PHILOSOPHICAL TRANSACTIONS.

I. *The Development of the Thymus, Epithelial Bodies, and Thyroid in the Marsupialia.* Part I.—Trichosurus vulpecula.

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[Plates 1–10.]

Contents.

Chapter I.—Introductory.

In recent years much attention has been given to the development of the thymus and thyroid in the Mammalia, with the result that we are now in possession of more or less adequate accounts of the developmental history of these structures in representatives of many of the mammalian orders, including the Monotremata (Maurer, 34). As concerns the Marsupialia, however, apart from a brief résumé of results communicated by the present authors to Section D at the Dundee (1912) Meeting of the British Association, no observations on the origin of these structures are extant. It is the object of the present paper to fill this blank in our knowledge so far as the

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Diprotodont Trichosurus is concerned. In Part II, one of us (E. A. F.) gives an account of the development of these glands in certain other Marsupials of which our material is less extensive than it is in Trichosurus.

Our work in this field is the outcome of an endeavour to prepare a normal table of the development of Trichosurus, but we had not proceeded very far with this task before it became evident that the work of tabulation of the conditions in the pharyngeal region could only be satisfactorily effected after we had made as thorough a study as possible of the development of the gill-pouches and their subsequent transformation. The results of that study are presented in this communication. They are, we venture to think, of considerable interest, inasmuch as they show that Trichosurus, in addition to being provided with a paired superficial cervical thymus, the epithelial basis of which is mainly of ectodermal origin, possesses two pairs of thoracic thymus glands derived exclusively, so far as their epithelial basis is concerned, from the entoderm of the third and fourth pairs of gill-pouches. In respect of the invariable development of these two thymus-metameres, Trichosurus exhibits more primitive relations than any of the mammals hitherto investigated. Further, in respect of the mode of origin of thymus III from the entire caudal as well as the ventral wall of gill-pouch III, Trichosurus would seem to furnish an example of the transitional stage between the Reptilian mode of thymus-development (the thymus being an exclusively dorsal product of the gill-pouch entoderm) and the Eutherian mode (the thymus arising as a ventral product of the gill-pouch).

i. *Material and Methods.*—For the purposes of our investigation we have had at our disposal an almost complete series of uterine embryos of Trichosurus ranging from a stage 5 mm. in greatest length (G. L.) to the embryo just before birth, 14 mm. G.L. In addition we have studied a series of pouch-young and have dissected two adults.

For descriptive purposes, we have arranged our material in twenty-two stages, of which Stages I–XV*a* comprise the uterine embryos from 5 to 14 mm. G.L., and Stages XV*b*–XXII, pouch-fœtuses ranging from the new-born young, 14·5 mm. G.L., to a pouch-fœtus, 5·2 cm. G.L.

Most of our embryonic material was fixed *in utero* in picro-nitric acid, and though for the most part excellently preserved for general work on organogenesis, it is not suited for a detailed study of the histogenesis of such an organ as the thymus, which necessitates, as is well known, not only the most careful fixation but the employment of special staining methods. We have accordingly confined ourselves in the main to a study of the organogeny of the gill-pouch derivatives. The first gill-pouch is not dealt with in this paper.

Our methods call for no special remark except that we may state here that we have prepared wax-plate reconstructions of part of the pharyngeal region in three stages, at a magnification of 300 diameters, reduced figures of the models being reproduced on Plates 2 and 3, figs. 4, 12 and 13, 16 and 17, 19 and 20.

ii. *Nomenclature.*—Thymus workers in recent years have evolved such a complicated and by no means always consistent terminology for the various parts derivative of the gill-pouches, their ectodermal grooves and the cervical sinus that it is often a somewhat difficult matter for anyone who is not a specialist in this particular field to follow the descriptive part of a paper on thymus-development. Having experienced this difficulty ourselves, we have adopted in this paper a conservative attitude and have endeavoured to select those terms which are in most general use and whose signification is most obvious. In a number of cases, we have adopted the terms suggested by HAMMAR (22) in a recent paper dealing with the nomenclature of certain branchial derivatives.

iii. *Literature.*—In view of the publication in 1911 of a very excellent review by HAMMAR (19), entitled 'Fünfzig Jahre Thymus-forschung,' in which is given a critical digest of the more important papers on the development and involution of the thymus that had appeared up to that date, we feel absolved from dealing in any detail with the older literature, and in the sequel have confined ourselves in the main to references to the literature published since the date of that review.

We have thought it best to give in the descriptive part of this paper (Chapter III) a statement of our own observations, largely unencumbered by references to the literature. In Chapter IV we attempt to give a more connected account of the development of the individual pharyngeal derivatives (thymus, epithelial bodies, thyroid) accompanied by such references to the work of others as seem to us of value from the comparative standpoint.

We take this opportunity of expressing our grateful thanks to Miss E. A. STEELE for the drawings of the models (figs. 4, 12, 13, 16, 17, 19, 20), to Mrs. R. H. PLIMMER for the drawing reproduced as fig. 1, Plate 1, and to Mr. F. PITTOCK, of the Zoological Department, University College, for invaluable help in the preparation of the microphotographs reproduced on Plates 9 and 10, and in other ways.

CHAPTER II.—THE ANATOMY OF THE THYMUS, EPITHELIAL BODIES, AND THYROID IN THE ADULT.

Historical.—Our knowledge of the topographical anatomy of the thymus in the Marsupialia we owe almost entirely to the work of SIMON (54), OTTO (40), SYMINGTON (60), and JOHNSTONE (26).

The existence of a thymus in the Marsupials was apparently first recognised by JOHN SIMON in his classical memoir, 'A Physiological Essay on the Thymus Gland,' published in 1845. He dissected specimens of Didelphys, Perameles, Trichosurus, Hypsiprymnus, and Macropus, "with the constant result of finding a thymus" in the form usually of two lobes (three in a mammary fœtus of the kangaroo) situated in relation to the anterior region of the pericardium or shortly in front of the same. In *T. vulpecula*, in particular, he "discovered a distinct rounded remnant situated on the vessels a little above the heart," and in his fig. 21 he illustrates it as consisting of two asymmetrical lobes, the left partially overlapping the right. As the result of his observations SIMON felt assured that "there is no difference as regards this organ between the present (Marsupial) and any other family of mammiferous animals."

No further observations appear to have been made on the Marsupial thymus until 1897, when OTTO (40) in a paper on the comparative anatomy of the thymus and thyroid glands in the Mammalia records his observations on these glands in a number of Marsupials, including Didelphys, Macropus (two species), Petrogale, and Hypsiprymnus, without, however, materially advancing our knowledge of the former structure. In *M. giganteus* and *M. leporoides*, he describes the thymus as consisting of two lobes situated in the upper part of the anterior mediastinum; in the other forms he failed to find any trace of thymus tissue.

In 1898 appeared a valuable paper by SYMINGTON (60), in which he gave an account of his observations on the anatomy of the thymus in the Diprotodont genera, Macropus, Trichosurus, Phascolomys, and in the Polyprotodonts, Didelphys and Dasyurus. He showed that in the Diprotodont genera examined there is present, in addition to the paired posterior or thoracic thymus observed by SIMON and OTTO, a hitherto unrecognised and entirely distinct anterior or cervical thymus in the form of paired lobes situated superficially in the ventral part of the neck, immediately behind the corresponding submaxillary glands and just internally to the skin and platysma. In the Polyprotodont genera mentioned he was unable to find any trace of the cervical gland. He was thus led to put forward the tentative conclusion that the Diprotodontia differ from the Polyprotodontia in the possession of an additional thymus, viz., the cervical. He further made the suggestion that "the superficial position of the cervical thymus may be associated with the origin from the epiblastic rather than the hypoblastic portion of the clefts," a suggestion we are able substantially to confirm.

In a paper also published in 1898, JOHNSTONE (26), as the result of the examination of a more extensive material than that of SYMINGTON, generally confirmed the results of the latter and added to our detailed knowledge of the anatomy of the Marsupial thymus. He likewise failed to find a cervical thymus in any of the Polyprotodonts examined (Didelphys, adult and fœtal, Dasyurus, Thylacinus, Myrmecobius, Antechinomys, Perameles). Amongst the Diprotodonts, he observed it in Trichosurus and Macropus, but not in Cuscus, Petaurus, and Phascolarctos, though SYMINGTON (61), in a later paper, records its existence in a young specimen of the latter. It may be noted that JOHNSTONE describes a four-lobed condition of the thymus in fœtal specimens of Didelphys, Dasyurus, and Trichosurus, but in the absence of a knowledge of the development he was unable to recognise its significance.

ZUCKERKANDL (70), in 1902, was the first to give an account of epithelial bodies (parathyroids) in a Marsupial. In *Didelphys azaræ* he states that an epithelial body is situated at the point of division of the common carotid artery on each side. It shows a lobed structure, is pierced by the internal carotid artery, and is characterised by its large size, the right body measuring 15·5 mm. in length by 7 mm. in breadth by 5 mm. in thickness, the left being somewhat smaller. In addition, there is present on the right side a smaller epithelial body situated on the medial wall of the internal carotid, and on the left, two. Besides these external epithelial bodies Didelphys possesses, according to ZUCKERKANDL, one or two inner epithelial bodies situated in the dorsal parts of the thyroid lobes.

As a basis for our embryological work, we have made careful dissections of the cervical and anterior thoracic regions in two adult Phalangers; in each case the glands displayed were subsequently removed, and cut either wholly or in part into serial sections, so as to determine their nature. We may preface our detailed account of these two specimens by a short general statement of our observations.

The *thymus* in Trichosurus is noteworthy in that it is represented typically by *three* pairs of glands, viz., (1) a large paired *superficial cervical thymus* situated internally to the platysma on the ventral side of the anterior region of the neck, immediately caudal to the sub-maxillary glands, the existence of which has previously been recorded by SYMINGTON and JOHNSTONE, and (2) two pairs of more deeply-seated glands, situated, the one pair cranial to the other, a short distance anterior to the pericardium, in relation to the common carotid arteries. They lie partly in the posterior region of the neck, partly in the thorax, on a level with or just behind the first rib. We may speak of them for convenience as the *thoracic* glands. Study of their development shows that they represent paired thymus III and paired thymus IV, which are here for the first time definitely recognised. They may remain distinct and independent, or they may fuse with each other on one or both sides. In the oldest fœtal specimen we have examined (Stage XXII, p. 41) a small accessory thymus is present on the right side, on a level with the lateral thyroid lobe, whilst in Stage XIV *b* an accessory lobe is present caudally to right thymus IV.

The *epithelial bodies* comprise at least two pairs, an anterior pair (epithelial body III), situated near the division of the common carotid arteries, and a posterior pair (epithelial body IV), either imbedded in thymus IV or not far removed from the same. In addition, accessory epithelial bodies may occur in connection with both the cervical and thoracic thymus. In view of ZUCKERKANDL'S statement (*cf. ante*), it may be emphasised here that in Trichosurus we have never met with epithelial bodies either close to or imbedded in the thyroid in any of the material (whether embryonic, fœtal, or adult) examined by us. Trichosurus thus affords no justification for the application of the name parathyroid to these structures.

The *thyroid*, as in the majority of other marsupials (*cf.* OTTO, JOHNSTONE, and others), consists of two lateral lobes connected by a slender median bridge. It lies, as usual, ventro-laterally to the hinder part of the larynx and the beginning of the trachea.

Specimen A.—Virgin female, measuring in dorsal contour length from snout to root of tail 45·5 cm. (Plate 1, fig. 1).

The *cervical thymus* (fig. 1, *s.tm.*) consists of two well marked lobes situated ventro-laterally in the anterior region of the neck, immediately caudal to the sub-maxillary glands (*subm.gl.*). As described by SYMINGTON (60), the two glands lie internally to the platysma, between the latter and the sterno-cleido-mastoid and sterno-hyoid muscles (*cf.* Plate 10, fig. 61), being covered on their ventral or outer surfaces by backward extensions of the parotid glands. Each gland appears externally as a compact flattened structure, roughly triangular in shape, the right gland measuring 13 mm. in length by 10 mm. in breadth by 4 mm. in thickness, the left measuring 15 × 9·5 × 4 mm. In section the glands are seen to be markedly lobulated. They exhibit the usual differentiation into cortex and medulla, Hassall's corpuscles being present in the latter, and, so far as we have observed, they differ in no respect histologically from the thoracic glands. In the medulla of the right gland there is present an elongated canal-like cavity, partially occupied by lymphocytes and multinuclear elements.

A large accessory *epithelial body* (0·49 × 0·43 mm. in diameter) indents the left gland on one side, being situated superficially between the lobules.

The *thoracic thymus* comprises four separate glands, two on the right and two on the left, asymmetrical both in size and in disposition.

Left thymus III (fig. 1, *tm.* III) is a small elongated gland, 5 mm. in length by 2 mm. in breadth, situated ventro-medially to the left common carotid artery, between it and the trachea, and shortly in front of the mid-region of the latter. It appears in section as a compact gland, little lobulated. A very short distance (0·35 mm.) from one end of the gland there is seen in the sections an epithelial body measuring 0·59 × 0·19 mm. in diameter.

Left thymus IV (*tm.* IV), measuring 6·5 × 6 × 3·5 mm., is an irregularly ovalish body, situated ventro-laterally to the left common carotid, on a level with the lower end of the clavicle and in front of the first rib. In section it is seen to be markedly lobulated. In connection with it three epithelial bodies are seen to be present in the sections, a larger one (0·5 × 0·36 mm. in diameter) imbedded between the lobes towards one end of the gland, and two smaller ones, completely imbedded in the thymus-tissue. One of these two is exceptional in the presence in it of a small patch of lymphocytes.

Of the two glands on the right side, one, much the larger of the two (*tm.'*) is pear-shaped in form and lies on a level with left thymus IV, close to the middle line, and just ventrally to the division of the innominate artery into the right subclavian and right common carotid. It measures 10·5 × 5 × 3 mm., and in section is seen to be distinctly lobulated. A relatively large epithelial body (0·72 × 0·67 mm. in diameter) lies imbedded between the lobes towards one end. From its position this gland might be regarded as right thymus III, but the presence of the large epithelial body in it is rather suggestive of thymus IV. The second gland (*tm.″*) (? right thymus III or IV) is small (measuring 5 × 2 mm.), and lies postero-laterally to the anterior gland on a level with the first rib. It is in process of involution; the thymus tissue has taken on a diffuse arrangement, and fatty degeneration is evident. No epithelial body was observed in the portion of the gland cut.

Epithelial body III (*ep.b.* III) appears on the left side as a small ovalish mass (2·25 mm. in length by 1·5 mm. in breadth) situated just medially to the origin of the internal carotid artery. On the right side it measures 2 × 1 mm. and lies in contact with the lateral surface of the common carotid, 4 mm. behind the point of division of the same.

The epithelial bodies in Trichosurus present everywhere the same histological appearance. They are compact bodies invested by a thin connective tissue capsule, and composed of closely packed pale-staining cells arranged in anastomosing columns and masses between which run fine sinusoids (*cf.* Plate 8, fig. 64). They appear to be identical in structure with the compact epithelial body of the sheep as figured by SCHAFER (53, *cf.* his fig. 1, Plate IX). Occasionally, sparsely distributed connective tissue cells may be observed between the cell masses, especially in sections stained by Mallory's method, but there can be no question of the existence of connective tissue septa such as Mrs. THOMPSON (63) states are present in the epithelial bodies of man.

Epithelial body III of Trichosurus would appear to differ widely from the epithelial body in Didelphys described by ZUCKERKANDL (*loc. cit. ante*) both as regards size and histological characters, so widely indeed as to suggest a doubt whether we are dealing with the same structures.

Thyroid.—The lateral lobes (fig. 1, *l.th.*) are elongate, ovalish bodies situated ventro-laterally to the hinder portion of the larynx and the commencement of the trachea. They are slightly asymmetrical, the left measuring 11 × 4 × 3 mm., and the right 14 × 5 × 3·5 mm. The bridge or isthmus arises from the hinder end of each lobe, runs forwards a short distance in contact with the medial surface of the same, and then extends transversely across below the trachea at about the level of the third tracheal ring. It has a transverse length of about 11 mm., and a thickness of 1–2 mm.

In this specimen the thyroid vesicles are lined by a cubical epithelium, and are irregular in shape, tending to be lobed or slightly branched. They possess only scanty contents.

Specimen B.—Adult ♂. Dorsal contour length, 51 cm.

In this specimen the thymus glands are all in a more or less advanced stage of involution.

Cervical Thymus.—The left gland is greatly reduced as compared with that of

A, measuring 8·5 mm. in length by 5 mm. in breadth. The bulk of the gland is formed of fibrous connective tissue through which the thymus tissue is diffused in masses and streaks. Hassall's corpuscles are abundant. There is no evidence of fatty degeneration.

The right gland was overlooked in the dissection.

The *thoracic thymus* is in this specimen represented by two glands only. The left gland lies ventrally to the left common carotid, approximately in the position occupied by left thymus IV in specimen A. It measures 5·5 × 2 mm. The involution-changes are well marked. The gland is penetrated by fatty tissue, and the fibrous connective tissue, especially in relation to the blood-vessels, is markedly increased. The thymus tissue is diffuse and broken up into larger and smaller masses of irregular form. Two imbedded epithelial bodies are present.

The right gland is an oval body, 5 mm. in greatest diameter, situated ventrally to the right common carotid, about the middle of its length. The main mass of the gland is here again formed of fibrous connective tissue, with fat-cells. The thymus tissue is diffuse and scanty in amount. Hassall's corpuscles are well marked. A typical imbedded epithelial body is present, and in addition there occurs a smaller epithelial mass whose ends are not sharply marked off from the adjoining thymus tissue. The fact that in some of the isolated nodules of thymus tissue the epithelial cells of the reticulum appear to have undergone hypertrophy suggests that this mass may have been formed from the reticulum after the withdrawal of the thymus cells.

Epithelial body III on the left side lies dorsally to the internal carotid, shortly in front of its origin. It measures 2·5 × 2 mm. On the right side it lies medially to the external carotid, and measures 2·5 × 1 mm.

The *thyroid* resembles that of A, the lobes being slightly larger, the left measuring 14 × 15 mm., and the right 16·5 × 6 mm. The bridge passes across between the fourth and fifth tracheal rings. The thyroid vesicles are here large and spherical, with thin flattened walls and abundant colloid.

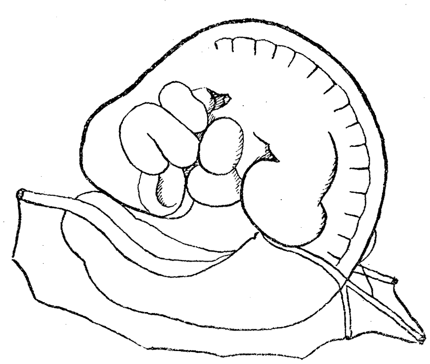
Cervical thymus in a third specimen (C).—In addition we have examined the cervical thymus in a second ♀ with a dorsal contour length of 48·5 cm. One of the nipples in the pouch is much enlarged, showing that this female had bred. The left gland measured 8·5 × 2·5 × about 1 mm., the right 8·5 × 3 × 1·5 mm. Both glands are in involution. The thymus tissue is diffuse, but is more abundant than in the left cervical thymus of B. Fat-cells are present in small numbers, and connective tissue containing numerous vessels is conspicuous. There are numerous Hassall's corpuscles. A well marked epithelial body is imbedded in the left gland.

As regards the onset of involution, the foregoing observations show that in the adult but virgin female (A) involution is apparent in only one of the thymus glands, viz., right thymus IV ? (fig. 1, *tm.″*), in the adult male (B) it is general, whilst in the multiparous female (C) it is presumably also general. The evidence, such as it is, indicates that in Trichosurus, as in other mammals, the onset of involution coincides with the attainment of sexual maturity (*cf.* HAMMAR, 19, p. 257).

CHAPTER III.—DESCRIPTION OF MATERIAL.

Stage I.—Three embryos: (*a*) δ '97, transverse, (*b*) 1*a* '01, longitudinal, and (*c*) 1 '01, transverse. G.L. from dorsal curvature above fore-limbs to hinder end = 5 mm. Plate 2, figs. 2 and 3 and text-fig. 1.

Embryo greatly curved (text-fig. 1), the frontal surface of the head almost in contact with the ventral surface of the hinder region of the trunk. Fore-limb differentiated into arm and manus, no indication of digits. Hind limbs in the form of undifferentiated low ridges.



TEXT-FIG. 1.

The *hyoid arch* is large and conspicuous. It lies immediately behind and parallel with the mandibular process of the first arch, from which it is separated by the first ectodermal groove (fig. 2, *hy.a.*, *ect.gr.* 1). Behind the hyoid arch is the *cervical sinus* (figs. 2 and 3, *s.c.*), an extensive depression, widely open to the exterior and of triangular outline, its apex directed posteriorly. It is bounded in front by the hyoid arch, above by a distinct curved ridge, the retrobranchial ridge of HIS, and below by a second ridge running forwards and inwards above the heart swelling. In the floor of the sinus are visible the first, second and third branchial (the third, fourth and fifth visceral) arches. The first branchial arch is the largest (fig. 2, *br.a.* 1), but is much smaller and narrower than the hyoid. Its upper end lies at the level of the retrobranchial ridge outside the sinus, and from there the remainder of the arch, now lying within the sinus, slopes downwards and inwards behind the hyoid, gradually becoming reduced in height. The *second arch* (fig. 3, *br.a.* 2) is much less prominent and more deeply placed in the floor of the sinus. The *third arch* is very short, and lies, disposed obliquely, in the deepest caudal part of the sinus: it is best developed in embryo (*c*) (fig. 3, *br.a.* 3). Ectodermal grooves are present between the arches, the second groove between the hyoid and first branchial arch being by far the largest. Behind the third branchial arch and occupying the extreme caudo-ventral part of the sinus is a distinct fifth groove, corresponding to the rudiment of the fifth gill-pouch and best seen in embryo (*c*) (fig. 3), where it is continued below the ventral margin of the sinus as a short cul-de-sac ending in the mesoderm. The ectoderm of the caudal wall of the sinus adjacent to the ganglion nodosum, it may here be noted, is distinctly thickened, the thickening constituting the placode of the tenth nerve* (fig. 3).

* For an account of the cranial ganglionic placodes ("Kiemenspaltorgane") in mammals, see the papers of FRORIEP (10) and H. RABL (49).

The *second gill-pouch* is well developed. It communicates with the pharynx by a wide opening and is provided with a small dorsal and an elongated ventral diverticulum (fig. 2, *cl.* 2). Its closing membrane (*cl.m.* 2) has a dorso-ventral extent of about 0·25 mm. and involves the entire lateral extent of the pouch, its upper third lying above the dorsal margin of the sinus, its remainder within the sinus. It is composed of ectoderm and entoderm intimately fused, and over the greater portion of its extent its free (ectodermal) surface is directed caudally (fig. 2). Below the termination of the pouch-lumen, the entoderm is prolonged for a distance of about 0·09 mm. as a solid ridge fused with the bottom of the second ectodermal groove.

The *third pouch* (fig. 2, *cl.* 3) is smaller than the second, although it has about the same dorso-ventral extent. It has no distinct dorsal diverticulum but its ventral one is well marked. The closing membrane (fig. 2, *cl.m.* 3) is rather thicker than that of the second pouch. It measures in dorso-ventral extent about 0·26 mm. and is co-extensive with the lateral margin of the pouch.

Behind the third pouch, the pharynx bulges out ventro-laterally to form a distinct bay (fig. 3, *ph.b.*), 0·16 mm. in antero-posterior extent in embryo (*b*), from the anterior region of which the fourth pouch passes off, whilst from the ventral wall of its posterior region, medially to the origin of the fourth pouch, there arises a tubular structure which we regard as probably representing the fifth pouch and ultimo-branchial body and which we may term the posterior pharyngeal complex.

The *fourth pouch* is small, having a dorso-ventral extent of about 0·13 mm., but is quite well developed. It consists of a transverse part (0·04 mm. in vertical extent) in communication with the pharyngeal bay and of a well marked ventral prolongation (about 0·09 mm. in length), tubular in form and thick walled (fig. 3, *cl.* 4). The entire lateral margin of the pouch lies in contact with the bottom of the fourth ectodermal groove, but the ectoderm and entoderm are not fused, so that the closing membrane (if we may speak of such) is very thick.

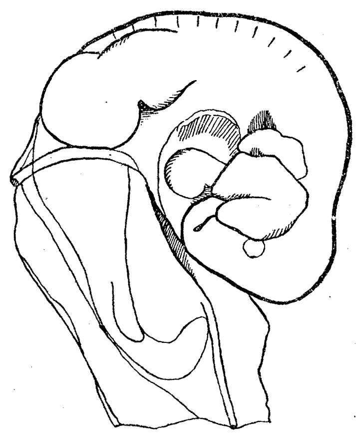
The *posterior pharyngeal complex* has the form of a tubular structure, with a total length in embryo (*c*) of about 0·12 mm., which runs from the pharyngeal bay ventrally and very slightly caudally. Its dorsal portion, comprising about one-third or rather more of its extent, is thicker and of greater transverse diameter than its remaining ventral portion, and measures in greatest transverse diameter 0·128 mm. and in cranio-caudal diameter 0·072 mm. (right side (*c*)). It runs down parallel with and quite close to the bottom of the fifth ectodermal groove. Indeed, shortly below its origin from the pharyngeal bay, its lateral angle (right side (*c*)) is prolonged slightly outwards and is separated by a distance of only about 0·025 mm. from the ectoderm of the groove, the latter being in embryo (*c*) well marked and prolonged down in the form of a short cul-de-sac, below the ventral margin of the sinus as already mentioned. The more ventral portion of the complex appears as a slightly tapering tubular prolongation, rather more definitely cylindrical than the dorsal portion and possessing thicker walls and a smaller lumen. At about its mid-region it measures 0·08 × 0·06 mm.

in diameter. From its relations, we are inclined to regard the dorsal portion of the complex as representing the remains of the fifth gill-pouch, and the remainder of it as being formed by the ultimobranchial body. In this connection it remains to be mentioned that in all three embryos, on one or both sides, there is present a small but perfectly distinct fifth aortic arch which runs up in the third branchial arch to open into the dorsal aortic root along with the sixth arch, the latter lying quite caudally to the complex (fig. 3, *aort.a.* 5).

The primordium of the *median thyroid* appears as a hollow median outgrowth of the entoderm of the pharyngeal floor, situated between the second and third gill-pouches and communicating with the pharynx by a slit-like aperture. It is roughly V-shaped in longitudinal section (embryo (*b*)), the apex of the V being directed backwards and downwards and projecting slightly behind the posterior margin of the opening. Its wall is formed of slightly thickened entoderm, with basally situated nuclei. It measures about 0·14 mm. in the antero-posterior direction and 0·11 mm. dorso-ventrally.

Stage II.—Two embryos: (*a*) β '98, and (*b*) γ '99. Plate 2, figs. 4 (of model) and 5, text-fig. 2.

Although only measuring in G.L. 4·5 and 5 mm. respectively, the two embryos of this stage (text-fig. 2) are distinctly in advance of those of Stage I. The head is more sharply flexed, the hinder region of the trunk is more straightened out, the hind limbs and tail are more advanced and the openings of the olfactory pits are now more slit-like.


TEXT-FIG. 2.

The *hyoid arch* is still large and prominent. Behind it lies the deep *cervical sinus*, less widely open to the exterior than in Stage I. The first branchial arch now lies wholly within the sinus and is overlapped to a greater extent by the hyoid. The second arch is small but distinct and is succeeded by the third, situated in the caudal part of the sinus.

The *second gill-pouch* (fig. 4, *cl.* 2) consists of a horizontal wider part, dorso-ventrally flattened and in open communication with the pharynx, together with a postero-ventral tapering prolongation, the ventral diverticulum (figs. 4 and 5, *v.pr.cl.* 2).

The closing membrane (fig. 5, *cl.m.* 2) has a dorso-ventral extent of 0·2 mm., and involves the horizontal part of the cleft and the ventral diverticulum. As in the preceding stage its dorsal third is situated above the sinus, its remainder in the latter. Beyond the termination of the pouch-lumen, the epithelium, as in the preceding stage, is continued on as a solid prolongation, fused with the bottom of the second ectodermal groove for a distance of about 0·07 mm.

The *third pouch* (fig. 4, *cl.* 3) is very wide dorso-ventrally, but is markedly flattened in the cranio-caudal direction. It has a well marked wide ventral diverticulum, also flattened cranio-caudally. The closing membrane is extensive, involving the entire lateral extent of the pouch. In dorso-ventral extent, it measures 0·23 mm.

The *fourth pouch* (fig. 4, *cl.* 4) shows no essential alteration. It is still small, with a narrow, cranio-caudally flattened lumen, and runs from the pharyngeal bay obliquely outwards and downwards. Its closing membrane is thick and quite similar to that of the first stage.

The *posterior pharyngeal complex* no longer shows any evidence of its composite character, and from now on we shall refer to it simply as the *ultimobranchial body.* It leaves the pharyngeal bay close behind and medially to the fourth pouch (fig. 4, *u.b.*), and runs caudally and ventrally without approaching the floor of the cervical sinus as in the embryos of the first stage. It is now bulbous in form and connected with the pharyngeal bay by a constricted neck. It possesses thick walls and a narrow lumen, and in embryo (*b*) has attained a length of 0·16 mm., so that it is already a relatively large structure.

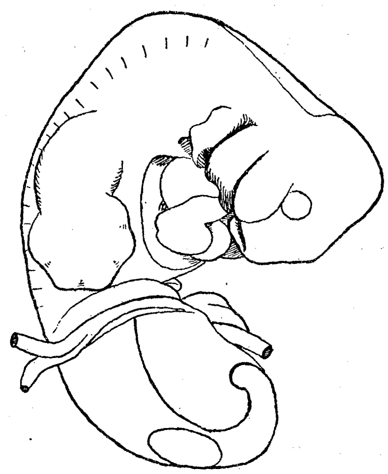
Ectodermal grooves corresponding to the second, third, and fourth pouches are present. The second (fig. 5, *ect.gr.* 2), as before, is by far the best marked, and is now somewhat deeper and narrower, owing to the greater backward growth of the hyoid arch. The fourth groove is quite shallow. Opposite the ultimobranchial body, though far removed from it by mesoderm, is a wide and deep pit-like depression occupying the hinder end of the sinus, and into which the fourth ectodermal groove appears to run. This depression corresponds with the groove in the corresponding position in the preceding stage, but is not so well marked as in embryo (*c*) of that stage. It apparently represents the fifth ectodermal groove *plus* the caudal portion of the sinus.

The *median thyroid* primordium, well seen in fig. 4 (*th.*), lies, as in the preceding stage, in the interspace between the second and third gill-pouches. In embryo (*a*) it is still connected with the pharynx in the region of its slit-like opening (fig. 5, *th.*) situated on a level with the ventral diverticulum of pouch 2, whilst its hinder half projects freely backwards as a bluntly ending tube which terminates about on a level with the anterior face of pouch 3. In embryo (*b*) it has lost its connection with the pharynx and appears as a closed, bluntly spindle-shaped tube lying below the pharyngeal floor and possessing thick walls and a narrow lumen. It has a length of about 0·14 mm. in embryo (*a*) and of about 0·16 mm. in embryo (*b*).

Stage III.—Embryo *a* '97. G.L. = 7 mm. (text-fig. 3).

The head of the embryo is more raised than in the preceding stage, and the neck-protuberance is much more prominent. Digits are distinctly indicated in the manus, and the hind-limb buds and the tail are further advanced.

The *hyoid arch* consists of a thick and prominent upper part and of a thinner lower part, directed ventro-medially and forming the hinder boundary of the primordium of the external auditory meatus which has now appeared.



TEXT-FIG. 3.

The *cervical sinus* is considerably reduced, but is still a well marked depression, measuring in horizontal section, at the level of the fourth cleft, about 0·3 mm. in depth by 0·28 mm. in antero-posterior extent. Its caudo-dorsal wall is thickened, as in the preceding stages, and is in proliferative continuity with the ganglion of the tenth nerve.

The *branchial arches* are now inconspicuous; the first is very low and the second is smaller than the third and hardly projects.

The *second pouch* runs from its pharyngeal opening (now somewhat narrowed), at first outwards, and then it turns downwards as the ventral diverticulum. The lumen of the latter in its upper part is wide and triangular in sectional outline, but it gradually narrows as the pouch is traced ventrally, whilst its walls thicken. The closing membrane is now considerably reduced in dorso-ventral extent as compared with the last stage, measuring only 0·11 mm. This reduction is evidently due to the commencing closure of the second ectodermal groove in the direction from above downwards as the result of the growth of the hyoid arch. Further, as the result of the closing-in of the cervical sinus itself, we now find that the closing membrane terminates just above the dorsal margin of the sinus. Here again, however, the entoderm of the pouch is continued on for a short distance beyond the termination of the closing membrane as a solid prolongation fused with the bottom of the ectodermal groove.

The *third pouch* is still more flattened than in the last stage and possesses a very narrow slit-like lumen. In this embryo it appears to be connected with the ectoderm of the sinus only towards its ventral end. Owing to the reduction of the sinus, its closing membrane now lies closer to that of pouch 2. Ectodermal groove 3 is not recognisable.

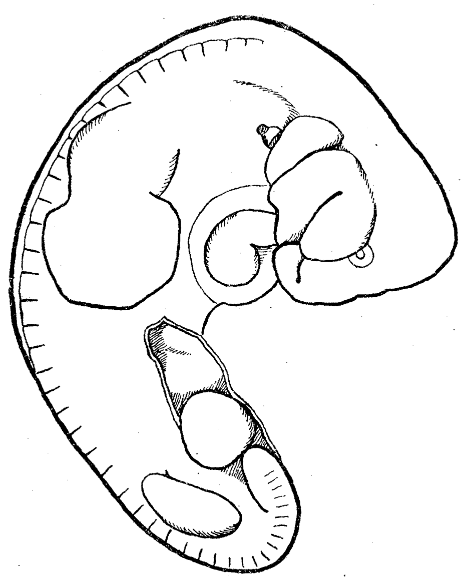
The *fourth pouch* essentially resembles that of the last stage. It is again very narrow and flattened. From its opening into the pharyngeal bay it runs almost directly outwards, and below the level of that opening is continued for a short distance ventrally. Its lateral margin joins the ectoderm of the fourth ectodermal groove, the closing membrane being very thick and the ectoderm and entoderm unfused.

The *ultimobranchial body* does not differ from that of the preceding stage except that it now arises immediately behind and dorsally to pouch 4 as the result of the narrowing of the pharyngeal bay. It has a total length of 0·15 mm., and is here, again, club-shaped in form.

The *thyroid* measures 0·2 mm. in length, and essentially resembles that of embryo (*b*) of the last stage.

Stage IV.—Embryo XIX '04. G.L. = 7·5 mm. (Plate 2, fig. 7, Plate 4, fig. 9, and text-fig. 4).

This embryo (text-fig. 4) closely resembles that of the preceding stage in its external characters, and indeed in respect of the condition of the hyoid arch and of the primordium of the external auditory meatus is rather less advanced, but taking the branchial region as a whole it appears slightly the older.



TEXT-FIG. 4.

The *hyoid arch* (fig. 7, *hy.a.*) is large and prominent, and consists, as in the preceding embryo, of a thicker dorsal part and a thinner ventral part, but the latter appears less reduced than in embryo *a* '97, and the primordium of the external auditory meatus is just indicated.

The *cervical sinus* (fig. 9, *s.c.*) is in much the same condition as in the latter embryo, but its caudal margin is more distinct owing to the persistence of the well marked depression observable in stages I and II at its hinder end.

The *branchial arches* are reduced: the first is small, and situated under cover of the backwardly projecting hyoid arch; the second is no longer distinct, whilst the third is represented by a ridge in front of the caudal depression of the sinus (fig. 9, *br.a.* 3).

The *second gill-pouch* is in much the same condition as in the preceding embryo. It has a wide connection with the pharynx, and ventral to that connection runs outwards and downwards as a relatively thick-walled tube—the ventral diverticulum —roughly triangular in cross-section in its upper part and flattened obliquely in the cranio-caudal direction in its lower part (fig. 7, *v.pr.cl.* 2). As it passes down it gradually becomes reduced in size; its lumen disappears about 0·1 mm. below the level of the pharyngeal connection, but, as in the preceding stages, the epithelium of the pouch continues on for some distance fused with the bottom of the ectodermal groove, this solid continuation being more marked than in the last stage. The closing membrane has a dorso-ventral extent of only 0·08 mm., the more dorsal part of the pouch having now lost connection with the ectoderm. It lies, as in the last embryo, entirely dorsal to the sinus. In the region of the closing membrane, the second ectodermal groove (figs. 7 and 9, *ect.gr.* 2) is narrow and fissure-like, and, as in the previous stages, the closing membrane involves the cranial wall of the groove.

The *third pouch* has now a greatly reduced pharyngeal opening, confined to two sections (= 0·02 mm.). It runs outwards and downwards as a thick-walled tube, flattened (though not so much as in the last stage) in the cranio-caudal direction, and with a well marked lumen. The closing membrane has a dorso-ventral extent of about 0·08 mm., and involves the greater part of the lateral aspect of the pouch. It now appears drawn inwards at right angles to the surface, having in horizontal section the form of a thickish cellular ingrowth connecting the lateral margin of the pouch with the ectoderm of the upper part of the sinus. Opposite it, is a slight ectodermal groove.

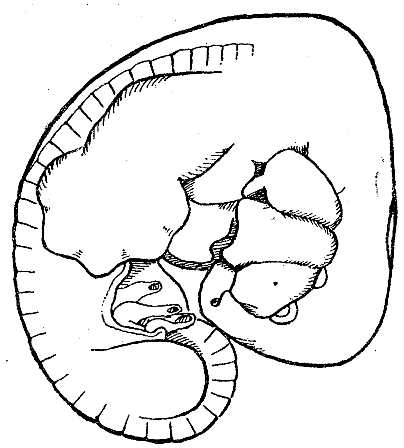
The *fourth pouch* (fig. 9, *cl.* 4) shows a well marked advance on that of the last stage. It is still in communication with the narrowed pharyngeal bay by a narrow opening situated just caudally to the level of the glottis, but is now distinguishable into proximal and distal portions. Its proximal part does not differ essentially from the corresponding part in the preceding embryo. It is enlarged and luminated, and runs ventrally and cranially, continuing the curvature of the pharynx. Its ventral wall is thickened and continues for a distance of 0·03 mm. as a solid tapering projection. The distal part of the pouch is disposed transversely like the corresponding part in the last stage. It is, however, no longer luminated, but has become transformed into a solid laterally directed process which is connected with the ectoderm of the caudal depression of the sinus by an irregular loose strand of cells containing numerous chromophile granules. In the following stage, this cellular strand is represented by a definite short ingrowth from the sinus-ectoderm. We therefore regard it and the solid lateral portion of the pouch as together forming a *ductus ecto-entobranchialis* IV (HAMMAR, 22), which is here precociously developed, being much more attenuated and reduced than it is in the next stage.

The *ultimobranchial body* (fig. 9, *u.b.*) has the same relations as in the last stage. It begins as a slender tube with a very small lumen, and runs caudally and ventrally, gradually increasing in thickness. It is, as before, club-shaped in form, and has a total length of 0·18 mm., which may be regarded as its maximum. It is thus evident that the ultimobranchial body attains its maximum length at a relatively early period in development.

The *median thyroid* resembles that of the last stage, but is slightly longer (measuring 0·23 mm.).

Stage V.—Embryo II '01. G.L. 6 mm. (text-fig. 5 and Plate 2, fig. 10, Plate 4, fig. 11, Plate 3, figs. 12 and 13, the two latter figures representing views of a wax-plate reconstruction of part of the pharyngeal region).

