicle, and others through the gelatinous mass. These vessels are of a capillary type, and remain so up to the time of their absorption. The vessels of the lens-sheath form a single layer, and external to the vessels we find a few fusiform cells. A few cells are found in the vitreous, mostly near the vessels. In the pig, at the posterior pole of the lens where the hyaloid

artery breaks up, a considerable number of cells are found (Fig. 7). It is impossible to say how many of these cells in the young vitreous belong to the vessels. A little later (Fig. 8) no nuclei are found except those belonging to the vessels. At a much later stage we find cells which are evidently simply wandering leucocytes.

When the lens is just formed, the vitreous in the rabbit has the appearance shown in Fig. 5. A little later the vitreous shows a fibrillar structure near its limits, and about the vessels are clear, highly refracting globules.

At no stage of its development can the vitreous be regarded as having a distinctly cellular structure, although in the earliest stages some few connective-tissue cells are found in it. Kölliker and the early writers believed the vitreous to be a degenerated connective-tissue structure. Kessler considers it an albuminous transudation from the blood-vessels. H. Virchow takes a middle ground, thinking each view true in part.

The inner surface of the vesicle-wall is bordered by a delicate membrane. The vitreous, however, adheres to it closely, and when in the process of hardening the vitreous shrinks and becomes detached, this membrane is detached with it. In Fig. 5 at the left the membrane is seen in position. To the right it is detached from the vesicle-wall, but where it is detached the cells beneath it are torn and irregular. It is not a membrane that can be stripped off leaving the cells intact. This membrane has been called the hyaloid membrane or limiting membrane of the vitreous, and it has been supposed to belong to the vitreous, partly for the reason that when the vitreous is detached the membrane usually remains adherent to it. This, however, is no conclusive proof, for, as we shall see, when the vitreous becomes detached at a later stage, it often takes with it also the nerve-fibre layer of the retina and the retinal vessels. This membrane extends to the anterior margin of the vesicle-wall. Later it forms the limitans interna of

the retina and the elastic membrane which rests on the cells of the pars ciliaris retinæ. A limiting membrane of the vitreous, in my opinion, does not exist.

c. Vessels of the vitreous. The inferior cleft closes about the mesoblastic vessels which enter the vitreous-cavity. These vessels then come to lie in the rudimentary papilla and here the main trunk breaks up into two systems of branches. The first system is composed of a trunk which, usually single, but sometimes dividing, runs from the papilla to the posterior pole of the lens and then breaks up into innumerable branches in the lens-sheath. This is the hyaloid artery shown in Fig. 8. The second system consists of a great number of branches which run at first near the vesicle-wall and anastomose anteriorly with the vessels of the lens-sheath (Fig. 8). At this stage there is no trace of vessels in the rudimentary retina, all the vitreous-vessels lying within the limitans interna.

A very little later small branches start from

the vessels in the papilla and run in the retina just external to the limitans interna (Fig. 10 to the left), but do not pass through the limiting membrane and therefore do not anastomose with the vessels of the lens-sheath or of the vitreous.

The blood from the retinal vessels is returned to the papilla. The blood from the vitreous-vessels circulates in the lens-sheath and is carried out of the eye by vessels of the iris, which anastomose with the vessels of the anterior portion of the lens-sheath. Most writers have considered the retinal vessels as being at first one system of the vitreous-vessels. The retinal vessels are, however, from their first appearance always separated from the vitreous by the limitans interna.

The vitreous has shown, up to this period, a slightly fibrillar structure, the direction of the fibrillæ being in general parallel to the margin of the vitreous (Fig. 9). Now, well-marked coarser striations appear about the blood-vessels and run parallel to them (Fig. 12).

The vitreous when shrinking in the process of hardening contracts in the direction of these striations, and, becoming detached, takes with it the layer of retinal vessels. When this occurs, the anterior portion of the retina is also often detached, ruptured at its origin, and drawn inward. The folds in the retina, which are almost always found in preparations, and which are represented in Figs. 7, 8, 9, 10, are probably all artificial, though many writers have described them as normally existing.

Some anatomists have described the vitreous as consisting of concentric layers, others have described it as homogeneous. The striations along the vessels certainly divide the vitreous to a certain extent, but I cannot confirm the observations of those who have described the vitreous in the embryo as showing a distinctly lamellar structure.

In Fig. G we have a diagram showing the vessels in a half-grown embryo, A being the hyaloid artery, B the system of vitreous arteries, and C the arteries and veins of the retina which are detached from the equator forward.

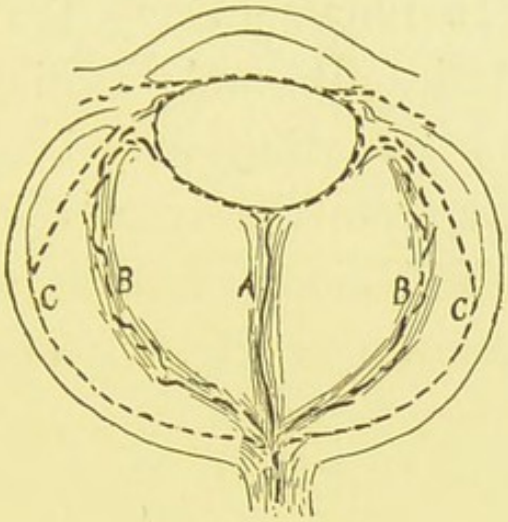


FIG. G.

Along the vessel A and the system of vessels B we find well-marked striations, so that the vitreous in such a section is apparently divided into four lamellæ. The intervening spaces show no striations. If the section be cut somewhat excentric, we have the vessels arranged as in Fig. H. Here the stria-

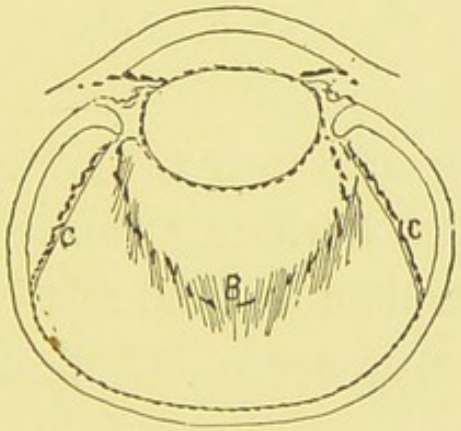


FIG. H.

tions are seen running along the system of vitreous arteries B, and crossing them at an angle, so that they may be followed a little distance from the vessels. If the section be cut still more excentric we find the appearance shown in Fig. I. The system of

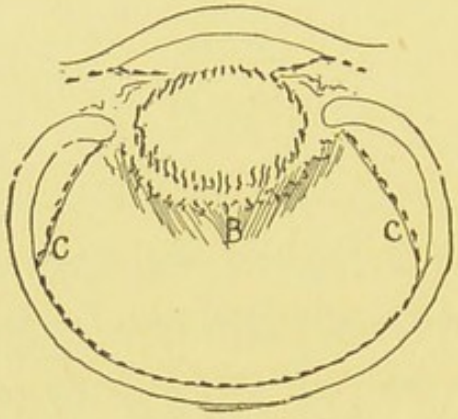


FIG. I.

vitreous-arteries here lies close to the lens, which is cut nearer to its equator, so that in a thick section the vessels of the lens-sheath may be followed some little distance. Here the striations are seen near the system of vessels, B. It is clear, if three such sections were examined at random and the relative location of the vessels was not noted, that an observer

might suppose the entire vitreous to be divided into lamellæ by the striations, and this mistake would seem to have been often made. Further than these striations along the vessels I believe there are no structural elements in the vitreous causing a stratification which can be demonstrated with the microscope.

d. Zonula. The anatomy of the zonula is still imperfectly understood, and its development is still more uncertain. Recent writers (Czermak, Berger, Topolanski, and others) have devoted considerable study to its normal structure, but there are many points on which there is not general agreement.

At the time when the ciliary processes are being formed the retinal vessels stop at the place where the retina gradually thins down into the pars ciliaris (Fig. 13). The limitans interna, however, continues over the ciliary body, and from this time on grows gradually thicker, forming a distinct homogeneous membrane on the pars ciliaris. The superficial portion of the vitreous anteriorly has a fibrillar

structure, and a few nuclei or round cells are seen in it, and also on and often apparently in the membrane of the pars ciliaris. The ciliary body at this period and later is adherent to the lens-capsule, and when the two are forcibly torn apart the membrane sometimes becomes detached from the pars ciliaris, and a continuous membrane with nuclei lying on it may then be seen extending from the ciliary body to the lens-capsule. This has often been mistaken for the zonula.

The vessels of the lens-sheath begin to atrophy at this stage. At times, when the ciliary body is torn away from the lens, long spindle-cells (which may be atrophic vessel-walls, since earlier no spindle-cells are found in the lens-sheath) run from the lens to the ciliary body. Later, when the vitreous-vessels have disappeared, the vitreous is here very fibrillar, and is adherent to the limitans interna just anterior to the ora serrata. Thick bundles of vitreous-fibrillæ, often wavy, run in a curved line from the ciliary body to the equator of the

lens and continue over its posterior surface. No distinct anterior hyaloid or limiting membrane of the vitreous can be found here. In the space anterior to and outside the vitreous we find zonula-fibres running from the ciliary body to the lens. Farther back we find similar fibres, with nuclei lying on or in them, running from one ciliary process to another or from the smooth portion of the ciliary body to a ciliary process, having their origin in and being inserted into the homogeneous membrane of the pars ciliaris.

Whether the zonula-fibres originate from the vitreous-fibrillæ entirely, or in part from cells of the vascular sheath of the lens is not shown by my preparations, and the rôle of the nuclei or cells which are found in the vitreous at a late stage is uncertain in my mind. Until very recently it was generally believed that the zonula was derived from the vitreous. Treacher Collins, however, in human embryos, has observed spindle-cells of the lens-sheath stretch out to form nucleated fibres

which later lose their nuclei and become zonula-fibres, and his view is supported by the study of two specimens showing congenital anomalies of the zonula. I cannot see, however, how such an explanation could hold good for the so-called orbiculo-ciliary and the inter- and intra-ciliary fibres which are not inserted into the lens-capsule.

4. *Crystalline lens.*—In Fig. 1 the primary vesicle A is in apposition with the external epiblast. In Fig. 2 the external epiblast has become thickened. This section is somewhat excentric and does not show the cupping, which is clearly seen in Fig. 3. According to the later writers a similar cupping occurs in most mammals. The opening shown in the cup in Fig. 3 soon closes, so that the external epiblast again forms a continuous layer and the cup becomes a closed sac.

This junction of two folds with the union of the outer and inner layers, and the entire separation of the two layers from each other, is the same process that occurs in the first

involution of the neural epiblast to form the cerebro-spinal axis, and again in the closure of the cleft in the ventral wall of the secondary optic vesicle.