Body of embryo (text-fig. 5) greatly curved, the snout region touching the tail. Neck protuberance very prominent. Digits of manus better marked than in the last stage. Hind limb in the form of a flattened lobe with medial and lateral surfaces. The *hyoid arch* (figs. 10 and 11, *hy.a.*) is still distinct but is less prominent, especially at its upper end. The external auditory meatus is better marked than in embryo α '97.



TEXT-FIG. 5.

The branchial structures in this embryo show a well marked advance on those of the two preceding stages.

The *cervical sinus* is now greatly reduced. It may be described as consisting of three parts: (*a*) an inner or deeper portion in the form of a laterally compressed narrow cavity, which we may speak of as the *sinus proper* (Plate 4, fig. 11, *s.c.*), (*b*) an oblique slit-like passage through which the latter communicates with the exterior, usually termed the *cervical duct* (*ductus cervicalis*) (fig. 11, *d.c.*, and text-fig. 5), and (*c*) a large globular sac with a well marked lumen, the *cervical vesicle* (*vesicula cervicalis*) (figs. 11 and 13, *v.c.*), connected with the caudal end of the sinus proper by a slightly narrowed portion, the *vesicle-duct* (*ductus vesiculæ cervicalis*) (fig. 11, *v.d.*).

The cervical vesicle measures 0·12 mm. in dorso-ventral and 0·16 mm. in transverse diameter. Its wall consists of a thick, deeply staining epithelium which lies in close proximity to the ganglion nodosum and is evidently constituted, at least in major part, by the well-marked placode which, in the preceding stage, occupies the dorso-caudal region of the sinus wall. It does not appear, however, to be any longer in actual proliferative connection with the ganglion. The medial wall of the vesicle-duct is formed by that part of the sinus floor which was previously occupied by the second and third branchial arches. It is thus clear that the cervical vesicle and its duct owe their origin to the growth of the caudo-dorsal margin of the sinus forwards so as to overlap the floor of the same. This forward growth indeed is the chief cause of the closing-in and reduction of the sinus which is such a marked feature of the present stage, but the backward growth of the hyoid arch on the cranial and dorso-cranial margins of the sinus is also contributory, though in lesser degree.

Turning now to certain further details in connection with the sinus, we find, as in the preceding stage, the second ectodermal groove occupying the cranial angle of the sinus proper (fig. 11, *ect.gr.* 2), the groove running upwards as well as downwards and forwards. On tracing the groove in the upward direction we see at once that there is a striking difference in its relations as compared with the preceding stage, inasmuch as it no longer runs dorsally above the margin of the sinus as an open groove but is continued above the dorsal margin of the cervical duct into what appears as a somewhat flattened and at first hollow prolongation of the sinus wall which extends obliquely upwards in the mesoderm and which gradually becomes reduced in width until it disappears. This prolongation is free from the ectoderm except below, but it is not free from the entoderm, since, throughout its extent, its cranio-medial edge is fused with the ventral continuation of the second gill-pouch, the line of union being of the nature of an oblique overlap. This overlapping line of junction of the ectodermal sinus-prolongation and the entodermal continuation of the second gill-pouch must include the region of the closing membrane of the preceding stage, where, it will be remembered, the closing membrane is situated entirely above the dorsal margin of the sinus, and no doubt the cellular tissue which intervenes between the upper end of the lumen of the ectodermal prolongation and the lower end of the pouch-lumen is actually a part of the closing membrane, but the fusion is so intimate that it is impossible to determine the exact limits of ectoderm and entoderm. We estimate, however, that the ectodermal prolongation extends upwards from the sinus for a distance of approximately 0·13 mm. on the left side and 0·2 mm. on the right side. In about the ventral half of its extent it contains a narrow lumen which widens out below to open into the sinus cavity and which forms the direct upward continuation of the sinus part of the second ectodermal groove (fig. 10, *d.b.*).

Consideration of the relations of this ectodermal prolongation shows that it consists of two parts not sharply separable : (1) a larger dorsal part formed by the closing-off and separation from the ectoderm of that part of the second ectodermal groove which in the preceding stage lies immediately dorsal to the sinus, and which is involved in the formation of the closing membrane of the second pouch, and (2) a smaller ventral part formed by the closing-off of the cranio-dorsal corner of the sinus occupied by the downward continuation of the ectodermal groove. If we suppose that, in the region of the persisting part of the closing membrane in the preceding stage, fusion of the lips of the ectodermal groove took place from above downwards, so as to leave the inner part of the groove as a tube fused with the ventral continuation of the second pouch, and if we further imagine the dorso-cranial part of the sinus, occupied by the ventral prolongation of the groove, also to become closed off at the same time, then we should arrive at the condition above described.

The second pouch is thus connected with the sinus-ectoderm through the intermediation of a short distal segment composed of the above described ectodermal prolongation, derivative of the second ectodermal groove and the sinus, fused with the ventral continuation of the entoderm of the second gill-pouch (fig. 12, *d.e.b.* II). This composite segment corresponds to the narrowed duct-like cord, which in the pig and certain other mammals connects the second pouch with the sinus-ectoderm. In the pig embryo, ZOTTERMAN (69) has shown that the cord in question is also a composite structure. Its dorso-medial part consists of a prolongation of the second gill-pouch, enclosing a narrow lumen, whilst its ventro-lateral part is formed from the closed-off second ectodermal groove, and contains a prolongation of the sinus-lumen, the closing membrane being situated at the junction of the two. There is thus close agreement with the condition above described for Trichosurus, except that the overlapping junction between the ectodermal and entodermal parts appears to be much more marked in our form than in the pig. ZOTTERMAN terms this connecting cord the "Kiemengang," or *ductus branchialis*. The term "Kiemengang," it should be noted, was originally applied by C. RABL (45) to the narrow ventral prolongation of the second pouch in the pig, FOX (8) subsequently distinguishing the same as the "filiform process." In the human embryo, HAMMAR (18), however, employed the same term to designate a quite different structure, viz., the ectodermal cord which connects the second pouch with the ectoderm, and which is formed from the second ectodermal groove. It has also been termed the *ductus branchialis* or *ductus branchialis* II (GROSSER, 17). It now seems established that in some mammals the second pouch is connected with the sinus-ectoderm by a purely ectodermal cord derived from the second ectodermal groove, as in the human embryo* (HAMMAR, 18) and the rabbit (HANSON, 23), whilst in others, *e.g.*, the pig (ZOTTERMAN, 69), the guinea-pig (RUBEN, 50; H. RABL, 49), and the mole (H. RABL, 46), it is formed partly of a narrowed ventral prolongation of the pouch-entoderm, partly of groove-ectoderm, the proportions of the two constituents varying in the different forms. Thus HAMMAR (22) has been led to suggest that the connecting cord should be termed the *ductus ecto-branchialis* II, where it consists exclusively of groove-ectoderm, and *ductus ecto-ento-branchialis* II, where it is of composite origin. The duct in Trichosurus being of the latter category, we shall speak of it under that name, and where it is necessary to refer to its constituent parts separately, we shall distinguish them as the ento- and ecto-branchial ducts respectively.

Returning to the sinus, it remains to be mentioned that the ventral continuation of the second ectodermal groove, referred to above, runs downwards and forwards, to fade away below in the cervical groove between head and trunk. Its floor is produced into the mesoderm in the form of a solid ridge (fig. 12, *ect.r.*), destined eventually to disappear.

As might be expected, branchial arches are now no longer recognisable.

The *second pouch* (figs. 12 and 13, *cl.* 2) still communicates with the pharynx by a narrow opening. The pouch as a whole is distinctly more elongated in the dorso-ventral direction than in the preceding stage and is also of smaller diameter. Proximally it is tubular, with a distinct lumen, but distally it narrows to form a tapering prolongation, the entobranchial duct, at first luminated but eventually becoming solid, which is fused with the cranio-medial side of the ectobranchial duct to form the *ductus ecto-entobranchialis* II above described. From the point of separation of the pouch from the pharynx, the lumen extends down, rapidly decreasing in diameter, for a distance of about 0·17 mm. on the left side and 0·21 mm. on the right. Towards its ventral end, the lumen is reduced to an exceedingly minute passage, which finally

* In the human embryo, however, HAMMAR states that the ductus branchialis joins the ectoderm of the cervical groove.

terminates about 0·05 mm. below what we estimate to be the upper extremity of the ectobranchial duct, which at this level is solid. Below the termination of the lumen, the entobranchial duct continues on apparently right down to the level of the sinus, as a solid prolongation fused with the ectobranchial duct, the ventral portion of which contains, as we have seen, a narrow lumen prolonged up from the sinus (fig. 10, *cl.* 2 and *d.b.*). The more ventral portion of this solid continuation of the pouch-entoderm is, without doubt, identical with the solid prolongation of the same described as fused with the bottom of the second ectodermal groove in the preceding stages.

The *third pouch* (figs. 10, 12 and 13, *cl.* 3) has still a narrow communication with the pharynx. The proximal part of the pouch is narrow and duct-like and runs outwards and downwards, medially and slightly dorsally to the second pouch, to open into the distal part, which is thick-walled and more expanded (figs. 12 and 13, *cl.* 3). This distal part runs ventrally and is connected by a solid cell-plate (the ductus ecto-entobranchialis III, representing the drawn-out closing membrane), with the ectoderm of the ductus ecto-entobranchialis II and the upper portion of the sinus (fig. 10, *cl.* 3 and *d.e.b.* III). The third pouch is thicker walled and of greater diameter than the second. It is luminated almost up to its ventral extremity, and has a total length of about 0·11 mm.

The *fourth pouch* (figs. 11, 12, 13, *cl.* 4) is still small, having a dorso-ventral extent of only 0·06 mm. The same proximal and distal portions are recognisable as in the last stage. The proximal part is expanded and flattened. It communicates with the pharyngeal bay by a narrow aperture and possesses a small lumen. Its ventral and cranial walls are thickened and produced into a short ventro-medial process (fig. 11, *cl.* 4, *vm.pr.*) already indicated in the preceding stage. The distal or lateral part is stalk-like but is less reduced than in the preceding stage, since it still retains a remnant of the pouch-lumen. It runs transversely outwards towards the sinus and is connected therewith by a very short but quite definite ingrowth from the ectoderm forming the medial wall of the vesicle-duct (fig. 11, *cl.* 4, and *d.e.b.* IV). The conjoint connecting strand so constituted thus forms a ductus ecto-entobranchialis IV like that of the last stage, only much less attenuated.

The *ultimobranchial body* leaves the pharyngeal bay shortly behind pouch 4 as in the preceding stage. Proximally it is thin and for a short distance solid, but distally it becomes luminated and thick-walled. In length, it measures about 0·15 mm.

The *median thyroid* primordium calls for no extended description. It has a length of only 0·14 mm. and lies above the ventral aorta on a level with the hyoid arch (fig. 10, *th.*). It possesses a minute lumen in front and is solid and rather more flattened behind.

Stage VI.—Embryo XX '04. G.L. 7·75 mm. (Plate 4, fig. 15).

In this embryo the trunk is again straightened out and the head is flexed at an acute angle. The digits of the manus are more delimited than in the preceding stage, and the hind-limb exhibits commencing differentiation into leg and foot. The *hyoid arch* (fig. 15, *hy.a.*) is less prominent, and the external auditory meatus is larger, and is extending upwards in the site of the ectodermal groove.

The branchial structures show a distinct advance on those of the last embryo.

The *cervical sinus* is connected with the exterior by a cervical duct (fig. 15, *d.c.*) of much the same size and extent as before, but the lumen of the sinus proper is still further reduced, more especially in the dorso-ventral direction, as the result of the fusion of the walls of the dorso-cranial region of the sinus with which the *ductus ecto-entobranchialis* II is connected. In this way there has been formed a solid thickening of the dorso-cranial angle of the sinus, just ventrally to and in direct continuity with the *ductus ecto-entobranchialis* II, whose lumen has also entirely disappeared. This thickening, which also involves the cranial and medial walls of the open portion of the sinus, is the first indication of the primordium of the *superficial cervical thymus* (fig. 15, *s.tm.*). It is now quite impossible to determine the relation of the entoderm of the second pouch (entobranchial duct) either to this thickening or to the ectobranchial duct, and from the examination of this embryo alone it might seem justifiable to conclude that the thickening under consideration consists exclusively of sinus-ectoderm, and that the superficial cervical thymus is accordingly a *thymus ectodermalis.* It may be so, but in view of the existence, in preceding stages, of a solid prolongation of the pouch-entoderm extending down in continuity with the ectodermal groove (or ectobranchial duct) as far as the sinus, the possibility of the inclusion of some entoderm in the primordium cannot entirely be excluded. All we can say is that the primordium of the superficial cervical thymus consists mainly of sinus-ectoderm, and probably also contains a small amount of pouch-entoderm. The still open part of the sinus, apart from size, differs from that of the preceding stage chiefly in the greater thickness of its cranial angle (resulting from partial closure of the ectodermal groove) and of its medial wall, both parts passing dorsally into continuity with the thymus primordium above described. The cervical vesicle is well marked, and has extended further in the dorso-medial direction (fig. 15, *v.c.*).

The *second pouch* shows a very marked advance on that of the preceding stage. It still communicates with the pharynx, but its lumen is present only for a very short distance (0·06 mm.) in its proximal thicker part. Beyond the termination of the lumen the pouch continues outwards and downwards as a solid cellular cord, which becomes of very small diameter (0·05 mm.), and which is greatly elongated in the dorso-ventral direction. After a course of about 0·2 mm. the cord begins to thicken again (this enlargement perhaps marking the upper extremity of the ectobranchial duct), and finally merges into the above described solid thickening of the dorso-cranial region of the sinus. The thicker ventral part of the cord no doubt consists of the fused ento- and ecto-branchial ducts, but from the sections it is quite impossible to determine the limits of the entoderm and ectoderm, the cord appearing as a perfectly uniform, solid structure (the ductus ecto-entobranchialis II).

The *third pouch* no longer opens into the pharynx, though it is still in definite cellular continuity with it. Proximally it has the form of a thick-walled tube (about 0·16 by 0·11 mm. in diameter) with a distinct but short lumen. Distally it is solid and tapering, and towards its ventral extremity it is connected with the thickened ectoderm of the cranio-medial wall of the sinus. On the left side there are two connections, viz., a more dorsal one in the form of a very thin cellular strand joining the dorsal part of the sinus thickening, and, 0·07 mm. further on, a much more extensive and thicker ventral connection, below the level of which the pouch continues for a distance of 0·03 mm. On the right side the dorsal connection is but indicated, the ventral connection is similar to that of the left side (fig. 15, *d.e.b.* III). There is no ventral prolongation. The pouch has a total length of about 0·16 mm.

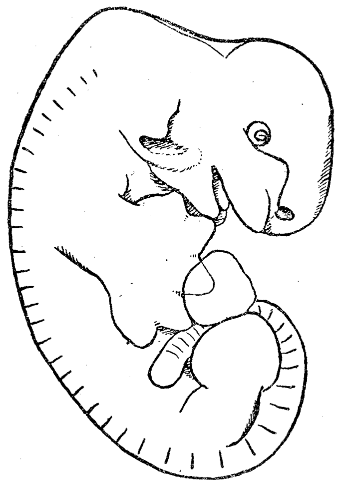
The *fourth pouch* and *ultimobranchial body* now communicate with the pharynx through a short duct formed from the pharyngeal bay and opening shortly behind the level of the glottis. This duct we may distinguish as the pharyngeal duct; it corresponds to the *ductus pharyngo-branchialis communis* IV and V of HAMMAR. The pouch at its origin from the pharyngeal duct is roughly circular in section. Almost immediately there passes off from it the now very thin and greatly elongated ductus ecto-entobranchialis IV, which joins the sinus-ectoderm just ventrally to and in front of the vesicle-duct. Below the origin of the ductus the pouch broadens transversely and continues caudo-ventrally as a well marked prolongation with very thick walls and a narrow lumen. The pouch has now a dorso-ventral length of 0·11 mm., *i.e.*, it is nearly twice as long as that of the preceding embryo. It is thus evident that marked growth in the caudo-ventral direction has taken place in the proximal part of the pouch in the interval between this stage and the preceding, this growth involving especially the ventral wall (including the ventro-medial process) of the proximal portion of the pouch. At the same time the *ductus ecto-entobranchialis* IV has become greatly elongated as the result apparently of the general growth in width of this region of the embryo.

The *ultimobranchial body* arises from the pharyngeal duct dorso-medially to pouch 4, and runs back dorsally and medially to the latter, and medially to the systemic arch. It begins as a relatively thin tube, but thickens considerably in its hinder region, the latter being thicker than in the preceding embryo. The body has a total length of about 0·16 mm., and is altogether a more massive structure than pouch 4.

The *median thyroid* has a length of 0·13 mm. Its walls have increased considerably in thickness, but a minute central lumen is still present. Its more dorsal part is thick and sub-cylindrical, its more ventral part is thinner, more flattened, and of greater transverse width.

Stage VII.—Embryo III '01. G.L. 7·25 mm. (text-fig. 6 and Plate 3, figs. 16 and 17 (of model), and Plate 4, fig. 18.)

This embryo, although smaller than the preceding, is distinctly older (text-fig. 6). The head is more raised and the snout is now marked off by a transverse groove. The digits of the manus project to a greater extent, and the hind limb is distinctly differentiated into leg and foot.



TEXT-FIG. 6.

The *hyoid arch* is now incorporated in the side of the head and the external auditory meatus is larger and deeper. The primordium of the pinna is well marked.

Cervical Sinus.—The fusion of the thickened walls of the sinus proper, already initiated in the preceding stage, has here made further progress, with the result that the entire cranial portion of the sinus has become converted into a bulbously swollen mass, solid except for the presence in its ventral part of a quite small remnant of the original lumen. This mass (figs. 16 and 17, *s.tm.*) we may now definitely characterise as *the primordium of the superficial cervical thymus.* The swollen region now extends down below the connection of the third pouch with the sinus-ectoderm, whilst dorsally, as in the preceding stage, it gradually tapers upwards and passes into direct continuity with the cord-like structure representing the ductus ecto-entobranchialis II and the drawn-out second pouch (figs. 16 and 17, *d.e.b.* II and *cl.* 2).

The cervical duct leading out from the remnant of the sinus-lumen above mentioned is greatly reduced and cleft-like and opens just below the ventral margin of the meatus into the cervical groove. The cervical vesicle (fig. 17, *v.c.*) lies as before in contact with the ventro-cranial surface of the ganglion nodosum, the third pouch now occupying a position almost directly cranial to it. It is somewhat smaller than in the preceding stage and more definitely spherical in shape. It possesses thick walls and a reduced lumen and is connected with the thymus primordium by a very thin vesicle-duct.

The *second pouch* (figs. 16 and 17, *cl.* 2) has undergone still further thinning and elongation and becomes converted into a slender, solid cord soon after it leaves the pharynx. After a course ventro-caudally of about 0·3 mm. it gradually enlarges and passes into continuity with the thymus primordium. It is now quite impossible to distinguish the limits of the ductus ecto-entobranchialis; probably it has become largely incorporated in the sinus thickening.

The *third pouch* (figs. 16 and 17, *cl.* 3) is now completely cut off from the pharynx, though an indication of the former connection is still apparent in the form of a solid tapering prolongation extending from the upper part of the pouch towards the same. The pouch as a whole has undergone elongation in the dorso-ventral direction and is roughly of an elongated pear-shape. Its thicker dorsal half is luminated, somewhat flattened in its upper quarter and then becoming more cylindrical below; its ventral half is solid and tapering and is connected with the sinus-thickening by a solid cellular cord arising from its lower end and forming the ductus ecto-entobranchialis III (figs. 16 and 17, *d.e.b.* III). On the left side, the pouch has a total length of about 0·2 mm.

The walls of the pouch now exhibit, for the first time, a highly important histological differentiation, marking out the primordia of the two derivatives of the pouch, viz., *epithelial body* III and *thymus* III. In following the serial sections of the pouch from above downwards, one finds, as the dorsal part of the pouch assumes its cylindrical form, that the caudal half of its wall thickens, whilst its constituent cells take on a looser, more irregular arrangement and stain only slightly, if at all, with eosin. On the other hand, the cells of the cranial half of the wall retain their original character as a columnar epithelium and stain deeply with eosin (fig. 18, *tm.* III, and *ep.b.* III). As the cleft is traced ventrally, the lumen becomes greatly reduced and finally disappears, and at the same time, the thickening, at first confined to the caudal wall, becomes more marked and extends so as to involve the lateral walls and eventually the entire solid ventral portion of the pouch. This differentiation, which is still better marked in the next stage, is the first indication of the primordia of *thymus* III and *epithelial body* III. As subsequent stages show, thymus III is formed from the caudal and ventral walls of pouch 3, whilst the related epithelial body is derived from the cranial wall of the more dorsal part of the pouch.

The *fourth pouch* and the *ultimobranchial body* have essentially the same relations to the pharynx and to each other as in the preceding stage, only the pharyngeal duct has now the form of an elongated thin tube, of considerably greater length than that of the last embryo. From the end of this pharyngeal duct, the fourth pouch runs caudally and slightly laterally as a thick-walled cylindrical tube with a narrow lumen, best marked in its thicker dorsal part and more reduced or absent in its tapering ventral part. On the left side, there is still present a slender ductus ecto-entobranchialis IV which runs upwards and outwards from the commencement of the pouch to join the sinus-ectoderm caudally to and at the same level as the connection of pouch 3 with the same. The duct is considerably longer than that of the last embryo. On the right side, it appears to have completely disappeared.

The *ultimobranchial body* has essentially the same form and relations as in the preceding embryo, and appears as the practically direct backward continuation of the pharyngeal duct. It has, however, undergone further thickening in its caudal region, where it exhibits dorso-ventral flattening with reduction of its lumen. Further, the caudal ends of the two bodies have now become more approximated towards the middle line, with the result that they have acquired an obliquely transverse position.

The *median thyroid* now exhibits increased growth activity. It has increased only slightly in length (0·15 mm.) but very markedly in thickness and in breadth (maximum = 0·35 mm.). Its surface contour is now somewhat irregular, and instead of a small central lumen it contains a number of disconnected flattened cavities.

Stage VIII.—Two embryos, *a* (XIIA '02) and *b* (XII '02). G.L. = 7·25 mm. Plate 3, figs. 19 and 20 (of model), Plate 4, figs. 21 and 25, Plate 5, figs. 26, 27, 29, 30, 31 and 32, Plate 6, figs. 33, 34, and 35.

The two embryos of this stage are identical as regards their external characters, but examination of the sectional series shows that embryo (*a*) (cut longitudinally) is slightly less advanced than (*b*) (cut transversely) in respect of the pharyngeal derivatives.

As compared with the preceding embryo, the differences in the external characters are only slight, and consist mainly in the greater freeing of the digits of the manus and in the sharper separation of the two divisions of the hind limb, but the pharyngeal derivatives have in the interval made more progress than these slight external differences would have led one to expect.

The *cervical sinus*, apart from the cervical vesicle, has now practically closed. A small remnant of its lumen is, however, still present in the form of a very small cavity situated caudo-ventrally to the superficial cervical thymus (figs. 21 and 34, *s.c.*), with which cavity in embryo (*a*) the duct of the cervical vesicle still communicates, and which opens into the groove between the head and trunk through the last remnant of the cervical duct (fig. 21, *s.c.* and *d.c.*). The cervical vesicle (figs. 19, 20, and 31, *v.c.*) has moved still further upwards, and its dorsal end is now on a level with the upper portion of pouch 3. It lies, as before, cranial to the ventral portion of the ganglion nodosum. In embryo (*a*), its lumen is well marked, but in (*b*) is reduced.

The primordium of the *superficial cervical thymus* (figs. 19, 20, 21 and 34, *s.tm.*) appears as a solid bulbous mass, the dorsal part of which projects upwards into the mesoderm whilst its lower part is joined by a narrowed connection with the ectoderm of the cervical groove. It is slightly larger than in the preceding stage and now possesses a rather more definite bulbous form as the result partly of its own growth, partly of the more complete closing of the sinus, and partly of the thinning out of the structures connected with it. Ventrally it tapers down into an ectodermal ridge projecting in from the bottom of the ectodermal groove, so that it is impossible to determine its exact ventral limit, but it may be said to have in embryo (*b*) a dorso-ventral extent of roughly 0·15 mm. Its maximum transverse thickness is about 0·2 mm., and its cranio-caudal thickness 0·11 mm.

The *second pouch* (figs. 19, 20, 21, *cl.* 2) has the same cord-like form as in the preceding embryo. It is still connected with the pharynx and in embryo (*a*) it is luminated in the dorsal half of its extent, in (*b*) it is much more attenuated and solid. At its ventral end it joins the superficial cervical thymus. It has approximately the same length as in the preceding embryo.

The *third pouch* (figs. 19 and 20, *cl.* 3, and 25, 26, 30, 31 and 33, *tm.* III and *ep.b.* III) still shows a remnant of its pharyngeal connection (fig. 30, *ph.c.*), rather better marked than in the preceding embryo, and is also joined to the primordium of the cervical thymus by a solid cellular cord (*the ductus ecto-entobranchialis* III) arising now, not from its ventral end as in the last embryo, but from about the mid-region of its length (figs. 19 and 20, *d.e.b.* III). On the right side in embryo (*b*), this connection has already disappeared. The pouch itself (figs. 19 and 20, *cl.* 3) has much the same general form as in the preceding stage. At its dorsal end it is cranio-caudally flattened but over the rest of its extent it is cylindrical. Below the connection with the cervical thymus, it tapers to a blunt point and is slightly curved in the caudo-ventral direction. The pouch differs especially from that of the last embryo in the fact that the ventral solid portion in that stage has now grown down for a distance of 0·08 mm. (left side) below the connection with the cervical thymus as the well-marked tapering process above referred to. The pouch has a total dorso-ventral extent of 0·26 mm. and is thus longer than that of the last embryo. As in the latter, it possesses a lumen in its dorsal half, the lumen being larger in embryo (*a*) than in (*b*), but is solid throughout its ventral half. At its dorsal end, the pouch extends for a short distance (0·05 mm. on left side) above the level of the remnant of the pharyngeal connection.

The walls of the pouch show the same differentiation into the primordia of thymus III and epithelial body III as in the last embryo, but the transformation is now more marked and is especially well seen in the longitudinal sections of embryo (*a*) (figs, 25, 26 and 31, *tm.* III and *ep.b.* III). In the sections, the cranial and caudal walls of the luminated dorsal part of the pouch are sharply distinguishable by their histological characters and staining reactions. The cranial wall (including the dorsal margin of the pouch) is composed of columnar cells with ovalish nuclei of fairly regular size and staining properties, and arranged in roughly alternating fashion in the mid-region of the cells. The cytoplasm appears homogeneous and is markedly eosinophilous (fig. 26, *ep.b.* III). This part of the wall, as already indicated, constitutes the primordium of epithelial body III. The caudal wall, together with the solid ventral prolongation of the pouch, presents a much less uniform and rather less compact appearance. The cells are less regularly arranged, and the nuclei vary in size and in staining properties and are frequently seen in mitosis, whilst the cytoplasm is only slightly eosinophilous (fig. 26, *tm.* III.). This part of the pouch forms the primordium of thymus III. At the extreme dorsal end of the pouch, where the lumen is absent, and especially in embryo (*b*), there are indications of the commencing separation of the thymus and epithelial body (fig. 30, *tm.* III and *ep.b.* III).

It may be noted that both in the cervical thymus and more abundantly in thymus

III, there are present numbers of small cells with rounded or ovalish cell-bodies and deeply staining nuclei. We incline to regard these elements, which are also present in the surrounding tissue, as lymphocytes (see fig. 26, *l.c.*).

The *fourth pouch* and the ultimobranchial body arise, as before, from the hinder end of the pharyngeal duct, which has undergone still further elongation, having now a length of 0·22 mm. in embryo (*b*) (figs. 31 and 33, *ph.d.*) In embryo (*a*), this duct is much shorter and runs more directly downwards.

The relations of the fourth pouch are best seen in the longitudinal series of embryo (*a*). It leaves the pharyngeal duct as a relatively narrow tube running almost transversely outwards to open into the main part of the pouch. The latter is now disposed obliquely, shortly above the pericardial cavity, its ventral end being directed downwards and forwards, and its thinner dorsal end, with which the proximal part is connected, looking upwards and backwards (fig. 27, *tm.* IV and *ep.b.* IV). The pouch has in embryo (*a*) (right side) a dorso-ventral length of 0·16 mm. It is cranio-caudally flattened, measuring 0·13 mm. in breadth and 0·06 mm. in greatest thickness, and, it is important to note, its ventral part is now thicker than the dorsal. In embryo (*a*) the lumen is distinct, but in (*b*) it is reduced and practically confined to the proximal part of the pouch. The *ductus ecto-entobranchialis* IV has completely disappeared. The walls of the pouch now exhibit a histological differentiation precisely similar to that seen in pouch 3 (fig. 35, *t.m.* IV and *e.p.b.* IV). Here, however, the primordium of epithelial body IV is furnished by the thinner dorsal part of the pouch, including both the cranial and caudal walls, whilst the primordium of thymus IV is constituted by the larger ventral portion of the pouch, whose wall (especially its ventral part) is markedly thickened (figs. 27 and 35, *tm.* IV and *ep.b.* IV).

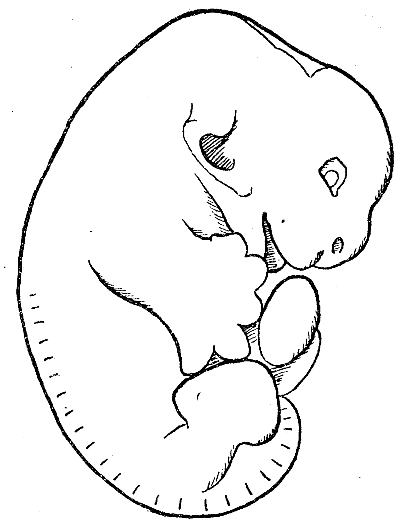
The *ultimobranchial body* (figs. 29 and 32, *u.b.*) does not essentially differ from that of the preceding stage. It has increased, however, in breadth in its hinder portion, measuring 0·19 mm. by 0·08 mm. in thickness.

The *median thyroid* (fig. 33, *th.*) is not quite so advanced as that of the last stage. In embryo (*b*) it is cylindrical in its upper part and possesses a small central lumen, but in its hinder region it has the form of a thin flat plate (0·32 mm. in greatest breadth), and shows several minute lumina, or indications of such. It has a total length of 0·17 mm. In (*a*) it is smaller (0·12 mm.), and possesses a distinct central lumen in its thicker upper part.

Stage IX.—Two embryos, *a* (5 '97), cut longitudinally, and *b* (IV '01), cut transversely. G.L. = 8·5 mm. Text-fig. 7 and Plate 6, figs. 36–39.

The interval between this stage and the last represents the greatest gap in our series of stages.

The embryos of this stage (text-fig. 7) are distinctly in advance of those of the last in their external characters. The trunk is more straightened out, and the head is more raised, though the neck protuberance is still prominent. The eye is ovalish in outline, the retina is pigmented, and the naso-lachrymal groove has disappeared. The digits of the manus are now freed, and the foot is well marked off from the leg and is spear-head-like in shape. The tongue projects slightly from the mouth. Of the two embryos, *a* is slightly the younger.



TEXT-FIG. 7.

The *cervical sinus* has completely closed, but the cervical vesicle still remains, appearing as a conspicuous mass with thickened walls and a central lumen, situated close against the cranial side of the ventral half of the ganglion nodosum (fig. 37, *v.c.*).

The *second pouch* has completely disappeared.

The *superficial cervical thymus* is now practically an independent structure, being connected with the ectoderm of the cervical groove only by a fine cellular strand (fig. 36, *s.tm.*). It has the form in embryo (*a*) of an elongated pear, measuring in dorso-ventral length about 0·3 mm., and in diameter, at its thickest region, 0·12 by 0·08 mm. In embryo (*b*), it is thickest below, near its connection with the ectoderm, and is cylindrical and tapering in its upper part. It shows a histological differentiation quite comparable with that of thymus III of the preceding stage, and in (*b*) is becoming encapsulated.

Third pouch.—The process of separation of the two derivatives of the third pouch which we saw commencing at its dorsal end in the preceding stage has now been completed and as the result the two parts in question, viz. thymus III and epithelial body III, are here quite independent.

Epithelial body III lies just cranio-dorsally to the cervical vesicle and appears as an elongate tubular structure with thickened, deeply staining walls and a central lumen (fig. 37, *ep.b.* III). It is disposed almost transversely and measures in embryo (*a*) 0·16×0·09 mm. in transverse and dorso-ventral diameters respectively; in (*b*) it is slightly smaller (0·14×0·07 mm.). In embryo (*a*), on both sides, the ventral wall of the epithelial body, directed towards thymus III, exhibits in a few consecutive sections a slight irregularity in the character and staining properties of its cells (fig. 37). This area doubtless marks the last point of separation from the thymus.

Thymus III (fig. 37, *tm.* III) is situated immediately below the cervical vesicle, ventrally and laterally to the corresponding epithelial body. It appears as an ovalish solid mass, elongated in the cranio-caudal direction, which extends back at first dorsal and then immediately lateral to the common carotid. Its hinder end lies just cranial to the anterior end of thymus IV. It measures 0·24 mm. in length and 0·09 in transverse diameter and has thus increased considerably in size since the last stage. A remnant of the former connection of the thymus part of the pouch with the sinus-ectoderm is still to be seen in the form of a fine cord prolonged inwards from the dorsal end of the cervical thymus. In embryo (*a*), on the left side, this cord can be traced up to the interspace between epithelial body III and thymus III and is possibly connected with the dorsal end of the latter. Thymus III is now becoming encapsulated.

The *fourth pouch* has now lost its connection with the pharyngeal duct, though its epithelial body in embryo (*a*) is still connected with the original cranial (now caudal) end of the ultimo-branchial body. Its derivatives, viz., thymus IV and epithelial body IV, have either just separated from each other (embryo *a*) or are in process of separation (embryo *b*).

Thymus IV (fig. 39, *tm.* IV) lies immediately caudal to thymus III and close above the dorso-cranial extremity of the pericardium. It is very similar to thymus III in structure but tends to be less elongate and more spherical in shape, averaging about 0·14 mm. in diameter. On the right side in embryo (*b*), however, it is practically as long as the corresponding thymus III, and measures $0{\cdot}23 \times 0{\cdot}12$ mm. In embryo (*a*), on the right side, a slender secondary connection has been established between thymus III and IV. As we shall see in later stages, secondary union of thymus III and IV to form a single gland on one or both sides is not uncommon.

Epithelial body IV, representing the inner dorsal portion of pouch 4, is, in embryo (*b*), still in continuity with thymus IV, but in (*a*) it has already separated, though it is not so far removed from the thymus as is epithelial body III from thymus III. In both embryos, the epithelial body lies dorsally and slightly caudally to the thymus. In embryo (*a*) it has the form of a narrow tube, averaging 0·13 mm. in length by 0·04 mm. in thickness, which runs upwards and inwards to become connected by a slender degenerating tract of cells with the hinder (originally cranial) end of the ultimobranchial body. In (*b*) the epithelial body, as already mentioned, has not yet completely separated from the thymus. It is less elongated than in (*a*) and is no longer connected with the ultimobranchial body. Fig. 39 shows a horizontal section through thymus IV (*tm.* IV) and epithelial body IV (*ep.b.* IV) at a level where the two are in process of separation. In this embryo (*b*) it is worthy of note that the remnant of the lumen of pouch 4 extends from the epithelial body into the dorsal part of the thymus, where it is enclosed by epithelially arranged cells. In (*a*) the separated epithelial body is luminated, whilst in the dorsal part of the thymus there is present a conspicuous rounded cavity likewise enclosed by epithelially arranged cells, and evidently formed from the part of the cleft-lumen formerly continued into it. Cavities of this sort, though not always directly traceable to remnants of the pouch-lumen, are of frequent occurrence in later stages in both thymus III and IV. They are not present in thymus III of this stage and, in fact, are always more numerous in thymus IV than in thymus III. We shall refer to them henceforth as *thymic cavities.*

The *ultimobranchial body* (fig. 38, *u.b.*) has also lost connection with the pharyngeal duct. It is situated just medially to the carotid artery, and has now undergone a noteworthy change in its relations, having moved forwards and upwards in such a way that its original ventral end is now directed cranially, and lies just postero-dorsally to the lateral lobe of the thyroid on each side. In this connection the reader should compare fig. 38 of this stage with fig. 29 of the preceding one. As in the preceding stage, its walls are markedly thickened at its cranial (originally ventral) end and its lumen is distinct.

Median thyroid.—The lateral extremities of the thyroid (fig. 38, *l.th.*) have now grown slightly upwards, and in embryo (*b*) especially have increased in thickness, so that it is now possible to distinguish between a median bridge and lateral lobes. The bridge appears as a flattened band stretching across immediately in front of the point of division of the aorta. Irregular spaces are present, especially in the bridge region, filled by an eosinophilous material.

Stage X.—Embryo V '01. G.L., 9·5 mm. Plate 7, figs. 40 and 42, Plate 6, fig. 41.

Apart from the difference in size, this embryo exhibits no great advance on the last in respect of its external characters. The neck protuberance appears less marked owing to the head being slightly more raised. The outline of the eye is approximately semicircular, and the external auditory meatus is becoming reduced.

The *cervical vesicle* (figs. 40 and 41, *v.c.*) is still conspicuous on the cranial side of the ganglion nodosum, and possesses a distinct lumen.

The *superficial cervical thymus* (fig. 40, *s.tm.*) has now increased in size, the increase being mainly in thickness. In its thickest region it measures 0·19 × 0·11 mm. in diameter. It occupies the same position as before, being situated immediately lateral to the lingual vein, and is still pear-shaped in form, and joined to the ectoderm of the cervical groove by a slender strand. The gland now consists of an apparent cell-reticulum, in the meshes of which lymphocytes are present in small numbers. It is definitely encapsulated, and blood-vessels are already present in the capsule.

Epithelial body III has not changed in position, and is of practically the same size as in the preceding stage. It lies immediately dorsal to the common carotid artery, shortly behind its point of bifurcation, and now appears as a compact, flattened cell-mass, in which only traces of the former lumen are perceptible.

Thymus III has now moved more caudally, its cranial end being situated 0·22 mm. behind epithelial body III, and its caudal end reaching almost as far back as the origin of the carotid from the aortic arch. It lies just below the vagus nerve, dorso-laterally to the carotid artery. It has increased in diameter (now measuring 0·16 × 0·11 mm.), but not in length, and is essentially similar histologically to the cervical thymus, except that lymphocytes are perhaps more abundant. It is encapsulated, as also is epithelial body III, and the capsule is vascularised. A large thymic cavity is now present in the gland.

Thymus IV (fig. 42, *tm.* IV) has also moved caudally, but only slightly, and lies immediately above the dorso-lateral corner of the pericardium. It has not increased much in size since the last stage, averaging in length 0·17 mm. It is similar in structure to thymus III, but possesses two thymic cavities, one of them being exceptionally large (fig. 42, *tm.c.*). Thymus III and IV are not connected, though the two glands are much nearer to one another on the right side than on the left.

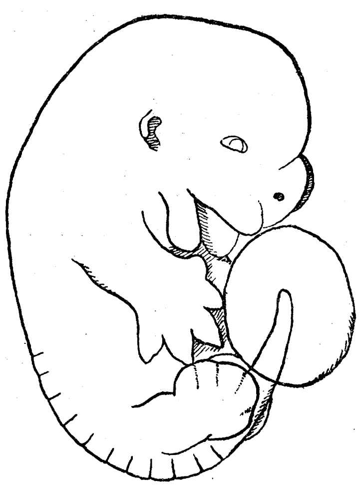
Epithelial body IV (fig. 42, *e.p.b.* IV) appears as a small, deeply-staining mass, with only a remnant of its former lumen. On both sides it indents the dorsal surface of the corresponding thymus.

The *ultimobranchial body* (fig. 41, *u.b.*) has approached still closer to the lateral lobe of the thyroid, and is further enlarged at its cranial end.