The wall of the lens-sac consists of a uniform layer of epithelial cells, four or five deep, both in the chick (Fig. 3) and in the rabbit (Fig. 4). The cells of the posterior layer lengthen out into fibres. The beginning of this process is shown in Fig. 4 below. These fibres, developing more rapidly in the centre, push forward until they reach the anterior layer, and thus obliterate the cavity of the sac (Fig. 6). Each fibre has a single nucleus, and is developed from a single cell. In the embryo-pig at the time when the lens is fully formed, the anterior epithelium is four or five cells deep (Fig. 7). The short fibres which develop at the angles of the lens-sac curve sharply outward to reach the anterior epithelium, those nearer the posterior pole curve less, and those arising in the polar region extend forward in a straight line (Figs. 6 and

7). The anterior epithelium at this stage is continued far back behind the equator of the lens, and the nuclei of the fibres are bunched together in the form of a crescent with its convexity forward. As the lens develops, the cells farthest back in the anterior epithelial layer become lens-fibres in their turn, and the limit of the epithelial layer gradually moves forward (Figs. 7, 8, 9). At the same time the layer decreases in thickness until it comes to consist of a single stratum of cells, which terminate near the equator of the lens (Fig. 9), and which are permanent. The nuclei of the fibres become more scattered, and lose to some extent their regular arrangement (Fig. 8), and the curve of the individual fibres changes, those near the equator of the lens curving but slightly outward, and those nearer the axis curving slightly inward. This change in curvature increases, and in the matured lens most of the fibres curve sharply inward and run concentrically.

From the time when the lens-sac is first

formed it is surrounded by a capsular membrane which gradually increases in thickness. It is to be considered a cuticular formation of the epithelial cells, and it becomes much thicker anteriorly where the epithelial cells remain permanently. Anteriorly also it may be split up into lamellæ, each of which represents in all probability a certain period of formation. The vascular sheath is for the nutrition of the lens during its rapid growth, and seems to play no rôle in the formation of the capsule (*cf.* p. 20).

5. *Cornea.*—When the lens-sac becomes separated from the external epiblast, an open space remains between the two (Fig. 6). In the rabbit (Fig. 4) the mesoblastic tissue passes over the margin of the secondary optic vesicle into the cavity of the latter. This mesoblastic tissue contains many vessels, and at this stage both the anterior space and the cavity of the vesicle are filled with a fluid which is probably transuded from the vessels.

Mesoblastic cells now push out from the

sides and cross the space between the external epiblast and the lens-sac. A layer of mesoblastic cells is thus formed, which may rest on the posterior surface of the external epiblastic layer, or which may at first lie slightly posterior to the external epiblast. After the first continuous layer has been formed from the mesoblast at the sides, it gradually increases in thickness, the new cells having their origin probably in the division both of the cells of the existing layer and of the cells at the sides. These cells become long spindle-cells, and the anterior cells, if at first they have not rested on the external epiblast, soon do so, and there is then no trace of any intervening material between corneal stroma and epithelium. For a time the rudimentary cornea is much thicker at its periphery (Fig. 7). At length the central portion fills up until the cornea is of a uniform thickness. Then a single stratum of endothelial cells, the origin of which is uncertain, passes out over its posterior surface (Fig. 8).

The endothelial layer lies on the stroma of the cornea for a time. Later in fœtal life a delicate double-contoured membrane appears between them. This membrane gradually thickens until, in the grown animal, it is a thick lamina which may be stripped off cleanly, and which is very resistant to pathological processes and does not stain like the stroma of the cornea. It is to be considered a product of the endothelium. When the endothelial layer in the human eye is displaced, it may proceed to the development of a new elastic membrane, altogether similar to the normal membrane of Descemet (Wagenmann).

In mammals, as we have seen, the stroma cells of the rudimentary cornea lie directly on the posterior surface of the epithelium (Fig. 7). The cells become spindle-shaped and fibres are formed, between the bundles of which the cells remain permanently as the fixed corneal corpuscles. When the cells have become long spindle-cells we find that no nuclei lie on the external epithelium, but

that the nearest nuclei are separated from the epithelium by a fibrous layer similar to the corneal stroma as the stroma appears somewhat later. This layer after it is formed has about the thickness of a corneal lamella, and does not increase in thickness in later fœtal life like the membranes of cuticular formation. It has a sharp outline next the epithelium, and the epithelium is readily stripped cleanly off it, but it is not at any period sharply limited from the corneal stroma and it cannot be readily separated from the latter. It stains much the same as the corneal stroma, and is similarly affected by pathological processes. It would seem to be an early product of the corneal cells, being fully formed at a time when the rudimentary cornea is still composed of spindle-cells, and distinct fibrous tissue has not yet made its appearance elsewhere.

In birds the development of Bowman's membrane is different. The space between the lens and the external epithelium is filled

in the chick with a homogeneous non-cellular material, and the mesoblastic cells which push out to form the stroma of the cornea do not rest directly on the posterior surface of the external epithelium, but lie a little distance from it. A layer of the homogeneous material remains between them, and this soon appears as a double-contoured membrane which is permanent. The epithelium often cannot be stripped off it cleanly, and fragments of the cells remain adherent to the membrane. This homogeneous material is probably a transudation from the vessels. The mesoblastic cells push out into it, and for a time it forms the intercellular matrix of the cornea.

The process occurring in birds has been supposed by many to hold good for mammals. In my opinion the development of Bowman's membrane is entirely different in the two. The first stroma-cells of the cornea in mammals have been often described and pictured as lying some distance behind the epithelium. This may sometimes be found at the beginning

of the corneal development. But after the rudimentary cornea is a few cells deep, the anterior cells lie directly on the epithelium. In birds the stroma-cells do not reach the epithelium at any period.

There has been much discussion as to whether the corneal cells are cells which have wandered in from the mesoblast, or whether they have been produced *in loco*. Some authors have described the cornea as consisting in the beginning of a non-cellular homogeneous material into which the corneal cells pass by migration. Others have described it as a homogeneous material containing a few cells which by their division produce the corneal cells. In mammals, the homogeneous material need not be taken particularly into account. It is in all probability simply an indifferent fluid filling a cavity. The mesoblastic cells at the sides proliferate and thus a thin layer of cells is pushed through the cavity. The cells of this layer and the cells at the sides continue to proliferate and form the

rudimentary cornea. When the mesoblāstic cells first push in from the sides to form the rudimentary cornea (Figs. 4 and 7), they have an oval nucleus and a large cell-body with two processes and occasionally more. In a vertical section of the cornea the cells have a parallel direction, and appear as separate bipolar cells, In a flat section the processes extend in various directions, and small offshoots from the processes anastomose with those of other cells. Very soon the cells become flattened. Then in a vertical section of the cornea the nucleus has a long spindle form, and the body of the cell appears only as a long delicate process from either end of the nucleus. In a flat section at this stage we see a slightly oval nucleus and a broad cell-body ending in two sharp processes. We now find delicate fibres resting on the cells, appearing similar to the delicate cell-processes as seen in a vertical section. These fibres rapidly increase in number, separating the cells in a vertical direction. The long processes of the cells finally become

shorter, and the cells remain as fixed corneal corpuscles between the lamellæ of fibres.

The external epithelium for a considerable time consists of a single stratum of cuboidal cells (Figs. 6 and 7). Then a stratum of flattened cells appears external to the cuboidal layer (Fig. 8). From this time on, the epithelium gradually thickens, the cells of the external layers remaining flat, those of the middle layers irregularly cuboidal, while those of the inner layers are columnar. Just beneath Bowman's membrane vessels are seen near the periphery of the cornea, continuous with conjunctival vessels.

6. *Sclera.*—At the time when the lens is being formed, the mesoblastic tissue outside the secondary optic vesicle consists of a mass of connective-tissue cells of various forms, the nucleus being round or nearly so, and the cells having no particular arrangement. Scattered through this tissue are thin-walled blood-vessels, and a network of these vessels lies on the vesicle-wall (Figs. 3, 6). A little later these vessels

come to form a simple layer of capillaries resting on the vesicle-wall (Fig. 8). The mesoblastic cells then become spindle-shaped and run parallel to the vesicle-wall, and later the spindle-cells form fibres. In Fig. 10 we see outside the vesicle-wall this thin fibrous layer, which is the rudimentary sclera. External to it and at this period not sharply differentiated from it is the general mass of indifferent mesoblastic cells filling the orbital cavity. A little later branched pigmented cells appear at the outer margin of the rudimentary sclera, separating it from the orbital tissue. These pigmented cells are rarely found in the human sclera.

External to the pigmented cells is a thin layer of loosely meshed cells, and external to these, particularly in the anterior segment, we find a very thin fibrous layer similar to the sclera, which represents the capsule of Tenon. Anteriorly the fibres of the sclera are continuous with those of the cornea (Fig. 9). The loose tissue external to the sclera continues

forward as the subconjunctival tissue, a loose meshwork of cells with many blood-vessels.

7. *Choroid.*—The fibres of the rudimentary sclera, as we have seen, lie at first just external to the capillary-vessel layer, which latter rests upon the vesicle-wall (Fig. 10). Internal to this fibrous layer the choroid is formed about the capillary vessels.

At this time we find the outer layer of the vesicle-wall consisting of a single stratum of hexagonal cells, darkly pigmented with rod-shaped particles of pigment. This stratum is the pigment-epithelium. The inner margin of this stratum is irregular; its outer margin is smooth, and resting on this outer margin may be seen the beginning of a delicate membrane, which keeps growing thicker throughout the entire course of fœtal life. In the grown animal this is a fairly thick homogeneous membrane, the so-called lamina vitrea of the choroid. This membrane would seem to be secreted by the pigment-epithelium.

Directly on this thin homogeneous membrane

rest the capillaries. The first change that occurs in the formation of the choroid is the arrangement of a considerable number of cells of various shapes about the capillaries and the development of a number of larger vessels just external to the capillaries. These changes all take place between the pigment-epithelium and the fibrous layer which is the rudimentary sclera, the latter being simply pushed outward by the development of the choroid beneath it.

After the appearance of the larger vessels, pigmented cells are seen just beneath the rudimentary sclera at the outer margin of the rudimentary choroid, and later pigmented cells are found deeper in the choroid, until finally in the pig they reach up to the capillary layer. In man the pigmented cells seldom extend into Sattler's layer of smaller vessels, and almost never reach the capillaries. The pigment is in the form of rods, shorter and more rounded at the ends than the rods in the pigment-epithelium.

With the appearance of the pigmented cells the vessels become more numerous and the pigmented and unpigmented cells form a delicate meshwork about them. The external cells form long fibres, which are readily detached from the rudimentary sclera, and among these fibres free endothelial cells are found.

8. *Iris, ciliary body, and pupillary membrane.*

a. The iris and ciliary body are composed of an epiblastic and a mesoblastic portion, each of which may be considered separately.

Epiblastic portion. In Fig. 3 we see the folded anterior margin of the secondary optic vesicle, to the left the two layers some distance apart, to the right the two layers in apposition. In Fig. 7 the outer layer has taken on its pigment, and the inner layer has become thinned near the margin. The folded margins turn it toward the lens, and in Fig. 8 they are in contact with it. At this stage we may notice a slight curving of the vesicle-wall near its folded margin, which becomes later a dis-

tinct fold where the ciliary body is to be formed.

The inner layer of the vesicle-wall becomes thinner in its anterior portion (Figs. 8 and 9), until, like the outer layer, it comes to consist of a single stratum of cells—the pars ciliaris retinæ (Fig. 11). Farther back the inner layer is thicker and passes imperceptibly over into the rudimentary retina. Anteriorly the single stratum of cells becomes pigmented in the portion that is to form the posterior layer of the iris, the pigmentation ceasing at the head of the ciliary body (Fig. 11). In specimens from the grown pig, bleached by Collins'[1] method, the posterior layer of the iris with the pigment removed consists of cells entirely similar to those of the pars ciliaris, the only difference being that the layer on the iris does not have a smooth posterior surface, but forms a succession of short curves.

Some time after the development of the equatorial fold to form the ciliary body, meridi-

[1] *Trans. Ophthal. Soc. Unit. Kingdom*, vol. xi.

onal folds are thrown out to form the ciliary processes.

The mesoblastic portion plays in the beginning a more passive rôle in the development of the iris and choroid. In Fig. 7 the rudimentary cornea and the general mass of mesoblastic tissue are seen to be entirely cellular. In Fig. 8 the mesoblastic tissue next the vesicle-wall is still cellular, more externally it is beginning to be fibrous. In Fig. 9 the fibrous layer is only separated from the vesicle-wall by the capillaries of the rudimentary choroid. The mesoblastic tissue of the rudimentary iris at this stage forms a thick cellular layer with many blood-vessels, some of which are continuous posteriorly with the choroidal vessels and anteriorly with the vessels of the lens-sheath. This mesoblastic cellular tissue later fills up the folds thrown out in the epiblastic portion, and forms the connective-tissue portion of the iris and ciliary body.

In Figs. 11 and 13 we see a wedge-shaped

mass of cells running transversely, which is intercalated between the sclera and the ciliary body, and encloses the angle of the anterior chamber. These cells form a meshwork of fibres which becomes the ligamentum pectinatum.

The layer of closely packed endothelial cells on the posterior surface of the cornea stops, as a layer, at the angle of the anterior chamber, but isolated endothelial cells lie in the spaces of the ligamentum pectinatum, and a thin endothelial layer with scattered nuclei continues over the iris and out into the pupillary membrane.

The sphincter iridis and the ciliary muscle develop late. The later stages of development of the iris and ciliary body differ considerably in the pig from those in man, and are of no particular interest here.

b. The pupillary membrane. When the mesoblastic portion of the iris is first forming it pushes out beyond the epiblastic portion and rests upon the lens (Fig. 8). In this

situation it at first retains its original thickness. A little later its margin becomes thinner (Fig. 9), and still later (Figs. 11, 13) we find nothing left of this mesoblastic outgrowth running to the vascular sheath of the lens but the endothelial layer, and a few spindle-cells from the anterior layer, which accompany vessels. The spindle-cells extend only a short distance into the pupillary membrane, and in its central portion the membrane consists only of a single layer of capillaries, much smaller than those which lie posterior to the iris and carry the blood from the vessels in the vitreous.

At a late stage the mesoblastic margin of the iris extends out some distance beyond the farthest iris vessels, and capillaries springing from vessels of the minor zone pass from the anterior surface of the iris, some millimetres from its margin, and run to the pupillary membrane. The membrane disappears just before birth, or just after birth in some animals, and usually there is no trace of it left.

Any of the fœtal vessels which are usually absorbed may, however, remain permanently in a degenerated form, so that we find as congenital anomalies, persistent pupillary membrane, in the form of plaques on the capsule of the lens or fibres arising from the region of the minor vascular circle of the iris; persistent posterior vascular sheath of the lens, in the form of plaques near the pole or striations running meridionally on the capsule; persistent hyaloid artery, either its lenticular or papillary insertion being preserved; persistent vitreous vessels of the 2d system; and last, connective-tissue masses of varying size in the physiological cup of the papilla (Fig. 12), or running from this point out into the vitreous or extending along the limitans interna, all of which anomalies are seen in the human eye.

In the upper portion of Fig. 4 we see how the vessels of the posterior lens-sheath run over the anterior margin of the vesicle-wall to reach the mesoblastic tissue outside. This communication remains throughout fœtal life,

although the development of the iris changes the relative positions. In cases of coloboma of the iris Hess[1] has in several cases found a fibrous cord extending from the optic disc to the posterior pole of the lens, and from this point running meridionally to the equator of the lens, where it was inserted into the ciliary body at the head of the coloboma. This he regards as a mesoblastic formation, which passing in front of the margin of the secondary vesicle has prevented the development of the iris at this point.

As is well known, in cases of incomplete or arrested development of the eye, we usually find remains of fœtal vessels that have not been absorbed. In my opinion, the cord that Hess has described is a remnant of the fœtal vessels, which has remained simply because the secondary vesicle has not developed anteriorly at some point, and the relations seen in Fig. 4 are therefore preserved permanently—in short, the persistent cord is not the cause

[1] *Græfe's Archiv*, xxxiv., 3.

of the coloboma of the iris, but the consequence.

9. *Retina and pigment-epithelium.*

a. Retina. When the secondary vesicle is fully formed its inner layer from which the retina develops, is bordered on either surface by a more or less distinct membrane, which membranes become respectively the limitans externa and the limitans interna of the retina (Fig. 4).

The cells of the stratum next the limitans interna are columnar and the nucleus lies some little distance from the membrane (Fig. 4). A little later, these columnar cells become spindle-shaped and small spaces appear between their internal prolongations. When the limitans interna is stripped off, these prolongations are seen to form a fine network (Fig. 7). A similar network is found on the margin of the wall of the cerebral vesicles. At the next stage we find nerve-fibres extending continuously from the cerebral vesicle through the optic nerve to the retina (Fig. 8). The inter-

nal prolongations of the inner stratum of retinal cells just mentioned, may now be seen to be continuous each with a nerve-fibre (Fig. 14). It is not possible to say whether the nerve-fibres originate peripherically or centrally, or whether they originate simultaneously at both extremities. At the earliest period in which I have found nerve-fibres they are apparently equally developed in their entire course.

After the nerve-fibres appear, the vessels soon develop. These spring from the vessels in the nerve, and quickly spread over the entire retina in the form of small capillaries lying just beneath the limitans interna (Fig. 10 at left).

At this stage the differentiation of the retinal cells becomes further advanced. The stratum of cells next the limitans externa become columnar with long oval nuclei which stain deeply (Fig. 10).

The mass of retinal cells have a round or oval nucleus, staining moderately dark, and a

small amount of protoplasm of a delicate spindle form.

The inner stratum of cells from which the nerve-fibres run—the rudimentary ganglion-cells (Fig. 14, A)—have a large nucleus at this stage staining deeply with hematoxylin, and a large cell-body with two distinct processes, one continuous with a nerve-fibre, the other extending back among the retinal cells.

The stratum of ganglion-cells is separated from the mass of the retinal cells by a stratum of rather large cells (Fig. 14, B), the nuclei of which stain very faintly, and which a little later disappear almost entirely to give place to a delicate network striated longitudinally—the inner reticular layer (Fig. 15, B). From this time on we notice long nucleated fibres staining deeply in the outer cellular layers (Figs. 14 and 15).

The outer reticular layer is formed later, exactly as the inner layer was formed. That is, there is a stratum of cells near the inner reticular layer which stain deeply, and just

external to this stratum is a second in which the cells stain faintly (Fig. 15, C). These faintly staining cells disappear to give place to the reticulum.

Near the ora serrata the nerve-fibre layer is very thin, and only in this region can the supporting fibres of Müller be studied with any degree of clearness. At a late stage coarse fibres may here be seen spreading out into a cone shape and inserted into the limitans interna, which previously has existed as a simple membrane. In this cone-shaped foot, both in the fœtus and in the grown animal, we may here and there distinguish a very faintly staining nucleus.

As the ganglion-cell grows, its nucleus increases greatly in size and comes to stain more faintly. Among the ganglion-cells there are from the beginning small bipolar cells which take a deep stain. These small cells have an oval nucleus with its long axis in the direction in which Müller's fibres run. Somewhat similar cells which stain less deeply lie in the

nerve-fibre layer, with the long axis of the nucleus in the direction of the nerve-fibres, and are called glia cells.

At a very late period the rods and cones are developed by the outer layer of columnar cells sending processes through the limitans externa. In my specimens from the fœtus and from new-born animals this layer is not sufficiently preserved to justify a description.

b. The pigment-epithelium is formed from the outer epiblastic layer of the secondary optic vesicle, which becomes reduced to a single stratum of cells hexagonal in flat section. In the chick these cells are for a time all cuboidal in vertical section and of nearly equal size (Figs. 3 and 6). In the pig the posterior cells are cuboidal, while the anterior ones soon become long columnar in vertical section (Fig. 7). In the pig, when the lens-sac is forming, rod-shaped bits of pigment are deposited in the cells along the *inner* margin of the cells, the nucleus lying in the outer portion (Figs. 4 and 7). This deposition of pigment begins

anteriorly, and here it is always denser and more resistant to the action of bleaching agents even in adult life. The margins of the inferior cleft are not pigmented until a considerable time after the cleft is obliterated. The pigment gradually fills the entire cell, excepting the nucleus and the outer margin, which always remains free.

In the chick the deposition of pigment occurs somewhat later and begins in the *outer* portion of the cell, the pigment extending to the outer margin. Later, when the anterior cells become columnar, the pigment is most dense in the inner portion of the cell.

10. *Optic nerve.*—Just before the lens is fully formed, and while the eyelids are only indicated by two small folds (Fig. 4), we find the inferior cleft of the secondary vesicle closed but still showing evidences of its recent closure. In Fig. 16, A is an equatorial section through the inferior wall of the vesicle, showing the inner layer folded where the cleft has closed; B is a section nearer the optic

nerve, showing the outer layer folded. It will be noticed that the pigment of the outer layer is wanting in the region of the fold. At a slightly later period these folds are obliterated and the pigmentation is uniform in the outer layer; C is the optic stalk near the vesicle, with its inferior cupping; D is the stalk a short distance from the vesicle; and E is the round stalk with a central lumen some distance from the vesicle. At this period the optic stalk is entirely cellular and shows no trace of nerve-fibres.

As we have seen, the cells of the retina are at first closely packed, but just before the appearance of the nerve-fibres the cells of the layer at the inner surface of the retina become branched, and the branches form a network and the cells lie farther apart. At the same time a similar change takes place in the cells of the cerebral vesicles. The walls of the cerebral vesicles increase in thickness until the cavity is almost obliterated. The central cells are closely packed, while those on the surface

of the vesicle in places become branched like the retinal cells. From these branched cells near the surface of the wall of the third vesicle arise the nerve-fibres. These nerve-fibres run anteriorly in a compact mass on the surface of the vesicle, thus forming the optic tract, and then, passing into the optic stalk, run without interruption to the retina.

In the optic tract, as in the wall of the cerebral vesicle, there are a number of capillaries which pass in from the surrounding mesoblast. Apart from the capillaries there are no connective-tissue elements, and the only cells in the tracts are a few branched neural-epiblastic cells, mostly lying among the peripheric fibres, and identical with the cells of the vesicle-wall.

At the point of origin of the optic nerve (Fig. 17, A) there is a considerable accumulation of these cells among the nerve-fibres, and passing up throughout the length of the optic nerve are the same cells arranged in short longitudinal rows which separate the fibres

into more or less distinct bundles, as the connective-tissue septa do later.

In a transverse section of the nerve we find fibres in every portion, but grouped into larger and more distinct bundles in the centre.

The cells among the fibres throw out lateral processes which anastomose so that a sort of loose membrane is formed grouping the fibres into bundles (Fig. 18, A). On the surface of the nerve there is a layer of similar cells (Fig. 18, B) which have a large, paler, round nucleus, and well-marked processes, the longer ones extending into the nerve, the shorter ones joining the branched and spindle-shaped mesoblastic cells (Fig. 18, C), which are beginning to form a sheath about the nerve.