Median thyroid.—The lateral lobes are less marked than in the last embryo, but the bridge is better developed, indeed it is here exceptionally thick (fig. 41, *th.*). The gland is becoming enclosed in a connective tissue capsule containing small vessels, and numbers of small irregular slit-like cavities are present throughout its substance.

Stage XI.—Embryo VI '01. G.L. = 10 mm. Text-fig. 8 and Plate 7, fig. 43.

This embryo shows considerable advance on the last. The head is raised, and the neck protuberance as such has disappeared. The tongue projects markedly. The triangular pinna stands out at right angles behind the now considerably reduced meatus. The primordia of vibrissæ are recognisable on the face. The elbow is indicated, whilst claws are forming on the digits of the manus. In the hind limb the digits are now indicated.



TEXT-FIG. 8.

Except in the case of the thyroid the pharyngeal derivatives show no great advance on those of the last stage.

The *cervical vesicle* has become smaller, and is imbedded in the cranial side of the ganglion nodosum. Its lumen is still retained.

The *superficial cervical thymus* shows no essential change, except that it has lost all connection with the ectoderm of the neck groove. It has increased in size, and now measures 0·24 × 0·16 mm. in diameter.

Epithelial body III has lost all trace of its lumen, and is now a compact solid structure.

Thymus III (measuring 0·16 × 0·16 mm. in diameter) and *thymus* IV (0·14 × 0·11 mm. in diameter) are quite separate, the latter lying slightly more dorsally than in the last embryo. The epithelial elements are still the most prominent constituents of both glands. There is a single thymic cavity in thymus III and two in thymus IV.

Epithelial body IV is solid and compact like epithelial body III, but is smaller than the latter. It lies on the dorsal or dorso-medial side of thymus IV.

The *ultimobranchial body* (fig. 43, *u.b.*) has much the same length as in the preceding stage, measuring about 0·18 mm. It appears as a relatively massive structure, with thick deeply-staining walls and a well marked lumen except towards its ends. On the right side, its ventral half now lies in close contact with the dorso-medial surface of the corresponding thyroid lobe, whilst on the left, the two are in close proximity.

The *thyroid* (fig. 43, *l.th.*) has made considerable progress. Its lateral lobes, situated shortly behind the larynx ventro-laterally to the trachea, have more than doubled in length as compared with the last stage, and now measure about 0·26 mm. They have apparently grown up dorsally so as to come into closer relationship with the ultimobranchial bodies. The median bridge contains numbers of rounded and cleft-like spaces, but these are less abundant in the lateral lobes.

Stage XII.—Two embryos, *a* (XXI '04), cut transversely, and *b* (XXII '04), cut longitudinally. G.L. = 11 and 11·5 mm. respectively. Text-fig. 9 and Plate 7, fig. 44.

The lips are now in process of fusion, the tongue is grooved, and the eye is nearly closed over. The external auditory meatus is largely filled up and the pinna is becoming soldered down. The elbow is well marked and the digits of the manus bear recurved claws. In the foot the digits are beginning to project.

TEXT-FIG. 9.

The *cervical vesicle* is very small. In embryo (*a*) on the left side it appears to be almost completely imbedded in the ganglion nodosum, whilst on the right side it is no longer distinguishable.

The *superficial cervical thymus* still shows a prolongation towards the ectoderm of the cervical groove, but the two are separated by a wide interval (fig. 44, *s.tm.*). Lymphocytes are not yet particularly abundant in the gland. Its capsule contains well marked vessels.

Epithelial body III (fig. 44, *ep.b.* III) shows traces of a lumen only in embryo (*a*). It occupies the same position as before and differs from that of the last embryo only in being more elongated, measuring in embryo (*b*) 0·17 mm. in length by 0·12 mm. in transverse diameter.

Thymus III and IV.—Thymus III appears to have moved caudally, and is now more remote from epithelial body III, a shifting which is perhaps due to the growth of the whole embryo. In embryo (*b*) there is only a single thymus on the left side. It is elongated, measuring 0·3 mm. in length by 0·15 mm. in dorso-ventral thickness, and no doubt represents thymus III and IV fused. On the right side the two glands are separate, each having a length of 0·17 mm., and that is also the condition on both sides in embryo (*a*), where the glands average each about 0·2 mm. in length. Right thymus III and right and left thymus IV have each a thymic cavity. In both glands lymphocytes are well marked though not very abundant.

Epithelial body IV is noteworthy in this stage mainly for its variability of position. In embryo (*a*) it lies on the lateral side of right thymus IV and on the dorsal side of the left thymus, whereas in (*b*) it is situated laterally to the thymus but caudally and dorsally to it on the left and immediately cranial to it on the right.

The *ultimobranchial body* in both embryos lies in close contact with the dorso-medial surface of the corresponding thyroid lobe. In embryo (*a*), on the right side, its middle part has extended down so as to invest the medial surface of the lobe, whilst on the left a corresponding downgrowth is indicated. In embryo (*b*) the wall of the body appears to be giving off short solid outgrowths. It is rather shorter than in the preceding embryo, measuring about 0·13 mm. in length.

Thyroid.—In embryo (*a*) the lateral lobes are compact and of much the same size as in the last embryo. In embryo (*b*) much progress has been made, for here under the influence of connective tissue invasions carrying blood vessels, the formerly compact tissue of the gland has become broken up into an irregular system of cellular cords, some solid but many of them containing a central lumen enclosed by a single layer of cells.

Stage XIII.—Embryo X '01. G.L. = 12 mm. H.L. = 6·5 mm. Plate 7, fig. 45.

Head and fore-limbs raised, the latter touching in mid-ventral line. Lip-fusion well advanced, lip-groove narrow and shallow. Tongue hardly projects. Eye and ear-pinna covered.

The *superficial cervical thymus* (the right alone available for examination) has further increased in size and measures 0·24 × 0·19 mm. in diameter. It shows for the first time a small thymic cavity quite similar to those met with in thymus III and IV.

Epithelial body III is exceptionally large for this stage of development and is further exceptional in being already well vascularised.

Thymus.—A single elongated gland is present on each side (fig. 45, *tm.*), the right measuring in length, 0·53 mm. and the left, 0·43 mm. It runs back to terminate a short distance in front of the pericardium, on a level with the first rib. We regard the single gland as being formed by the union of thymus III and IV and the fact that the right gland is somewhat constricted and stains less deeply in its mid-region, on a level with the laterally placed *epithelial body* IV (fig. 45, *ep.b.* IV), supports that conclusion. The left gland is shorter and thicker than the right and shows no trace of division into two parts.

Two thymic cavities (the caudal one, the larger) are present in each gland.

The *thyroid* and *ultimobranchial body* are now enclosed in a common capsule and are so closely associated that from this stage onwards they are best described together.

The lateral thyroid lobes as an individual variation are markedly asymmetrical. The right lobe is shorter (0·28 mm. in length) but much thicker than the left, which is remarkably long (0·44 mm.) and very attenuated. The median bridge is very slender. Histologically the right lobe is in much the same condition as in embryo (*b*) of the last stage but is more compact. The ultimobranchial body now closely invests the medial side of the cranial part of the lateral lobe and is much more closely connected with the same than in the preceding stage. The right body is the larger of the two. It is thick walled and luminated and in the sections not sharply separable from the tissue of the thyroid lobe. It is possible that it is already sending cellular outgrowths into the latter. The left body is reduced as compared with the right, it possesses much thinner walls, and is altogether less active looking. This reduced condition of the ultimobranchial body, associated as it is with attenuation of the corresponding thyroid lobe, would thus seem to afford an interesting example of growth-correlation.

Stage XIV.—Two embryos, *a* (XXV), transverse, and *b* (XXIV), longitudinal. G.L. = 13 and 13·5 mm. respectively. Plate 8, figs. 46, 50, and 50A, Plate 7, figs. 47 and 48, and Plate 9, fig. 49.

The *cervical vesicle* is still visible in embryo (*a*), imbedded in the cranial side of the ganglion nodosum, but in (*b*) it is no longer distinguishable.

The *superficial cervical thymus* has increased in size and is now a large and conspicuous ovalish gland, measuring in (*a*) 0·25 mm. in length and about 0·28 × 0·24 mm. in diameter. It begins just medial to the hinder end of the primordium of the submaxillary gland and runs back close above the developing panniculus muscle in the region of the cervical groove. It is invested in a well marked vascular capsule and is devoid of thymic cavities.

Epithelial body III lies as in the preceding stages just caudal to the division of the common carotid. It now shows a distinct advance since in both embryos connective tissue ingrowths from the capsule carrying capillaries have penetrated into it, with the result that the gland in the region of these ingrowths presents a lobed appearance (fig. 48, *sin.*).

Thymus III and IV (fig. 47, *tm.* III and IV) are united in embryo (*a*) on the right side, to form a single gland 0·54 mm. in length, the gland showing a constriction in its mid-region indicative of the point of union, as in the right gland of the preceding stage. On the left, the two glands are separate but the caudal end of thymus III, which measures 0·28 mm. in length, closely overlaps the cranial end of thymus IV, measuring 0·25 mm. in length. The glands are now situated more caudally than in the preceding stage. There is a single thymic cavity in thymus III and two in thymus IV on each side, the hinder one being the larger (fig. 47, *tm.c.*).

In embryo (*b*), thymus III and IV are quite separate, with no overlapping, and an extra but small thymus is present caudally to right thymus IV. Cranially to this accessory thymus is an extra epithelial body. Owing no doubt to the presence of this additional thymus, right thymus IV is situated cranially to left thymus IV and nearer to thymus III. On the left side, thymus III (0·28 mm. in length) lies immediately cranial to the pericardium, while thymus IV, measuring only 0·19 mm. in length and therefore of small dimensions, is situated some distance caudally and dorsally to the pericardium.

Epithelial body IV on the right side, in embryo (*a*), occupies the same position as in the last embryo, but on the left it lies dorso-laterally to the caudal end of thymus IV. In embryo (*b*), it also lies caudal to thymus IV but medially to the latter on the left and dorso-laterally on the right. It is thus evident that epithelial body IV is subject to considerable variation in its position relative to thymus IV.

Thyroid and Ultimobranchial Body.—The lateral lobes (figs. 49, 50, 50A, *l.th.*) are more massive than in the preceding stage and reach a length of 0·36 mm. Ingrowths of vascular connective tissue are now more numerous and are especially marked between the lateral lobe and the ultimobranchial body (figs. 46 and 49, *l.th.* and *u.b.*).

The ultimobranchial body (0·21 mm. in length) occupies the same position on the medial side of the lateral lobe as in the last stage but begins a short distance behind the cranial end of the latter. It possesses a well marked lumen and is surrounded by thick deeply-staining walls, so that it is readily distinguishable from the tissue of the lateral lobe. It now shows marked activity (fig. 46, *spr.*) inasmuch as its walls, especially that next the thyroid lobe, have grown out in the form of sprout-like solid processes, some of which actually penetrate into the substance of the lobe (figs. 46, 49, 50, and 50A, *u.b.* and *l.th.*). In embryo (*a*) and especially noticeable on the left side, there is present a thick sprout which, instead of passing towards the thyroid lobe, is directed ventro-medially. It has stained differently from the other sprouts and quite deeply with eosin, and is apparently in process of degeneration.

Stage XV.—Embryo, *a* (XXIII), G.L., 14 mm., cut transversely; and newly-born pouch-young (*b*), G.L., 14·5 mm., cut longitudinally. Plate 9, fig. 51.

Head at right angles to trunk, which is now straight. Lip-fusion complete. In (*a*) tongue protrudes and is grooved dorsally, in (*b*) it is retracted. Position of eye just recognisable, that of the pinna indicated by a slight elevation. Claws of digits of manus strongly developed and markedly recurved. Digits of foot project as short processes, two and three syndactylous. Faint indication of knee. Tail reaches in front of umbilicus.

The *cervical vesicle* has now completely disappeared.

The *superficial cervical thymus* has much the same size as in the last stage. In embryo (*a*), it is still a compact gland of rounded outline in cross section, but its capsule is now more vascular and has begun to grow inwards into the substance of the gland. This same feature is much better marked in the new-born (*b*), where the gland presents a distinctly lobulated appearance. In the right cervical thymus of (*b*) there occurs imbedded in the centre of the gland a small solid strip of deeply staining epithelium which may possibly represent the primordium of an epithelial body, since such may occur in the cervical thymus of later fœtal specimens and also in the adult (*cf.* pp. 6 and 36).

Small thymic cavities (one or two) in each gland are observable in embryo (*a*).

Epithelial body III is rather more vascularised than in the last stage and occupies the same position except that on the right side in (*a*) it lies dorso-laterally to the carotid artery.

Thymus III *and* IV (fig. 51, *tm.* III and *tm.* IV) are separate in both specimens. In embryo (*a*), they are smaller than in the last few stages and also than in (*b*), having each a length of 0·17 mm. In (*b*) right thymus III measures 0·27 mm. in length and the corresponding thymus IV, 0·22 mm. They occupy a rather more cranial position than in (*a*) and are distinctly further advanced in differentiation. Not only are they becoming lobulated as the result of the penetration of connective tissue ingrowths, but each gland now consists of two regions distinguishable by their histological characters, viz., a very small central zone, lighter staining, and formed almost exclusively of epithelial elements, and a more extensive, more darkly-staining marginal zone in which numerous lymphocytes are present in the epithelial matrix. A thymic cavity is present in each gland.

Epithelial body IV in embryo (*a*) lies cranio-dorsally to thymus IV. In the new-born (*b*) it lies dorso-laterally to the thymus, separate from it on the right and partially imbedded on the left (fig. 51, *ep.b.* IV). It is now becoming vascularised. In addition, in the new-born, there is present between thymus III and IV on both sides a large irregularly shaped accessory epithelial body (fig. 51, *ep.b.* V).

Thyroid and Ultimobranchial Body.—In (*a*), the lateral lobes happen to be smaller than in the last stage (measuring 0·28 mm. in length). The ultimobranchial body is much reduced, having a length of only 0·1 mm., and its walls have become thinner, evidently as the result of continued proliferation. Distinct sprouts passing into the thyroid tissue are still visible, whilst at some points it is difficult to determine the limits between the two structures.

In the new born, the thyroid lobes are distinctly lobulated, especially towards their hinder ends, and are now well vascularised.

Stage XVI.—Pouch-young. G.L., 16 mm.

The *superficial cervical thymus* is of much the same length as in the new-born fœtus, measuring 0·34 mm. in length by 0·38 mm. in diameter, but its cranial end has now broadened out and lies in contact with the medial aspect of the submaxillary gland. Cortical and medullary zones are now indicated, and the peripheral part of the cortex is divided into distinct though small deeply-staining lobules. Blood vessels have penetrated between the lobules, especially at the hinder end of the gland, and are well marked in its capsule. Lymphocytes are not very abundant, not nearly so abundant as in thymus III and IV of the preceding stage. Many of them are in mitotic division.

Epithelial body III lies dorso-medially to the carotid on the left side and dorso-laterally on the right, as in embryo (*a*) of the last stage.

Thymus III *and* IV are separate but lie in close proximity and indeed actually overlap on the right side, the cranial end of thymus IV lying immediately lateral to the caudal end of thymus III. Thymus III is now in contact with its fellow in the middle line, ventrally to the common carotids. It has increased considerably in length, now measuring 0·36 mm., whilst thymus IV has a length of about 0·2 mm. Both glands are more markedly lobulated than the cervical thymus. Cortical and medullary zones are distinguishable but lymphocytes are not very abundant. On the left side two thymic cavities are present in thymus IV and one in thymus III.

Epithelial body IV appears to be absent on the left side but there are three on the right, one situated ventro-laterally to the mid-region of thymus III, a second dorso-laterally to the cranial end of thymus IV, and a third, very small, situated caudally to the latter.

Thyroid.—The lateral lobes have increased in thickness, and are now more lobulated and more markedly invaded by vascular connective tissue than in the preceding stage. The *ultimobranchial body* lies imbedded in the anterior part of the lateral lobe on its medial side and appears as a vesicular structure with a wall varying in thickness from one to several layers of cells. In places the wall is in active proliferative connection with the thyroid tissue, as evidenced by the presence of mitotic figures and the impossibility of determining the limits between the two. In this fœtus, as the result of the penetration of a capillary vessel, the lumen of the ultimobranchial body on both sides is completely occupied by blood-corpuscles.

Stage XVII.—Two pouch-young: (*a*) G.L., 17 mm., cut longitudinally, and (*b*) G.L., 17·5 mm., cut transversely. H.L., 7·5 mm. Plate 8, fig. 52; Plate 9, figs. 53 and 55.

The *superficial cervical thymus* shows a further increase in length, and is now distinctly lobulated and very vascular. In the left cervical thymus of (*b*) there is present an unmistakable though small epithelial body, lying imbedded in the ventro-lateral side of the gland between two of its lobes, whilst there also occurs in (*b*) a short closed duct of unknown significance, situated midway between the gland and the epidermis.*

* We may state here that we have not attempted to make any detailed study of the various varieties of epithelial structures (apart from the "epithelial bodies") met with in, or in relation to, the cervical and thoracic thymus glands in the later fœtuses of Trichosurus.

Epithelial body III is especially large in both specimens. In (*b*) on the left, it lies medially to the point of division of the common carotid; on the right, caudally and dorsally to the same. Capillaries are in process of penetrating into it, and its cells show indications of becoming arranged in columns, two cells thick.

Thymus III and IV are very similar in appearance to the cervical thymus. In (*a*) they are separate on the left side, but united on the right (fig. 52, *tm.* III and IV), the conjoint gland overlapping left thymus III in the middle line, and having left thymus IV caudally to it (fig. 52, *tm.* IV). Three thymic cavities are present in thymus IV, and one in each of the others. In (*b*) the glands are united on both sides (fig. 53, *tm.* III and IV), and average 0·33 mm. in length.

Epithelial body IV is very inconstant in position. In (*a*) on the left, it lies caudally and laterally to thymus IV. On the right, it appears to have failed to move back with thymus IV and lies ventrally to the trachea well in front of the latter gland (fig. 52, *ep.b.* IV). In (*b*) it lies dorso-laterally to the thymus on the right and ventro-laterally on the left (fig. 53, *ep.b.* IV). The centre of each body is occupied by a vascular connective tissue strand, and its cells are taking on the same arrangement as in epithelial body III.

Thyroid.—The lateral lobes (fig. 55, *l.th.*) are thicker than in the preceding stage, and their sub-division into lobules by vascular connective tissue invasions is more marked, especially in their caudal regions. The cellular epithelial cords, some solid, others enclosing minute lumina, are now better marked, but the formation of the definitive thyroid vesicles does not appear to have commenced.

The *ultimobranchial body,* more especially in (*b*), is exceptionally well developed, and its walls are in much more active proliferation than in the last fœtus, numbers of solid sprout-like processes passing off from them into the thyroid tissue (fig. 55, *u.b.* and *spr.*). We think the evidence from this stage alone justifies the conclusion that the ultimobranchial bodies in Trichosurus contribute to the formation of the lateral lobes of the thyroid.

Stage XVIII.—Pouch-young. G.L., 23 mm. H.L., 9 mm. Cut transversely.

The *superficial cervical thymus* has increased greatly in size, being now twice as long as that of the last stage. It measures 0·63 mm. in length and 0·8 mm. in thickness, and has almost attained its adult condition so far as lobulation is concerned. It is distinctly more massive and more markedly lobulated than the thoracic glands, but essentially resembles the latter in its histological structure. Thymus cells (lymphocytes) are fairly abundant both in the cortex and medulla, and in the latter, for the first time, we meet with Hassall's corpuscles in process of differentiation. On the medial aspect of the gland there is present an epithelially lined duct, closed at both ends and recalling that of (*b*) of the last stage. It is convoluted on the left side, straight and very short on the right, and lies, unlike that of XVII *b*, between the thymic lobes, inside the capsule. It is, therefore, probably of thymic origin.

Further, in addition to developing Hassall's corpuscles, there are present small spherical cavities (cystic vesicles) bounded by a wall apparently syncytial, with nuclei arranged fairly regularly in one layer and evidently derived from elements of the epithelial reticulum. The cavity contains either a group of degenerating cells or a deeply-staining mucoid-like material. We believe these structures are purely secondary formations, not related to the thymic cavities but rather of the same order of structure as Hassall's corpuscles.

Epithelial body III has advanced considerably in differentiation, and has practically attained to the adult condition. It appears as a rounded compact body with a well-developed capsule, situated on the right side laterally to the common carotid, and on the left medially to the same. Its cells are now more definitely grouped in irregular laminæ and cords, two cells thick, separated by sinusoids.

Thymus III and IV.—On the right side, the two glands are fused to form a single mass, 0·96 mm. in length. On the left, they are widely separate, thymus III measuring 0·64 mm. in length and lying laterally to the common carotid and the lateral thyroid lobe, thymus IV (of the same length) being situated on a level with the cranial portion of the conjoint right thymus. The thoracic thymus is well lobulated and in this stage has not only increased greatly in size as compared with that of the last, but has progressed in histological differentiation, being now well advanced towards the adult condition. Cortical and medullary zones are now clearly recognisable. The cortex presents a uniform appearance and stains deeply. It contains very numerous small thymus cells (lymphocytes) supported in the epithelial reticulum, the nuclei of which are larger and stain less deeply than those of the thymus cells. The central medullary region is distinguishable into two parts, (*a*) a zone next the cortex in which the epithelial elements are more conspicuous and the thymus cells less abundant, and (*b*) a mass occupying the centre of the gland, composed of more or less closely packed hypertrophied epithelial elements and containing relatively few thymus cells. In this central portion Hassall's corpuscles are seen in process of differentiation, indeed some of them are already well formed and show the typical concentric arrangement of the cells. No thymic cavities appear to be present.

Epithelial body IV.—A large epithelial body, similar to epithelial body III, is present on the lateral side of the cranial end of the left thymus. On the right side, two are found, one imbedded in the dorsal side of the right thymus, the other quite minute, situated dorso-laterally to the common carotid, far cranial to the thymus. They are not yet vascularised.

Thyroid.—The lateral lobes are only slightly longer than in the last stage, now measuring 0·5 mm. The irregular cell cords of that stage are now becoming broken up into cell-masses, many of them luminated. Differentiation of the definitive thyroid vesicles may therefore be said to be now in progress. The connective tissue, which, relatively to the epithelial constituents of the gland, is abundant, is now beginning to form thin but distinct investing layers around the vesicles.

The *ultimobranchial body* lies imbedded on the dorsal side of the lateral lobe. On the left side, it appears as a short tubular structure about 0·09 mm. in length, with a large lumen enclosed by moderately thin walls which do not appear to be proliferating. On the right, it appears as an irregularly lobed, darkly staining structure with only traces of a lumen.

Stage XIX.—Pouch-young. G.L. 19 mm. (curved). H.L. 11 mm. Cut longitudinally. Plate 8, figs. 56 and 57, and Plate 9, fig. 58.

The *cervical thymus* (figs. 56 and 58, *s. tm.*) measures 0·67 mm. in length and is markedly lobulated. Thymic cavities identical with those of the thoracic thymus are present in it (fig. 56, *tm. c.*), and a small epithelial body occurs imbedded superficially on the ventral side of the left gland. As in the preceding stages, a closed duct (fig. 56, *d.t.*) is present in relation to the thymus; on the right it is situated wholly outside the gland, but on the left, part of it lies inside the capsule.

Epithelial body III lies just below the carotid fork.

Thymus III and IV (figs. 57, *tm.* IV, and 58, *tm.* III and *tm.* IV).—On the right side there is but a single gland, 0·38 mm. in length, situated cranio-laterally to left thymus IV, the two overlapping in the middle line. On the left, the glands are separate. Left thymus III (0·48 mm. in length), much as in the last stage, has failed to pass back, and lies ventral to and just behind the carotid fork. Thymic cavities are present, but Hassall's corpuscles are not yet fully formed.

Epithelial body IV (fig. 57, *ep.b.* IV) on the right, lies caudo-laterally to the single thymus, and on the left, on the lateral side of thymus IV. It is less advanced than epithelial body III.

Thyroid.—The lateral lobes (fig. 58, *l.th.*) are asymmetrical, the right being thicker but shorter than the left. Cell-cords are well marked and vesicle formation is less advanced than in the last stage.

The *ultimobranchial body* lies imbedded in the cranial part of the lateral lobe. The right body measures 0·1 × 0·08 mm. in diameter, the left, 0·07 × 0·04. Both are luminated and possess moderately thick walls but are no longer in active proliferation.

Stage XX.—Two pouch-young; G.L. 30 mm.: (*a*) H.L. 12 mm., cut transversely, and (*b*) H.L. 12·5 mm., cut longitudinally. Plate 9, fig. 59, and Plate 8, fig. 60.

The *superficial cervical thymus* (fig. 59, *s.tm.*) has almost trebled in length since the last stage, now measuring 1·9 mm. The two glands overlap in the middle line and now exhibit the characters of the adult structure. The definitive cortical and medullary zones are clearly distinguishable. The central patch of epithelial elements to which attention was directed in Stage XVIII (p. 38) is no longer recognisable as such, and thymus cells are abundant throughout its entire extent. Many fully formed Hassall's corpuscles are present and others are in course of formation. A well developed epithelial body lies imbedded between the lobes at the hinder end of each gland. The right one is larger than the left and is already vascularised (fig. 60, *ep.b'.*). Intra-thymic cystic vesicles as well as intra- and extra-thymic duct-like structures similar to those already noted in preceding stages, and whose walls are variable in their histological characters, are present in connection with the thymus in both embryos.

Epithelial body III has increased markedly in length but shows no further change as compared with those of the preceding stage. In (*a*) it lies dorso-medially to the internal carotid on the left and dorso-laterally to the same on the right. In (*b*) it lies between the internal and external carotids, cranial to the carotid fork.

Thymus III and IV.—In (*a*) there is only one large thymus on each side, with a length of about 1·2 mm. In (*b*) thymus III and IV are separate on both sides and lie remote from each other. The former (1·3 mm. in length) has failed to move back and lies on a level with the cervical thymus (fig. 59, *tm.* III). It is an exceptionally large, elongated, many-lobed gland. The latter (0·75 mm. in length) is situated just cranial to the pericardium (fig. 59, *tm.* IV). A cystic vesicle filled with cellular elements is present in left thymus III. Hassall's corpuscles are present in both specimens.

Epithelial body IV lies laterally to the mid-region of the thymus in (*a*) on both sides. In (*b*) it is imbedded in the dorsal side of right thymus IV, and lies just cranial to the corresponding left gland (fig. 59, *ep.b.* IV). In (*a*) small accessory epithelial bodies (three or four on the right and one on the left) are present within the thymus lobes.

Thyroid.—The lateral lobes (fig. 59, *l.th.*) have increased greatly both in thickness and in length, especially in (*a*), where they attain a length of 0·9 mm. The two lobes as in preceding stages are connected by a stout bridge. They still present a compact solid-looking appearance, the differentiating thyroid vesicles being mostly small and possessing quite minute lumina in which a material staining deeply with eosin may sometimes be seen. The connective tissue matrix of the gland is prominent between the developing vesicles.

Imbedded in the centre of the right lobe in (*a*) is the remnant of the *ultimo-branchial body* in the form of a closed tubular structure (0·1 mm. in length by 0·06 mm. in diameter), the walls of which vary in thickness. It is clearly distinguishable from the thyroid tissue and shows no signs of activity, on the contrary it is in evident process of degeneration. No such remnant is recognisable in the opposite thyroid lobe or in those of specimen (*b*).

Stage XXI.—Pouch-young, G.L. 28 mm. H.L. 13·5 mm.

The *cervical thymus* resembles that of the preceding stage but is smaller (averaging 1·2 mm. in length). A small epithelial body occurs in each gland and here again closed duct-like structures are present. On the right side, at the cranio-medial end of the gland, is an extra-thymic duct which runs out towards the ectoderm and joins the solid inner end of what appears to be a subcutaneous gland prolonged in from the epidermis. On the left side, between the lobes of the thymus there is a closed intra-thymic duct.

Epithelial body III lies as before cranial to the division of the common carotid.

Thymus III and IV.—A single gland is present on each side, averaging only 0·63 mm. in length. In each gland there occurs, curiously enough, one very large Hassall's corpuscle, in addition to numerous smaller ones.

Epithelial body IV has increased in size and lies on the left, dorso-laterally to the thymus, whilst on the right, it is situated far cranial to the same. A small accessory epithelial body is present within the left thymus, and at the caudal end of the right there occurs a closed tubular structure, almost completely imbedded in the gland and probably of the nature of an epithelial body.

Thyroid.—The lateral lobes show no marked advance on those of the last stage. The majority of the vesicles are still small, and their lumina are inconspicuous, but a few larger vesicles, containing an orange-staining substance, are now present. No remains of the ultimobranchial bodies are recognisable. The gland is now very vascular.

Stage XXII.—Pouch young. G.L. 5·2 cm. H.L. 19·5 mm. Dorsal contour length 8 cm. Cut transversely. Plate 10, figs. 61, 62, 63, and Plate 8, fig. 64.

The *cervical thymus* (fig. 61, *c.tm.*) is now a very large, flattened and markedly lobulated gland, which reaches a length on the right side of 2·17 mm., and on the left of 1·6 mm. Cranially, both glands lie dorso-medially to the hinder ends of the sub-maxillary glands. They take a slightly more ventral position as they run back on either side of the middle line between the sterno-hyoid and sterno-mastoid muscles dorsally and the platsyma ventrally. Large thymic cavities are present with epithelial walls of varying character and thickness, and with cellular elements in their lumina. Hassall's corpuscles are well marked, but no epithelial bodies are present. The medulla is now relatively more extensive than in the preceding stages, and, as in the last two stages, fat-cells are now present in the connective tissue between the lobules.

Epithelial body III lies cranial to the division of the common carotid, dorso-medially to the internal carotid on the right, and lateral to the same on the left. Histologically, it resembles epithelial body IV (*cf.* below).

Thymus III *and* IV (figs. 62 and 63, *tm.* III, *tm.* IV).—The thymus glands have increased very considerably in size, and now form large elongated structures, stretching back from the level of the first rib, to terminate just ventral to the anterior end of the pericardium. Thymus III and IV are distinguishable on both sides. On the right side they overlap, and are actually joined at one point. On the left they are separate, but they overlap more than on the right, the anterior end of thymus IV lying immediately dorsal to the hinder end of thymus III; on this side thymus III has a length of 1·36 mm., and thymus IV 0·96 mm. In addition, a small accessory thymus is present on the right side, situated laterally to the carotid artery, on a level with the lateral thyroid lobe (fig. 61, *acc.tm.*). It measures 0·54 mm. in length, and contains Hassall's corpuscles. The thoracic thymus essentially resembles the cervical histologically; they are markedly lobulated, and Hassall's corpuscles are present, but there are no cavities of any kind.

Epithelial body IV (fig. 63, *ep.b.* IV) is now a conspicuous structure, measuring 0·22 mm. in length on the left and 0·12 mm. on the right. On the left, it lies ventro-laterally to the œsophagus, a very short distance cranially to thymus III, but dorsally to the latter, being separated from it by the carotid artery and the jugular vein. On the same side a small accessory epithelial body is present laterally to thymus IV, in the form of a small lobulated nodule of epithelium penetrated by a capillary. On the right side, the epithelial body lies laterally to the cranial end of thymus III, whilst there also occurs a small accessory body imbedded in the thymus itself.

Histologically, the epithelial bodies now exhibit the structure of those of the adult (fig. 64). The gland is invested in a connective tissue capsule (fig. 64, *c.t.sh.*), and consists of irregular anastomosing lamellæ, each composed of two layers of cubical or columnar cells in close apposition. Between the lamellæ there are present sinusoidal capillaries (fig. 64, *sin.*).

Thyroid.—The lateral lobes (fig. 61, *l.th.*) are large and conspicuous, measuring 0·97 mm. in length on the right and 1·08 mm. on the left, where the lobe has extended back a short distance behind the level of the connecting bridge. The vesicles have increased in size since the last stage, and their lumina are better marked, still they are of very small size as compared with those of the adult, and the formation of colloid does not yet appear to have commenced.

In the lateral lobe, on each side, there is present in this fœtus a probable remnant of the *ultimobranchial body* in the form of a cavity enclosed by deeply-staining thickish walls, though the thickness varies. On the right side, the remnant lies nearer to the medial border of the lobe, and consists of two dismembered parts, a more anterior measuring 0·06 × 0·09 mm. in diameter, and a posterior, quite small part, 0·02 × 0·09 mm. in diameter. On the left side, the remnant measures 0·06 × 0·11 mm. in diameter, and is situated nearer the centre of the lobe. Such a tubular remnant of the ultimobranchial body has been termed the central canal of the thyroid by PRENANT (44).

CHAPTER IV.—SUMMARY AND DISCUSSION.

1. *Superficial Cervical Thymus.*

Our observations show that the epithelial basis of the superficial cervical thymus in Trichosurus is derived in greater part, if not exclusively, from the ectoderm of the cranial portion of the cervical sinus, but the possibility of the participation of the ventral extremity of the second gill-pouch in its formation cannot wholly be excluded. On the whole, we think it probable that a small amount of pouch-entoderm *is* actually included in the primordium, in which case the cervical thymus is to be regarded as a *thymus ento-ectodermalis*, in which the ectodermal constituent greatly preponderates.

The cervical sinus in its general features resembles that of such Eutheria as the Pig and Mole (H. RABL, 46). It seems to have attained its maximum development in Stage I (Plate 2, fig. 3, *s.c.*), where it appears as a well marked depression of triangular outline, bounded in front by the hyoid arch, above by the curved retrobranchial ridge, and below by a less marked ridge running forwards and inwards above the heart-swelling. On its floor are situated branchial arches 1–3 (fig. 3); the first arch is the largest, its upper end lying outside the sinus depression, on a level with the retro-branchial ridge, its remainder within the same. The second arch is smaller and more deeply placed than the first, whilst the third is still smaller and lies obliquely in the deepest caudal part of the sinus-depression. Between the hyoid and first branchial arches is the well marked second ectodermal groove, its upper part lying outside the sinus, its remainder within the same. The third and fourth grooves are both shallow, whilst the fifth groove appears as a distinct depression behind the small third arch and occupying the extreme caudal end of the sinus.

During the succeeding stages, the branchial arches and the ectodermal grooves (with the exception of the second) become indistinguishable and the sinus gradually closes, as the result partly, and indeed mainly, of the growth of its dorso-caudal margins (*i.e.*, of the retrobranchial ridge) in the cranial and ventral direction, and partly of the growth backwards of the hyoid arch Thus by Stage V, the widely open sinus of Stage I has become converted into an irregularly shaped vesicular structure which is in communication with the exterior only by an oblique slit-like passage representing the original opening now greatly reduced and known as the cervical duct (Plate 4, fig. 11, *d.c.*). The vesicular part of the sinus is distinguishable into two portions, respectively cranial and caudal. The cranial portion or sinus proper, as we have termed it, contains a laterally compressed narrow cavity into which the cervical duct leads, and whose cranial angle is formed by the sinus-part of the second ectodermal groove (fig. 11, *ect. gr.* 2), now deepened as the result of the growth of the hyoid arch. The caudal portion or cervical vesicle (vesicula cervicalis, fundus cervicalis) has the form of a thick-walled sac-like structure, with a well marked lumen, which is connected with the sinus proper by a somewhat narrowed region, the vesicle-duct (fig. 11, *v.c.* and *v.d.*).

Its wall includes the placode of the ganglion nodosum and it lies in contact with the cranio-ventral surface of that ganglion just as does the homologous part of the sinus in the human embryo (*cf.* GROSSER, 17, fig. 326), in Talpa and Cavia (H. RABL, 46, 49), and in the pig (ZOTTERMAN, 69). The cervical vesicle persists up to Stage XIV but is of no significance from the point of view of thymus formation. The cranial portion of the closed sinus, the sinus proper, on the other hand, is of the first importance, since its thickened and coalesced walls give origin to the major portion, if not to the whole, of the primordium of the cervical thymus.

Turning now to the history of the second gill-pouch, this pouch, like the cervical sinus, appears to have attained its maximum development in Stage I. It consists of a horizontal part in open communication with the pharynx (Plate 2, fig. 2, *cl.* 2), a small dorsal diverticulum (of no particular significance in the present connection), and a well marked ventral diverticulum. The closing membrane (fig. 2, *cl. m.* 2) is extensive and involves the lateral extent of the pouch, its upper third lying dorsal to the sinus, its remainder within the same. It is to be noted, however, that the ventral margin of the closing membrane does not coincide with the ventral limit of the pouch entoderm, since the latter continues on for a short distance as a solid ridge fused with the bottom of the second ectodermal groove, a condition which is also found in the succeeding stages. As development proceeds, the pouch assumes a more tubular form and, as the result of growth-changes correlated with the closing of the sinus, its closing membrane suffers a progressive reduction in its extent. Thus in Stage IV, the closing membrane has a dorso-ventral extent of only 0·08 mm. as compared with 0·24–0·26 mm. in Stage I, that part of it which is situated above the dorsal margin of the sinus alone persisting (Plate 2, fig. 7, *cl.m.* 2). In Stage V, the second pouch has acquired a more definitely tubular form and it has become reduced in diameter as the result of elongation in the dorso-ventral direction. Proximally, it possesses a well marked lumen in communication with the pharynx; as it passes ventrally, however, the lumen rapidly becomes smaller and the pouch narrows to form a tapering prolongation, at first minutely luminated but eventually becoming solid. This distal tapering part of the pouch we have distinguished as the entobranchial duct. It corresponds to the "Kiemengang" of C. RABL (45) and the "filiform process" of FOX (8) in the pig. The entobranchial duct is not free but is fused throughout its extent with the cranio-medial edge of a flattened, upwardly tapering prolongation from the wall of the cervical sinus which we have termed the ectobranchial duct. This corresponds to the ectodermal tube which in the human embryo (HAMMAR, 18) and in the rabbit (HANSON, 23) connects the second pouch with the ectoderm of the cervical groove in the former and of the sinus in the latter and which is now generally known as the ductus branchialis. HAMMAR has shown that it represents the closed-off second ectodermal groove and there can be no doubt but that in Trichosurus it has a similar origin. We regard it as being formed by the closing off and separation from the ectoderm of that part of the second ectodermal groove which in Stage IV is involved in the formation of the closing membrane, supplemented by the closing-off of the dorso-cranial corner of the sinus which is occupied by the direct downward continuation of the ectodermal groove. That mode of origin is in agreement with the fact that the ectobranchial duct is connected with the ectoderm only at its lower end where it passes into continuity with the sinus-wall, whilst the narrow lumen which is present in the ventral half of its extent appears as the direct upward continuation of the persisting sinus-portion of the ectodermal groove. The line of fusion of the ecto- and ento-branchial ducts is of the nature of an oblique overlap and includes the region of the closing membrane, but the latter is no longer distinguishable as a distinct structure, with the result that it is impossible to determine the exact limits of the ectoderm and entoderm. The evidence indicates, however, that, as in the preceding stages, the pouch-entoderm is continued as a solid process fused with the ectobranchial duct right down to the sinus.

For the very short composite segment which thus intervenes between the second pouch and the sinus-ectoderm, we adopt the designation suggested by HAMMAR (22) viz. ductus ecto-entobranchialis II. The corresponding structure in the pig (ZOTTERMAN, 69, p. 527) and guinea-pig (RUBEN, 50, p. 591) differs from that of Trichosurus mainly in the fact that the union of its two constituent parts is not of such a markedly overlapping character as in Trichosurus, but is more of the nature of an end-to-end junction.