At this stage the cells of the mesoblast and the branched cells of the neural epiblast bear a remarkable resemblance to each other, and most authors have considered the cells in the nerve to be mesoblastic. At this stage, however, no mesoblastic cells can be seen to extend into the nerve, and the cells of the

nerve are directly continuous with the epiblastic cells of the cerebral vesicles and of the retina, and in my opinion are to be considered the epiblastic cells of the optic stalk.

At a somewhat later stage in the pig I have found the optic nerve much larger, and consisting only partially of fibres. The remainder consists of closely packed cells continuous with the cells of the cerebral vesicle and of the retina, and identical with the closely packed cells found in these localities (Fig 10). These cell-masses in the nerve have a sharp, smooth peripheric margin bordered by the mesoblastic cells of the nerve-sheath. These can be nothing but proliferated cells of the primitive optic stalk.

A little later the optic nerve, which so far has had no direct blood-supply, becomes pervaded with capillaries which push in from the sheath, and entering the nerve run for the most part in a longitudinal direction (Fig. 12).

The nerve-fibres have now begun to take on their medullary sheath and lose their sharp

outline, so that the substance of the nerve appears as a gelatinous mass with a great number of cells (epiblastic). About the capillary vessels delicate connective-tissue membranes appear forming the septa and dividing the nerve-fibres into bundles. The epiblastic cells remain among the medullated fibres as glia cells.

A mesoblastic sheath forms early just about the nerve and gradually grows thicker and more fibrous. Later the fibrous sheath divides into two distinct layers separated by a loose cellular layer which becomes the arachnoid sheath, while the fibrous layers become respectively the pial and the dural sheath.

The central vessels lie in the cup of the optic stalk which closes about them (Figs. 16, C and 17, B). Connective-tissue membranes form about the capillaries of the nerve, and a thicker membranous capsule surrounds the central vessels.

11. *Eyelids.*—After the secondary vesicle has formed, the surface of the rudimentary

eye projects considerably beyond the general surface of the head, and a groove which forms about it makes the eye apparently project still more (Fig. 19, A and B). The bottom of this groove corresponds more or less accurately to the equator of the ball. The epiblast at the outer margin of this groove is thrown up as a fold about the eye. This fold develops particularly in the superior and inferior portions, and thus two folds of epiblast filled with mesoblastic tissue gradually approach each other over the cornea (Fig. 19, C) and finally unite. The epithelium of the free margins of the lids becomes very thick, and the lids are joined, particularly in the neighborhood of the commissures, by a continuous layer of epithelium long before the mesoblastic portions of the folds have come near each other. Finally the lids are joined by a thin layer of epithelium in their entire length, the line of junction being convex upward. A somewhat similar thin fold develops nasally just within the lids and forms the nictitating membrane (Fig. 9).

At first the epithelium of the lid consists of a single layer. The epithelium of the outer surface and of the margin becomes several cells deep, and that of the inner surface two or three cells deep (Fig. 9). The basal stratum of columnar cells stains deeply and soon becomes pigmented (Fig. 20). Very early we find the external epithelium dipping in in places to form hair follicles (Fig. 8). After the lids unite similar indippings at the margins form the follicles for the cilia. Just behind these, larger solid epithelial processes push a considerable distance into the lids, and later break down in the centre to form tubes, which give off short processes, and become Meibomian glands (Fig. 20).

At an early stage we find long fusiform cells developing into clear muscle-fibres (Fig. 9), which appear first near the orbital margin of the lids and much later near the free margin. These muscle-fibres are finally collected into bundles separated by loose connective tissue, and form the orbicularis muscle.

While the Meibomian glands are developing, the mesoblastic tissue forms a dense sheath of spindle-cells about them. This sheath becomes denser and forms a very tough fibrous layer in which the glands lie imbedded—the tarsus. Between the tarsus and the posterior epithelium there is only a trace of loose connective tissue, but beneath the external epithelium there is a thin layer of loosely meshed tissue without fat cells. The epithelium joining the lid margins degenerates, and the cilia pushing through break it up and the lids separate.

Lachrymal apparatus. In the young fœtus there is a groove between the lateral nasal process and the superior maxillary process, extending from the eye to the nostril, and called the lachrymal furrow (Fig. 19, A and B). This furrow soon disappears, and we see only a trace of its former existence near the eye (Fig. 19, C). In frontal sections at the stage shown in Fig. 19, A, B, we find a short distance from the nostril a thickening of the epi-

thelium in the furrow (Fig. 21, A). Farther toward the eye we find an epithelial mass deep in the tissue but still connected with the external epithelium (Fig. 21, B). At a slightly later stage, the mass of epithelium is entirely separated from the external epithelium and a central channel has appeared in it, forming the lachrymal duct.

The lachrymal gland is formed like other secreting glands by a solid epithelial process extending from the conjunctival epithelium back into the orbit, and giving off branches all of which become hollow tubules.

The extensive bibliography may be found in the general treatises of Manz, Kölliker, His, Kessler, and Quain.

EXPLANATION OF THE FIGURES.

Fig. 1.—Chick, 1st day, showing at A A the primary optic vesicles.

Fig. 2.—Chick, 2d day. Thickening of external epiblast to form lens.

Fig. 3.—Chick, 3d day. Formation of lens-sac and secondary vesicle.

Fig. 4.—Rabbit, sagittal section. Lens-sac fully formed.

Fig. 5.—Rabbit; early vitreous; x 200.

Fig. 6.—Chick; lens fully formed.

Fig. 7.—Pig, 4 cm. long; horizontal section.

Fig. 8.—Pig, 4½ cm. long; horizontal section.

Fig. 9.—Pig, 6 cm. long; horizontal; ant. segment.

Fig. 10.—Pig, 6 cm. long; horizontal; post. segment.

Fig. 11.—Pig, about 9 cm. long; horizontal; ant. segment.

Fig. 12.—Pig, 9 cm. long; horizontal; post. segment.

Fig. 13.—Pig, 12.5 cm. long; horizontal.

Fig. 14.—Retina pig; A, ganglion-cells; B, pale cells.

Fig. 15.—Retina pig near term; A, ganglion-cells; B, reticular layer; C, layer of pale cells.

Fig. 16.—Pig, $3\frac{1}{2}$ cm. long; A and B, frontal sections through inferior wall just after closure of cleft; C, D, E, optic stalk.

Fig. 17.—Pig, $4\frac{1}{2}$ cm. long; sagittal section optic nerve; A, collection of epiblastic cells among nerve fibres; B, entrance of central vessels.

Fig. 18.—Optic nerve, pig. A, nerve-fibres; C, sheath.

Fig. 19.—A and B, pig, 3 cm. long; C, pig, 4 cm. long.

Fig. 20.—Pig; vertical section, junction of lids; M, Meibomian glands; S, sweat-gland.

Fig. 21.—Pig, 3 cm. long, frontal section. Lach. duct: A, near nostril; B, near eye.

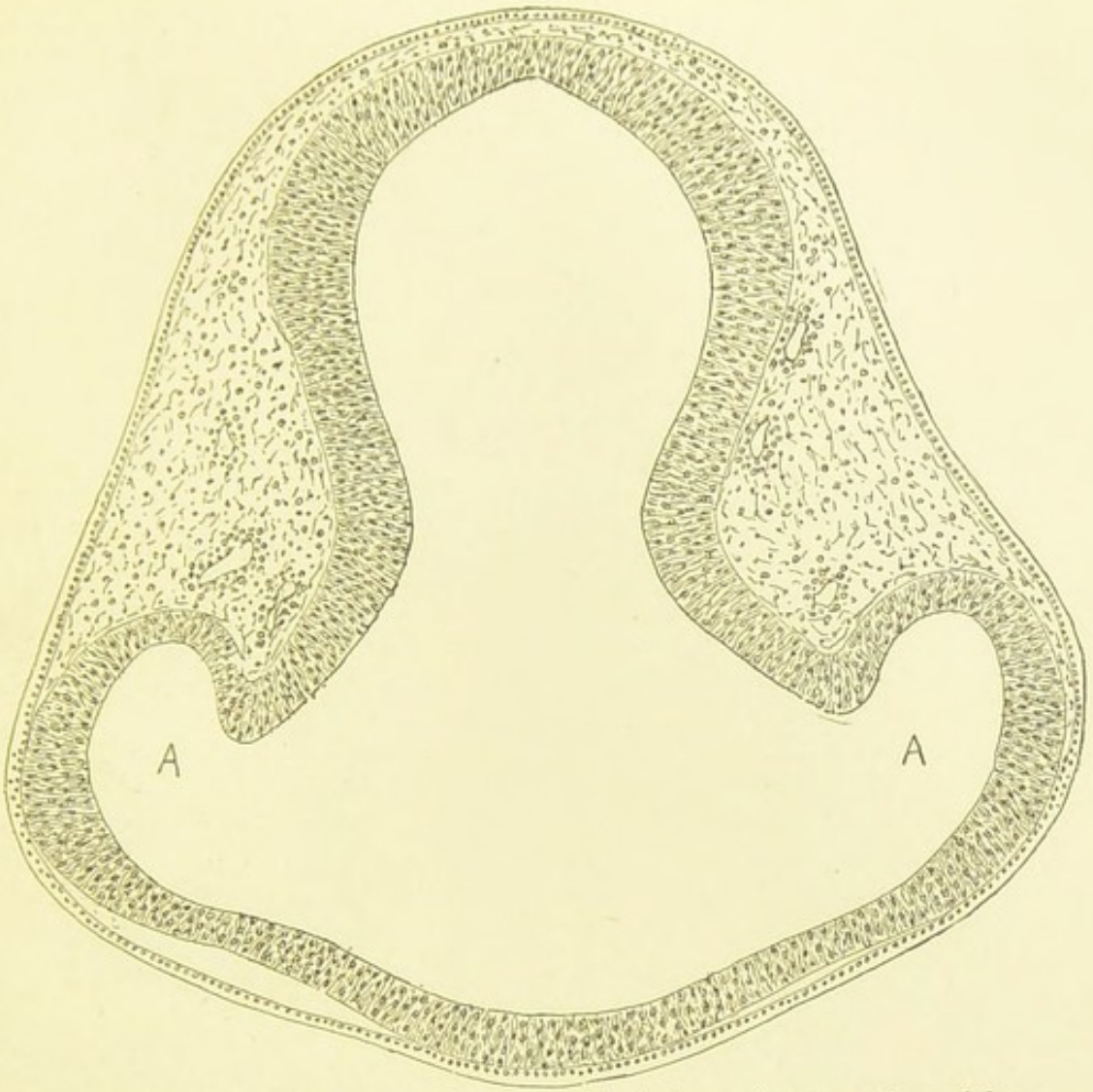


FIG. 1.—Chick, first day, showing at A A the primary optic vesicles.