In Stage VI (embryo of G.L. 7·75 mm.), the walls of the dorso-cranial angle of the sinus proper, with which the ductus ecto-entobranchialis is continuous, have become thickened and fused together to form a solid mass which is the first indication of the primordium of the cervical thymus (Plate 4, fig. 15, *s.tm.*). The second pouch has now the form of a thin cord with only a proximal remnant of its lumen, distally it passes into continuity with the slightly thickened ductus. In Stage VII, fusion of the thickened walls of the sinus proper has proceeded still further with the result that only a small ventral remnant of its lumen now remains. The bulbously swollen mass so formed constitutes the primordium of the cervical thymus (Plate 3, fig. 16, *s.tm.*). The swollen region extends down below the connection of the third pouch with the sinus-ectoderm and has still a wide connection with the general ectoderm. Dorsally it tapers upwards to become continuous with the thin cord representing pouch 2. This upper tapering part of the primordium includes at least the lower part of the ductus ecto-entobranchialis II, but it is now quite impossible to determine the limits of that structure.

In Stage VIII, the thymus primordium (Plate 4, fig. 21, and Plate 6, fig. 34, *s.tm.*) has increased somewhat in size, measuring about 0·15 mm. in dorso-ventral length by 0·2 × 0·11 mm. in diameter. It has now acquired a more definitely bulbous form, whilst its connection with the ectoderm of the cervical groove has become considerably narrowed. Pouches 2 and 3 and the vesicle-duct are still joined to it but pouch 4 has lost connection. In Stage IX, marked progress has been made. The thymus primordium is solid throughout, the last remnant of the sinus-lumen having disappeared, and it forms now a practically independent structure, being connected with the ectoderm only by a fine cellular strand (Plate 6, fig. 36, *s.tm.*). Pouch 2 and the cervical vesicle (Plate 6, fig. 37, *v.c.*) have both lost connection with it and only a remnant remains of the connecting cord of pouch 3. It is pear-shaped in form and measures 0·3 mm. in length by 0·12 × 0·08 mm. in diameter. In Stage X, histological differentiation, already indicated in Stage VIII, is making progress, the gland consisting of a cell-reticulum, in the meshes of which lymphocytes are present in small numbers. It is now enclosed by a definite capsule containing blood-vessels (Plate 7, fig. 40, *s.tm.*). The last remnant of the connection of the gland with the ectoderm has disappeared by Stage XI and by Stage XIV the gland, now ovalish in form, measures 0·25 × 0·28 × 0·24 mm. in diameter. In the new-born fœtus (Stage XV), it is beginning to be lobulated, and in the following stage central and marginal zones are distinguishable and blood vessels are beginning to penetrate between the lobules. In Stage XVIII, developing Hassall's corpuscles are recognisable for the first time in the central zone. The glands are now much larger (measuring 0·63 mm. in length by 0·8 mm. in diameter. They are distinctly lobulated and contain fairly abundant lymphocytes throughout their matrix. In Stage XX, the two glands overlap in the middle line and may now be said to have attained their adult characters (Plate 9, fig. 59, *s.tm.*). The definitive cortical and medullary zones are clearly distinguishable, lymphocytes are abundant and many fully formed and developing Hassall's corpuscles are present.

The not infrequent occurrence of an epithelial body, structurally identical with epithelial bodies III and IV, in one or both of the cervical glands of later fœtuses as well as adults of Trichosurus, is a feature of considerable interest, to which reference will be made later (p. 62).

Remarks on Cervical Thymus.—The facts that in certain Eutheria the ectoderm of the cervical sinus participates along with the entoderm of the third gill-pouch in the formation of the epithelial basis of thymus III and that it gives origin by itself to the epithelial basis of an independent cervical thymus gland may now be regarded as definitely established, thanks to the labours of, amongst others, KASTSCHENKO (27), H. RABL (46), ZOTTERMAN (69), RUBEN (50), NIERSTRASZ (39).

According to their constitution, it is thus possible to recognise, as ZOTTERMAN has already done (*loc. cit.* p. 528), three categories of thymus glands: (1) a thymus with a purely entodermal basis, derived from the gill-pouch entoderm, *e.g.* thymus III in Man, the Rabbit, and many other Eutheria and in the Monotremes, thymus III and IV in Trichosurus, (2) a thymus with a purely ectodermal basis, developed exclusively from the ectoderm of the cervical sinus and forming a gland situated in the neck (the cervical thymus) and primarily independent, *e.g.* the cervical thymus of the Pig, which co-exists with and indeed later joins a thymus III of mixed origin, and the superficial thymus of the Mole, which, as the result of the early atrophy of the major portion of the entodermal thymus III, persists as the main representative of the thymus in the adult; and lastly (3) a thymus with a mixed ecto-entodermal basis, formed in varying proportions partly from the gill-pouch entoderm and partly from sinus-ectoderm, *e.g.* the mixed thymus III of the Pig, Guinea-pig and Tarsius and probably also the superficial cervical thymus of Trichosurus.

It is evident then that amongst the forms mentioned in the foregoing, Sus and Talpa, in respect of their possession of a cervical thymus of ectodermal origin, approach most nearly to the condition in Trichosurus, and of the two there can be no doubt Talpa shows the greatest agreement both as regards adult relations and development.

Our detailed knowledge of the morphology and development of the cervical thymus in Talpa, we owe to the work of SCHAFFER (52) and H. RABL (46), indeed SCHAFFER was the first to describe the occurrence of this gland in the Mole. Both RABL and he, at the outset of their papers, direct attention to the close agreement it exhibits in its topographical relations with the superficial cervical thymus described by SYMINGTON (*loc. cit.*) in Diprotodont Marsupials, RABL even hazarding the suggestion that the Marsupial gland would probably be found to develop much in the same way as that of the Mole.

As in Trichosurus, so in the Mole, SCHAFFER shows that the cervical gland in the adult is a large paired distinctly lobulated structure, situated superficially in the neck immediately below the skin-musculature, at the cranial limit of the powerfully developed pectoral muscles. Histologically he describes the lobules of the gland as consisting of a broad small-celled cortex in which occur large pale reticulum-cells and of a clearer, rather sharply limited medulla with well developed Hassall's corpuscles.

He states that a thoracic thymus is not present in the adult but accessory thymus lobes are regularly met with in the region of the lateral lobes of the thyroid, caudally or dorsally to them, whilst other remnants of thymus tissue are usually present further cranially or caudally. In the embryo, however, there is present a thoracic thymus (shown by RABL to be the main body of thymus III). This was previously observed by SOULIÉ and VERDUN (57) and by GROSCHUFF (13), and was regarded by them as the only thymus present. The thoracic thymus undergoes atrophy and is not found in the adult, but the entire primordium of thymus III does not disappear, since its anterior portion fragments to form the persistent accessory lobes referred to above. In his paper, SCHAFFER gives a detailed account of the histology and of the involutionary changes in the gland, with which we are not here concerned.

According to the investigations of RABL, the cervical thymus takes origin from the ectoderm of the cervical sinus. The latter in its general features is very similar to that of Trichosurus. It closes in much the same way as in the latter to form a vesicular structure, to which RABL applies the name of *vesicula cervicalis*,* its original opening becoming narrowed to form the *ductus cervicalis.* In his

* It should be noted that RABL'S use of this name differs from our own, inasmuch as he applies it to the closed sinus cervicalis as a whole, and not simply to its vesicular caudal part, as we have done.

Stage VIII (embryos of 8 mm.) he describes pouch 2 as arising from the pharynx by a wide funnel-shaped opening, and as consisting of two parts, a proximal transverse part which gradually narrows outwards, and a thin distal part directed caudally. The latter, after a short course, joins the inner end of a solid cord, prolonged in from the cranio-lateral corner of the closed sinus, and derived from the second ectodermal groove. This cord and the distal segment of the pouch together form the ductus ecto-entobranchialis II or "Kiemengang," as RABL terms it, which differs from that of Trichosurus in that it consists in greater part of ectoderm, whilst, in the absence of the overlapping junction characteristic of that form, its entodermal component ends remote from the sinus-ectoderm.* The third pouch is also connected with the vesicula cervicalis by an epithelial cord (or ductus ecto-branchialis III), but that has already disappeared in Stage VIII. By Stage IX (embryo of 8·75 mm.) the ductus ecto-entobranchialis II is interrupted, and the *ductus cervicalis* is becoming reduced. The degeneration of the former duct begins at its central origin and progresses outwards, so that for a time the cranio-lateral tip of the vesicula cervicalis is seen to be continued into a short process representing the remnant of the ectodermal part of the duct. The *ductus cervicalis* eventually disappears, and the *vesicula cervicalis* now forms a completely closed sac, with thick epithelial walls and a narrow lumen. It lies free in the mesoderm, ventrally to the sterno-cleido-mastoid muscle and just internally to the platysma and skin, thus occupying precisely the same position as the cervical thymus in Trichosurus. In embryos of 10–11 mm., as the result of lateral compression by the surrounding tissue and of the growth in thickness of its walls, the vesicle loses its lumen and becomes converted into a solid epithelial mass, the *corpus cervicale*, representing the definitive primordium of the cervical thymus. Blood-vessels and connective tissue strands next penetrate into it, and as the result its peripheral region becomes divided up into spherical lobules. Thus the epithelial primordium of the cervical thymus takes on the same appearance as that of the thoracic thymus. It is noteworthy that, in embryos of G.L. 11 mm., "lymphoid" cells have not yet made their appearance according to SCHAFFER, though in places the epithelial cells are becoming transformed into the epithelial reticulum.

It is evident, then, that the cervical thymus in Trichosurus and Talpa develop in essentially the same way, but whereas in the former the epithelial basis of the gland is derived from the cranial portion only of the closed-off sinus, with the

* RABL points out that the relations of the ductus ecto-entobranchialis II to the cervical sinus in the Mole, and one may add the same holds true for Trichosurus and for the Rabbit (HANSON), differ from those of the ductus ectobranchialis II in the human embryo, inasmuch as in the latter, according to HAMMAR'S observations, the ductus leads not into the sinus but directly to the exterior, its opening being situated in the cervical groove along with that of the ductus cervicalis. In the human embryo, accordingly, the epithelium of the second ectodermal groove does not participate, as it does in the Mole, Trichosurus, and Rabbit, in forming the wall of the cervical sinus.

possible inclusion of the entoderm of the extreme ventral end of pouch 2, in the latter the epithelial basis is furnished exclusively by the ectoderm of the whole of the closed-off sinus, the entoderm of pouch 2 ending far remote from the latter, and disappearing before the establishment of the definitive primordium of the gland.

Turning now to Sus, KASTSCHENKO (27), in an important paper published in 1887, distinguished three parts in the thymus: (1) the *thymus superficialis*,* of purely ectodermal origin, and derived from the medial wall of what he terms the *ductus præcervicalis*, this latter corresponding, so far as we can judge, to our vesicle-duct, and probably also to part of our sinus proper; (2) the *caput thymi*, developed partly from the entoderm of pouch 3 and partly from the ectoderm of the *fundus præcervicalis* (our cervical vesicle); and (3) the *cauda thymi*, developed exclusively from a ventral outgrowth of pouch 3, and therefore purely entodermal. The caput and cauda always remain in connection, and together form the *thymus profunda*, in contradistinction to the *thymus superficialis*. The latter, however, fuses later on with the former, and becomes enclosed with it in a common connective tissue capsule. The more recent observations of ZOTTERMAN (69) essentially agree with those of KASTSCHENKO. He confirms the purely ectodermal origin of the superficial thymus, pointing out that the ductus ecto-entobranchialis II (which is very similar to that of Talpa) atrophies, taking no part in thymus formation, and the mixed (ecto-entodermal) origin of the "Thymuskopf," the pouch-entoderm taking by far the larger part in its formation. He states that there is no structural difference between the thymus ectodermalis and the thymus entodermalis: "Beide besitzen typische Thymus-struktur" (p. 528).

Lastly, in this connection, it may be noted that in Cavia, where the thymus is situated in the neck, not superficially, however, like the superficial cervical gland in Talpa and Trichosurus, but much deeper, at the sides of the trachea, the observations of ANIKIEW (1), RUBEN (50), and H. RABL (48 and 49) have shown that the gland is a thymus ecto-entodermalis III, formed partly from the lateral segment of pouch 3, partly from the sinus-ectoderm, whilst in Tarsius, NIERSTRASZ (39) has reached the conclusion that the thoracic thymus is also of the same nature, and thinks it is highly probable that the same holds true for the thoracic thymus of Nycticebus, the fourth pouch also probably taking part in its formation.

We claim to have shown in the foregoing that in Trichosurus the epithelial basis of the cervical gland is derived in major part from the ectoderm of the cranial portion of the cervical sinus, but the developmental relations are such as to prevent us from affirming that it is exclusively ectodermal, since it is possible, indeed we think probable, that a small amount of entoderm, derivative of the ventral end of the second gill pouch, is also included in the primordium of the gland. In any case, there can be no

* Presumably, in employing this name, KASTSCHENKO intended to emphasise the superficial origin of this part of the thymus, since, unlike the corresponding glands in Trichosurus and Talpa, it does not retain a superficial position in the full-grown animal.

question as to the ectodermal derivation of by far the larger portion of the primordium. That being so, we would lay special emphasis on the fact that the cervical gland, so far as we have been able to observe, differs in no essential histological respect from the thoracic glands which are unquestionably of purely entodermal origin so far as their epithelial basis is concerned. In both glands, cortical and medullary regions of apparently identical constitution are recognisable, in both Hassall's corpuscles are developed, and in connection with both accessory epithelial bodies may be present.* It would appear then that we have here a remarkable case of parallelism in histological differentiation between two glands, one with an epithelial basis largely ectodermal in origin, the other with a purely entodermal basis, and the question arises what significance are we to attach to this phenomenon? In this connection the bearing of the facts above set forth on the much discussed question of the origin of the "lymphoid" cells of the thymus (referred to elsewhere in this paper as lymphocytes), which, after all, form the characteristic and essential elements of the fully developed organ, is perhaps worthy of brief consideration. If, as certain observers (amongst whom may be mentioned BEARD (2), PRENANT (44), STÖHR (59), BELL (3)) hold, the "lymphoid" cells arise *in situ* by the transformation of certain of the cells of the original epithelial basis, then the parallelism between the cervical and thoracic thymus becomes still more remarkable, since in the former these cells would be mainly (Trichosurus) or entirely (Pig and Mole) of ectodermal derivation, whilst in the latter they would be purely entodermal and at the same time histologically indistinguishable in the two glands. But if, as various other observers (HAMMAR (21), MAXIMOW (35), and others) maintain, the thymus lymphocytes are to be regarded as immigrant elements which arise in the surrounding mesenchyme and only secondarily migrate into the epithelial basis of the gland, then the exact derivation of that basis becomes a matter of secondary importance, since it is possible to conceive of it as derived indifferently from either the ectoderm or the entoderm and to regard the differentiation of the gland as primarily induced by and dependent on the immigrant elements.

KASTSCHENKO and ZOTTERMAN, as already pointed out, have also been struck by the correspondence in histological structure between the thymus ectodermalis and thymus entodermalis in the Pig and, as concerns its significance, the latter writer has come to the conclusion "dass vom phylogenetischen Gesichtspunkte aus die Thymus ectodermalis und entodermalis als zwei verschiedene Organe betrachtet werden müssen, die durch den Parallelismus der Entwickelung gleiche Struktur erhalten haben" (p. 528). If that view is correct, and ZOTTERMAN regards it as so obvious as scarcely to need mentioning, then there is nothing further to be said except to point

* Epithelial ducts such as occur in connection with the cervical thymus of later fœtuses of Trichosurus (fig. 56, *d.t.*) are not met with in relation to the thoracic glands, but we are not inclined to attach any importance to this difference. It may be noted that PAPPENHEIMER (41) describes such structures in connection with thymus III in Man.

out that the histological parallelism between the two glands is all the more noteworthy if the "lymphoid" cells in the one are of ectodermal origin and in the other entodermal, and still noteworthy enough, if the "lymphoid" cells in both are immigrants. For our part, we are not convinced that the cervical and thoracic glands are so different phylogenetically as ZOTTERMAN assumes. We must confess we find it difficult to picture to ourselves the first origin of the cervical gland, and especially to conceive of it as arising *de novo* from the sinus-ectoderm, altogether without relationship to an entodermal thymus. That difficulty would be surmounted could it be shown that it took origin from a purely entodermal thymus II as the result of a gradual process of substitution whereby the original entodermal basis of the gland became more or less completely replaced by ectodermal cells derived from the walls of the cervical sinus, but it must be admitted that the evidence for such a mode of origin is not of a very convincing character. It may be pointed out, however, that the cervical gland of Trichosurus probably does include an entodermal component, even if small, and might consequently be regarded as more primitive than the purely ectodermal gland of Talpa or Sus, whilst the possibility of the occurrence of such a process of substitution as is indicated above is testified to by the fact already set forth that in certain mammals (Sus, Cavia, Tarsius) the primordium of thymus III does actually receive a contribution from the sinus-ectoderm. Then, as concerns thymus II, it may be noted that, although it is unknown in any adult mammal, its supposed primordium has been described by PIERSOL (43), and by SOULIÉ and VERDUN (57) in the Rabbit (though HANSON (23) expressly states he failed to find it), whilst amongst reptiles, thymus II has been described in Lacerta and other lizards by a number of investigators [DE MEURON (36), VAN BEMMELEN (4), MAURER (33), PETER (42)], and also by SAINT-RÉMY and PRENANT (51) in Anguis.

Lastly as regards the occurrence of the cervical gland in the Marsupialia, so far as we know at present, the gland is confined to the Diprotodontia, but the evidence is not yet sufficient to justify the statement that it occurs in all of them. So far, it has not been met with in any Polyprotodont, and we may state here that we have failed to find any trace of it in the embryos and fœtuses of Perameles and Dasyurus that we have examined. If, as SYMINGTON was the first to suggest and as we think probable, the presence or absence of a cervical thymus should turn out to be an ordinal character, then it adds to the Diprotodonts another of those peculiar features which so sharply mark them off from the Polyprotodonts, but as to why the gland should occur in the one group and not in the other we have no explanation to offer, nor do we think adequate the suggestion of SYMINGTON (60) that its presence in the Diprotodontia is to be correlated with their prevailing herbivorous habit, since in other mammals there is, so far as we know, no evidence whatever of any correlation between thymus and diet. Various authorities in recent years have suggested a functional relationship between the thymus and the reproductive system, but the only difference between the Polyprotodonts and Diprotodonts in respect of that system which occurs to us, relates not to the reproductive organs themselves but to the number of young, which is large in the former and small in the latter. This difference, however, as also an histological difference which Dr. C. H. O'DONOGHUE informs us he has noticed in the ovaries of the two sub-orders, can have no bearing in the present connection, since they affect the one sex.

2. *Thymus* III *and Epithelial Body* III.

The third gill-pouch (Plate 2, fig. 4, *cl.* 3) in Stages I and II appears as a well marked sac, wide dorso-ventrally, but markedly flattened in the cranio-caudal direction. It possesses a distinct ventral diverticulum and an extensive closing membrane, which involves the entire lateral margin of the pouch. In Stage IV, the pouch has assumed a more flattened tubular form, its pharyngeal opening has become greatly reduced, whilst its closing membrane, somewhat reduced in extent, has thickened as the result of the growth inwards of the ectoderm of the third ectodermal groove, so as to form an inwardly projecting cellular plate. In Stage V, the pouch has still a narrow communication with the pharynx, and is now distinguishable into a narrower duct-like proximal portion and a more expanded ventral part, connected by a solid cell-plate with the ectoderm of the ductus ecto-entobranchialis II and the upper portion of the sinus (Plate 2, fig. 10, *cl.* 3). It is luminated almost up to its ventral extremity, and measures in total length about 0·11 mm. In the following stage (VI), the pouch has advanced considerably in development. It no longer opens into the pharynx, though it is still in cellular continuity with the same, and has increased in length, now measuring 0·16 mm. Its proximal part has still the form of a tube, thick-walled, and with a distinct but short lumen. Its distal part, however, is now solid, and tapers towards its ventral extremity. The connecting plate of the two preceding stages has become interrupted, and is represented by two cellular cords, which arise from the ventral region of the pouch, and pass across to join the cranio-medial wall of the cervical sinus. One of these cords is very slender (indeed, is just indicated on the right side), and lies a little above the other, which is much thicker, and arises from the ventral extremity of the pouch (Plate 4, fig. 15, *d.e.b.* III).

By Stage VII still further progress has been made. The pouch, now finally free from the pharynx, has increased in length, measuring 0·29 mm. It has also altered in form as the result of the increase in thickness of its dorsal or proximal portion, which is still luminated. Its ventral or distal part, as in the preceding stage, is solid and tapering, and at its ventral extremity is connected, as in that stage, by a cellular cord or ductus ecto-entobranchialis III with the medial surface of the primordium of the cervical thymus. Much more important, however, than these changes is the histological differentiation which is now visible in the walls of the pouch, marking out as it does the primordia of the two derivatives of the pouch, viz., thymus III and epithelial body III. Examination shows that over the cranial wall of the dorsal luminated half of the pouch the cells are enlarged, columnar in form, and arranged so as to form a definite columnar epithelium, which stains deeply with eosin. This part of the wall constitutes the primordium of epithelial body III. Over the remainder of the pouch, including the caudal wall of its dorsal half and its ventral solid half in its entirety, the cells exhibit a looser, more irregular arrangement, and stain only slightly, if at all, with eosin. This part of the pouch forms the primordium of thymus III (Plate 4, fig. 18, *tm.* III and *ep.b.* III). In Stage VIII, the pouch exhibits the same general form as in the last, but its ventral portion or thymus primordium has now grown down below the origin of the ductus ecto-branchialis III as a well marked tapering process (Plate 3, figs. 19 and 20). The walls of the pouch exhibit precisely the same differentiation as in the last stage, only it is better marked (Plate 5, fig. 26, *tm.* III and *ep.b.* III), and at the extreme dorsal end of the pouch there are indications, in embryo (*b*) especially, of the commencing separation of the two primordia (Plate 5, fig. 30). Furthermore, small cells are present in the epithelial basis of the primordium, which we are inclined to regard as lymphocytes (fig. 26, *l.c.*). By the next stage (IX), the separation of the primordia has been completed, thymus III and epithelial body III being now quite independent. Thymus III (Plate 6, fig. 37, *tm.* III) has the form of an ovalish solid mass, situated dorso-laterally to the common carotid artery and immediately below the cervical vesicle. It measures 0·24 mm. in length by 0·09 mm. in transverse diameter, and is already becoming encapsulated. A remnant of its former connection with the primordium of the cervical thymus (sinus-ectoderm) is still present.

Epithelial body III (Plate 6, fig. 37, *ep.b.* III) lies dorsally and medially to thymus III, immediately above the common carotid artery and shortly behind the point of bifurcation of the same. It appears as an elongate tubular structure with thickened deeply-staining walls and a central lumen. It is disposed almost transversely, and measures in (*a*) 0·16 × 0·09 mm. in diameter. In Stage X, thymus III has increased somewhat in diameter, and has now shifted more caudalwards, its cranial end being situated 0·22 mm. behind epithelial body III, its caudal end reaching almost as far back as the origin of the common carotid artery from the aortic arch. Histologically, the gland essentially resembles the superficial cervical thymus, *i.e.* it consists of a cell-reticulum in whose meshes lymphocytes are present, but the latter are not yet very abundant. It contains a single large thymic cavity, and is now enclosed in a thin connective tissue capsule carrying blood-vessels. Epithelial body III occupies the same position as in the last stage, and appears as a compact flattened cell-mass, with only traces of its former lumen. It is now encapsulated.

Remarks on Thymus III.—Thymus III, *the* mammalian thymus, as HAMMAR terms it, is noteworthy in Trichosurus on account of the mode of origin of its primordium from the entire caudal, as well as the ventral wall of the third gill-pouch. In other words, thymus III is here not an exclusively ventral product of the gill-pouch, but also involves the caudal wall of the dorsal portion of the pouch. The interest of this mode of origin lies in the fact that, whereas in the majority of Eutheria, as well as in the Monotreme Echidna, thymus III is developed exclusively from the ventral portion of the gill-pouch, in the Reptiles, as the observations of DE MEURON (36), VAN BEMMELEN (4), MAURER (33), PETER (42), SAINT-RÉMY and PRENANT (51) have shown, the primordia of the thymus arise in the form of bud-like outgrowths (primitively of the nature of evaginations according to the last-named observers) from the dorsal ends of the gill-pouches (1, 2, and 3 in the case of Lacerta, thymus I being vestigial). In the case of the third pouch in Lacerta, however, MAURER finds that the dorsal thymus primordium is directly continued into a small ventrally directed appendage, representing the last remnant of the ventral diverticulum of the pouch. This he regards as a vestigial ventral thymus primordium, which is destined to disappear without forming thymus tissue. SAINT-RÉMY and PRENANT also record the existence of this ventral primordium of the third pouch; in Anguis they state it soon disappears, whereas in the case of Lacerta they affirm it participates with the dorsal in the formation of thymus III. In the opinion of MAURER, "in diesem Gebilde haben wir ein Rudiment vor uns, das bei Säugethieren den wesentlichen Theil der Thymus ausbildet" (34, p. 437), and which is to be regarded as a new acquisition by the Reptilia. However that may be, we think it will be generally agreed that we have here in Trichosurus a developmental condition which is transitional between the Reptilian mode of thymus formation and that which is met with in the majority of Eutheria.

The only other mammals in which, so far as we are aware, a corresponding mode of origin of thymus III has been observed are Homo and Cavia. In the human embryo, according to GROSSER (17, p. 463), "the formation of the thymus is preceded by the elongation of the ventral diverticulum, which extends ventrally and medially, and whose epithelium, consisting of closely-packed cells, increases in height on the aboral wall of the diverticulum. *This thickening of the epithelium extends also upon the aboral and dorsal walls of the pouch itself*" (italics ours). Compare also the remarks of GROSSER in the discussion on the paper of RABL (48, p. 161) and the account of HAMMAR (20, p. 208).

In Cavia, according to RABL (49), the third pouch becomes divided through a constriction into a medial part, the primordium of the epithelial body, and a lateral part, the primordium of the thymus. RABL remarks, "In dieser Anordnung spricht sich eine bedeutungsvolle Aehnlichkeit mit den Verhältnissen bei den niederen Wirbeltieren aus" (p. 121).

In the Rabbit, HANSON (23) describes the primordium of thymus III as appearing in the 7·2 mm. embryo in the form of a funnel-shaped diverticulum from the ventral wall of the third pouch. So also in the Mole, thymus III is a purely ventral derivative of the pouch. According to RABL (46), its primordium is first seen in the 6·5 mm. embryo in the form of a medio-caudally directed outgrowth from the caudal end of the ventral (earlier cranial) wall of the third pouch. It is at first solid but later becomes tubular.

As concerns the differentiation of pouch 3 as a whole we have seen that in Trichosurus, the cranial wall of the dorsal luminated half of the pouch, composed of a definite columnar epithelium, gives origin to epithelial body III, whilst the remainder of the pouch, comprising the caudal wall of its dorsal half and the ventral solid portion of the pouch in its entirety, gives origin to the primordium of thymus III. The entire epithelium of the pouch proper is thus used up in the formation of these two structures. The same holds true for Talpa and Cavia according to RABL, whereas in the rabbit (HANSON, 23) and in the human embryo (HAMMAR, 20), part of the pouch-wall remains unused and later degenerates.

Precise statements in regard to the differentiation of the walls of pouch 3 into the primordia of thymus III and epithelial body III are not numerous in the literature. In the human embryo, according to GROSSER (17, p. 463), the primordium of thymus III, as already noted, is furnished by a thickening of the epithelium of the aboral wall of the ventral diverticulum as well as of the aboral and dorsal walls of the pouch itself, whilst that of epithelial body III is constituted by a proliferation of "the oral and lateral walls of the dorsal diverticulum and of the pouch itself," the cells of which appear to be vacuolated, whilst their plasma is reticular and lightly staining, and their cell-boundaries are at first indistinct.

According to the observations of HAMMAR (20) in the human embryo, the histological differentiation of the thymus-complex begins first with epithelial body III, which appears as a thickening of the dorsal wall of the pouch in the 8·3 mm. embryo and then extends from there over the adjacent portions of the lateral and oral walls. At first the thickening has the character of a diffuse cell-mass, whose cells are distinguishable from those adjacent by their somewhat large size and their clear transparent character. The thymus-primordium differentiates somewhat later than the epithelial body, and here again the cells are characterised by their somewhat larger size and paler staining qualities as compared with those of the "Schlundtaschenrest."

In Cavia, RABL (49) first recognises the histological differentiation of the pouch-walls in an embryo of 10·7 mm. In the primordium of the epithelial body "ist nämlich das Epithel der Taschenwand geschichtet, die Kerne sind rundlich, das Plasma hell, zwischen den einzelnen Zellterritorien sind an günstigen Stellen blass rosenrote Grenzlinien wahrzunehmen": in the primordium of thymus III "wird die Wand noch wie früher von einem mehr-reihigen Epithel gebildet, in welchem sämtliche Kerne längsoval, die Zellkonturen senkrecht zur Oberfläche gerichtet sind." In the case of the Mole, the same author states that the thymus arises as an outgrowth from the caudal end of the ventral (earlier cranial) wall of the pouch, as already mentioned above, whilst the epithelial body is derived from the whole of the secondary pouch and not simply from a dorsal diverticulum of the same. According to HANSON (23) in the 7·2 mm. embryo of the Rabbit, the thymus arises as a diverticulum from the ventral wall of the pouch, whilst the epithelial body is first recognisable as a proliferation of the epithelium of the dorsal wall of the pouch, the cells exhibiting a different appearance to those of the remainder of the pouch, the nuclei being less compactly arranged and the protoplasm more transparent (*cf.* Trichosurus). In the 8 mm. embryo this differentiation has extended into the adjoining parts of the cranial, caudal and lateral walls.

In Echidna, according to MAURER (34), the primordium of epithelial body III is recognisable in embryo 42 of SEMON'S series as a vesicular enlargement of the dorsal end of pouch 3. From this swelling, the pouch runs ventrally to terminate as a slightly curved, thickened tube. This ventral part of the pouch represents the primordium of thymus III.

3. *Thymus* IV *and Epithelial Body* IV.

The fourth gill-pouch (Plate 2, fig. 4, *cl.* 4) is much smaller than the third. In the earlier stages (I, II and III), it is seen to take origin from a wide but shallow lateral outbaying of the pharyngeal wall, from the hinder portion of which the fifth pouch also arises. This outbaying represents the primordium of the common duct (the pharyngeal duct as we have termed it or *ductus pharyngo-branchialis communis* IV and V such as exists in the human embryo, and in Talpa and Cavia), through which the fourth pouch and ultimo-branchial body come to communicate with the pharynx, and which is distinct in Stage VI. From the pharyngeal bay, the fourth pouch runs outwards and downwards to join the ectoderm of the fourth ectodermal groove. It is flattened obliquely in the cranio-caudal direction and possesses a narrow lumen. Its closing membrane involves the entire lateral margin of the pouch and is much thicker than that of the third, ectoderm and entoderm never becoming completely fused. In Stage IV, the pouch (Plate 4, fig. 9, *cl.* 4) exhibits a distinct advance on that of the earlier stages. It is now distinguishable into proximal or medial and distal or lateral portions. The proximal part is enlarged and luminated and extends ventrally and cranially, its ventral wall being thickened. The distal part is disposed transversely and has the form of a solid process which is connected with the ectoderm of the caudal depression of the sinus by an irregular loose cellular cord (of ectodermal derivation, as comparison with the next stage shows). This cord and the solid lateral process of the pouch together form a ductus ecto-entobranchialis IV, here precocious in its degree of development since it is already much more attenuated than that of the next stage (V). In the latter stage, the same proximal and distal portions of the pouch are again recognisable. The proximal part presents much the same features as before but its ventral and cranial walls are more thickened and are produced into a short but distinct ventro-medial process. The distal part is stalk-like but is less reduced than that of the last stage, a remnant of its lumen being still present. It is connected with the sinus-ectoderm forming the medial wall of the vesicle-duct by a quite short ectodermal ingrowth, the distal part of the pouch and the latter together forming the *ductus ecto-entobranchialis* IV (Plate 4, fig. 11, *d.e.b.* IV), which is much thicker than that of the last stage.

In Stage VI, the pharyngeal bay has become transformed into a short duct (the pharyngeal duct above mentioned), appearing as a backward prolongation of the caudo-lateral region of the pharynx, from which the fourth pouch and the ultimobranchial body arise. The fourth pouch at its origin is roughly circular in section and almost immediately there passes off from it the ductus ecto-entobranchialis IV, now very thin and greatly elongated, which joins the sinus-ectoderm just below and in front of the vesicle-duct. Below the origin of this duct, the pouch broadens transversely and continues caudo-ventrally as a well marked prolongation with thick walls and a narrow lumen. The pouch has now a dorso-ventral length of 0·11 mm. as compared with 0·06 mm. in the preceding stage. It is thus evident that marked growth in the caudo-ventral direction has taken place in the interval between this stage and the preceding. In Stage VII, the pharyngeal duct has increased in length and the fourth pouch has acquired a more definitely tubular shape. It possesses thick walls and a narrow lumen, best marked in the thicker dorsal part of the pouch, and more reduced or absent in its tapering ventral part. On the left side the ductus ecto-entobranchialis IV is still retained but on the right it has disappeared.

In Stage VIII, the fourth pouch has increased still further in length, now measuring 0·16 mm., but its most marked advance is in histological differentiation, since the primordia of thymus IV and epithelial body IV are now clearly recognisable. It also shows alteration in the details of its form as compared with the last stage. It leaves the pharyngeal duct as a short transversely disposed tube which enters the main part of the pouch, now disposed obliquely, shortly above the pericardial cavity. The ventral portion of this region of the pouch is now thicker than the dorsal and is directed downwards and forwards. In embryo (*a*), the pouch-lumen is distinct, but in (*b*) it is reduced and practically confined to the duct-like upper part of the pouch. The ductus ecto-entobranchialis IV has completely disappeared. The wall of the pouch exhibits a histological differentiation quite comparable with that shown by pouch 3 in Stage VII. Here, however, the primordium of epithelial body IV is formed by the dorsal part of the pouch, including both its cranial and caudal walls, whilst the primordium of thymus IV is formed by the larger ventral portion of the same, whose walls are markedly thickened (Plate 5, fig. 27, and Plate 6, fig. 35, *tm.* IV, *ep.b.* IV). In Stage IX, the pouch has lost its connection with the pharyngeal duct (though its epithelial body is still connected in embryo (*a*) with the original cranial (now caudal) end of the ultimobranchial body) and its derivatives have either just separated (embryo (*a*)) or are in process of separation (embryo (*b*)). Thymus IV (Plate 6, fig. 39, *tm.* IV) lies just caudally to thymus III and close above the dorso-cranial extremity of the pericardium. It is very similar to thymus III in structure but is smaller and more spherical in shape. In (*a*), on the right side, a slender secondary connection has already been established between thymus III and thymus IV. Epithelial body IV lies dorsally and slightly caudally to thymus IV. In (*a*), where it is completely separated from the thymus, it has the form of a narrow tube with epithelial walls, which is still connected by a degenerating tract of cells with the hinder (originally cranial) end of the ultimobranchial body. In (*b*) the epithelial body is still in continuity with the dorsal end of the thymus and its lumen extends into the latter, where it is enclosed by epithelially arranged cells. It is possible that this portion of the pouch-lumen may persist in the thymus as a thymic cavity.

In Stage X, thymus IV and epithelial body IV are quite separate and independent structures. Thymus IV is similar to thymus III in structure but possesses two thymic cavities, one of them being very large (Plate 7, fig. 42, *tm.c.*). It has also shifted caudally but only to a slight extent. Epithelial body IV lies on the dorsal side of the thymus and appears as a small deeply staining mass with only a remnant of its lumen.

Remarks on Thymus IV.—HAMMAR in his review (19, p. 208) points out that no case is known of the constant occurrence of a thymus IV amongst the Mammalia, and goes on to remark "da ganze Säugerordnungen diesbezüglich unerforscht sind, ist allerdings die Möglichkeit zurzeit nicht ausgeschlossen, dass es wirklich Säuger mit konstant dimetamerem Thymus-Typus gibt." That possibility is now seen to be realised in Trichosurus, which thus acquires the distinction of being the first mammal to be described in which thymus III and thymus IV are constantly present.

The fact that thymus IV may occur amongst the Eutheria appears to have been first definitely established by GROSCHUFF (13) in a paper published in 1896. He stated that it occurs constantly in the Calf and Cat, occasionally in the Sheep, as traces in the Horse and Goat and he inferred its presence in Man. In a later paper (14) he corrects his former statement in regard to its constancy in the Calf and Cat and states that it is not of constant occurrence in any mammal but is to be regarded only as more or less frequent in those mammals which possess an epithelial body IV. GROSCHUFF showed that the small masses of thymus tissue associated with an epithelial body which had been observed by KOHN (29) and others imbedded in the lateral lobes of the thyroid in the Cat, Dog, and Rat, and which were distinguished by KOHN as "inner thymus-lobes," really represent thymus IV which has become secondarily included in the same along with epithelial body IV through the intermediation of the ultimobranchial body.

HAMMAR (19, p. 208) summarizes the observations of NICOLAS, SCHMID, VERDUN, and CRISPINO in the statement that "die Thymus IV ist bei Katze, Kaninchen, Igel, Kalb, Schaf, spurenweise auch beim Pferd und bei der Ziege angetroffen werden," and states that "JOHNSTONE (1898) vermutet sie bei gewissen Marsupialiern." What JOHNSTONE did say is that "the cervical thymus may probably arise from the fourth branchial pouch" (26, p. 554).

In the human embryo, the presence of thymus IV has been recorded by

GROSCHUFF (14), HERRMANN and VERDUN (24) and others. According to GROSSER, the ventral diverticulum of the fourth pouch is much more feebly developed than that of the third, and "it only occasionally undergoes development into thymus-tissue." ERDHEIM (6) also states that thymus IV in Man is rarely developed, and even when formed is a quite small nodule.

Lastly it may be noted that amongst the Reptilia, the constant occurrence of thymus III and IV has been recorded for certain snakes by VAN BEMMELEN (4) and SAINT-RÉMY and PRENANT (51).

As concerns the occurrence of thymus III and thymus IV in other Marsupials, we may state that we have observed both glands in Dasyurus and Perameles and also in Macropus, where they have already been observed and figured by JOHNSTONE (26), although he did not recognise them as such. It is, therefore, clear that this condition must have occurred in the common ancestor of the Polyprotodontia and Diprotodontia, and since rudiments of thymus IV have been met with in various Eutheria we are further justified in concluding that this condition was also characteristic of the common ancestral stock from which the Marsupials and Eutheria diverged.

With regard to the differention of the fourth pouch it may be recalled that the primordium of thymus IV, unlike that of thymus III, but like that of thymus III in many Eutheria, is furnished exclusively by the ventral portion of the pouch, whilst the primordium of epithelial body IV is constituted by the dorsal portion of the same, including both its cranial and caudal walls. In the human embryo, GROSSER (17) states that epithelial body IV "is formed from the dorsal and lateral portion of the pouch." In Echidna (MAURER), the Rabbit (HANSON), and in the Guinea-pig (RABL), the whole pouch is converted into the epithelial body.

4. *Later History of Thymus* III *and* IV.