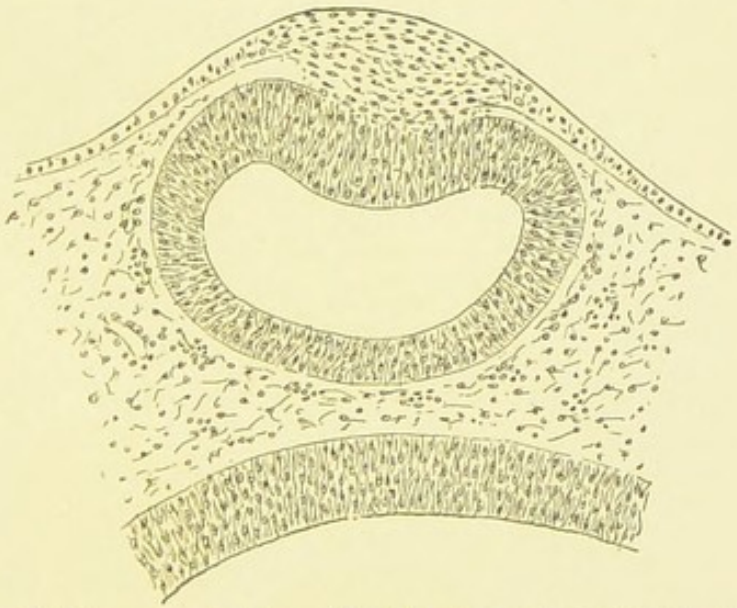


FIG. 2.—Chick, second day. Thickening of external epiblast to form lens.

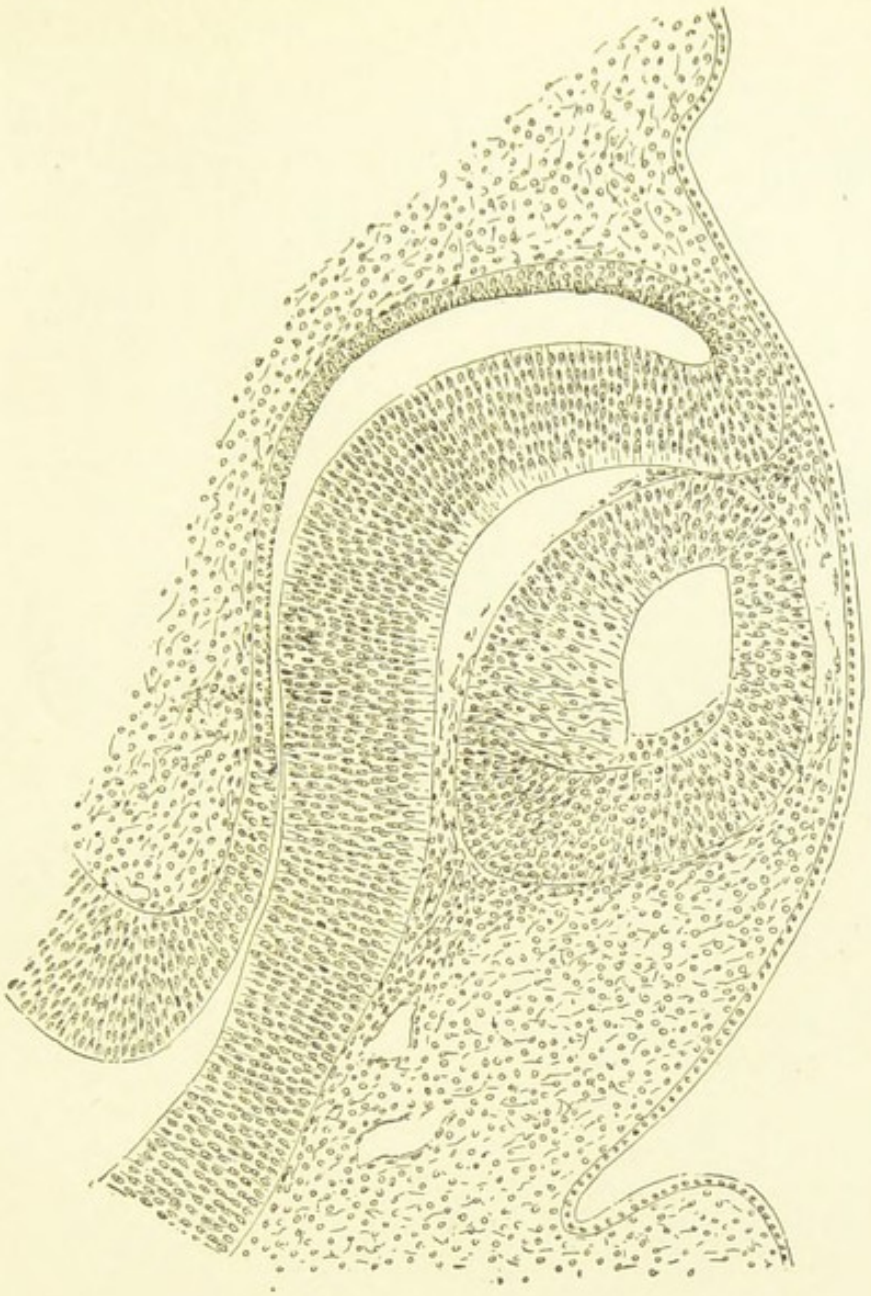


FIG. 4.—Rabbit, sagittal section. Lens-sac fully formed.

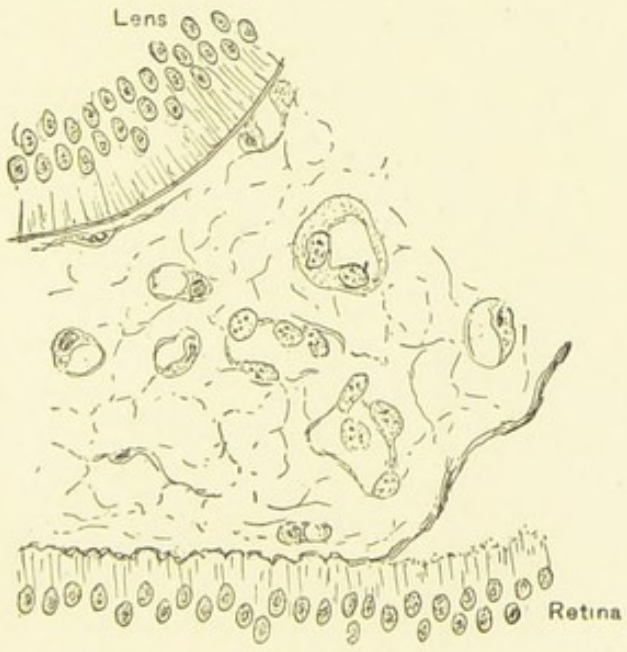


FIG. 5.—Rabbit; early vitreous; highly magnified.

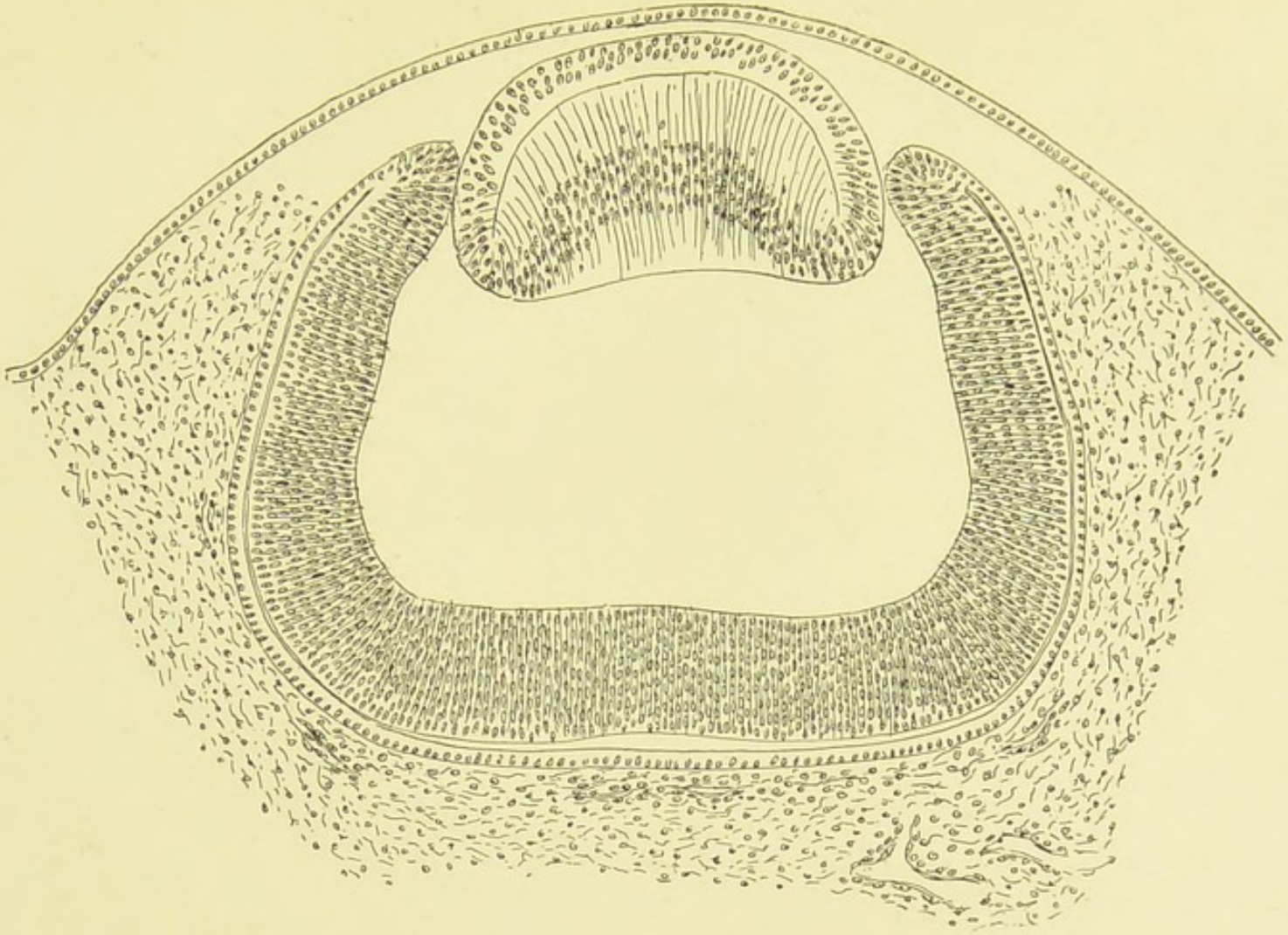


FIG. 6.—Chick ; lens fully formed.

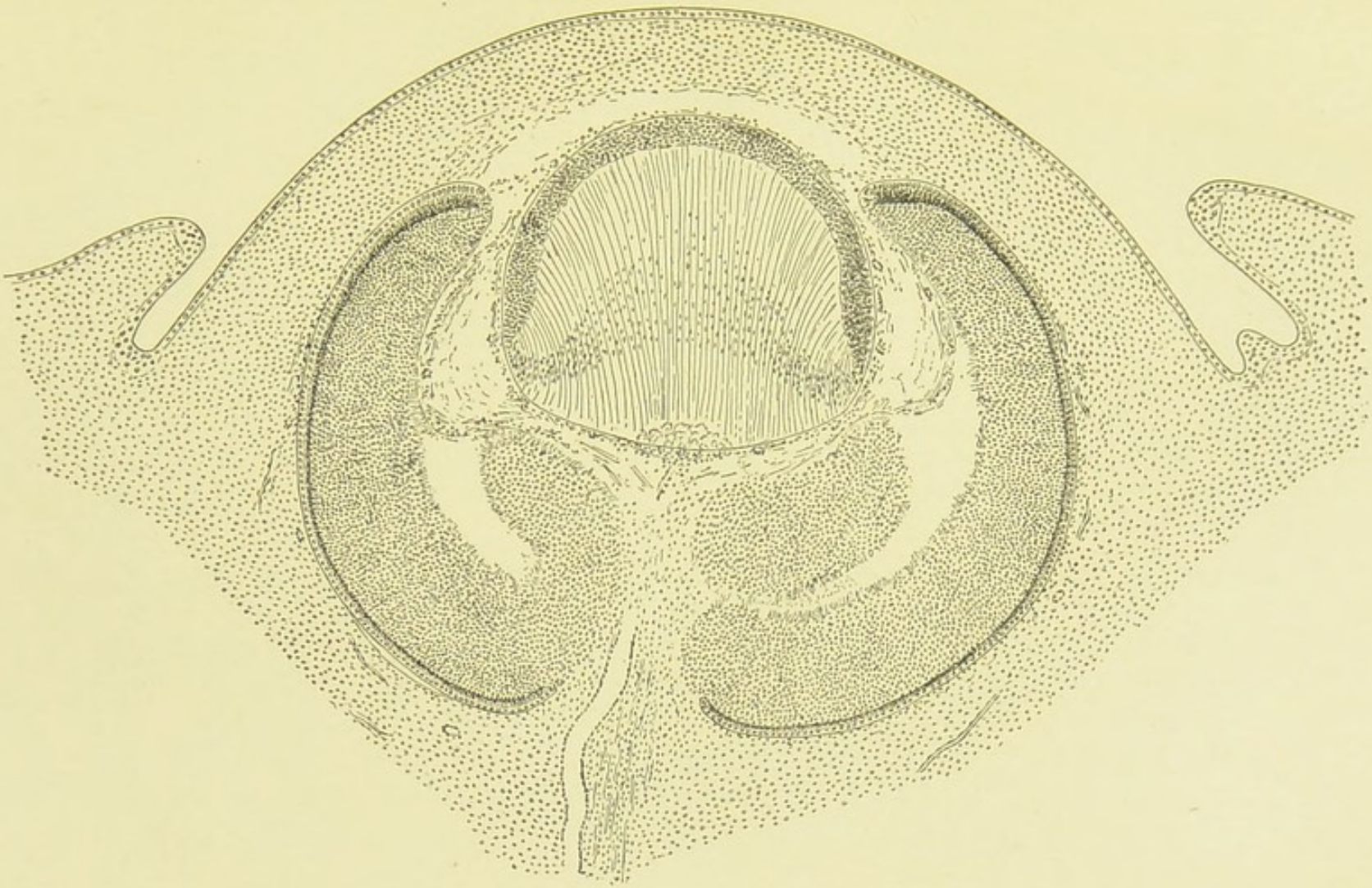


FIG. 7.—Pig, 4 cm. long ; horizontal section.

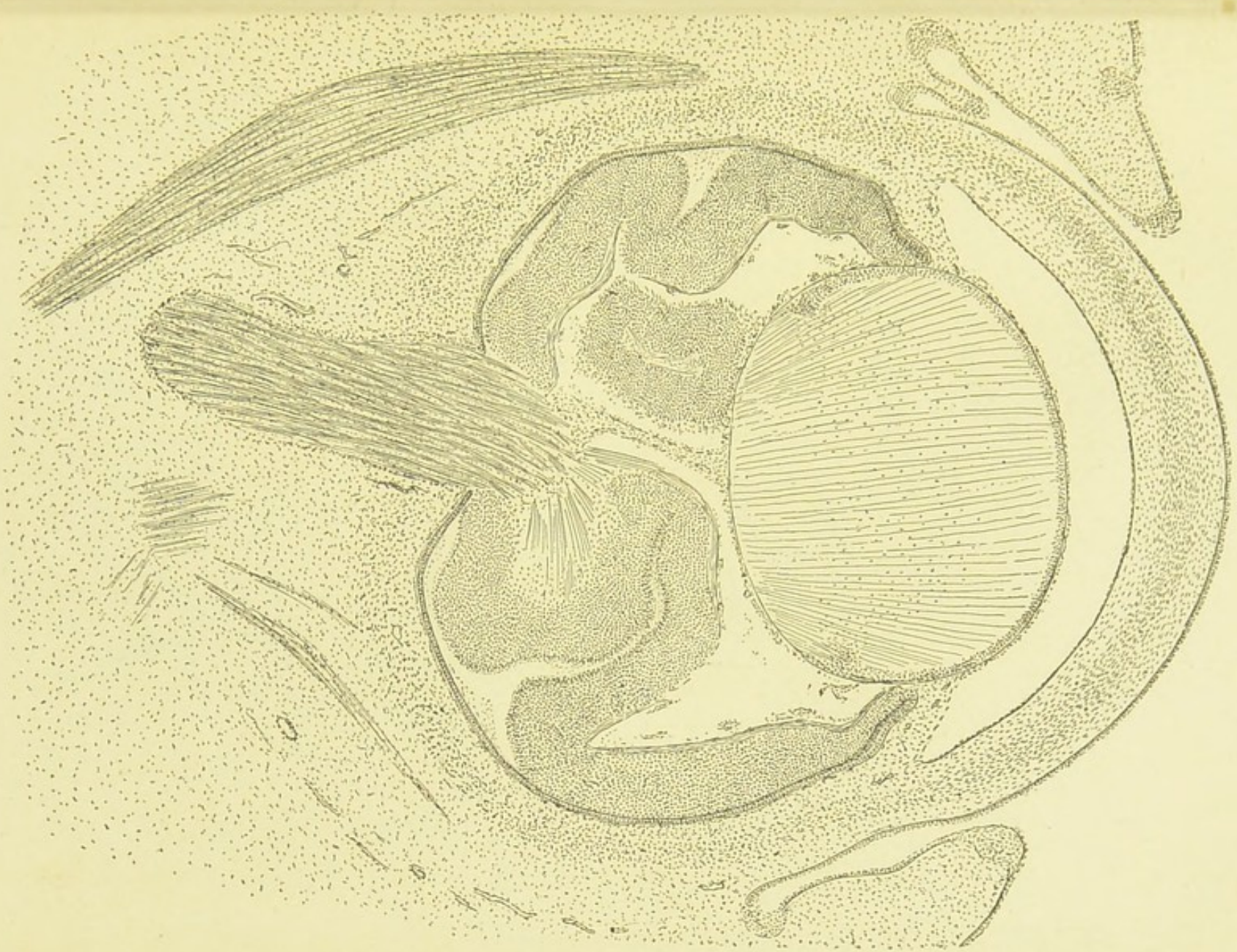


FIG. 8.—Pig, 4½ cm. long; horizontal section.

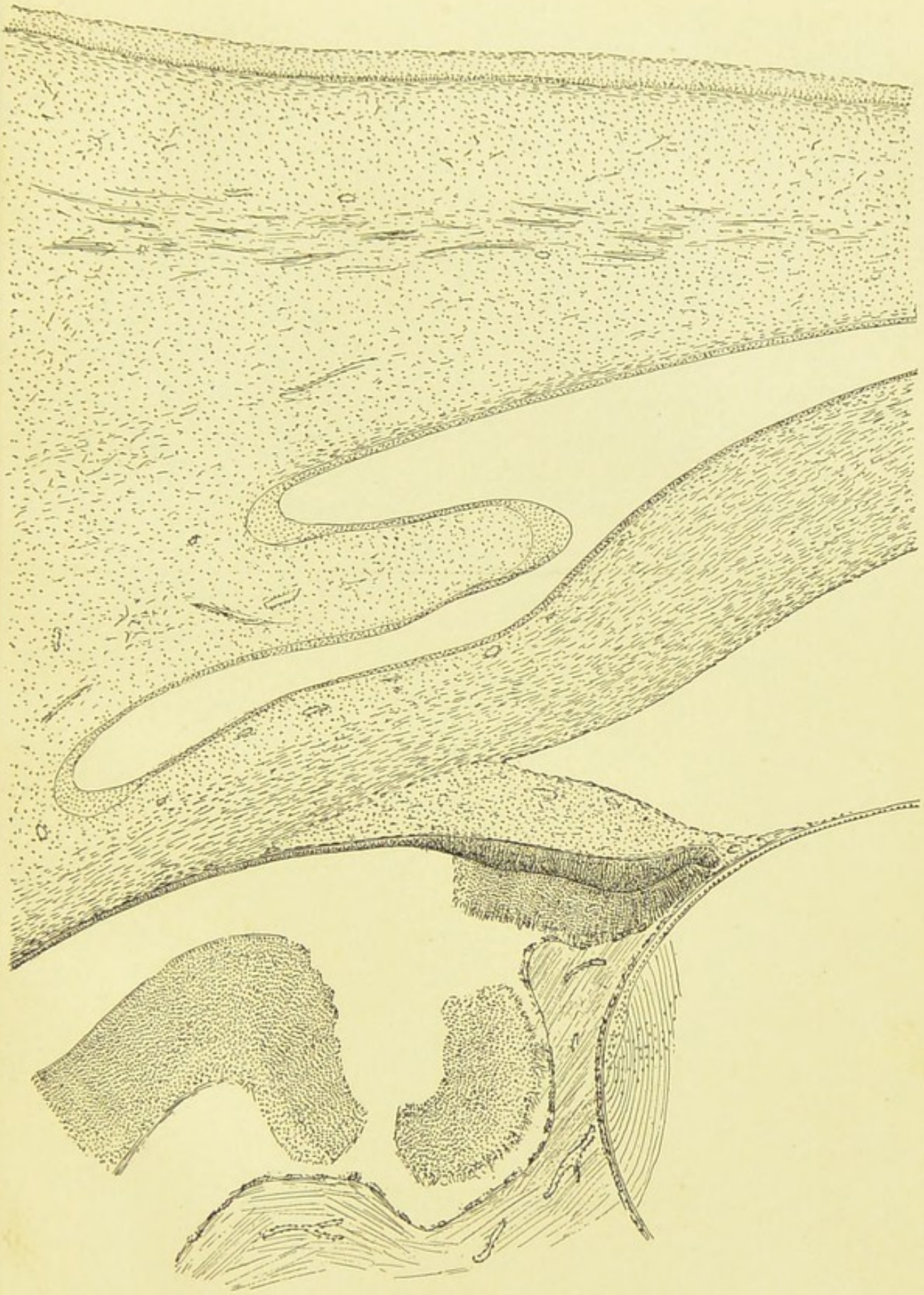


FIG. 9.—Pig, 6 cm. long; horizontal ant. segment.