The epithelial basis of thymus III is derived, as we have seen, from the caudal wall of the dorsal luminated half of pouch 3 as well as from the solid ventral portion of the pouch, the latter forming the main part of the primordium, whilst that of thymus IV is furnished exclusively by the larger ventral portion of pouch 4, including both its cranial and caudal walls. The primordium of thymus III first becomes recognisable in Stage VII after pouch 3 has lost its connection with the pharynx, and that of thymus IV in Stage VIII, the pouch being still connected with the pharynx. Lymphocytes first appear in both the cervical thymus and thymus III in Stage VIII, but do not become numerous until much later. By Stage IX, thymus III has become an independent structure and thymus IV is either independent or is in process of becoming so. By Stage IX, they have practically acquired their adult positions and have become encapsulated. The further differentiation of the thoracic glands is essentially similar to that of the cervical gland. Apart from growth in size, no great advance is seen until we reach the new-born fœtus (Stage XV). At this stage, right thymus III measures 0·27 mm. in length, and right thymus IV, 0·22 mm. Both glands are now becoming lobulated as the result of the ingrowth of vascular connective tissue septa from the enveloping capsule, and they now exhibit differentiation into a very small central zone formed almost exclusively of epithelial elements and a more extensive marginal zone containing numbers of lymphocytes. By Stage XVIII, the glands are well advanced towards the adult condition. They are lobulated and vascular, whilst cortical and medullary zones are now clearly recognisable. In the former there are numerous lymphocytes, whilst in the latter Hassall's corpuscles are present, some well advanced, others in process of formation. In our last fœtal specimen (XXII), left thymus III (Plate 10, fig. 62, *tm.* III) measures 1·36 mm. in length and left thymus IV (fig. 63, *tm.* IV), 0·96 mm. Apart from size, the glands differ in no essential respect from those of the adolescent animal.

Our observations demonstrate that two pairs of thoracic glands are invariably formed in Trichosurus, but that number is not always found in later fœtuses since secondary fusion may take place between the two glands of each side. In our Stages XI to XXII inclusive, we find seven specimens in which thymus III and IV are separate on both sides, four in which they are fused on both sides and five in which they are fused on one side (four having the right glands fused, and one the left glands). Thymus IV is usually smaller than thymus III, and the latter, it may be noted, is normally considerably smaller than the cervical thymus.

An accessory thymus lobe is present in embryo (*b*), Stage XIV, situated caudally to right thymus IV and cranially to it is an extra epithelial body. In Stage XXII also, an accessory lobe occurs on the right side, laterally to the carotid artery and on a level with the lateral thyroid lobe.

The occurrence in the cervical and thoracic thymus of thymic cavities, cystic vesicles (related to Hassall's corpuscles), and closed epithelial ducts (in connection with the cervical glands only) is recorded in the descriptive part of this paper but no attempt has been made to deal with these structures in any detail. For information in regard to their occurrence in other forms, the reader is referred to the summary of HAMMAR (19, p. 120) and to the paper of PAPPENHEIMER (41). As regards the thymic cavities, it is possible, indeed probable, that in the thoracic glands these may sometimes be primary formations, *i.e.* they may represent persistent remnants of the original pouch-lumen, and in this connection it may be noted that they are most constant in thymus IV, the lumen of which is originally more extensive than that of thymus III. In other cases, as for instance in the cervical thymus, these cavities are undoubtedly secondary. As regards the epithelial ducts which occur exclusively in connection with the cervical thymus, it is to be noted that these make their first appearance in a relatively late stage (XVII). We regard them as purely secondary structures. Such ducts have been described by various observers in Man and also in the Cat and Rabbit; according to PAPPENHEIMER (41), they are found in the human thymus chiefly in fœtal life or early childhood and occur principally in the interlobular septa and cortex. He thinks "it is probable that they are derived from a partial persistence of the original invagination of the third branchial cleft" but it is clear that in Trichosurus they can have no such origin.

5. *Epithelial Bodies.*

The two principal epithelial bodies (III and IV) originate, as already described, from gill-pouches III and IV.

Epithelial body III is derived from the cranial wall (including the extreme tip) of the dorsal luminated half of pouch III, the remainder of the pouch forming thymus III. Its primordium first becomes recognisable at Stage VII, and by Stage IX it has separated from the thymus and appears as a short tubular structure, situated dorso-medially to the latter, just above the common carotid artery and shortly behind its point of bifurcation (Plate 6, fig. 37, *ep.b.* III). By Stage X, it has acquired the form of a compact flattened cell-mass, already encapsulated and with only traces of its former lumen. It soon becomes quite solid and it gradually increases in size. At Stages XIII and XIV, vascular ingrowths from its capsule are penetrating into it, with the result that it presents a lobed appearance (Plate 7, fig. 48). Under continued penetration of capillaries, its constituent epithelial cells become arranged in irregular anastomosing lamellæ and cords, formed of two cell layers in close apposition. Between the lamellæ run sinusoidal capillaries. Thus by Stage XVIII, the epithelial body is well advanced towards the adult condition. It retains its primitive position dorsal to the common carotid and shortly behind the fork of the same, until Stage XVIII. After that, it usually moves forwards slightly and comes to lie cranial to the carotid fork, between the external and internal carotid arteries or in close proximity to one or other of them.

Epithelial body IV is derived from both the cranial and caudal walls of the dorsal portion of the fourth pouch, its primordium first becoming distinguishable in Stage VIII. It separates from thymus IV in Stage IX (*a*) and, like III, has at first the form of a short closed tube with deeply staining walls, situated dorsally to thymus IV. It soon loses its lumen, and by Stage XI has become solid and compact. Its further development (see Plate 8, fig. 57, *ep.b.* IV, and fig. 64) is precisely similar to that of III, and though it commences to be vascularised a little later than the latter, viz., at Stage XV (*b*), by Stage XVIII it is quite as far advanced as III.

As concerns its position, epithelial body IV is less constant than III; usually it retains its primitive position, close to thymus IV, lying either dorsally or laterally to the same, but it may lie far cranial to it as in Stages XVII (*a*) (Plate 8, fig. 52, *ep.b.* IV), XXI and XXII, on one or both sides, or it may lie caudally to it as in Stages XIV (*b*), XVII (*a*), and XIX. Frequently the glands of the two sides exhibit an asymmetrical disposition. Where thymus III and IV are fused, the epithelial body is usually situated laterally to the mid-region of the single gland. Only exceptionally is it included in the thymus as in Stage XX (*b*) and perhaps XVIII, though in the latter it is possible the body imbedded in the right thymus is an accessory one.

In addition to the paired epithelial bodies III and IV which we may distinguish as the primary epithelial bodies, since they are developed directly from the epithelium of pouches III and IV, accessory epithelial bodies, not necessarily paired and either extra- or intra-thymic in position, are met with in later stages in connection with thymus IV and with fused thymus III and IV. We have no direct observations as to the mode of origin of these accessory bodies and can only suppose that they originate from persistent remnants of the original pouch-epithelium.* Their occurrence is recorded in the descriptive part of this paper for Stages XV (*b*), XVIII, XX (*a*), XXI, and XXII.

Such accessory epithelial bodies are also met with, not infrequently, in the superficial cervical thymus, either imbedded superficially in the thymus tissue or situated between the lobes of the gland. They are recorded for one or both cervical glands in Stages XVII (*b*), XIX, XX (Plate 8, fig. 60), XXI, and probably also in XV (*b*), and it may be recollected they may also occur in the adult gland (*cf.* p. 6).

It is worthy of emphasis that the accessory epithelial bodies, whether related to the thoracic or to the cervical thymus, differ in no respect histologically from the primary. In this connection the origin of the epithelial body of the cervical thymus is a matter of interest but unfortunately it is impossible to determine whether it develops from the ectodermal constituents of that gland or from its presumed entodermal component. If from the former, and if the Hassall's corpuscles present in the cervical thymus are also derived from the same,† then we have further instances of that extraordinary parallelism in differentiation between the mainly ectodermal cervical thymus and the purely entodermal thoracic thymus to which attention has already been directed (p. 50).

For a general account of the epithelial bodies in Eutheria the reader is referred to the article of KOHN (30).

Epithelial bodies III and IV of Trichosurus resemble those of Echidna and of the lower vertebrates in general in that they acquire no secondary relationship with the thyroid, as do those of nearly all Eutheria. Epithelial body III retains throughout life its primitive position in relation to the carotid fork, as is also the case in the Sheep (PRENANT, 44) and as may occasionally happen in Man (GROSSER, 17, p. 471), whilst epithelial body IV remains in proximity to thymus IV. In Echidna, according to MAURER (34), an epithelial body II is present in addition to III and IV. It lies in

* In this connection it may be recalled that in the involuting adult thymus we have observed that the thymus-reticulum may assume a histological character suggestive of that of the epithelial bodies.

† Hassall's corpuscles occur in the cervical thymus of the Mole, according to SCHAFFER (52), and also in that of the Pig, according to ZOTTERMAN (69), but in neither case is the occurrence of an epithelial body recorded for the gland. In both cases the glands are described as being of purely ectodermal origin (H. RABL, ZOTTERMAN).

the carotid fork, thus occupying the same position as epithelial body III in Trichosurus, whilst III lies imbedded in the anterior end of thymus III and IV just anterior to the latter. In Anguis, according to SAINT-RÉMY and PRENANT (51), epithelial bodies III and IV are laid down, but only the former persists, lying close to thymus III. In Tropidonotus, according to the same observers, epithelial bodies III, IV, and V are laid down, III and IV persisting; III lies in the neighbourhood of the carotid artery and IV adjoins the thymus.

Amongst the Eutheria, epithelial body III usually migrates back with thymus III until it reaches the thyroid and may either become imbedded in the same or remain outside it; epithelial body IV also comes into relation with the thyroid through the intervention of the ultimobranchial body and usually becomes more or less completely enclosed in the same, along with thymus IV when that is present. There is, however, a good deal of variation in the relations of the epithelial bodies to the thyroid in the Eutheria, and in a number of the latter, epithelial body IV is absent.

It is clear that the relations of these bodies in Trichosurus and Echidna afford no justification for the employment of the name parathyroids as designatory of these structures.

As concerns the origin of the epithelial bodies we need only point out here that whereas in the Reptilia (MAURER, SAINT-RÉMY, and PRENANT) the epithelial bodies arise from the portion of the gill-pouch situated ventrally to the thymus-primordium (from the middle region of the pouch where a ventral thymus-primordium is recognisable), in the Mammals generally they arise from the dorsal region of the pouch, from the cranial wall of its dorsal half in the case of epithelial body III in Trichosurus and from the entire dorsal portion of the pouch in the case of epithelial body IV.

In the details of their differentiation, the epithelial bodies of Trichosurus would appear to agree closely with those of the human embryo as described by HAMMAR (20, p. 207). He writes:—"Schon beim Embryo 11·7 mm. bis zeigen die Zellen eine trabekuläre Anordnung: diese macht sich anfangs nur durch die reihenartige Anordnung der Zellenkerne bemerkbar, bald findet man aber spärliche Bindegewebskerne spindeligen Aussehens zwischen den Reihen, noch etwas später sind unter ihnen Gefässe bemerkbar."

Lastly, as concerns the occurrence of accessory epithelial bodies in Eutheria, it may be noted that such have been recorded by ERDHEIM (7) for the Rat, Rabbit, and Hedgehog and by ZUCKERKANDL (70) and KÜRSTEINER (31) for Man.

6. *Thyroid.*

The primordium of the median thyroid is present in Stage I in the form of a hollow median outgrowth of the entoderm of the pharyngeal floor, situated between the second and third gill-pouches. It is sessile, no distinct thyro-glossal duct being present, and communicates with the pharyngeal lumen by a slit-like aperture.

In the succeeding stage it is still connected with the pharynx in embryo (*a*) (Plate 2, figs. 4 and 5, *th.*), but in (*b*) it has separated, appearing as a closed, bluntly spindle-shaped tube 0·16 mm. in length, with thick walls and a narrow lumen. In the following stages it gradually increases in length and in thickness, and at the same time it broadens out behind, and its original lumen becomes replaced by a number of small disconnected flattened cavities. By Stage IX the lateral portions of the primordium have grown slightly upwards, and in embryo (*b*) have increased in thickness, so that it is now possible to distinguish between a median connecting bridge and lateral lobes. By Stage XI (Plate 7, fig. 43, *l.th.*) marked progress has been made. The lateral lobes, situated ventro-laterally to the trachea shortly behind the larynx, have increased markedly in size, and now measure 0·26 mm. in length. They have extended still further in the dorsal direction, and, owing to the forward growth of the ultimobranchial bodies, they now lie in close proximity to these structures, indeed, the right ultimobranchial is already in contact with the corresponding thyroid lobe. Cleft-like cavities are present in the bridge, and more sparsely in the lobes.

The gland is now becoming enclosed in a connective tissue capsule carrying small blood-vessels. In the following stage (XII) the thyroid lobes and ultimobranchial bodies have come into close contact, whilst, under the influence of vascular connective tissue ingrowths, the formerly compact tissue of the gland is now becoming broken up into an irregular system of cellular cords, some solid, others luminated. In Stage XIII the thyroid and ultimobranchial bodies have become enclosed in a common capsule. The ingrowth of vascular connective tissue septa proceeds actively, with the result that, in the new-born fœtus (Stage XV), the lateral lobes appear distinctly lobulated, and are well vascularised. In the following stages the lobulation, as well as the vascularity of the lobes, increases, and the cell-cords become better defined. In Stage XVIII the lateral lobes have reached a length of 0·5 mm., and the cell-cords are now beginning to break up into small cell-masses, many of them luminated, so that the formation of the definitive thyroid vesicles may now be said to have commenced. The connective tissue, which relatively to the epithelial constituents of the lobes is abundant, is now beginning to form delicate investments around the differentiating vesicles. By Stage XXII the vesicles have increased in size, and their lumina are better marked, but they are still quite minute as compared with those of the adult, and the formation of colloid has apparently not yet commenced.

The relation of the ultimobranchial bodies to the thyroid is discussed in the following section. We need only say here that, whilst we are inclined to believe that the ultimobranchial bodies contribute to some extent to the formation of the lateral lobes, unquestionably by far the major portion of the epithelial constituents of the thyroid is furnished by the median primordium.

The developmental history of the median thyroid primordium appears to differ in no essential respect from that in other mammals. The primordium itself agrees with that of reptiles and birds, as well as with that of the human embryo in its vesicular form (though in the latter the occurrence of a lumen is said to be variable), but it is rather more posteriorly situated, since it lies just behind the level of the second gill-pouch, and not between the first and second pouches, as appears to be usual.

In Talpa, RABL (46) describes the primordium as a small solid body connected with the pharyngeal floor by a short stalk, whilst in Cavia, according to the same author (49), the primordium is exceptional in that it appears as a group of short luminated processes arising from a median pharyngeal groove, close behind the level of the first gill-pouch. In the 5 mm. Pig, according to MOODY (37), the median primordium appears as a compact syncytium, forming a bilobed elongated mass, situated at about the level of the second gill-arch. He states that follicles with completed walls are first met with in embryos of 70 mm. According to GROSSER (17), follicles first begin to appear in human fœtuses of about 50 mm. vertex-breech length. Most observers agree in stating that the follicles arise by the breaking-up of the thyroid epithelial cords into groups of cells, some luminated, others solid.

7. *Ultimobranchial Body.*

In Stage I there arises from the hinder region of the pharyngeal bay, from which also the fourth pouch takes origin, a ventrally directed tubular structure which we think probably represents the fifth gill-pouch as well as the ultimobranchial body. We have accordingly termed it the posterior pharyngeal complex. It measures in embryo (*c*) about 0·12 mm. in total length and consists of a thicker dorsal part with a distinct lumen, and a thinner, more cylindrical, and slightly tapering ventral part with thickened walls and a narrow lumen. The dorsal part runs down close below, and is even slightly prolonged towards, the bottom of the fifth ectodermal groove, and from its relations, as well as from the existence of a distinct fifth aortic arch in the third branchial arch, we are inclined to regard it as representing the fifth gill-pouch. The ventral part undoubtedly belongs to the ultimobranchial body. In the absence of the immediately preceding stages of development we cannot be quite certain of the correctness of the identification of the dorsal part of the so-called complex as the fifth pouch. It may be that the whole of the tubular structure in question should be regarded simply as ultimobranchial body but we favour the first interpretation. In Stage II, the complex shows no evidence of its presumed composite character and is now a typical ultimobranchial body. It appears externally as an elongate somewhat bulbous structure (Plate 2, fig. 4, *u.b.*) connected with the pharyngeal bay by a narrow neck. It possesses thick walls and a narrow lumen and in embryo (*b*) has already reached a length of 0·16 mm. In Stage III, owing to the narrowing of the pharyngeal bay, it has come to open from the same shortly behind and dorsally to pouch 4. It is club-shaped in form and measures 0·15 mm. in length. In the next stage, it has attained a length of 0·18 mm., so that it reaches a large size at a relatively early stage.

By Stage VI, the pharyngeal bay has become converted into the pharyngeal duct, from the hinder end of which the fourth pouch and ultimobranchial body take their origin practically together. The latter runs back dorsally and medially to the former and medially to the systemic arch. It begins as a relatively thin tube but thickens considerably in its hinder part and is now more massive than in the preceding stages. In the succeeding stages, the pharyngeal duct (Plate 6, fig. 33, *ph.d.*) lengthens, and the hinder portion of the ultimobranchial body thickens still more and at the same time becomes flattened, whilst the hinder ends of the two bodies move nearer to the middle line, with the result that the bodies (Plate 5, fig. 32, *u.b.*) as a whole acquire an obliquely transverse position.

By Stage IX they have undergone a further noteworthy change in their relations, since they have moved forwards and upwards in such a way that their original hinder or ventral ends are now directed cranially and have come to lie just postero-dorsally to the lateral lobes of the thyroid (*cf.* Plate 6, fig. 38, with Plate 5, fig. 29). They have now lost connection with the pharyngeal ducts and their cranial ends are markedly thickened. In the next stages, the ultimobranchial body approaches still closer to the corresponding thyroid lobe and finally, in Stage XII, has come to lie in close contact with the dorso-medial surface of the same. In Stage XIII, the two structures are enclosed in a common connective tissue capsule and then in the following Stages, XIV to XVII, the ultimobranchial body enters on a period of marked proliferative activity, traces of which are indicated as early as Stage XII. In Stage XIV, the body lies in close contact with the medial side of the anterior two-thirds of the thyroid lobe. It measures 0·21 mm. in length and appears as a conspicuous structure with a well-marked lumen surrounded by thick deeply staining walls. The latter, especially on the side next the thyroid, are now in process of producing solid sprout-like cellular processes which penetrate into the tissue of the lobe and become so intimately related thereto that it is frequently impossible to say where the sprout ends and the thyroid tissue begins (Plate 8, figs. 46, 50, and 50A, and Plate 9, fig. 49, *u.b.*, *spr.*, and *l.th.*). The same sprouting is seen in Stages XV and XVI and is especially well marked in Stage XVII, where the ultimobranchial body is a conspicuous massive structure (Plate 9, fig. 55, *u.b.* and *spr.*).

It is thus clear that in Trichosurus the ultimobranchial body actively proliferates and produces cellular sprouts which penetrate into the tissue of the thyroid lobe. We have to admit, however, that we have no conclusive evidence as to the fate of these sprouts, since they are only distinguishable so long as they are connected with the parent body. They must either participate in the formation of the lateral lobes or undergo degeneration. As regards the latter alternative, the evidence we have (*cf.* Stage XIV, p. 34) indicates that those sprouts which fail to pass into the tissue of the thyroid lobe do degenerate just as the main mass of the ultimobranchial body usually does after proliferation has ceased, but we have no such evidence in the case of those which penetrate into the thyroid tissue, and they are such well defined and conspicuous formations that we should certainly expect to find some evidence of cellular degeneration going on in the thyroid lobe, if that is their fate. Nor have we any evidence that the sprouts, whilst still connected with the parent body, undergo a gradual process of atrophy at the same time as the latter. In favour of the former alternative the following considerations tell. The sprouts, beyond staining at first rather more deeply than the thyroid tissue, differ in no essential respect from it. They frequently appear to pass over into direct continuity with that tissue, and small cavities quite similar to those in the thyroid tissue also make their appearance in them. In this connection also it may be emphasised that the ultimobranchial bodies themselves undergo a progressive development right up to and including the proliferative stage, and that, when fully formed, they are relatively massive, active-looking structures, showing no signs of decrepitude. We find it difficult to understand their persistence in such an apparently well developed and active condition if they are purely vestigial organs. Our study of them leads us to regard it as probable that they do in some degree contribute cellular material to the lateral lobes. At the same time we feel bound to add that that contribution must be a relatively small one, since it is unquestionable that by far the greater part of the lateral lobes is furnished by the median thyroid primordium.

At Stage XVIII the ultimobranchial body lies imbedded on the dorsal side of the lateral lobe, and is already reduced. On the left it appears as a short tubular structure, about 0·09 mm. in length, with a large lumen enclosed by moderately thin walls, which are apparently no longer proliferating. On the right it is still further reduced and almost solid. In Stage XX a remnant of it is visible in the centre of the right thyroid lobe in fœtus (*a*), but it is not distinguishable in the left lobe or in fœtus (*b*), and the same holds good for Stage XXI. In Stage XXII, however, remnants of it are again observable as tubular cavities surrounded by darkly staining walls, more or less deeply imbedded in the thyroid lobes.

Remarks on the Ultimobranchial Bodies.—The paired structures which, following Greil (12), we now distinguish as the ultimobranchial bodies have passed under a variety of names (suprapericardial bodies, van Bemmelen; accessory, lateral, or posterior thyroid primordia, Born, de Meuron and others; postbranchial bodies, Maurer), and have been variously interpreted. The older investigators (Born and others) regarded them as diverticula of the fourth pair of gill-pouches. Maurer (32), from his observations on Amphibia, came to the conclusion that they were not of gill-pouch origin, but developed independently from the pharyngeal entoderm immediately behind the last existing pair of pouches, whether that be the sixth, fifth, or fourth. Accordingly, he termed them the *postbranchial* bodies, a name which passed into general use. Greil (12), however, as the result of a comparative study of these structures in Fishes and Amphibia, reached the conclusion that they are not postbranchial in the sense of MAURER, but are derived in all cases from the actual last pair of gill-pouches, which has become more or less vestigial, viz., the seventh in Selachii and Dipnoi, the sixth in Amphibia. He therefore proposed to term them the *ultimobranchial* bodies, a designation which has been adopted by RABL, GROSSER and others. Amongst the Mammalia, later writers, SOULIÉ and BONNE (56), TOURNEAUX and SOULIÉ (64), H. RABL (46), GROSCHUFF (13), TANDLER (62), GROSSER (16) and others have recognised the occurrence of a fifth pouch, and have regarded the ultimobranchial body as derived from it. More recently, however, H. RABL (49), on the basis of his own observations on the Duck (47), as well as those of PETER (42) on Lacerta, and of GREIL on Rana and Hyla, has seen reason to alter his former view, and has come to the conclusion that the ultimobranchial body in mammals is to be regarded not simply as a diverticulum of the fifth pouch, but as the derivative of the sixth pouch, as it has been held to be in the lower forms mentioned. He points out that, in the Bird, the fourth, fifth, and sixth pouches, in consequence of the reduction of the intervening arches, communicate with the pharynx, not directly, but by way of a common lateral outbulging of the same. The complex so formed, RABL has termed the caudal pharyngeal diverticulum, and he regards it as comparable with the caudal pharyngeal complex (GROSSER, 17), which, in the human embryo, is held to include the primordia of the fourth and fifth pouches. In RABL'S view, however, the supposed primordium of the fifth pouch, though appearing as a single groove in the human and other Mammalian embryos, really includes that of the sixth pouch also, the two primordia forming a single groove as the result of the complete suppression of the sixth visceral arch, which already in the Sauropsida is greatly reduced.

So far as our own observations go, all we can say is that in our Stage I the ultimobranchial body appears as the direct prolongation of what we believe is the fifth gill-pouch. The latter, as in various other mammals (human embryo, Cavia, Talpa, etc.), takes origin from a lateral pharyngeal bay in common with the fourth pouch, the bay in question narrowing to form in later stages the common pharyngeal duct through which the fourth pouch and the ultimobranchial body communicate with the pharynx. We have not observed a closing membrane in connection with pouch 5 in Trichosurus, though such is sometimes present in the human embryo (*cf.* HAMMAR in KEIBEL and ELZE, Normentafel (28, p. 103)).

There has been much discussion as to whether or not the ultimobranchial bodies contribute to the formation of the thyroid since WÖLFLER (68) and STIEDA (58) first described the occurrence of these structures in the mammalia and advanced the view (*contra* KÖLLIKER) that they give origin by themselves to the entire thyroid. In 1883 BORN (5) reached the conclusion that the thyroid in the Pig is formed by the union of two distinct primordia, viz., the median primordium, which he regarded as giving rise to the isthmus alone, and the posterior or lateral primordia, from which he held the lateral lobes are exclusively formed. In 1885, FISCHELIS (9) described the fusion of the lateral primordia with the lateral extremities of the median primordium, reaching much the same conclusion as BORN. In 1886, DE MEURON (36) combated BORN'S view and showed that in the mammals the lateral primordia or accessory thyroids do not form the lateral lobes by themselves but " se réunissent à la glande primitive et se fusionnent complètement avec ses parties latérales dont elles forment le centre." In 1887 KASTSCHENKO (27) reached a similar conclusion. He showed that the lateral thyroid primordia come to lie medially to the lateral portions of the median primordium and eventually become more or less completely enclosed by the latter. At the same time they give off many sprout-like solid processes and become transformed into aggregates of epithelial cell-strands, indistinguishable structurally from the tissue of the median primordium. From the small size of the lateral primordia relatively to the median, KASTSCHENKO concluded they play no great *rôle* in the development of the entire mass of the thyroid.

The researches of all subsequent investigators on Eutherian mammals as well as our own on representatives of the Marsupialia have confirmed the results of DE MEURON and KASTSCHENKO so far as concerns the more or less complete enclosure of the ultimobranchial bodies by the lateral lobes of the median primordium, but the further history of the ultimobranchial bodies has been very variously interpreted. Some authorities [SIMON (55), ZUCKERKANDL (71)] hold that the solid sprouts they give off are directly utilised in the formation of thyroid vesicles, others, perhaps the majority, deny that they take any part in the formation of the thyroid proper, but give varying accounts of their fate. HERRMANN and VERDUN (24) indeed go so far as to regard them as functionless rudiments.

Amongst the lower vertebrates, the ultimobranchial bodies always remain quite separate from the median thyroid and give rise to independent organs with a glandular structure.

Amongst the Reptilia, in *Anguis fragilis*, where, as in Lacerta (MAURER), the left body usually alone persists, SAINT-RÉMY and PRENANT (51) describe it in 6 cm. embryos as an ovoid gland situated behind the thyroid. It possesses a central cavity bounded by an epithelial wall composed of several layers of cells. Connected with the epithelium are convoluted cords of cells, separated by vascular conjunctive tissue and sometimes luminated, which have arisen by proliferation from the epithelium. In Coluber, where both bodies persist, VERDUN (67) describes them as two irregular elongated organs situated near the median thyroid, behind the thymus and consisting of glandular acini leading into a common connecting canal. In Tropidonotus also, according to SAINT-RÉMY and PRENANT, both bodies persist, the adult gland resembling that of Coluber as described by HERRMANN and VERDUN (24). SAINT-RÉMY and PRENANT state " la cavité persiste, assez importante, excentrique, avec un épithélium très spécial et remplie d'un fort coagulum (substance colloïde ?)." In *Chrysemys picta* and in *Pseudemys scripta*, according to the observations of F. D. THOMPSON (63), the organs are paired, intimately united with the corresponding parathyroids and placed anteriorly to the thyroid. They consist of vesicles of varying size and shape, some of which contain a material which appears to be true colloid: "at any rate it gives the same microchemical reaction as the substance in the colloid vesicles of the thyroid of the same species." The authoress remarks that "the occasional presence of colloid in the vesicles of the postbranchial body is not without significance."

In Echidna, MAURER (34) made the very interesting discovery that the ultimobranchial bodies also remain quite distinct from the thyroid and appear in the adult as two glands situated one on either side of the commencement of the trachea, close behind the cricoid cartilage and far cranial to the thyroid whose normal position they have usurped. In his own words: "Sie bilden längliche Knötchen, die mikroskopisch ein verschiedenes Bild zeigen: neben colloidhaltigen Epithelbläschen, die also typisches Schild-drusengewebe darbieten, findet man auch kleine Kugeln von compact zusammenliegenden, epithelialen Zellen, ein Bild, das auch in Epithelkörperchen gefunden wird. Im wesentlichen zeigt aber das Gebilde den Bau der Schilddrüse." Our own observations on the ultimobranchial bodies of Ornithorhynchus are in essential agreement with those of MAURER for Echidna. Vesicles containing a colloid-like substance and varying somewhat in size and in the detailed characters of their walls are present but are not very abundant in our material, the main mass of the gland consisting of spherical masses of compactly arranged epithelial cells (solid acini).

With reference to the above mentioned "colloid," GROSSER (15, p. 339) remarks: "doch ist das Kolloid nur nach seiner Färbbarkeit identifiziert, und wir müssen heute annehmen, dass jedes länger stagnierende eiweisshaltige Sekret die färberische Kolloidreaktion gibt (KOHN, ERDHEIM)."

Even so, it remains to be shown that the substance in question is not colloid, and, until that is done, we prefer to regard the facts above set forth as affording support to the view that in the higher mammals the ultimobranchial bodies participate in some degree in the formation of the lateral lobes of the thyroid.

This latter view receives its strongest support from the investigations of SIMON, set forth in an important paper (55) published in 1896 and which in our view has not received from subsequent writers the attention it deserves. SIMON studied the evolution of the ultimobranchial bodies, or lateral thyroid primordia as he termed them, in a representative series of embryos of Eutheria (including Rabbit, Guinea-pig, Calf, Sheep, Dog, Cat, Pig) and arrives at the conclusion that the lateral thyroid primordium, after active multiplication of its elements, gives origin to epithelial cords which, remaining distinct from those of the thyroid, become transformed into thyroid vesicles. He distinguishes two periods in the developmental history of the lateral primordia after they have come into relationship with the lateral lobes of the median primordium and characterises them as follows, to quote his own words (Conclusions, p. 140):—

"(A) La première, dite d'activité, est caractérisée par ce fait qu'après avoir subi un bourgeonnement actif, l'ébauche latérale se divise dans ses assises externes en cordons ou lobules qui ne s'anastomosent pas avec ceux de l'ébauche médiane, contrairement à l'opinion de BORN, STIEDA, KASTSCHENKO, PIERSOL. De même, certains cordons restent adhérents à l'ébauche latérale et se transforment directement en vésicules thyroïdiennes sans s'anastomoser avec l'ébauche médiane.

"(B) La seconde période, dite de survivance, est caractérisée par la persistance d'une vésicule, derniers vestiges de l'ébauche latérale. Celle-ci peut se trouver au centre du lobe latéral et y former un *canal central* (embryons de Lapin, Cobaye, Brebis, Chat), ou se trouver en debors (embryons de Veau). Cette vésicule disparait totalement dans la suite chez les Rongeurs, se transforme chez les Ruminants sans que nous ayons pu fixer le terme de son existence; enfin semble avoir une évolution très variable chez le Chat."

Our own observations on the history of the ultimobranchial bodies in Trichosurus agree closely with those of SIMON except that we are unable to draw such a sharp distinction between the ultimobranchial sprouts and the thyroid tissue as he has done.

In the Rat, ZUCKERKANDL (71, p. 18) states that the ultimobranchial body (lateral thyroid primordium as he terms it) appears after its separation from the pharynx as a thick-walled vesicle which becomes applied to the dorso-medial wall of the median thyroid primordium and later fuses with it. He goes on to say: "sie bildet nach eingetretener Verwachsung einen nicht gerade beträchtlichen Anteil des Seitenlappens und scheint sich später in Schilddrüsengewebe umzuformen, da an der betreffenden Stelle von Erscheinungen der Rückbildung nichts zu sehen ist." He adds that remains of the lumen of the ultimobranchial body are still present in later stages.

Most of the investigators, however, who have discussed this question of the fate of the ultimobranchial bodies in Eutheria (VERDUN (66), SOULIÉ and VERDUN (57), HERRMANN and VERDUN (24), GROSSER (15), RABL (49) and others) have come to the conclusion that they do not take part in the formation of the thyroid tissue of the lateral lobes, and hold that they either disappear completely, or persist for a longer or shorter period in later stages as cystic or other remnants of no functional importance. Other investigators, like PRENANT (44), leave the question undecided.

With special reference to the human embryo, GROSSER (17, p. 469) expresses the opinion that, "up to the present, no evidence has been advanced in favour of the widely accepted view that the (ultimobranchial) bodies become converted into thyroid tissue, and such a transformation is rendered highly improbable by the results of comparative investigation," and he is further of opinion that "the so variable behaviour of the ultimobranchial bodies throughout the Mammalian series may be explained on the supposition that, in the Mammalia, they constitute functionless rudiments (HERRMANN and VERDUN)" (p. 472).

Whilst we are prepared to recognise a certain amount of variability in the degree of development of the ultimobranchial bodies in the higher Mammalia, and even within the limits of the Marsupials themselves, we are of opinion that "the so variable behaviour" of these structures, referred to by GROSSER, is observable chiefly in SIMON'S second period, when the ultimobranchial bodies have reached what we may term their spent stage, and in any case we feel bound to say, from the point of view of our own observations on Trichosurus, we are unable to accept GROSSER'S conclusions.

Lastly, as concerns the persistence of the ultimobranchial bodies in later, and even adult stages, it remains to be mentioned that cystic remnants, comparable with those noted by us in late fœtuses of Trichosurus, have been described by a large number of investigators in Eutheria (PRENANT (44), SIMON (55), KOHN (29), NICOLAS (38), SCHAFFER (52), and others), the "central canal" of PRENANT in the Sheep and the "vésicule postbranchiale" of HERRMANN and VERDUN (24) being of this nature, whilst the latter authors have described in a 1-year-old dromedary an interesting case of the ultimobranchial body persisting independently of the thyroid. In this connection it may be noted that GETZOWA (11) has given detailed accounts of what she regards as remnants of the ultimobranchial bodies in the atrophic thyroids of cretins and idiots, in the normal thyroids of a 9-cm. fœtus and a new-born child and in a three-weeks' athyrotic individual, and has come to the conclusion (which we regard as still standing in need of embryological confirmation) that the ultimobranchial gill-pouch furnishes in rudimentary form the same derivatives as the preceding third and fourth gill-pouches, viz., an epithelial body and a thymus metamere, and, in addition, a specific glandular tissue (*Glandula postbranchialis*), together with a duct (*Ductus postbranchialis*).

CONCLUSIONS.

1. Trichosurus possesses three pairs of thymus glands, viz. :—

(*a*) A paired superficial cervical thymus situated posteriorly to the submaxillary glands and internally to the platysma on the ventral side of the anterior region of the neck.

(*b*) Two pairs of thoracic or posterior cervical glands representing paired thymus III and IV, which may remain separate or the two glands of the same side may unite with each other on one or both sides.

2. The epithelial basis of the superficial cervical thymus is furnished in greater part by the ectodermal walls of the cranial portion of the closed-off cervical sinus and to a smaller extent by the distal portion of the ductus ecto-entobranchialis II. It is probable that a small amount of entoderm derived from the ventral prolongation of the second pouch is also included in the primordium, in which case the cervical thymus is to be regarded as a *Thymus ecto-entodermalis*.

3. The primordia of thymus III and IV are purely entodermal in origin.

The epithelial basis of thymus III is furnished by the caudal wall of the dorsal luminated portion of the third pouch and by the solid ventral prolongation of the same. That of thymus IV is derived exclusively from the ventral portion of the fourth pouch, including its solid ventral prolongation.

4. Two pairs of primary epithelial bodies (III and IV), developed directly from portions of the walls of the third and fourth pouches, are always present. In addition, accessory epithelial bodies, not necessarily paired and either intra- or extra-thymic in position, are frequently found in connection both with the cervical thymus and the thoracic glands.

Epithelial body III arises from the cranial wall of the dorsal luminated portion of the third pouch and comes to lie close to the bifurcation of the common carotid artery.

Epithelial body IV takes origin from the cranial and caudal walls of the dorsal half of the fourth pouch. It usually lies in the neighbourhood of thymus IV.

The epithelial bodies of Trichosurus are never associated with the thyroid.

5. The main portion of the thyroid takes origin from the median thyroid primordium. It is probable that the ultimobranchial bodies, which become closely united with the lateral thyroid lobes and undergo active proliferation, also contribute in some degree to the formation of the latter.

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DESCRIPTION OF PLATES.

All the figures are from specimens of *T. vulpecula*. Drawings of sections were made with the aid of the camera lucida or the projection apparatus of Zeiss.

The following is a list of the reference letters common to the various figures :—

a.l. X	Anterior laryngeal branch of vagus.
aort.a. 1, 2, 3, 4, 5	Aortic arch 1, 2, 3, 4, 5.
br.a. 1, 2, 3	Branchial arch 1, 2, 3.
c.c.	Common carotid artery.
c.e.	External carotid artery.
c.f.	Cervical groove.
c.i.	Internal carotid artery.
cl. 1, 2, 3, 4	Gill-pouch 1, 2, 3, 4.
cl.m. 2, 3, 4	Closing membrane 2, 3, 4
clv.	Clavicle.
d.a.	Dorsal aorta.
d.b.	Ectobranchial duct.
d.c.	Ductus cervicalis.
d.e.b. II, III, IV	Ductus ecto-entobranchialis II, III, IV.
ect.gr. 1, 2, 3, 4	Ectodermal groove 1, 2, 3, 4.
ep.b. III, IV	Epithelial body III, IV.
g.n.	Ganglion nodosum.
hy.a.	Hyoid arch.
in.a.	Innominate artery.
jug.	Jugular vein.
l.	Larynx.
l.th.	Lateral lobe of thyroid.
l.v.	Lingual vein.
m.	Manubrium sterni.
m.cl.-m.	Cleido-mastoid muscle.
m.st.-h.	Sterno-hyoid muscle.
m.st.-m.	Sterno-mastoid muscle.
m.st.-th.	Sterno-thyroid muscle.
mnd.a.	Mandibular arch.

œs.	Œsophagus.
pc.v.	Precaval vein.
per.	Pericardium.
ph.	Pharynx.
ph.b.	Pharyngeal bay.
ph.d.	Pharyngeal duct.
rb. 1, 2	Rib 1, 2.
r.l. X	Recurrent laryngeal branch of vagus.
s.c.	Sinus cervicalis.
s.tm.	Superficial cervical thymus.
spr.	Sprout growing out from ultimobranchial body.
subcl.	Subclavian artery.
subm.gl.	Submaxillary gland.
sym.	Cervical sympathetic.
th.	Median thyroid.
tm. III, IV	Thymus III, IV.
tm.c.	Thymic cavity.
tr.	Trachea.
u.b.	Ultimobranchial body.
v.a.	Ventral aorta.
v.c.	Vesicula cervicalis.
v.d.	Ductus vesiculæ cervicalis.
v.pr.cl. 2	Ventral prolongation of pouch 2.
IX	Glossopharyngeal nerve.
X.	Vagus nerve.
XII	Hypoglossal nerve.

SPECIAL DESCRIPTION OF FIGURES, PLATES 1–10.

[The reader is asked to note that there are no figures corresponding to the numbers 6, 8, 14, 22, 23, 24, 28, and 54.]

Fig. 1, Plate 1.—Drawing [about nat. size] of dissection of adult, Specimen (A). For description see text (pp. 6–7). *m.dig.*, digastric muscle; *m.g-h.*, genio-hyoid muscle; *m.mass.*, masseter muscle; *m.th-h.*, thyro-hyoid muscle; *par.*, parotid gland; *pc.v.r.*, right precaval vein; *tm′*, *tm″*, thoracic thymus glands of right side.

Fig. 2, Plate 2.—Stage I, (*a*) δ '97. G.L. 5 mm. Trans. sect. showing the widely open cervical sinus (*s.c.*) and the second and third gill-pouches (*cl.* 2, *cl.* 3) of the right side with their closing membranes (*cl.m.* 2 and *cl.m.* 3).
[Sl. 4–1–4.] ×75.

Fig. 3, Plate 2.—The same, (*c*) 1 '01. Trans. sect. right side, showing the three branchial arches (*br.a.* 1–3) within the sinus, the fifth aortic arch (*aort.a.* 5), and the pharyngeal bay. [Sl. 3–2–9.] ×75.