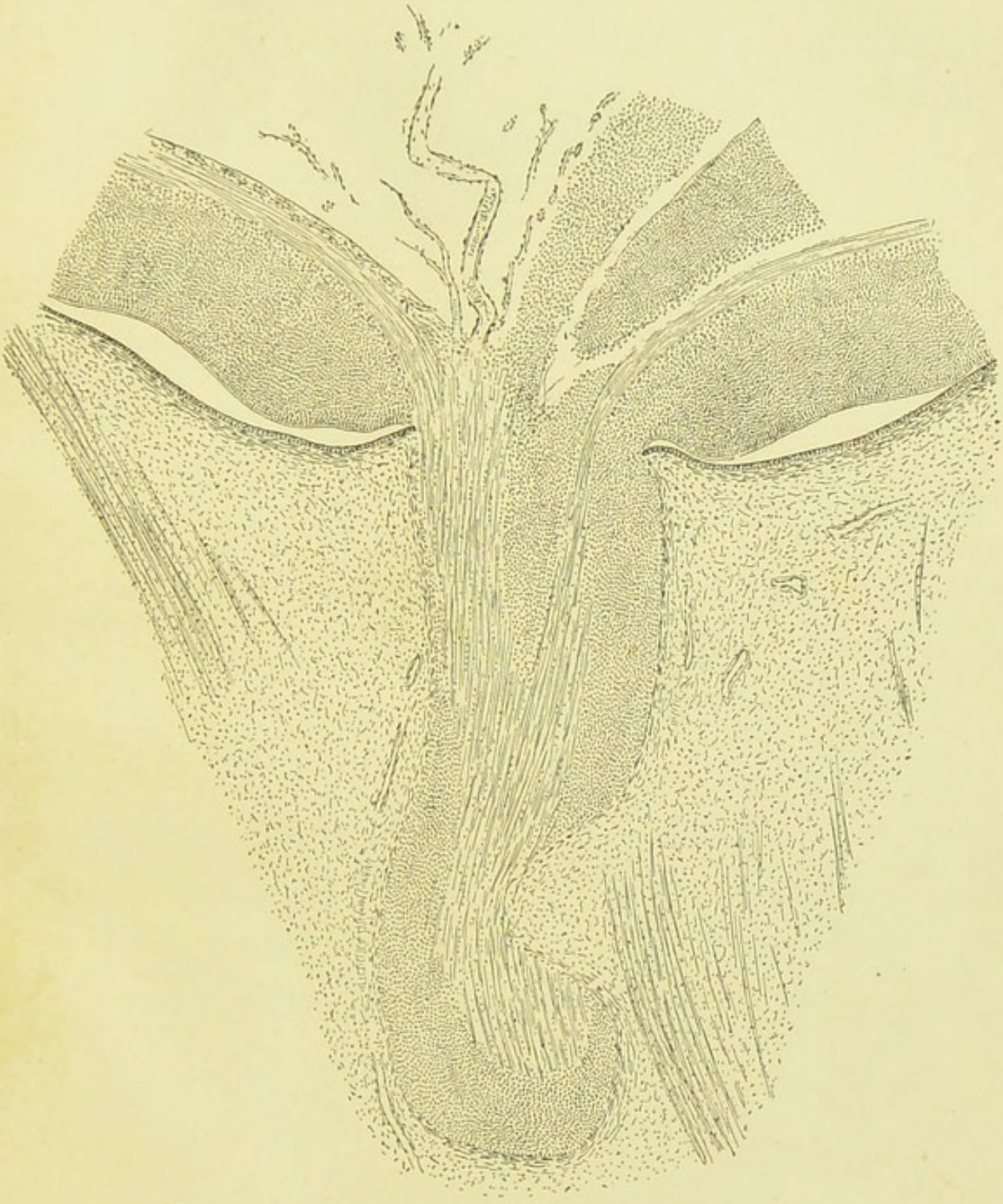


FIG. 10.—Pig, 6 cm. long; horizontal post. segment.

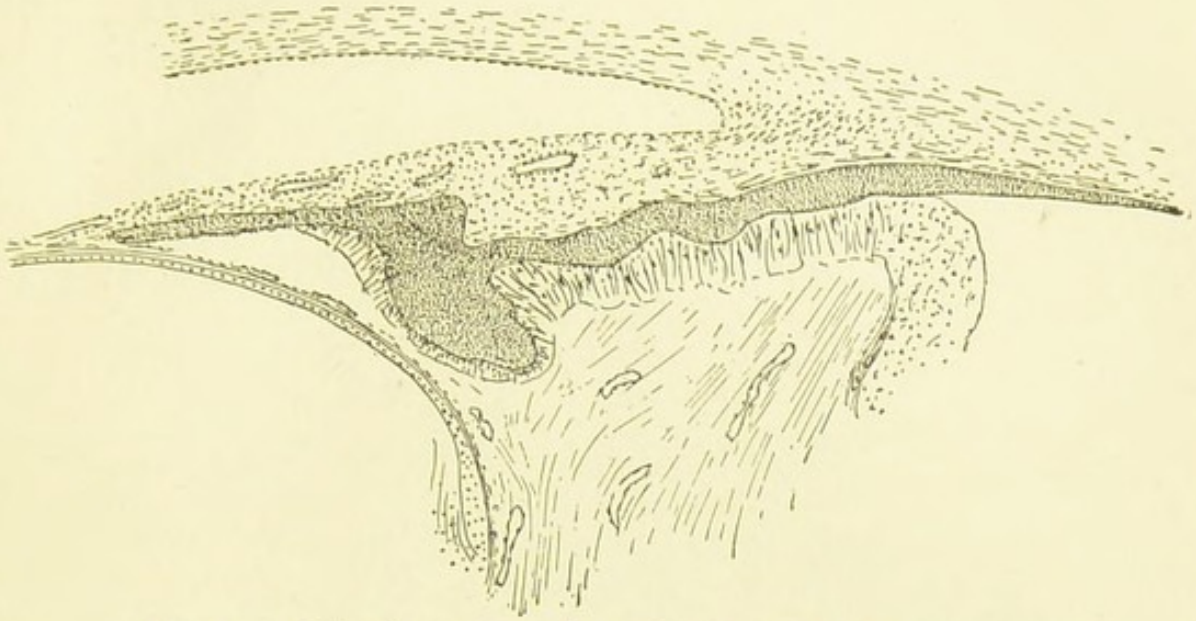


FIG. 11.—Pig, about 9 cm. long; horizontal ant. segment.

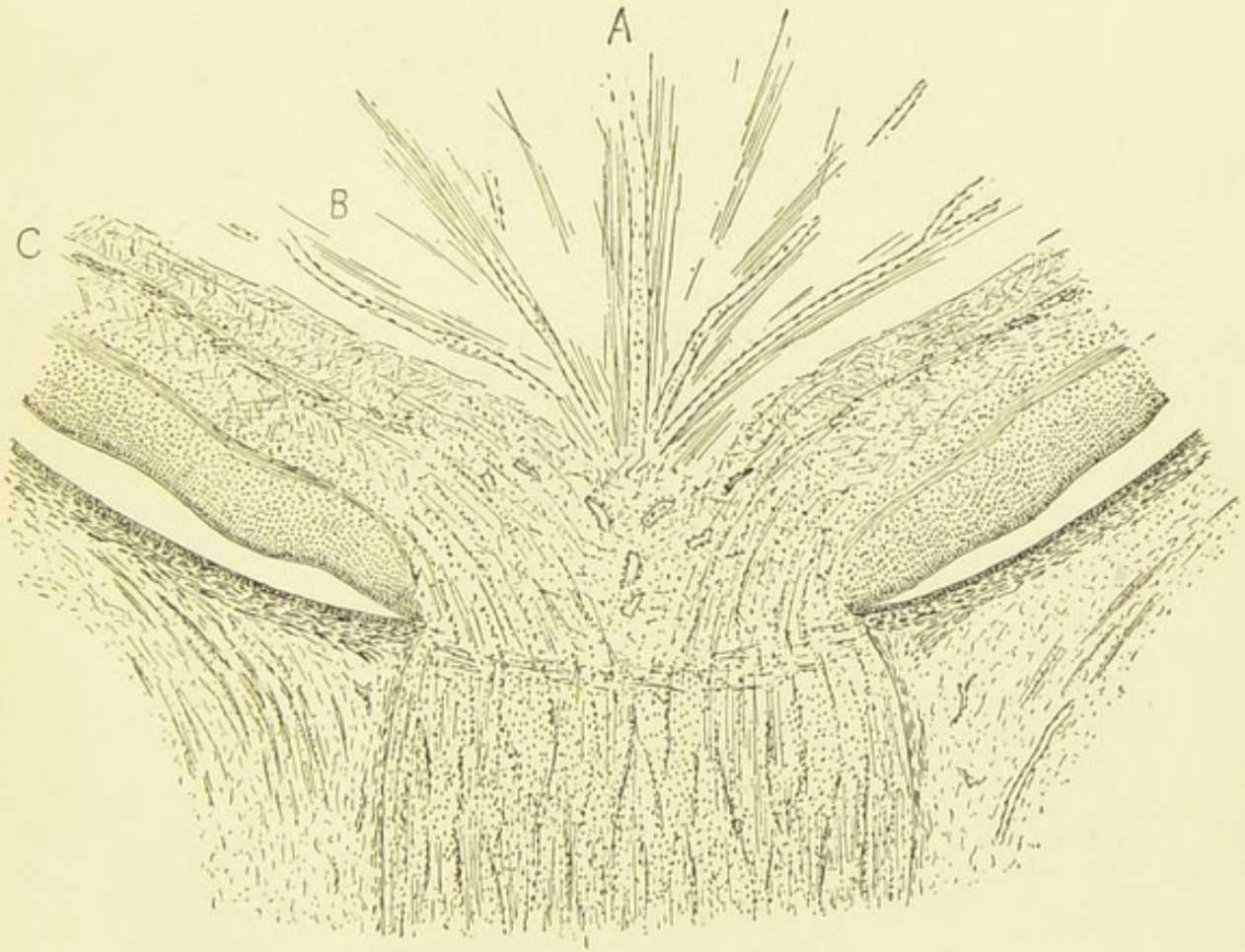


FIG. 12.—Pig, 9 cm. long; horizontal post. segment.