Fig. 4, Plate 2.—Stage II, (*a*) β '98. G.L. 4·5 mm. Ventral view of model of left half of pharynx, showing gill-pouches 2, 3, and 4 (*cl.* 2–4), the sinus cervicalis with a portion of the hyoid arch (*hy.a.*), the median thyroid primordium (*th.*), and the laryngo-tracheal groove (*ltr.gr.*). ×100.

Fig. 5, Plate 2.—The same. Trans. sect. showing the origin of the median thyroid primordium (*th.*) and the ventral prolongation of the second pouch of right side (*v.pr.cl.* 2). [Sl. 5–1–7.] ×75.

Fig. 7, Plate 2.—Stage IV (XIX '04). G.L. 7·5 mm. Trans. sect. showing the ventral prolongation of pouch 2 (*v.pr.cl.* 2) of the left side with its closing membrane. [Sl. 2–4–5.] ×75.

Fig. 9, Plate 4.—The same. Trans. sect. showing pouch 4 (*cl.* 4) and the ultimo-branchial body (*u.b.*) of right side, separating off together from the pharynx. The sinus cervicalis (*s.c.*) is also seen and the third branchial arch (*br.a.* 3). [Sl. 3–1–6.] ×75.

Fig. 10, Plate 2.—Stage V (II '01). G.L. 6 mm. Trans. sect. showing pouch 3 (*cl.* 3) of left side and the ductus ecto-entobranchialis III (*d.e.b.* III) connecting it with the now closed upper portion of the cervical sinus and the solid ventral portion of pouch 2 (*cl.* 2) fused with the ectobranchial duct (*d.b.*) to form ductus ecto-entobranchialis II. The posterior end of the thyroid primordium (*th.*) is seen below the ventral aorta. [Sl. 3–3–4 and 5.] ×75.

Fig. 11, Plate 4.—The same. Trans. sect. showing the reduced cervical sinus (*s.c.*) communicating with the exterior by the narrow cervical duct (*d.c.*), the cervical vesicle (*v.c.*), and its duct (*v.d.*). Pouch 4 (*cl.* 4) and its connection (*d.e.b.* IV) with the ectoderm of the sinus is also seen. *Vm.pr.*, ventro-medial prolongation of pouch 4. [Sl. 3–4–8.] ×75.

Fig. 12, Plate 3.—The same. View of cranial side of model, showing pouches 2–4 (*cl.* 2–4) of left side and their relations to the cervical sinus (*s.c.*). *ect.r.*, ectodermal ridge formed by prolongation of ectodermal groove 2. ×100.

Fig. 13, Plate 3.—The same. View of model from caudal side. The cervical vesicle (*v.c.*) is well seen. ×100.

Fig. 15, Plate 4.—Stage VI (XX '04). G.L. 7·75 mm. Trans. sect. showing the upper solid portion of the cervical sinus which forms the first indication of the primordium of the superficial cervical thymus (*s.tm.*). The extreme ventral end of pouch 3 (*cl.* 3) is seen with its connection (*d.e.b.* III) with the sinus, also the upper portion of the cervical vesicle (*v.c.*) closely approximated to the ganglion nodosum (*g.n.*). [Sl. 3–5–9.] ×75.

Fig. 16, Plate 3.—Stage VII (III '01). G.L. 7·25 mm. Cranial view of model, left side, showing the now greatly elongated pouch 2 (*cl.* 2), the ductus ecto-entobranchialis II (*d.e.b.* II), pouch 3 (*cl.* 3), and the developing superficial cervical thymus (*s.tm.*). ×100.

Fig. 17, Plate 3.—The same. Caudal view of model. Note the cervical vesicle (*v.c.*) now situated more dorsally, and its narrowed duct (*v.d.*) *Cf.* fig. 13. ×100.

Fig. 18, Plate 4.—The same. Trans. sect. passing through the dorsal portion of pouch 3 of right side, and showing its differentiation into the primordia of thymus III (*tm.* III) (caudal wall) and epithelial body III (*ep.b.* III) (cranial wall). [Sl. 5–2–1.] ×75.

Fig. 19, Plate 3.—Stage VIII, *b* (XII '02). G.L. 7·25 mm. View of cranial side of model. Note the conspicuous primordium of the cervical thymus (*s.tm.*), the ductus ecto-entobranchialis II (*d.e.b.* II), pouch 3 (*cl.* 3), which has now extended down as a solid prolongation below the ductus ecto-entobranchialis III (*d.e.b.* III), and the position of the primordia of thymus III (*tm.* III) and epithelial body III (*ep.b.* III). ×100.

Fig. 20, Plate 3.—The same. View of caudal side of model, the cervical vesicle (*v.c.*) and its duct (*v.d.*) are better seen. *d.c.*, outer end of the narrowed cervical duct. ×100.

Fig. 21, Plate 4.—The same, embryo *a* (XII A '02). Long. sect., left side, showing the elongated pouch 2, the ductus ecto-entobranchialis II (*d.e.b.* II) (less attenuated than in embryo *b*, fig. 19) passing below into the primordium of the superficial cervical thymus (*s.tm.*), the cervical sinus (*s.c.*), and its duct (*d.c.*). [Sl. 5–3–6.] ×75.

Fig. 25, Plate 4.—The same. Long. sect. showing the position of pouch 3 with its dorsal tubular portion and its solid ventral prolongation. [Sl. 6–3–6.] ×75.

Fig. 26, Plate 5.—The same. Same section as preceding, showing pouch 3 under higher magnification. The cranial wall of the dorsal luminated portion of the pouch is composed of a regular columnar epithelium, and forms the primordium of epithelial body III (*ep.b.* III). The caudal wall and the solid ventral prolongation are composed of more irregularly arranged cells, and form the primordium of thymus III (*tm.* III). Lymphocytes (*lc.*) are already present in the latter. [Sl. 6–3–6.] ×300.

Fig. 27, Plate 5.—The same. Long. sect. nearer the median plane than fig. 25, showing the form and position of pouch 4, left side. [Sl. 7–2–1.] ×75.

Fig. 29, Plate 5.—The same. Long. sect., right side, showing the hinder end of the ultimo-branchial body (*u.b.*) and its position in relation to the thyroid gland. The latter occurs eight sections further medially, its position being shown by a dotted outline (*th.*). [Sl. 9–3–1.] ×75.

Fig. 30, Plate 5.—The same, embryo *b* (XII '02). Composite figure from two adjoining transverse sections, showing the extreme dorsal portion of pouch 3, now almost separated from the pharynx. Thymus III (*tm.* III) and epithelial body III (*ep.b.* III) are beginning to separate from each other, especially on the left side (right of figure). *ph.c.*, pharyngeal connection of pouch. [Sl. 5–1–7 and 8.] ×75.

Fig. 31, Plate 5.—The same. Trans. sect. passing through pouch 3 of right side, further ventrally, and showing the primordia of thymus III (*tm.* III) and epithelial body III (*ep.b.* III), also the cervical vesicle (*v.c.*) in intimate relation with the ganglion nodosum (*g.n.*). [Sl. 5–2–1.] ×75.

Fig. 32, Plate 5.—The same. Composite figure from transverse sections, showing pouch 4 and the thickened ultimobranchial body (*u.b.*) after their separation from the pharyngeal duct. The two derivatives of pouch 4 (thymus IV and epithelial body IV) are seen on the right side (left in figure) and epithelial body IV, and the attenuated connection (*ect.c.*) of pouch 4 with the sinus ectoderm on the left side (right in figure). The sections are slightly oblique, the left side being in front of the right. [Sl. 5–3–11 and 13.] ×75.

Fig. 33, Plate 6.—The same. Trans. sect. anterior to fig. 32, showing the thyroid gland (*th.*) spread out below the ventral aorta (*v.a.*) and the ventral end of thymus III (*tm.* III). The ventro-lateral portion of pouch 4 (*cl.* 4) here appears in trans. sect. dorsal to the ventral end of pouch 3, owing to the growth of the newly developed solid ventral prolongation of the latter. [Sl. 5–3–5A.] ×75.

Fig. 34, Plate 6.—The same. Trans. sect. showing the superficial cervical thymus (*s.tm.*) still connected with the ectoderm of the cervical groove (*c.f.*). The last remnant of the lumen of the cervical sinus (*s.c.*) is seen on its postero-lateral side. [Sl. 5–2–13.] ×200.

Fig. 35, Plate 6.—The same, embryo *a* (XII A '02). Long. sect. showing pouch 4 of fig. 27 under higher magnification. Note the regular columnar structure of the dorsal portion of the pouch, forming the primordium of epithelial body IV (*ep.b.* IV), and the ventral portion of the pouch, formed of more irregularly arranged and lighter staining cells constituting the primordium of thymus IV (*tm.* IV). The ventral prolongation of the pouch is less marked than in the case of pouch 3, and into it the pouch lumen is continued for a short distance. Compare with fig. 26. [Sl. 7–2–1.] ×300.

Fig. 36, Plate 6.—Stage IX, *a* (5 '97). G.L. 8·5 mm. Long. sect. showing the superficial cervical thymus of the left side in the form of a pear-shaped mass of cells still connected by a fine strand with the ectoderm of the cervical groove (*c.f.*). [Sl. 7–3–3.] ×75.

Fig. 37, Plate 6.—The same. Long. sect. showing thymus III (*tm.* III) and epithelial body III (*ep.b.* III) now separated from each other. The wall of the epithelial body directed towards the thymus is irregular in contour, indicating that it has only recently separated from the latter. The cervical vesicle (*v.c.*) is seen close below the ventral side of the ganglion nodosum (*g.n.*). [Sl. 7–1–7.] ×75.

Fig. 38, Plate 6.—The same. Long. sect., right side, showing the position of the ultimobranchial body (*u.b.*) in relation to the lateral lobe of the thyroid (*l.th.*). It has moved forward and now lies close behind the latter. Compare with fig. 29. *b.c.* = bulbus cordis. [Sl. 5–2–6.] ×75.

Fig. 39, Plate 6.—The same, embryo *b* (IV '01). Trans. sect. showing thymus IV (*tm.* IV) and epithelial body IV (*ep.b.* IV) of the right side still unseparated. [Sl. 7–3–6.] ×75.

Fig. 40, Plate 7.—Stage X (V '01). G.L. 9·5 mm. Trans. sect. showing the inner end of the superficial cervical thymus (*s.tm.*) of the left side, now definitely encapsulated and consisting of an epithelial reticulum in which lymphocytes in spare numbers are present. The cervical vesicle (*v.c.*) is becoming imbedded in the ganglion nodosum. *l*, laryngeal cavity; *cr.*, cricoid cartilage. [Sl. 6–4–3.] ×75.

Fig. 41, Plate 6.—The same. Trans. sect. showing the thickened cranial end of the ultimobranchial body (*u.b.*) and its position in relation to the thyroid. The central bridge of the latter is here seen; it is exceptionally thick and contains many cavities. The lateral lobes, which are small in this embryo, lie further cranially. [Sl. 7–3–1.] ×75.

Fig. 42, Plate 7.—The same. Trans. sect. showing thymus IV (*tm.* IV) containing a very large thymic cavity (*tm.c.*) on each side and epithelial body IV (*ep.b.* IV). [Sl. 8–2–8.] ×75.

Fig. 43, Plate 7.—Stage XI (VI '01). G.L. 10 mm. Trans. sect. showing the ultimobranchial body (*u.b.*) lying on the dorso-median side of the lateral lobe of the thyroid. [Sl. 7–4–6.] ×75.

Fig. 44, Plate 7.—Stage XII, *b* (XXII '04). G.L. 11 mm. Composite figure from two longitudinal sections, right side, showing the solid epithelial body III (*ep.b.* III) lying dorsal to the common carotid artery (*c.c.*) and the superficial cervical thymus (*s.tm.*), which still has a prolongation directed towards the ectoderm of the cervical groove (*c.f.*). [Sl. 14–1–7 and 8.] ×75.

Fig. 45, Plate 7.—Stage XIII (X '01). G.L. 12 mm. Trans. sect. showing the large solid epithelial body IV (*ep.b.* IV) of the right side and the single thoracic thymus (*tm.*) on each side, representing thymus III and IV united. [Sl. 4–3–3.] ×75.

Fig. 46, Plate 8.—Stage XIV, *a* (XXV). G.L. 13 mm. Trans. sect. showing the ultimobranchial body (*u.b.*) of the left side, with a solid sprout (*spr.*) passing into the lateral lobe of the thyroid. [Sl. 9–1–2.] ×75.

Fig. 47, Plate 7.—The same. Composite figure from two transverse sections, showing the single thymus (*tm.* III and IV) of the right side (left in figure) and thymus IV (*tm.* IV) of the left side. Each gland possesses a conspicuous thymic cavity (*tm.c.*). [Sl. 11–4–4 and 5.] ×75.

Fig. 48, Plate 7.—The same, embryo *b* (XXIV). G.L. 13·5 mm. Long. sect. through epithelial body III. A vascular ingrowth (*sin.*) has penetrated into the gland. [Sl. 9–1–4.] ×300.

Fig. 49, Plate 9.—The same, embryo *a* (XXV). Microphotograph of transverse section, showing the ultimobranchial body (*u.b.*) and the lateral thyroid lobes, two sections behind fig. 46. [Sl. 9–1–4.] ×87.

Fig. 50, Plate 8.—The same. Trans. sect. three sections in front of fig. 49, showing the ultimobranchial body and lateral thyroid lobe of right side; the walls of the former have sent out broad cellular sprouts, which pass into apparent continuity with the tissue of the lateral lobe. In the more dorsal sprout is a cavity quite similar to those in the thyroid tissue. [Sl. 9–1–1.] ×250.

Fig. 50A, Plate 8.—The same. Trans. sect., one section behind fig. 49, passing through the hinder end of the ultimobranchial body, here produced into lobe-like sprouts, with cavities similar to those in the thyroid tissue. [Sl. 9–1–5.] ×250.

Fig. 51, Plate 9.—Stage XV, *b* (new-born fœtus). G.L. 14·5 mm. Microphotograph of longitudinal section, showing thymus III and IV of the right side, epithelial body IV partially imbedded in the thymus and also an accessory epithelial body (*ep.b.′*). [Sl. 16–2–8.] ×60.

Fig. 52, Plate 8.—Stage XVII (*a*). G.L. 17 mm. Composite figure from two longitudinal sections, showing the single thymus of the right side (*tm.* III and IV) and behind it thymus IV (*tm.* IV) of the left side. Epithelial body IV (*ep.b.* IV) of the right side is seen far cranial to thymus IV, dorsal to the vagus nerve (X). Cortical and medullary zones are already developed in the thymus. [Sl. 10–2–5 and 6.] ×75.

Fig. 53, Plate 9.—The same (*b*). G.L. 17·5 mm. Microphotograph of a transverse section showing the single large thoracic thymus (*tm.* III and IV) on each side and epithelial body IV (*ep.b.* IV) of the left side. *sc.*, scapula; *hm.*, humerus. [Sl. 13–2–1.] ×15.

Fig. 55, Plate 9.—The same. Microphotograph of transverse section, showing a well marked sprout from the ultimobranchial body running indistinguishably into the thyroid tissue. [Sl. 9–3–8.] ×270.

Fig. 56, Plate 8.—Stage XIX. G.L. 19 mm. Long. sect. through the lobed superficial cervical thymus (*s.tm.*) of the left side (*tm.c.*, thymic cavity) and the outer portion of the closed epithelial duct (*d.t.*) in relation to the thymus. [Sl. 13–1–4.] ×75.

Fig. 57, Plate 8.—The same. Long. sect. through the lateral portion of thymus IV, showing the very large and compact epithelial body (*ep.b.* IV) imbedded in it. *b.c.*, body cavity. [Sl. 16–2–1.] ×75.

Fig. 58, Plate 9.—The same. Microphotograph of longitudinal section, showing the positions of the superficial cervical thymus (*s.tm.*), the single thymus of the right side, and thymus IV and the lateral thyroid lobe of the left side. [Sl. 14–2–5.] ×20.

Fig. 59, Plate 9.—Stage XX (*b*). G.L. 30 mm. Microphotograph of longitudinal section, right side, showing the large superficial cervical thymus (*s.tm.*), the well developed thymus III (*tm.* III) lying dorsally to it, the smaller thymus IV (*tm.* IV), and the lateral thyroid lobe (*l.th.*). Epithelial body IV (*ep.b.* IV) lies cranial to thymus IV. [Sl. 13–1–4.] ×17·5.

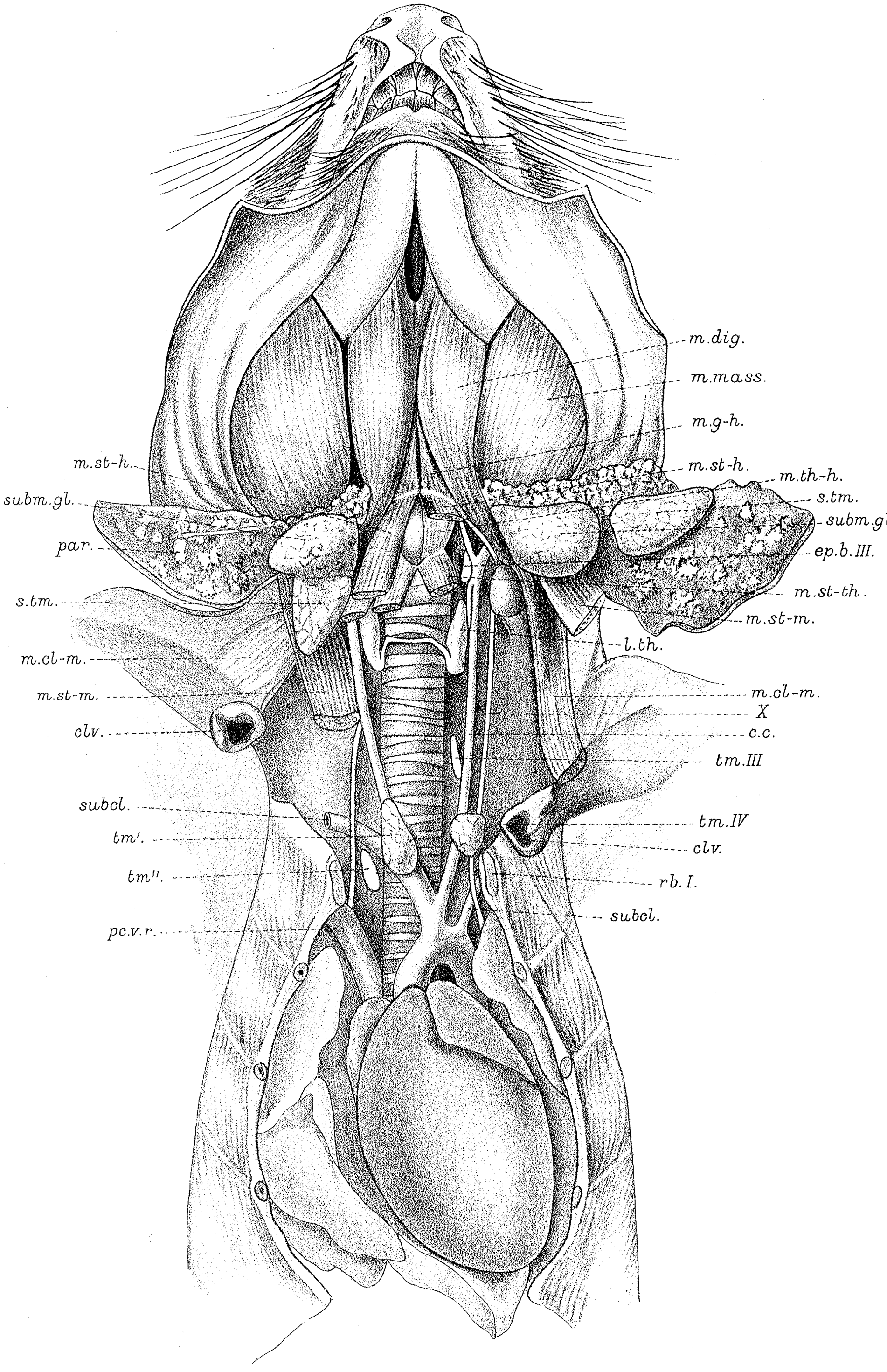
Fig. 60, Plate 8.—The same, fœtus (*a*). Trans. sect. through the epithelial body (*ep.b.'*) imbedded between the lobes of the superficial cervical thymus of the right side. The cells are becoming arranged in columns and vascular ingrowths (*sin.*) have penetrated into it. [Sl. 17–1–1.] ×75.

Fig. 61, Plate 10.—Stage XXII. G.L. 5·2 cm. Microphotograph of transverse section, showing the form and position of the superficial cervical thymus (*s.tm.*) The lateral lobes of the thyroid (*l.th.*) and the posterior end of the accessory thymus (*acc.tm.*) of the right side are also visible. [Sl. 12–2–1.] ×15.

Fig. 62, Plate 10.—The same. Microphotograph showing position and relations of thymus III (*tm.* III). *lym.*, lymphatic gland. [Sl. 47–1–1.] ×15.

Fig. 63, Plate 10.—The same. Microphotograph showing thymus IV (*tm.* IV) and epithelial body IV (*ep.b.* IV) lying dorso-laterally to left thymus IV. *st.*, sternum. [Sl. 50–1–5.] ×15.

Fig. 64, Plate 8.—The same. Trans. sect. through epithelial body IV of left side. It is composed of cords of cells (*cell. cd.*), mostly formed of two cell layers, in between which run sinusoids (*sin.*). *c.t.sh.*, connective tissue sheath. [Sl. 38–2–5.] ×150.



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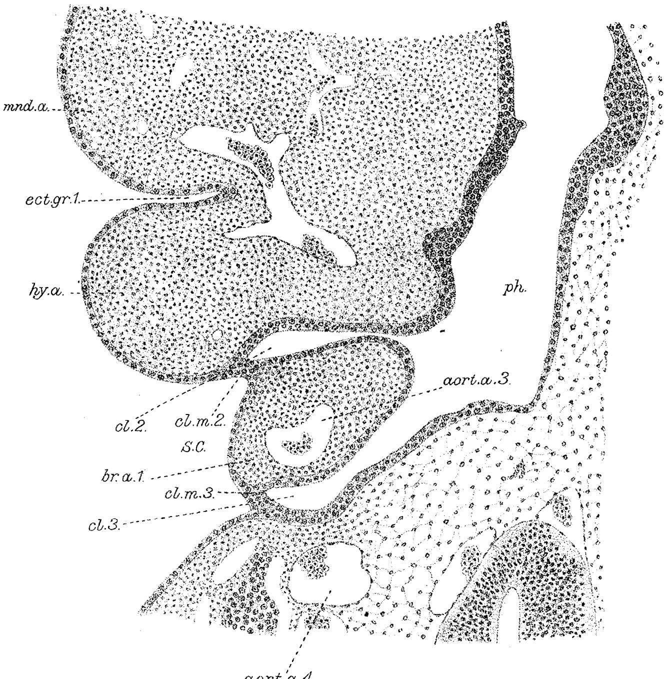

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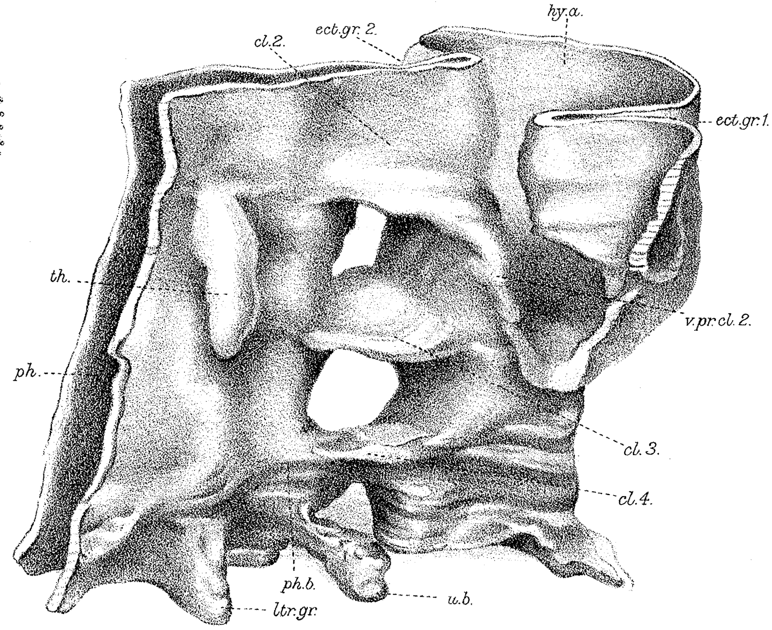

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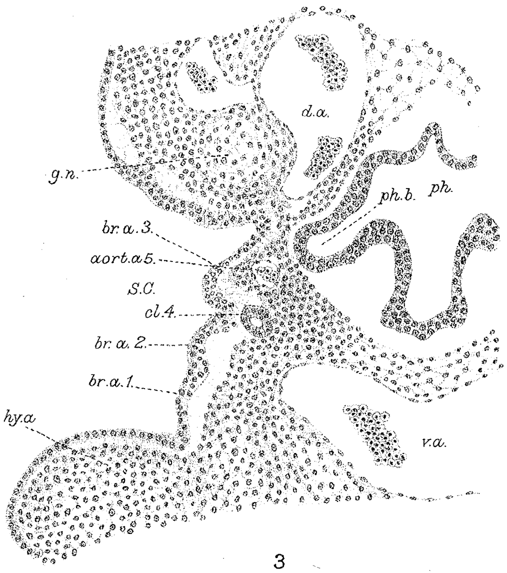

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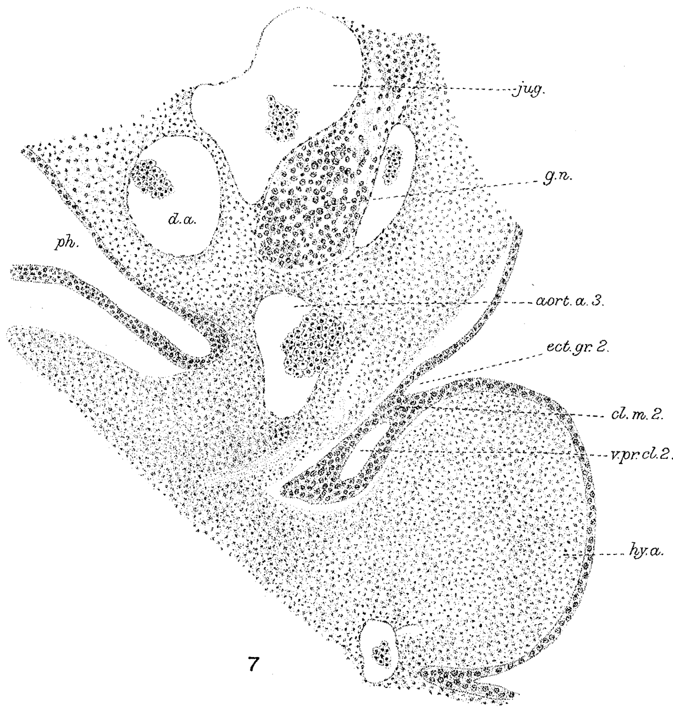

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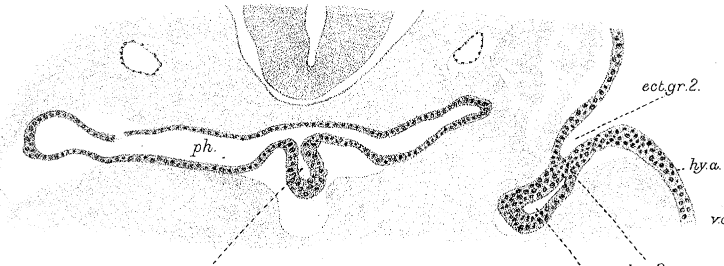

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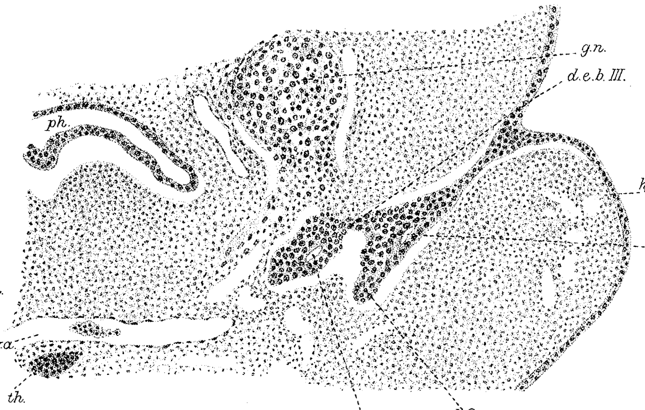

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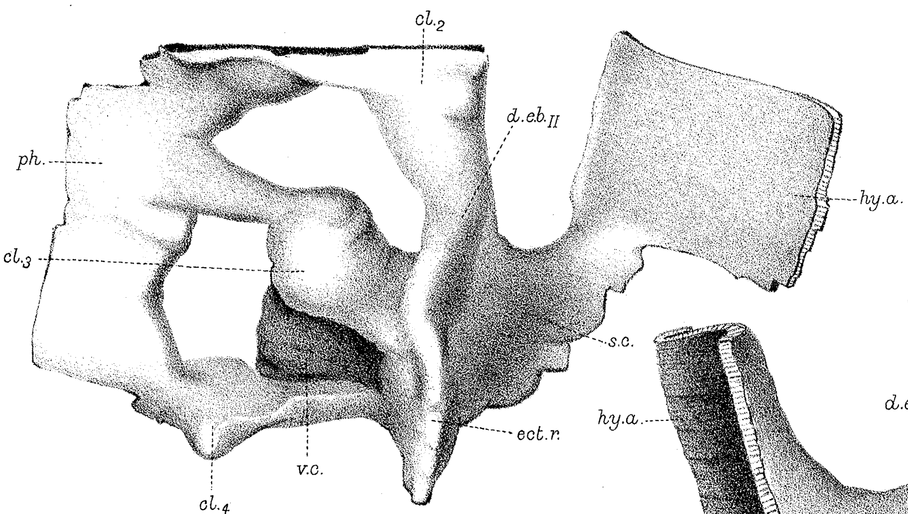

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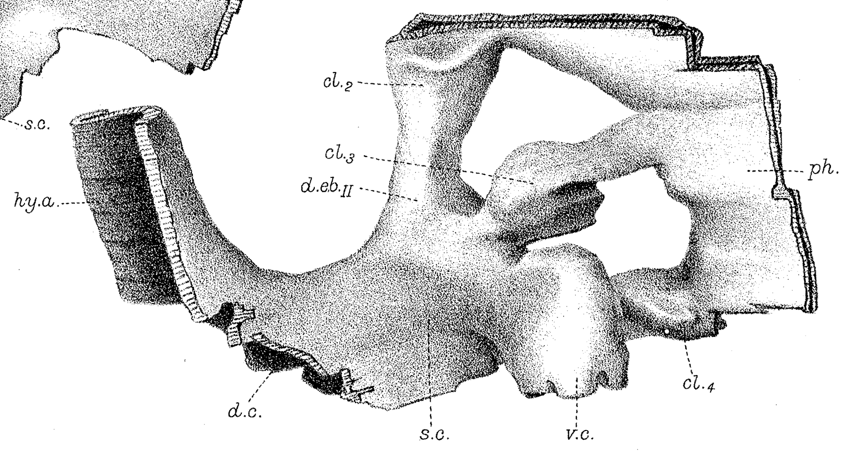

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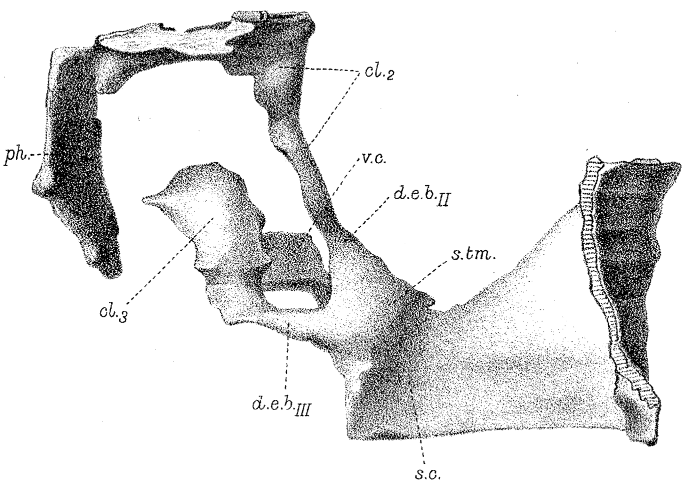

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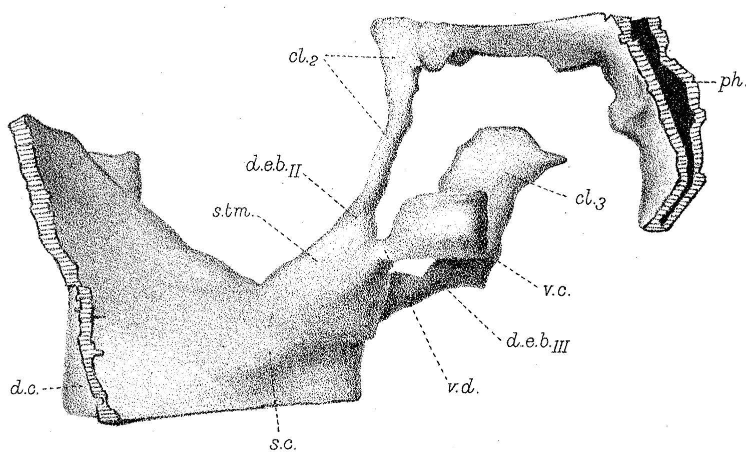

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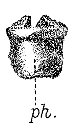

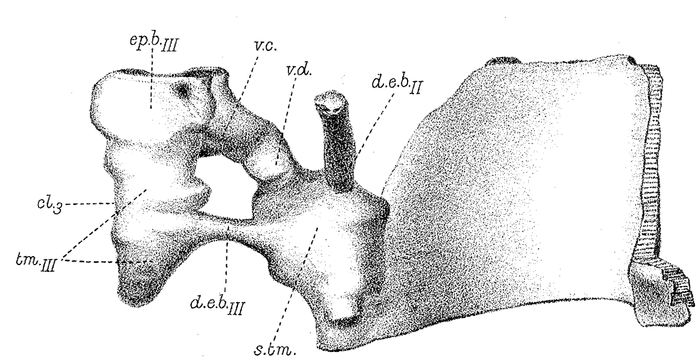

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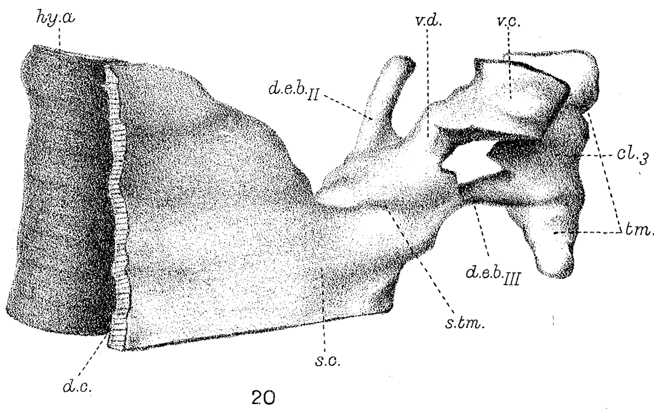

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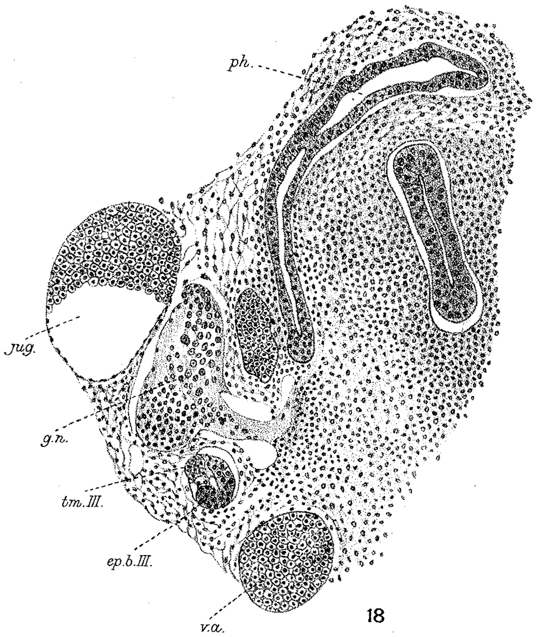

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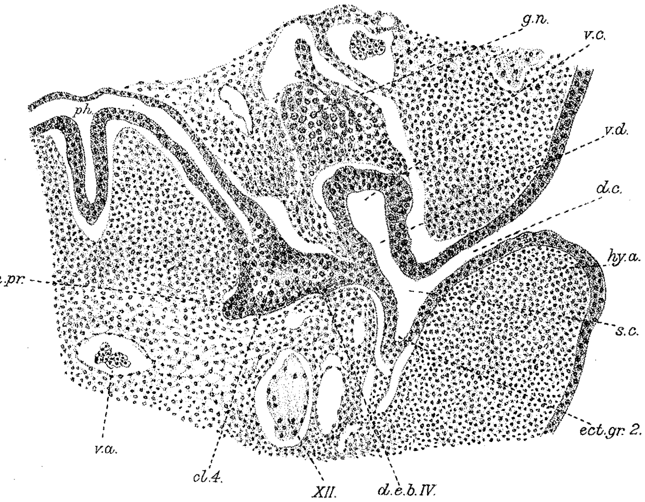

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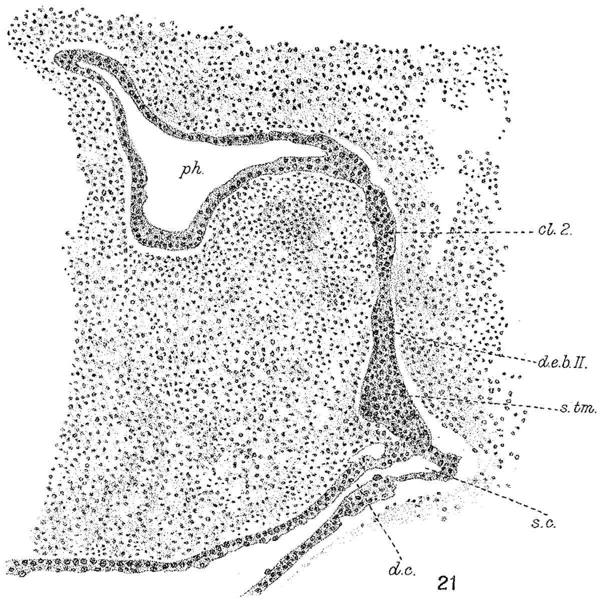

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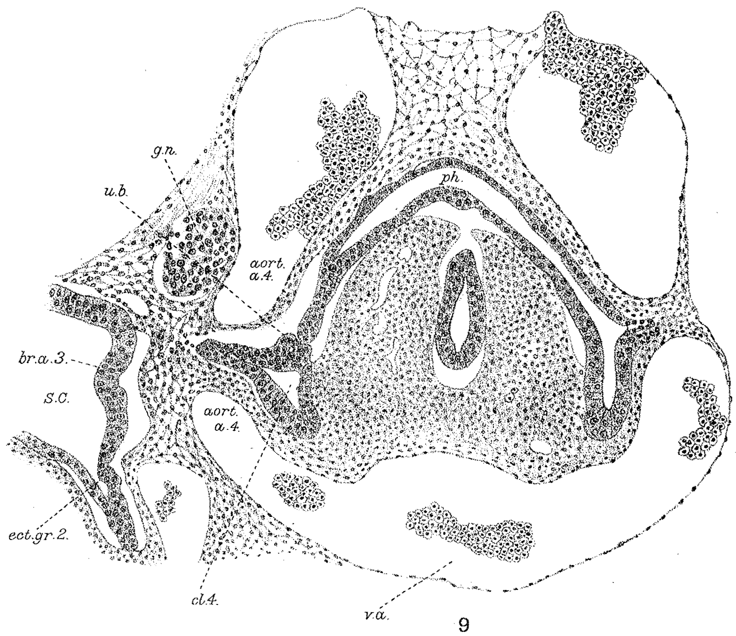