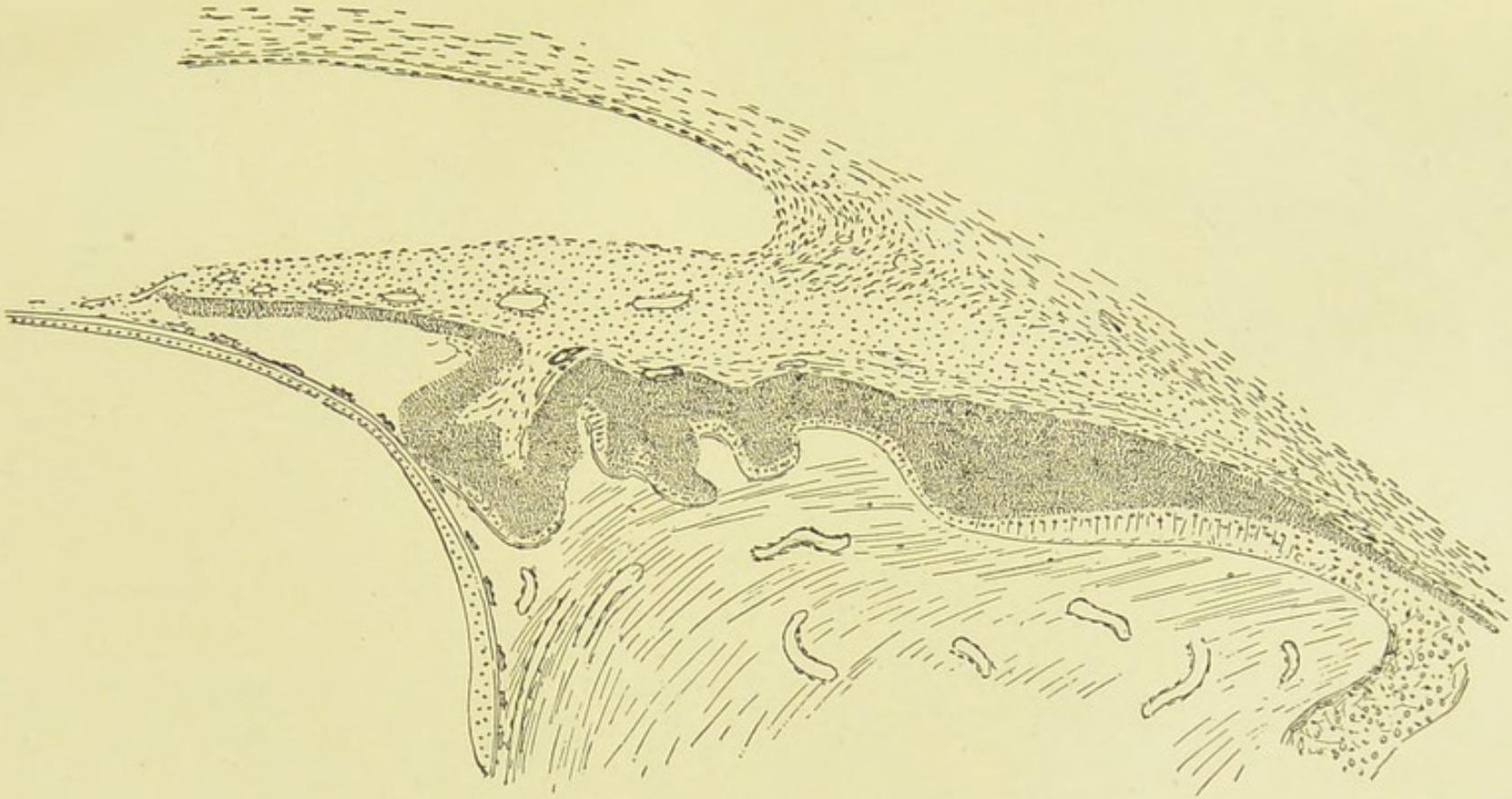


FIG. 13.—Pig, 12.5 cm. long; horizontal.

FIG. 14.—Retina pig; A, ganglion cells; B, pale cells.

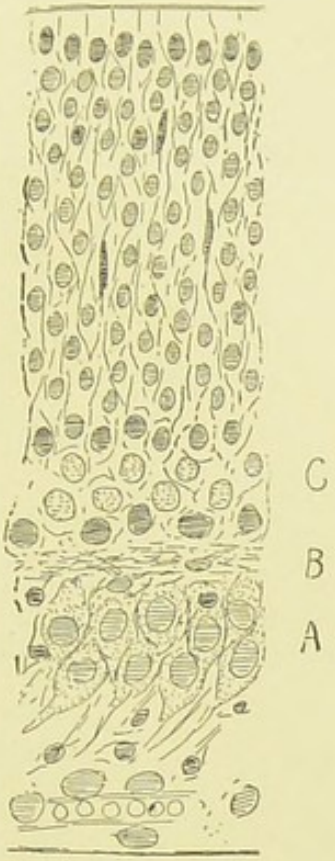
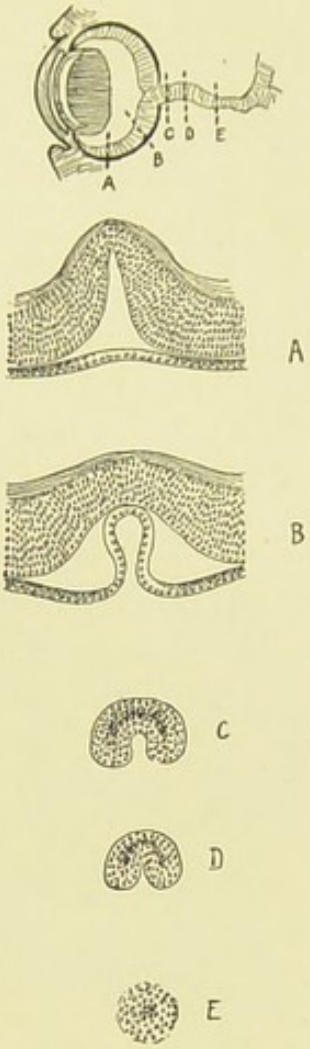


FIG. 15.—Retina pig; A, ganglion cells; B, reticular layer; C, layer of pale cells.



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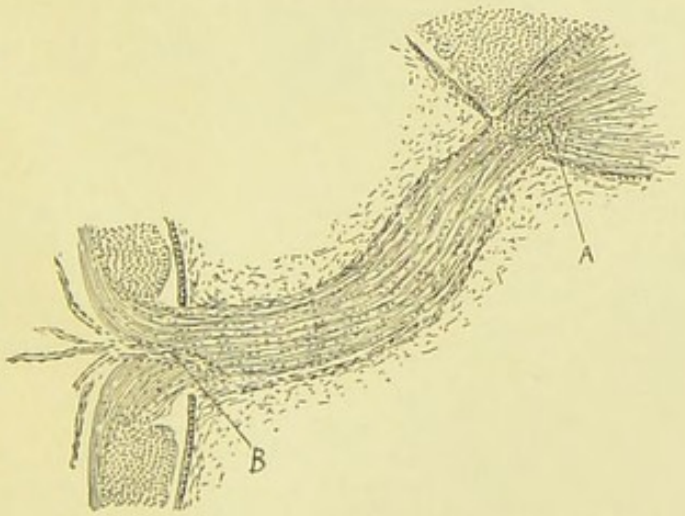

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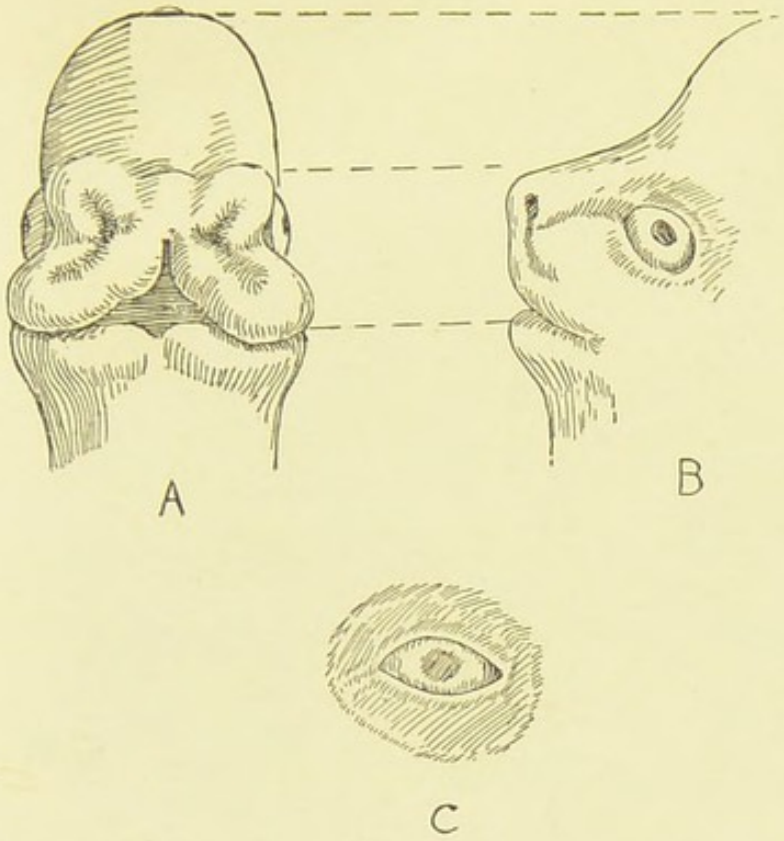
FIG. 18.—Pig, Optic nerve; A, nerve fibres; C, sheath.



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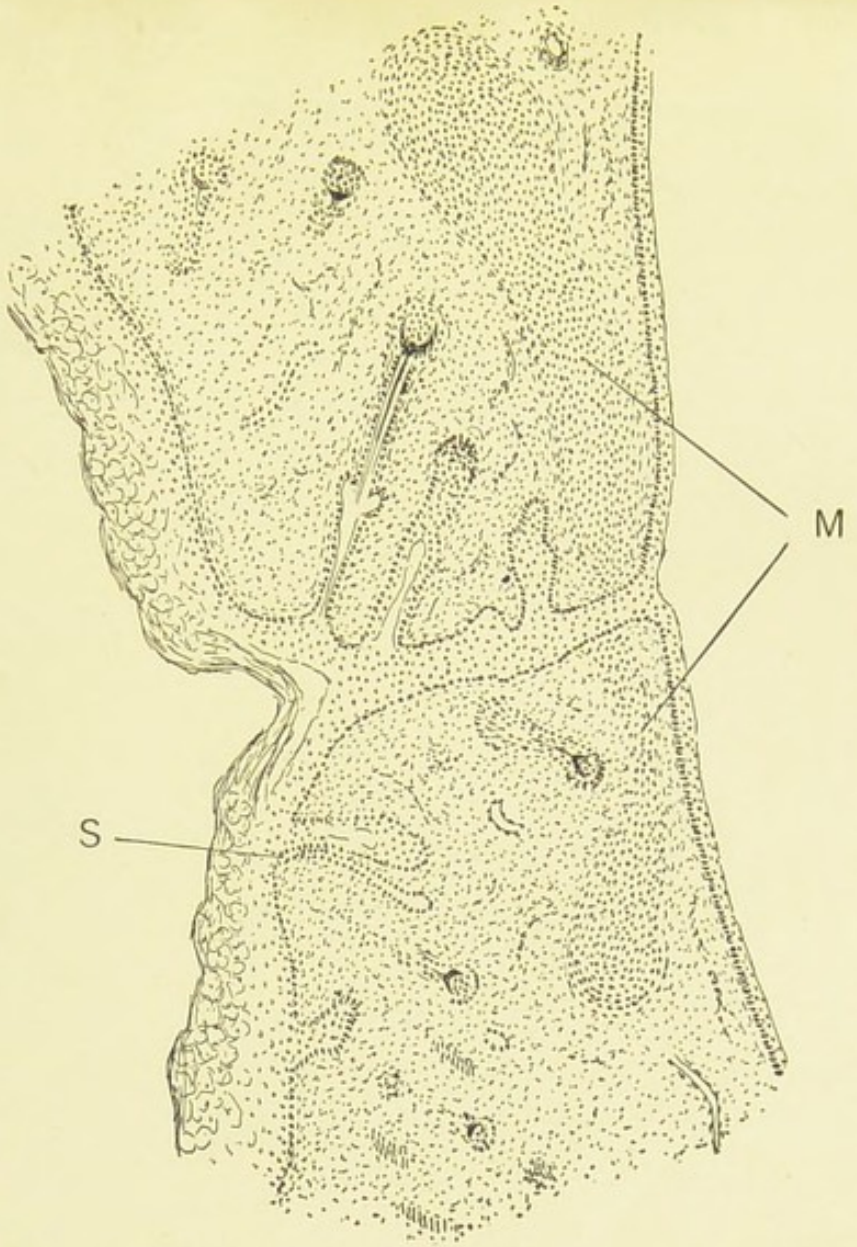

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