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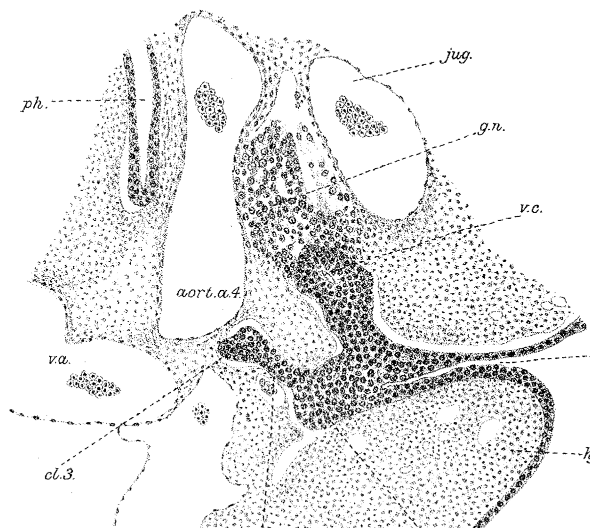

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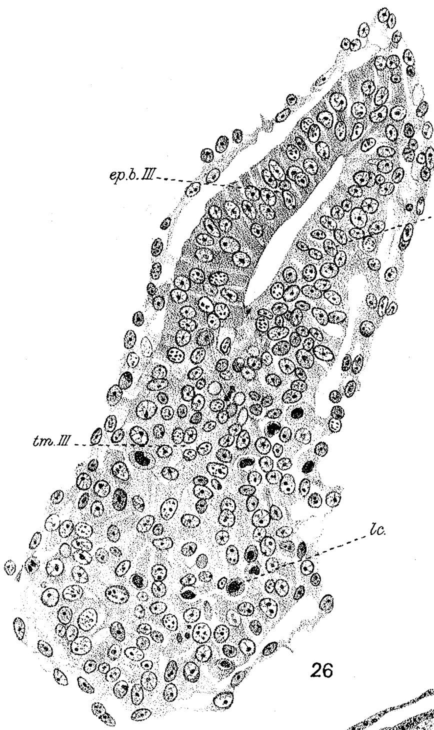

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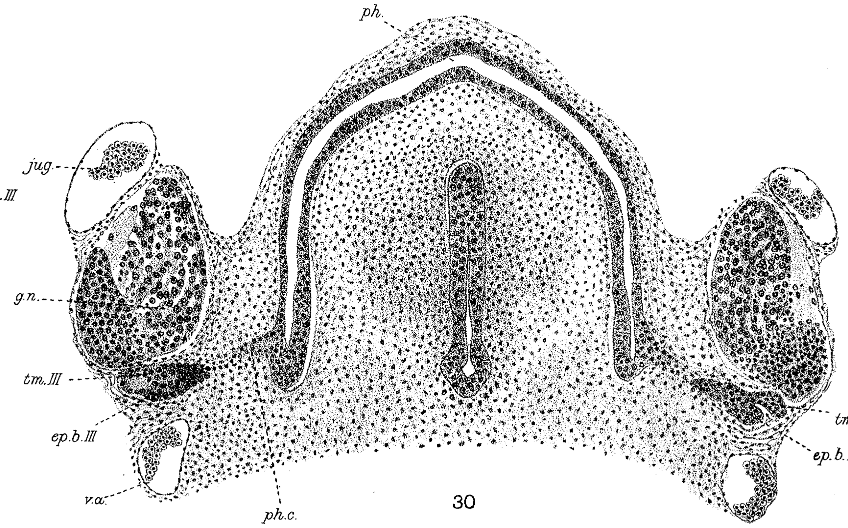

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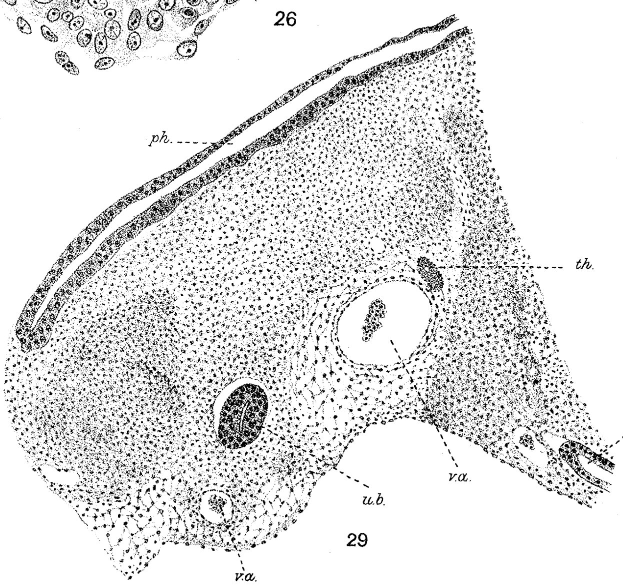

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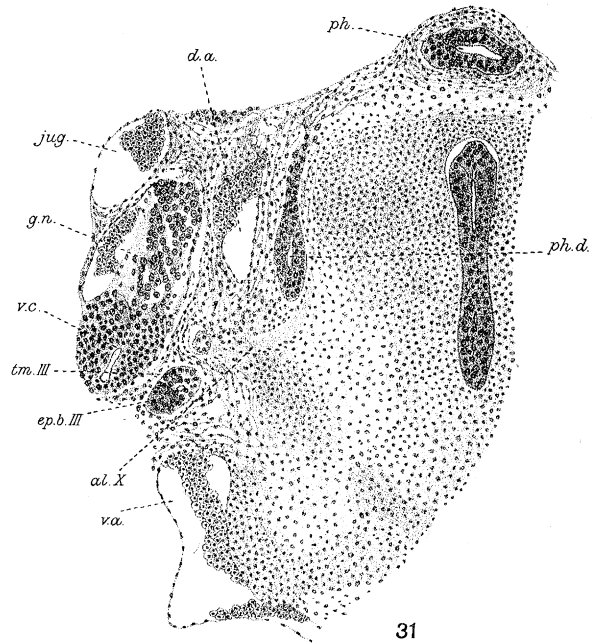

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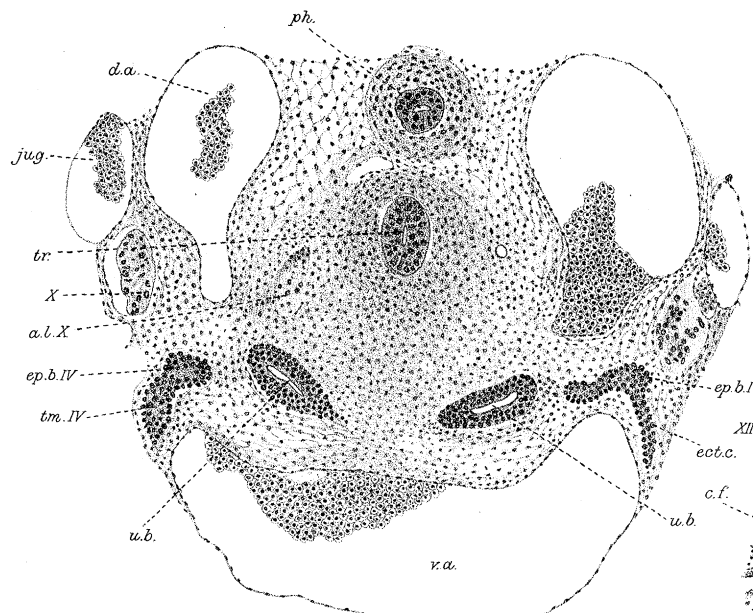

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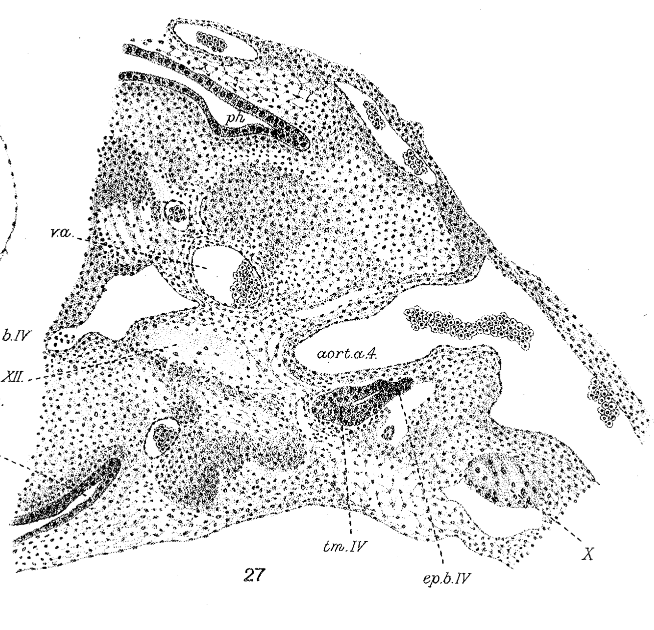

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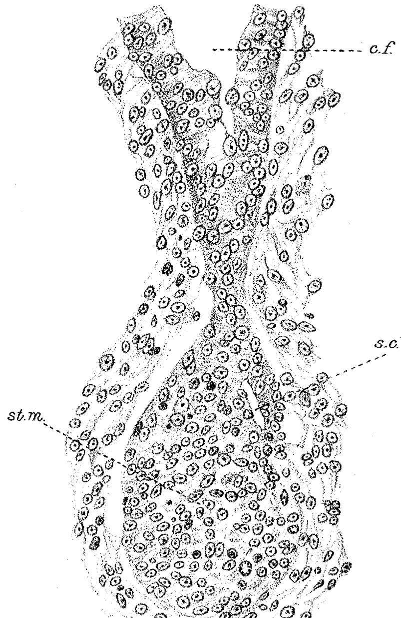

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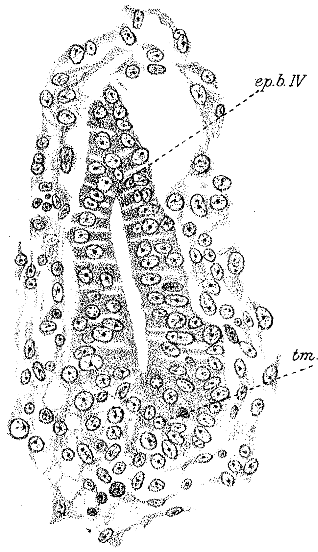

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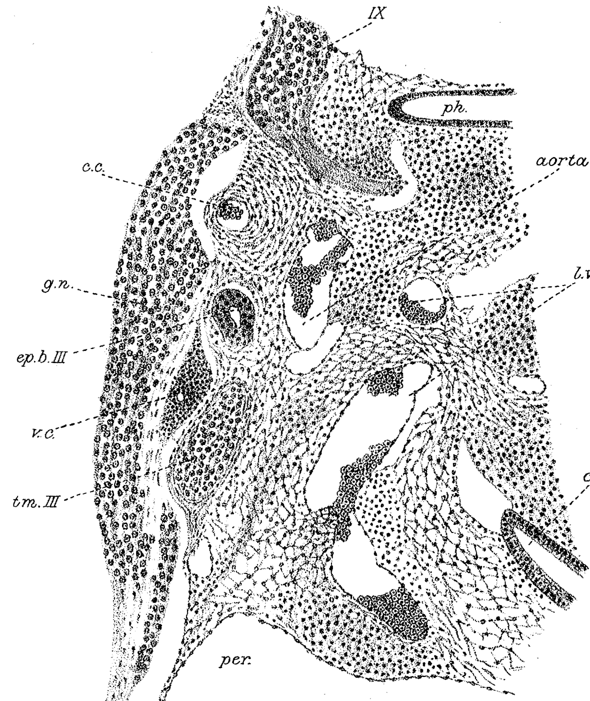

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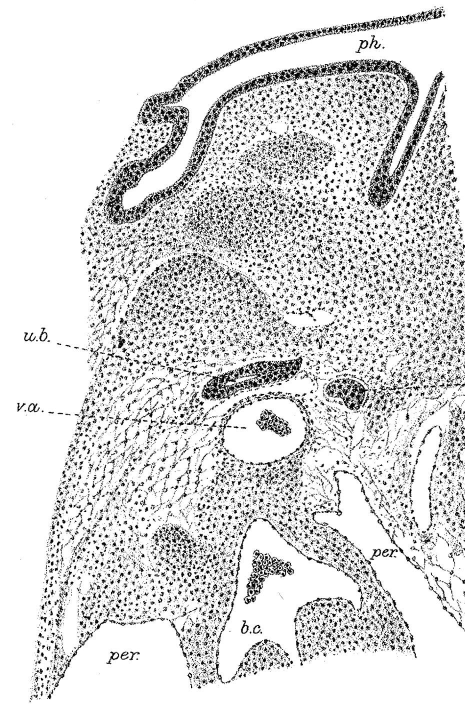

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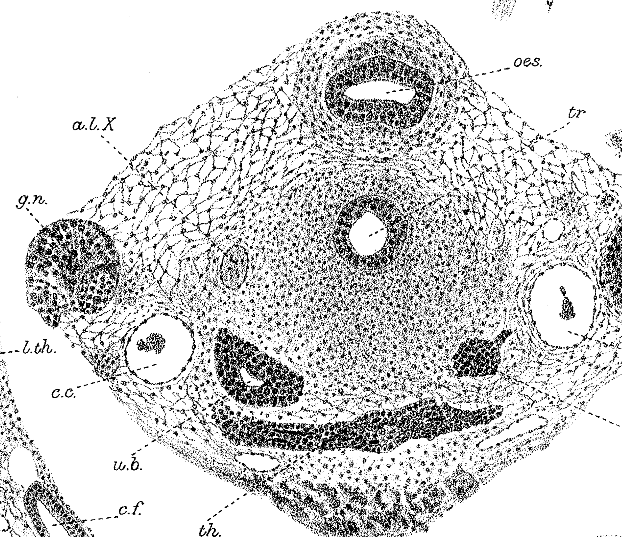

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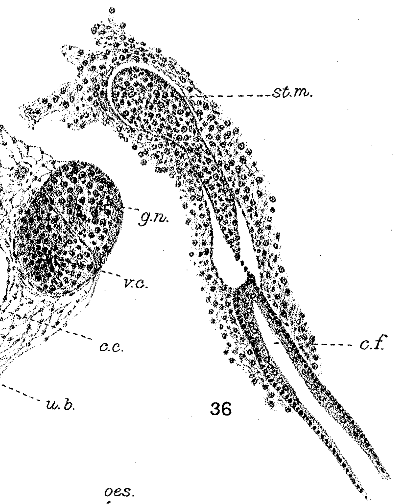

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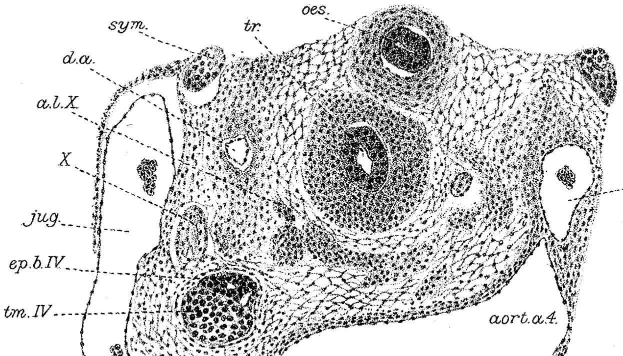

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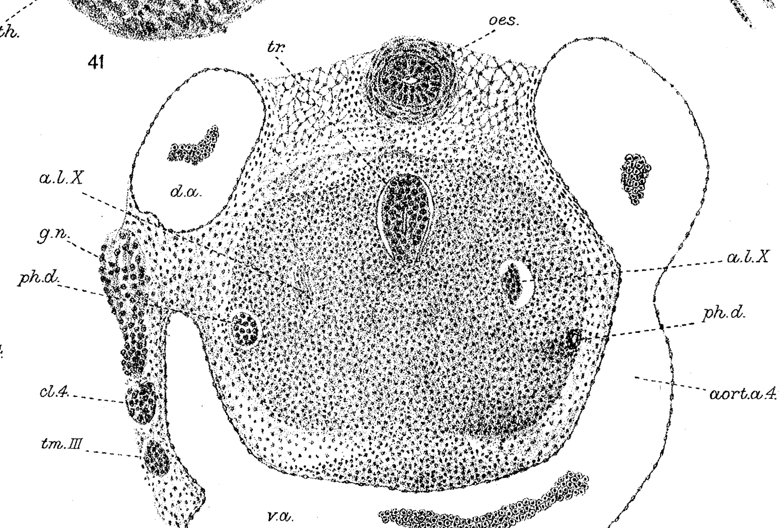

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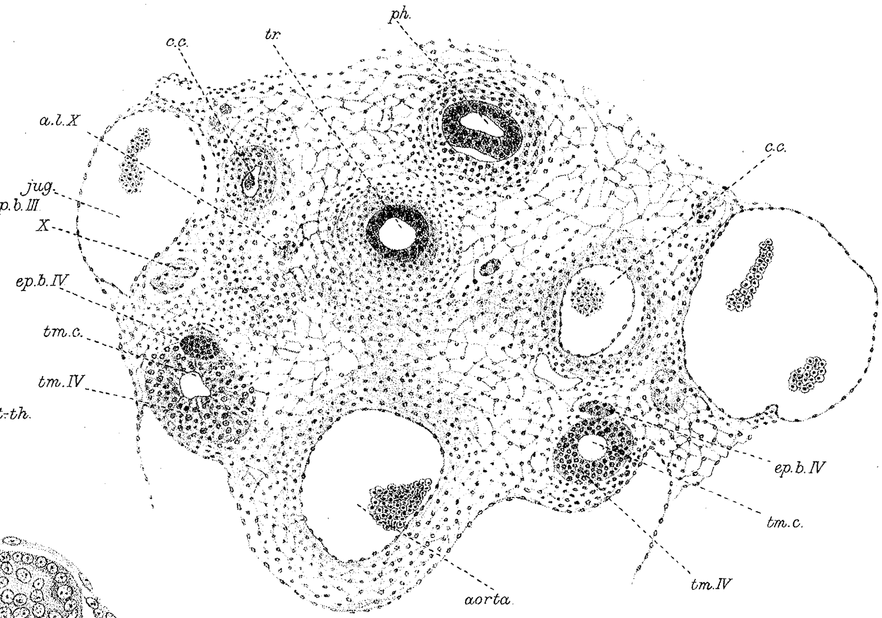

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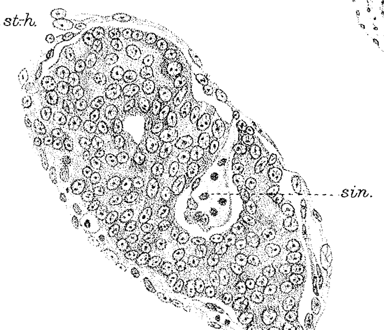

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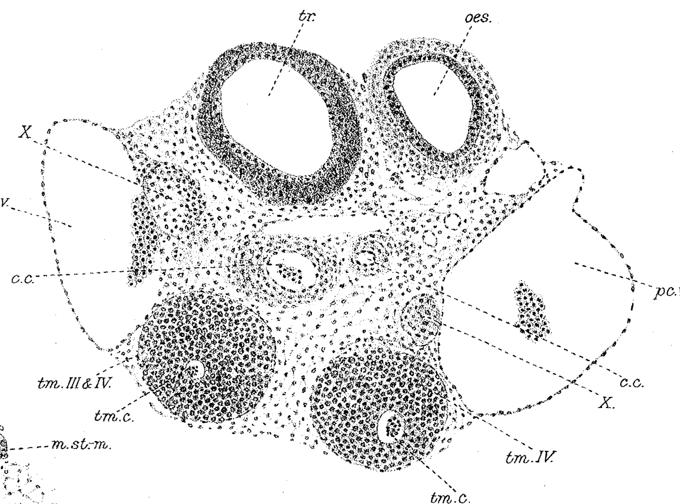

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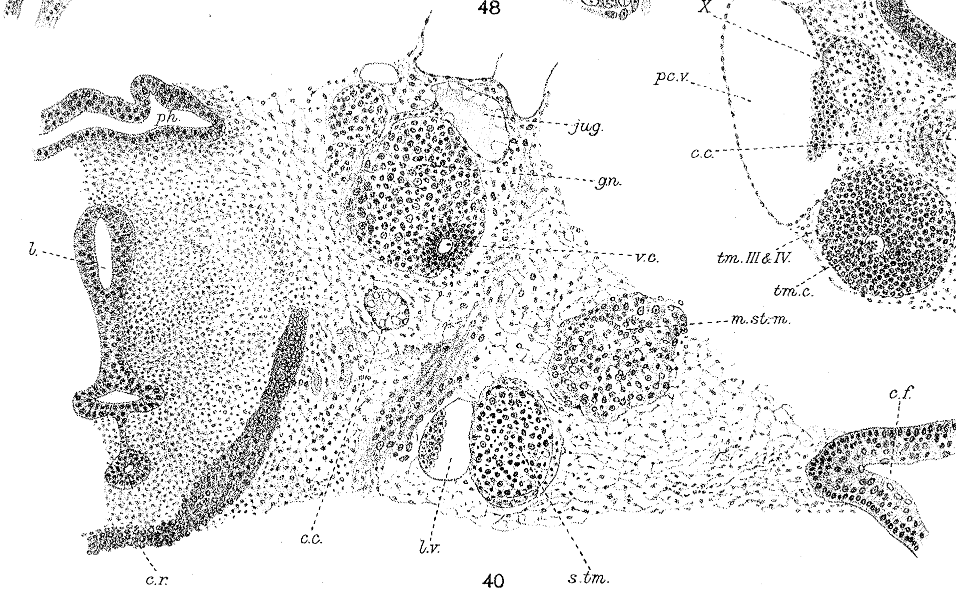

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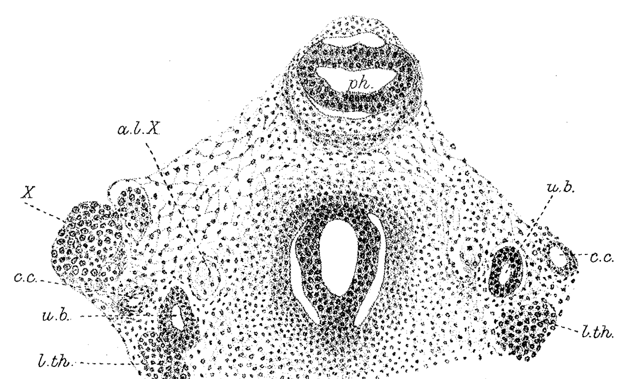

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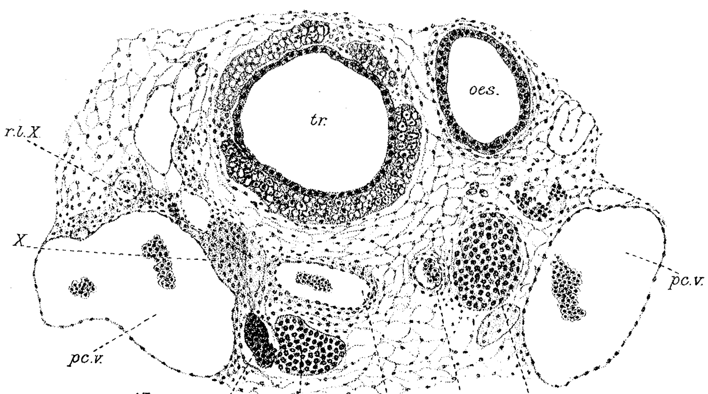

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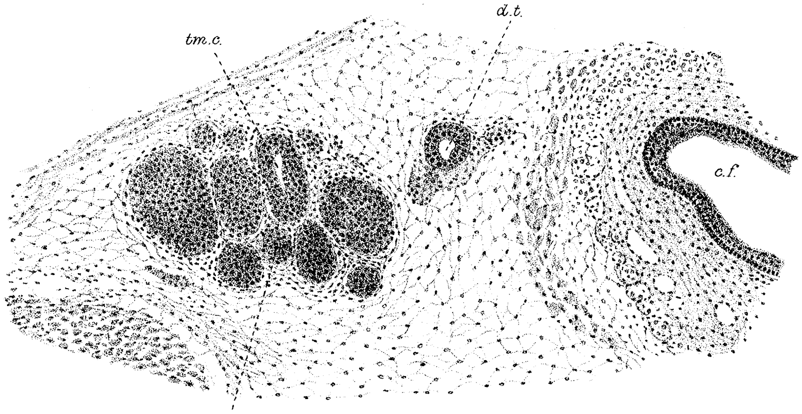

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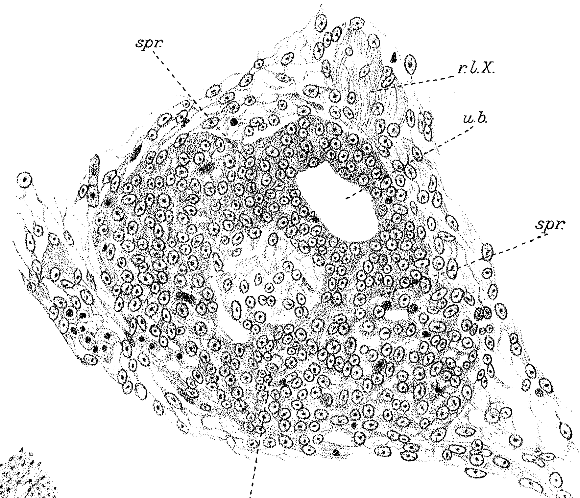

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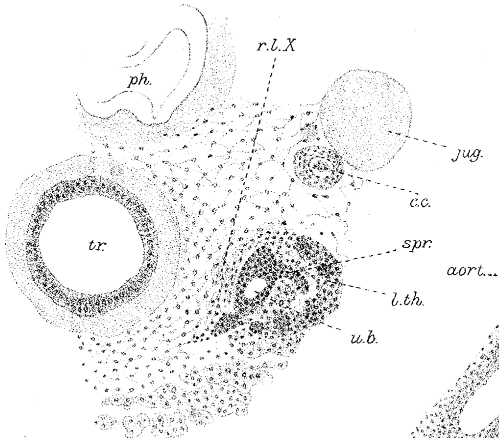

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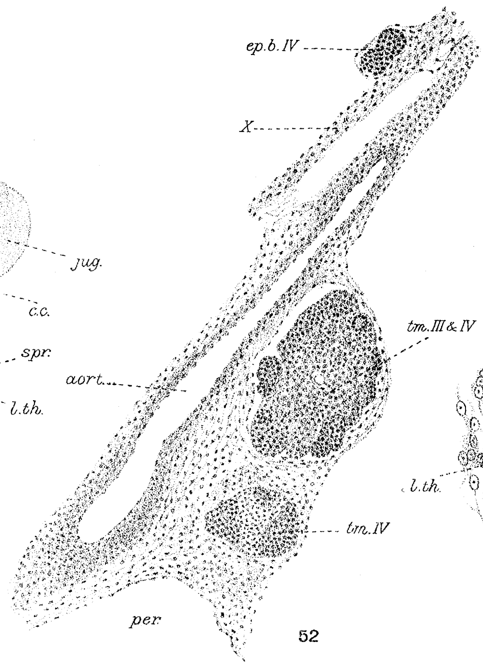

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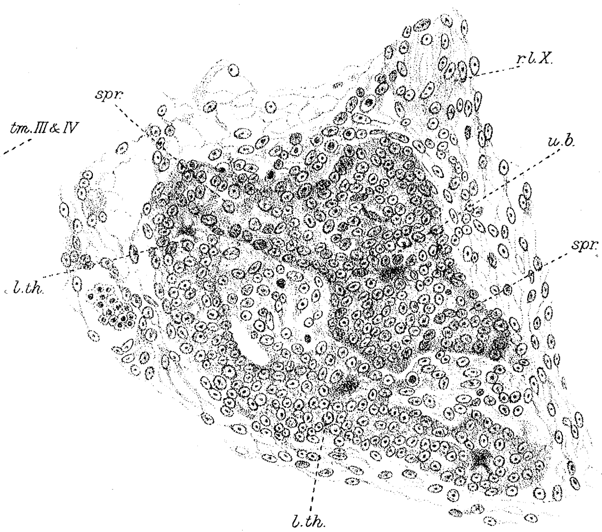

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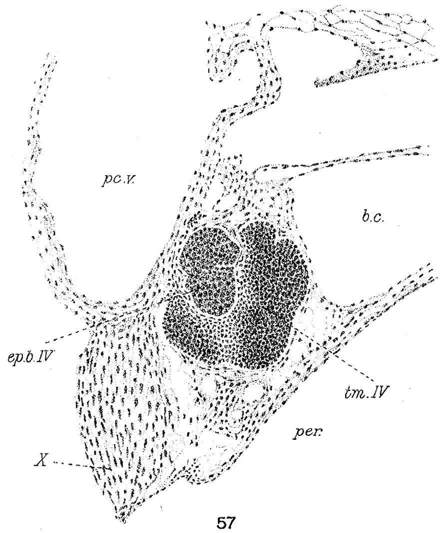

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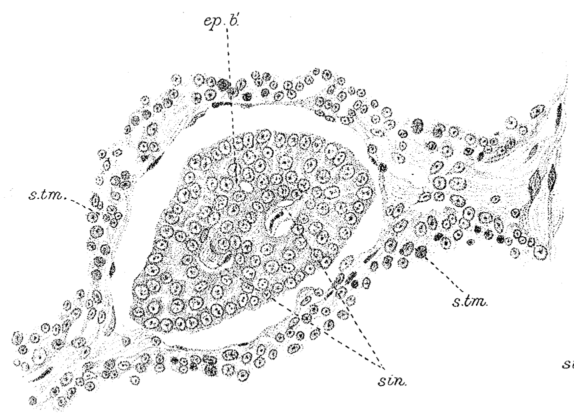

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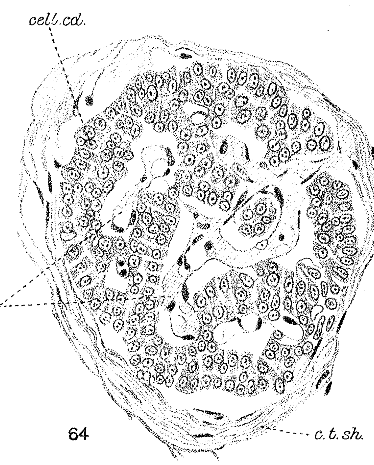

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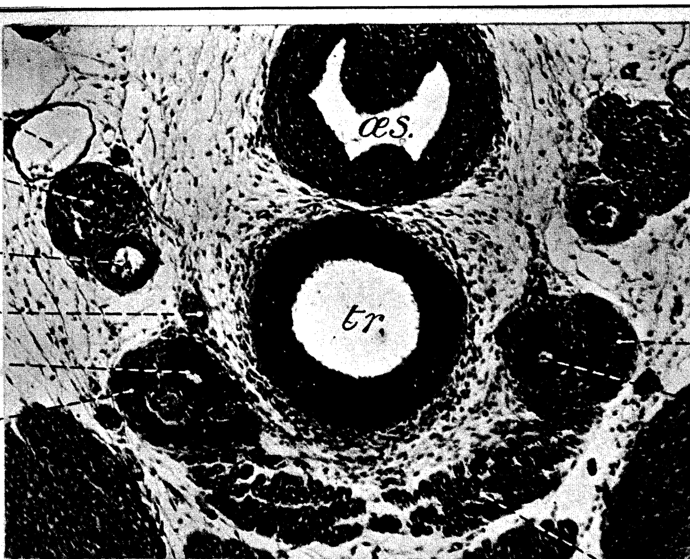

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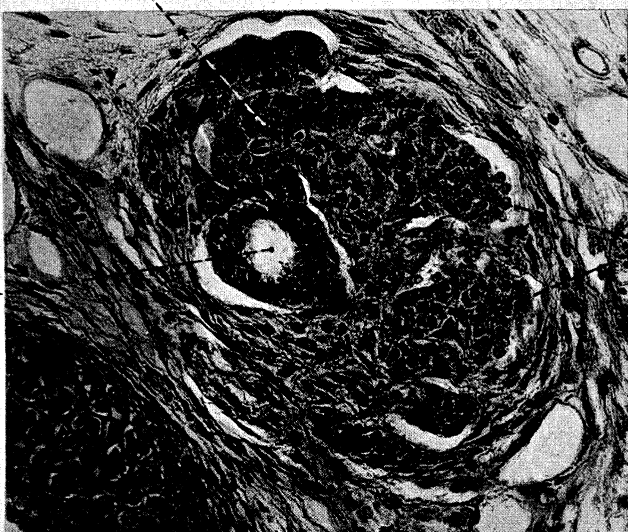

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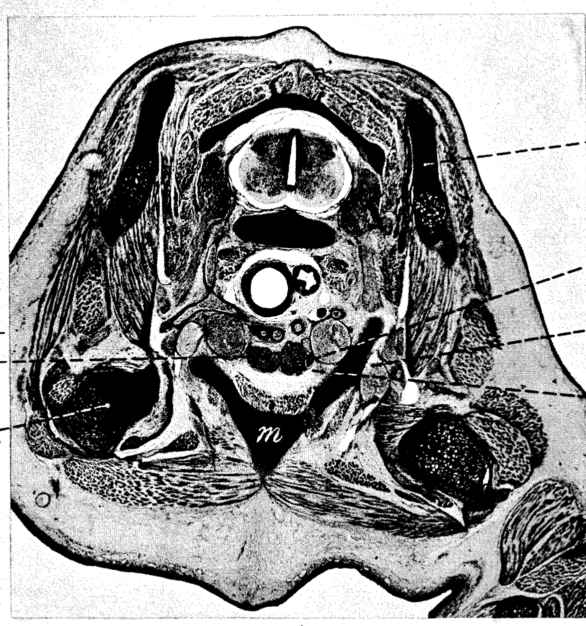

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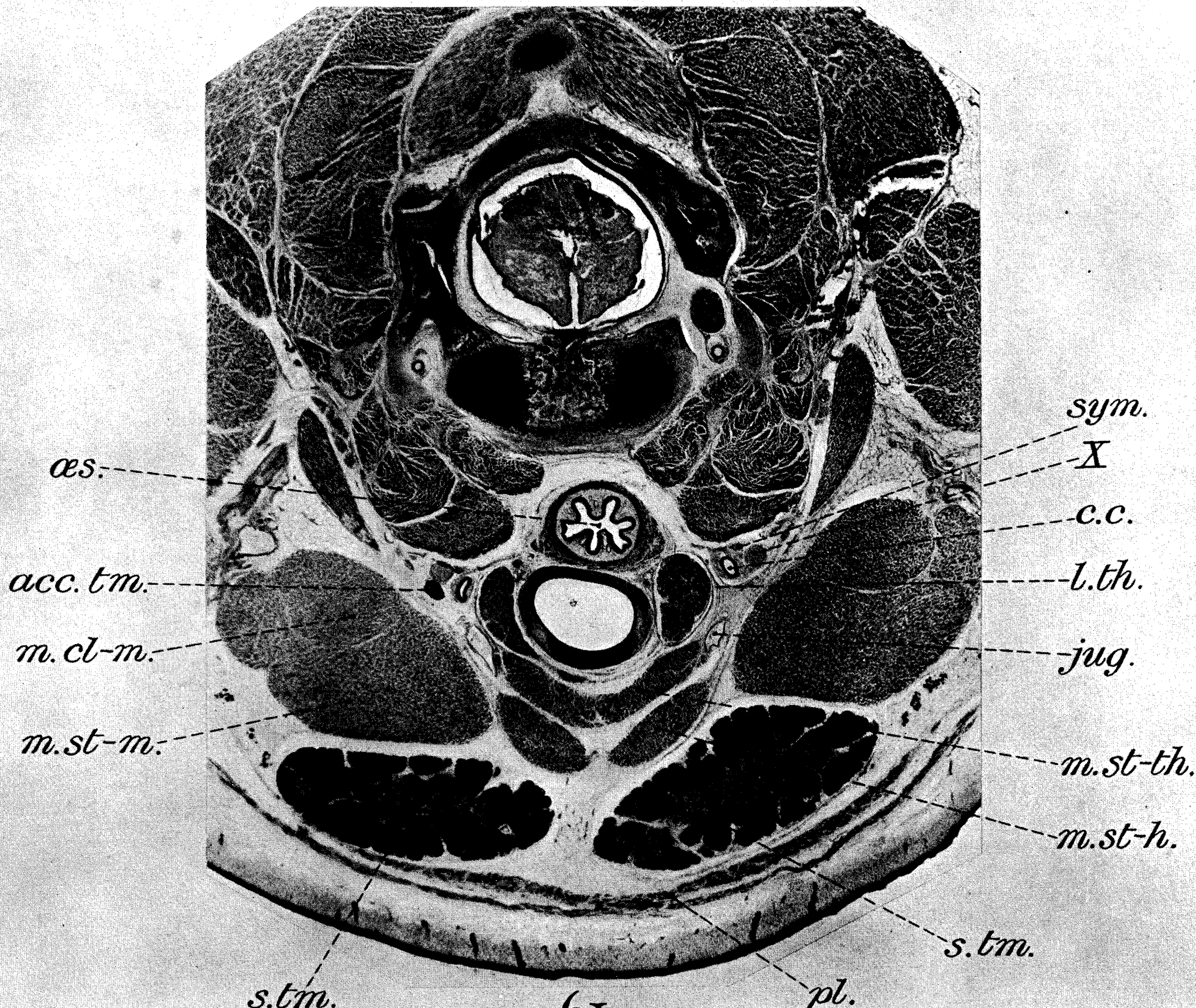

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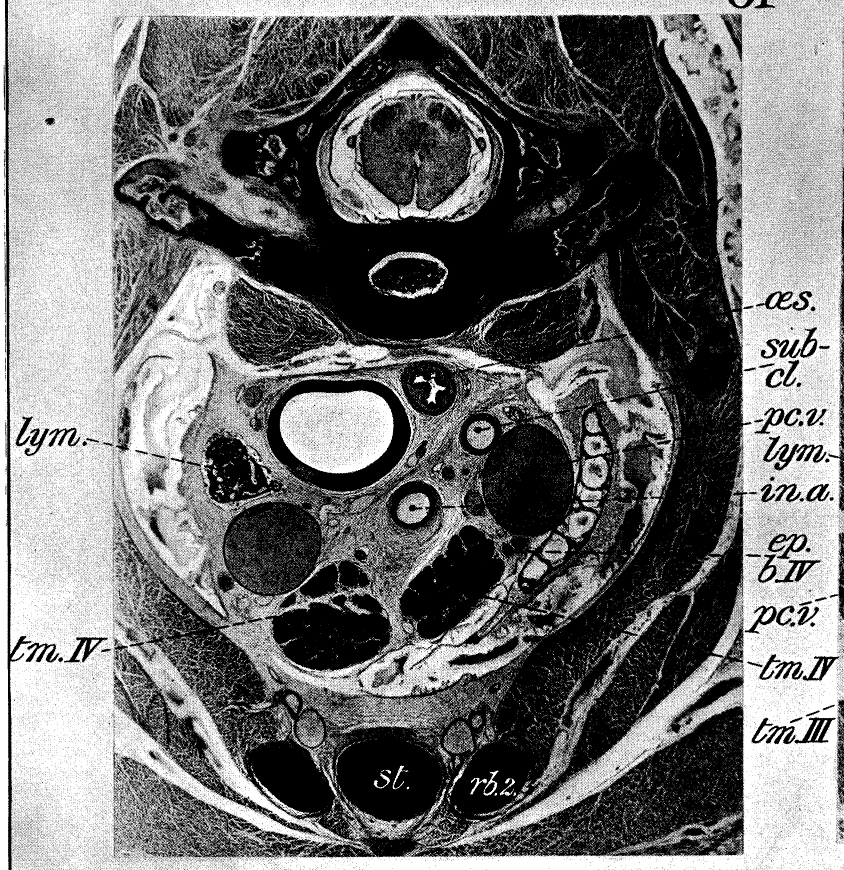

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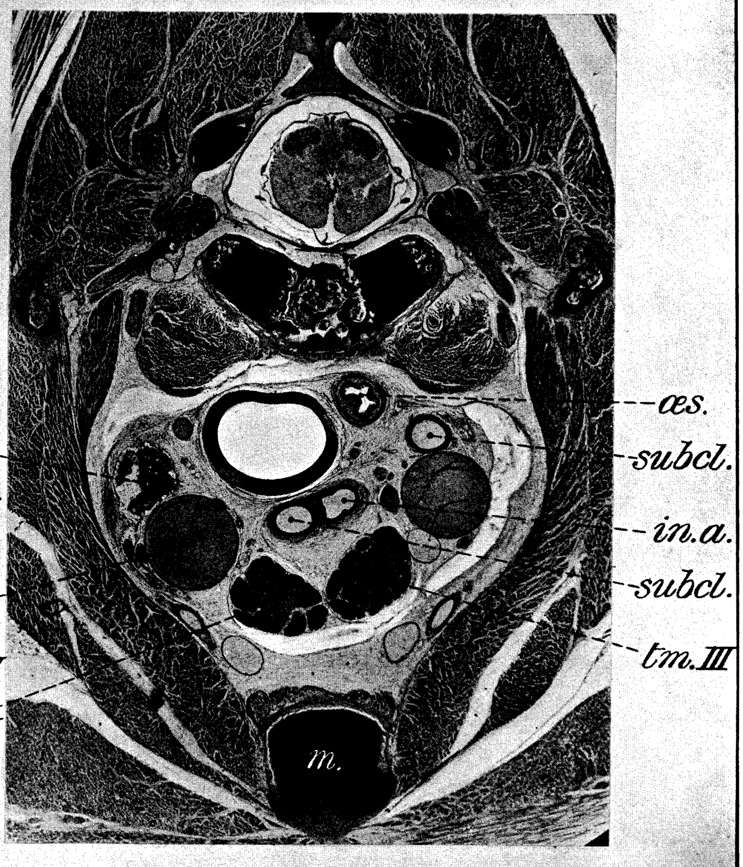

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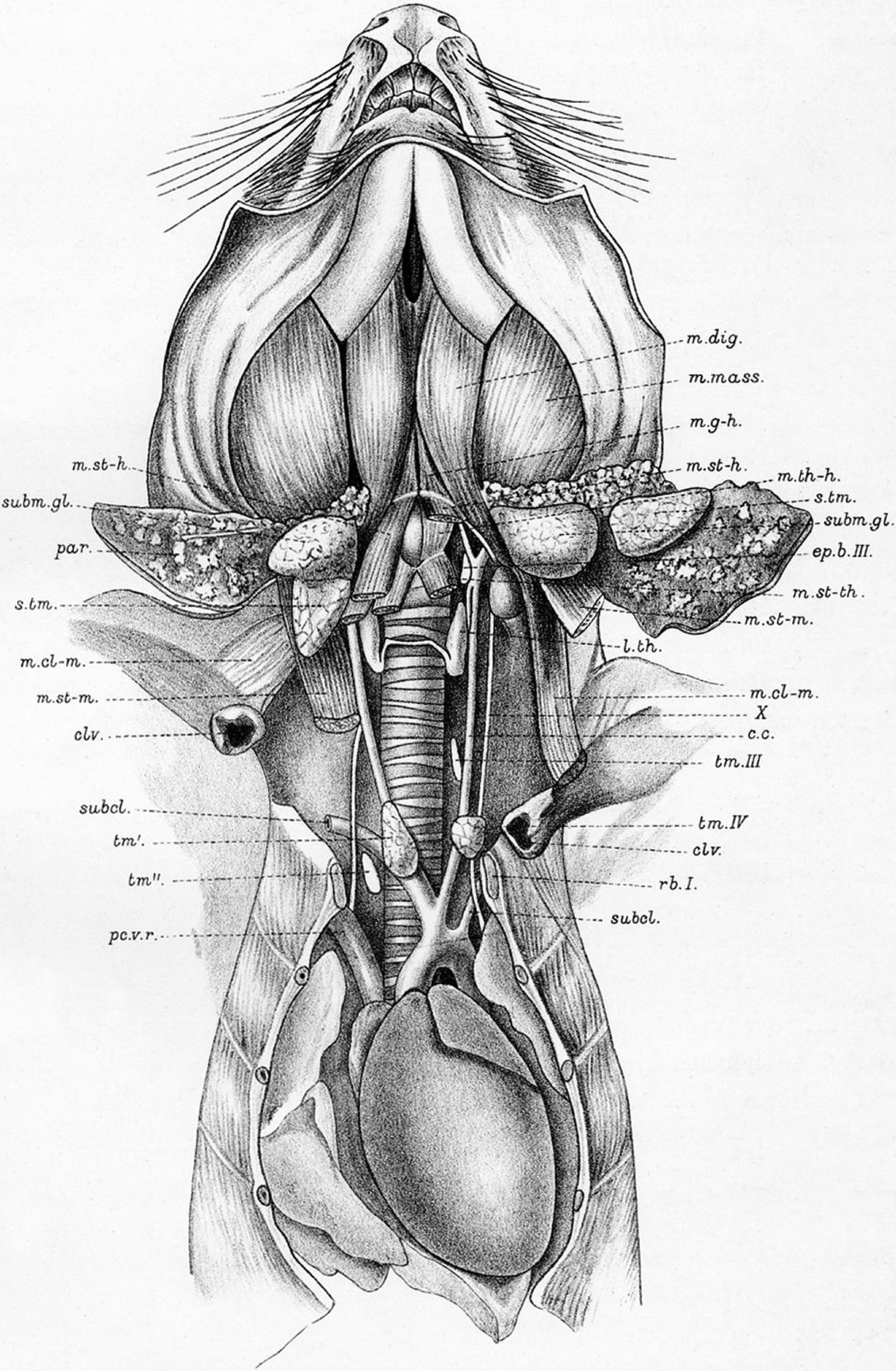
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par.
ep.b.III.
s.tm.
m.st-th.
m.st-m.
l.th.
m.cl-m.
m.cl-m.
m.st-m.
X
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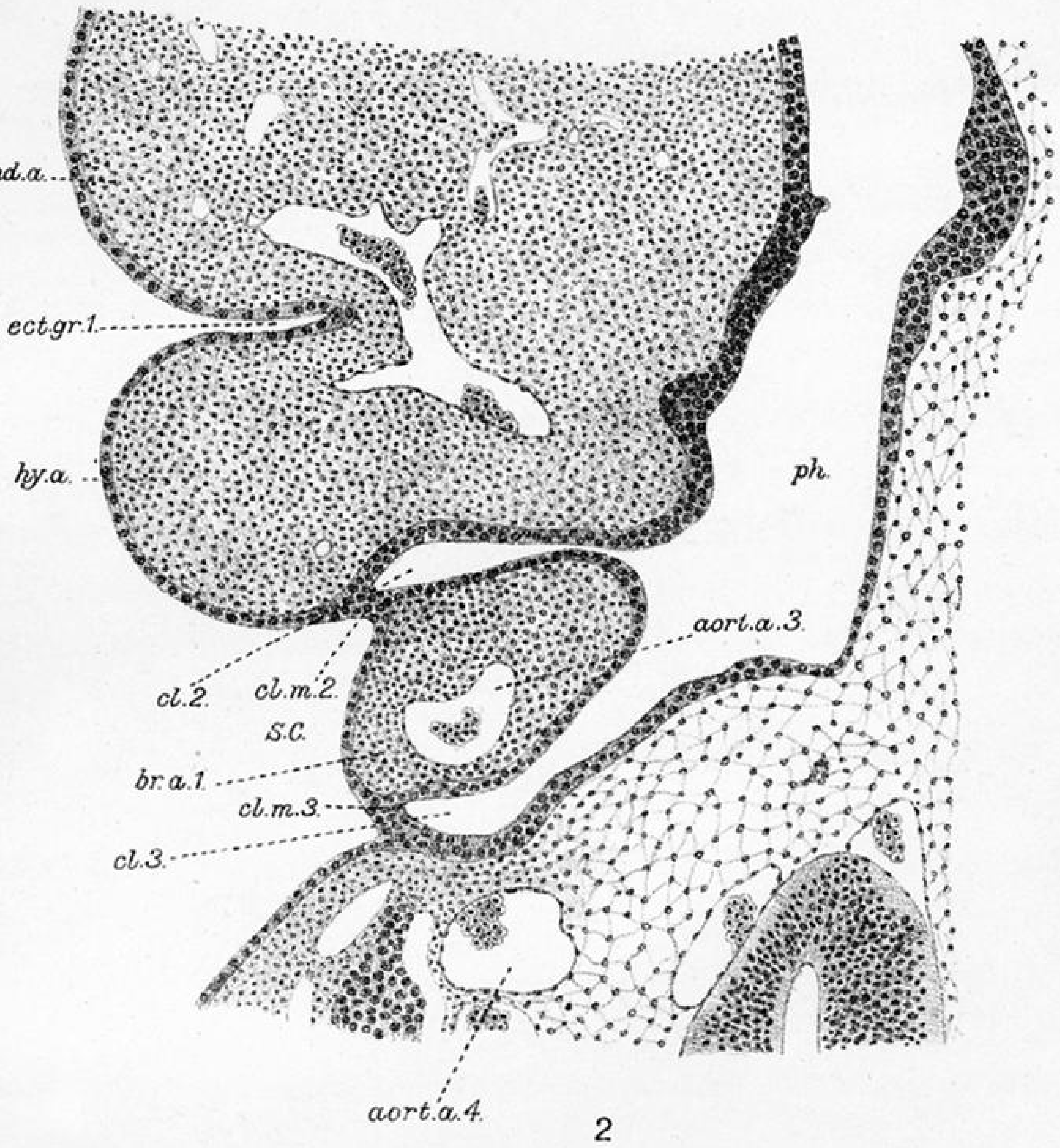
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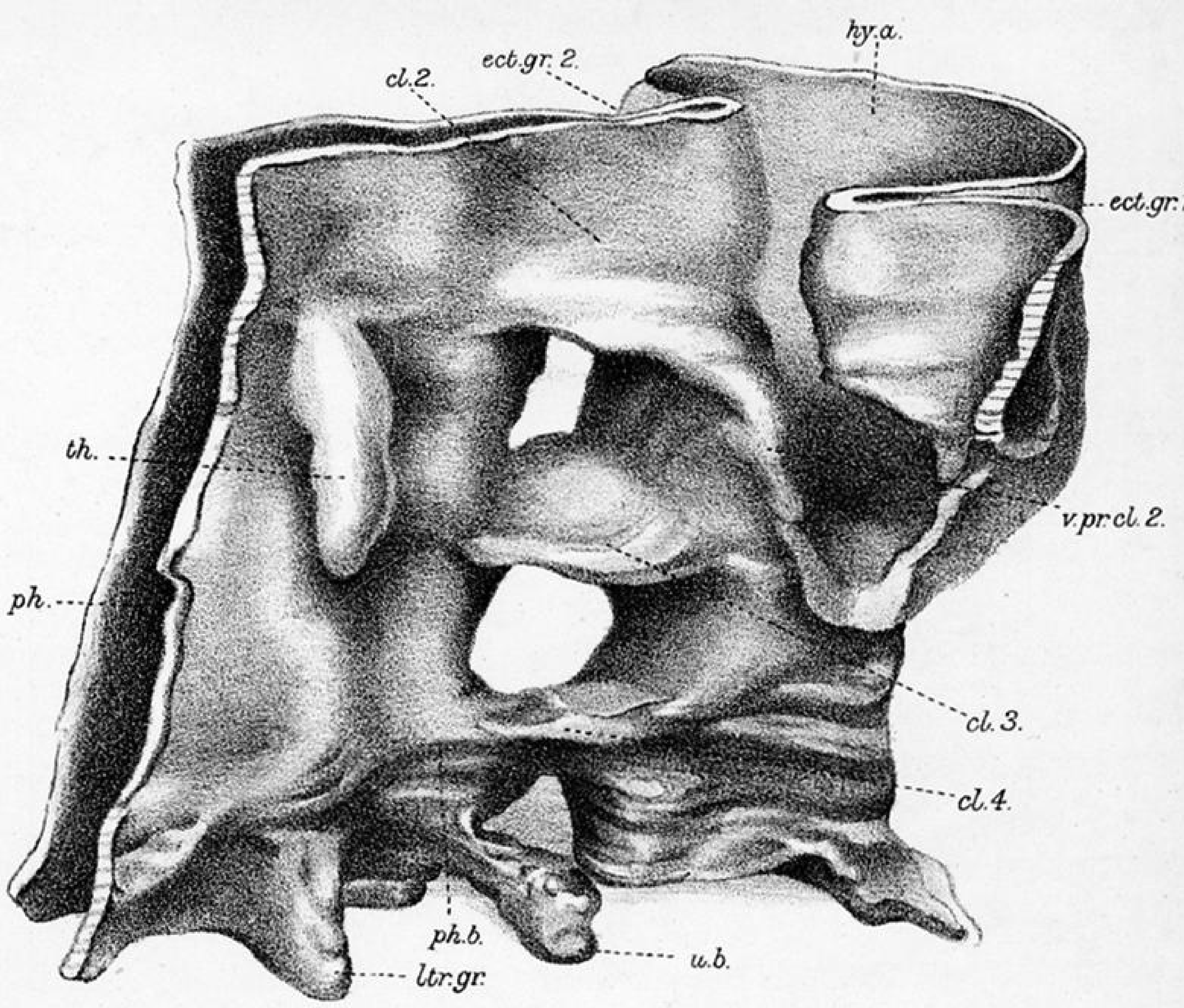
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ltr.gr.
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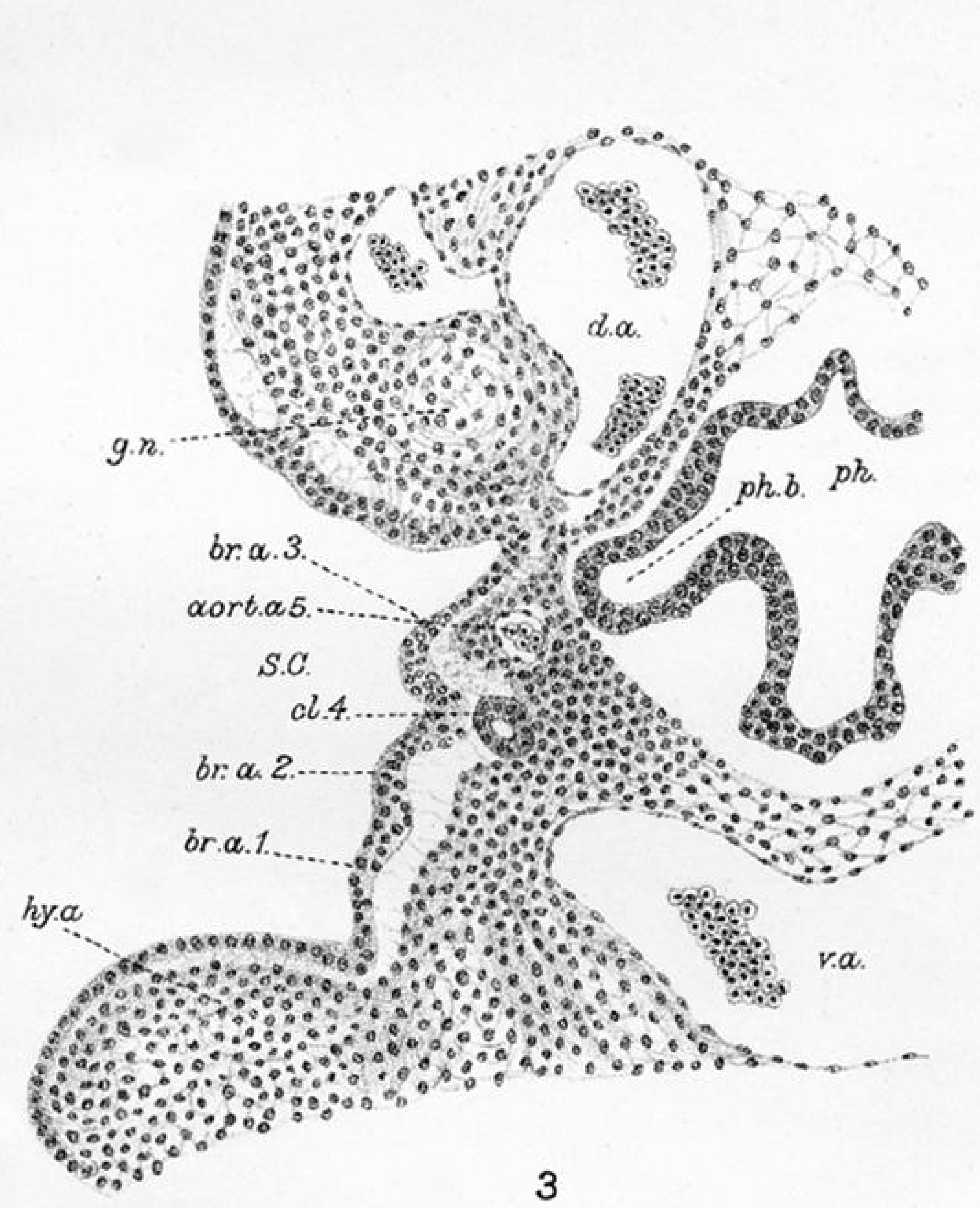
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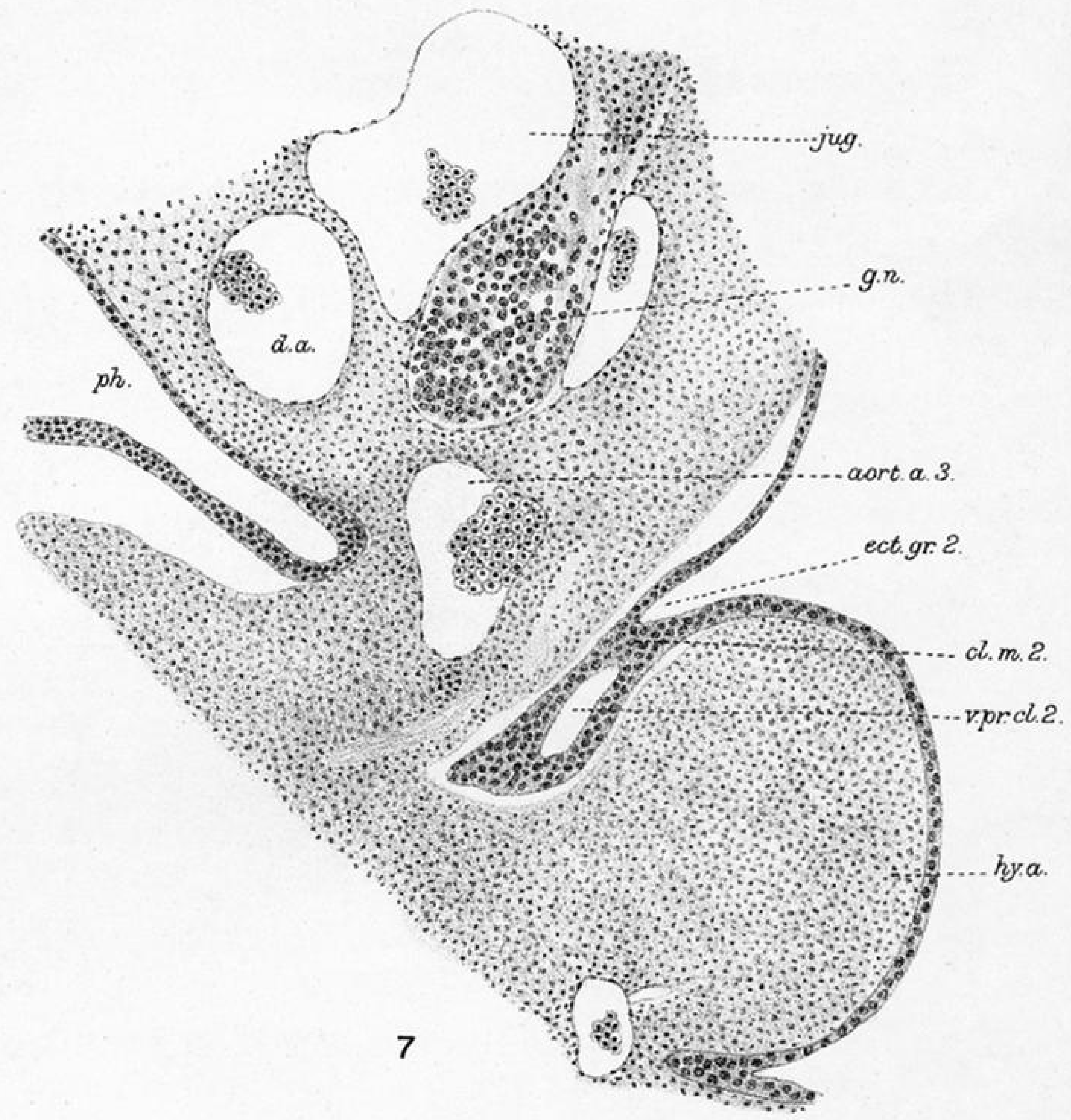
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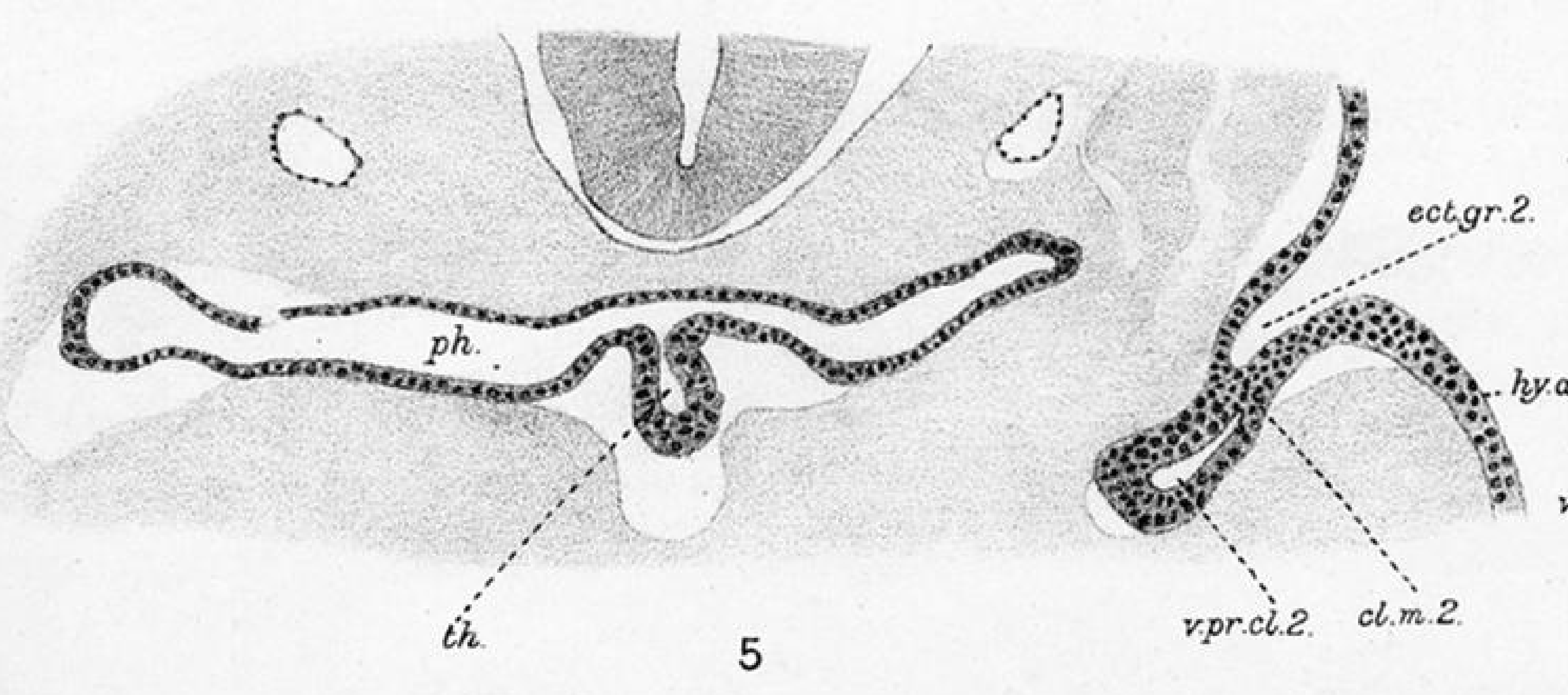
7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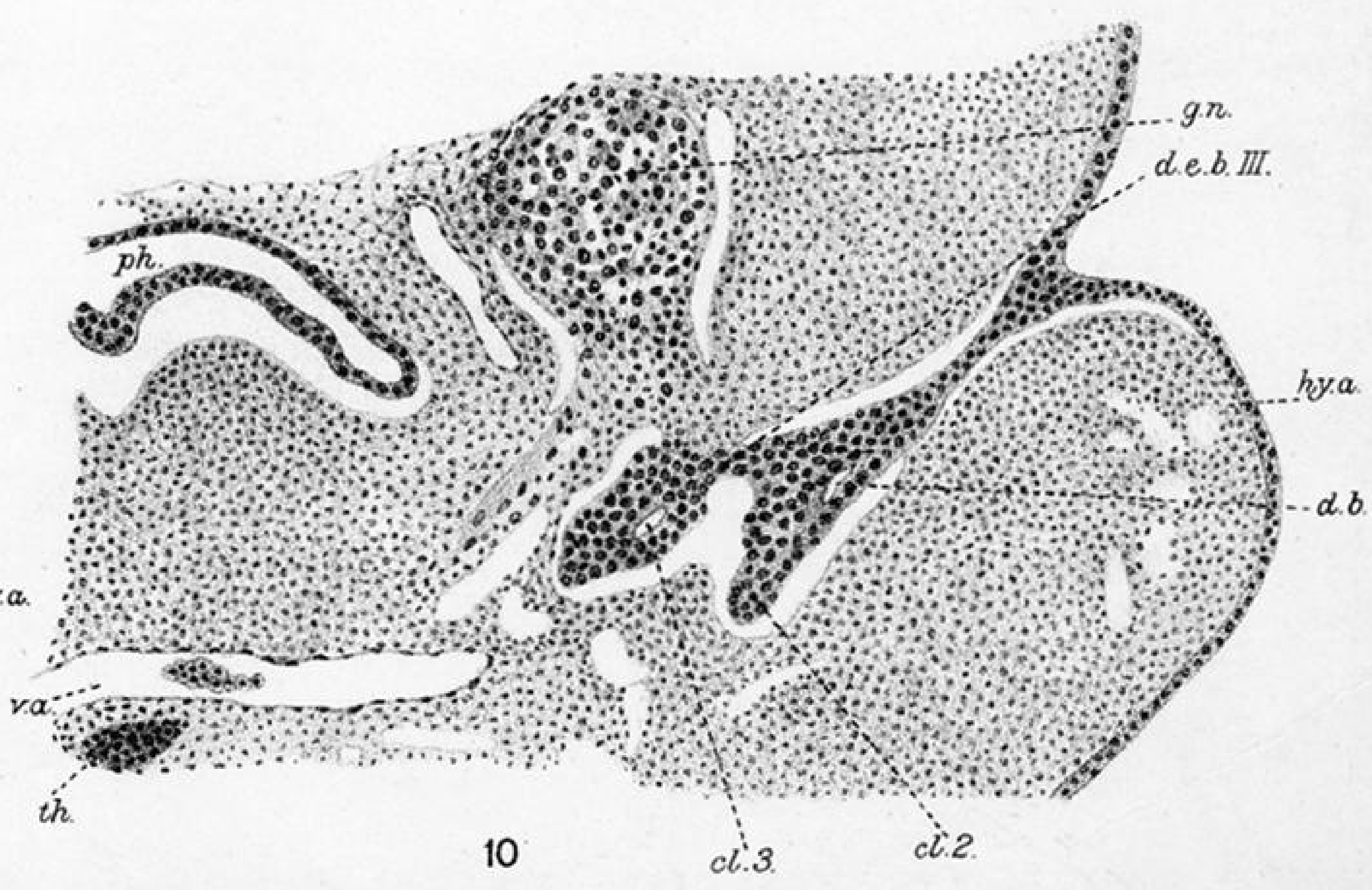
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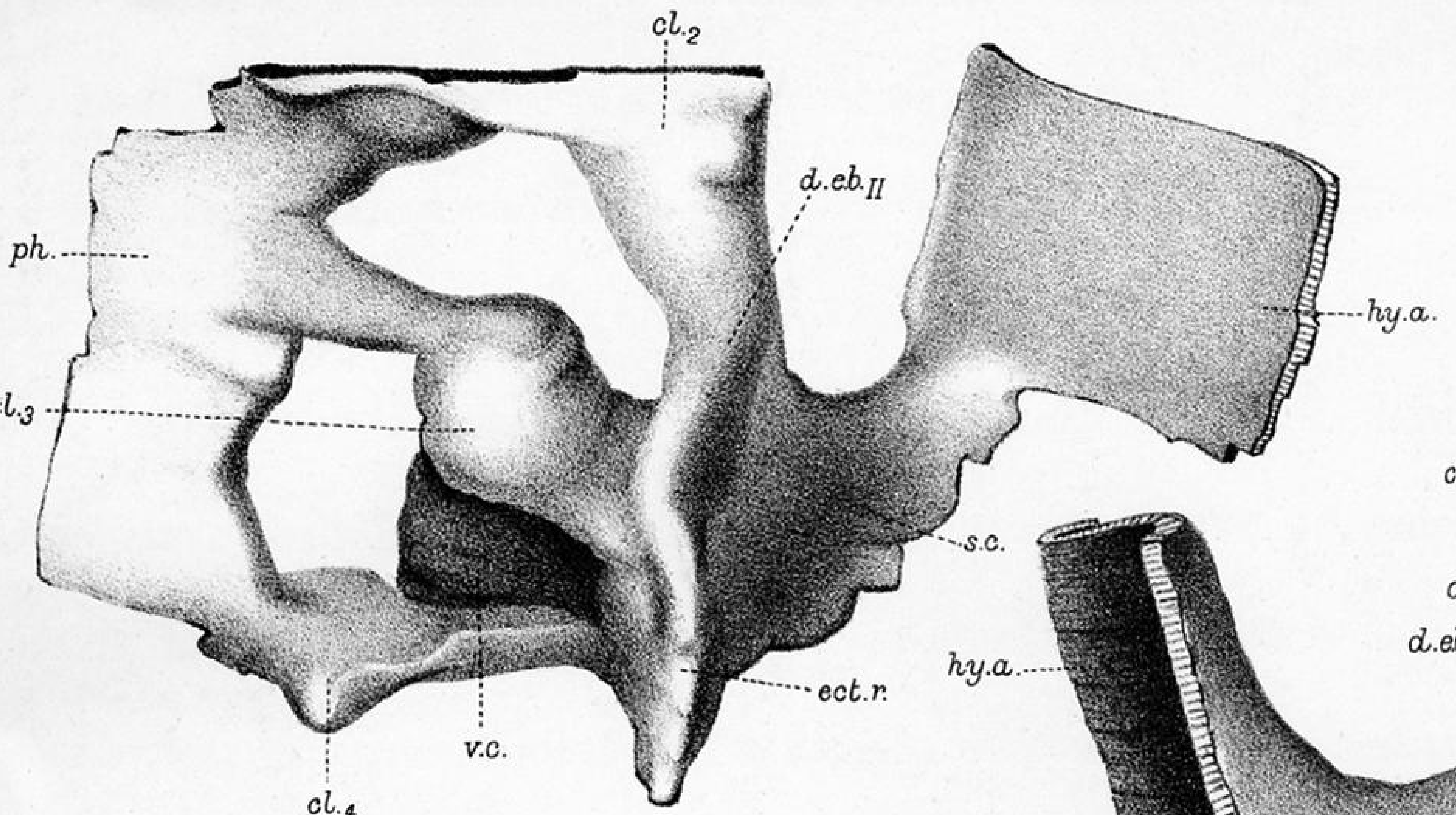

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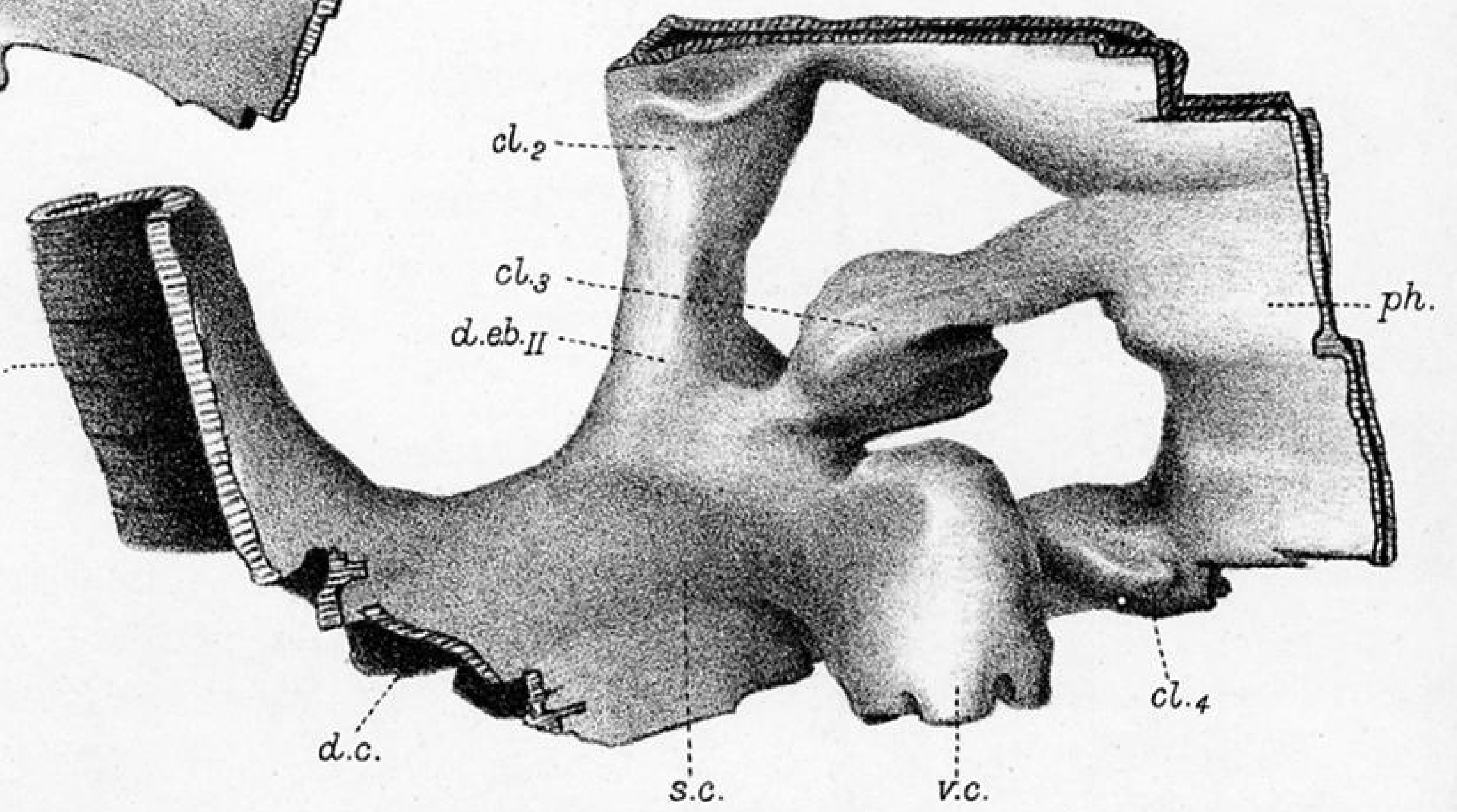

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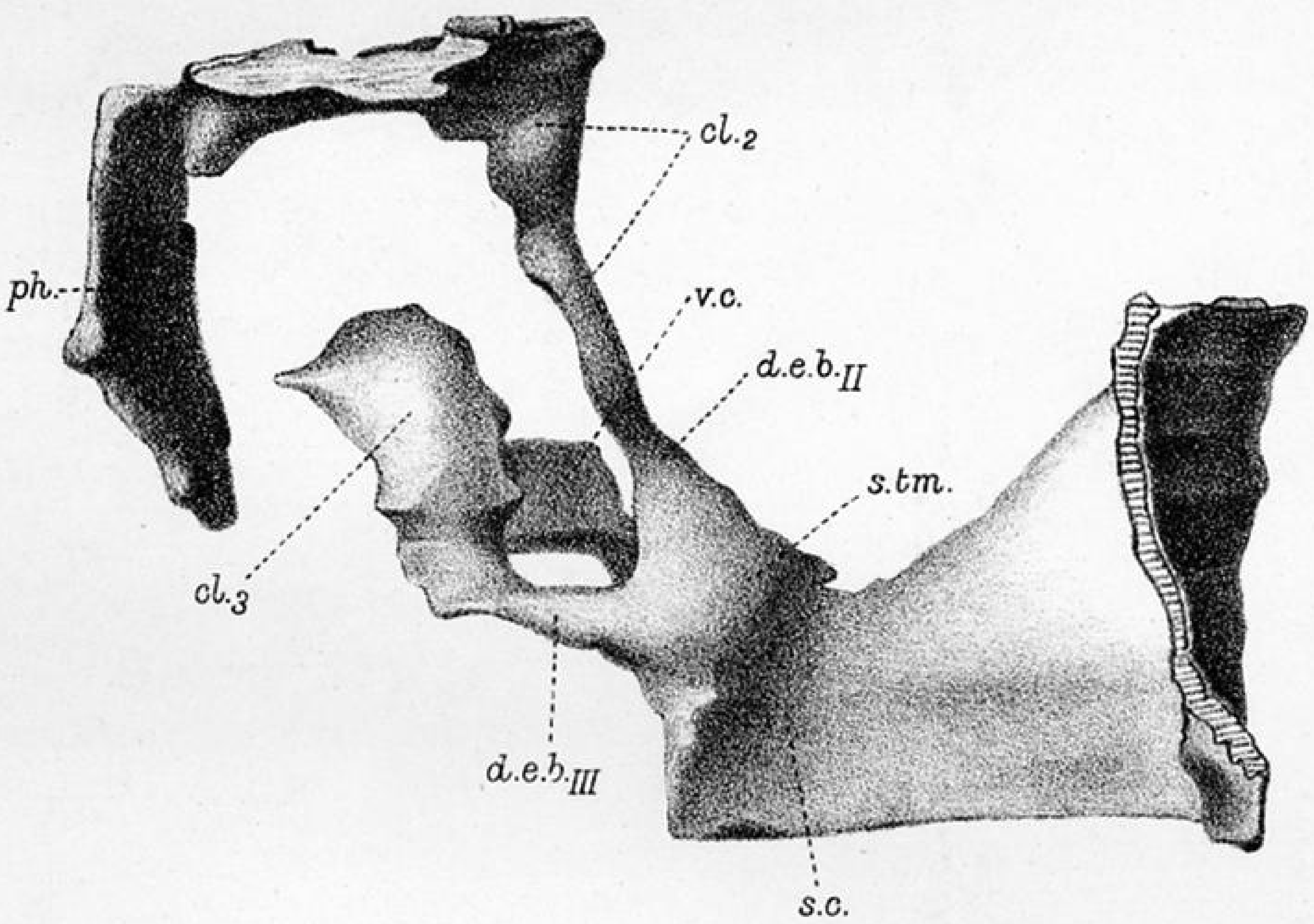

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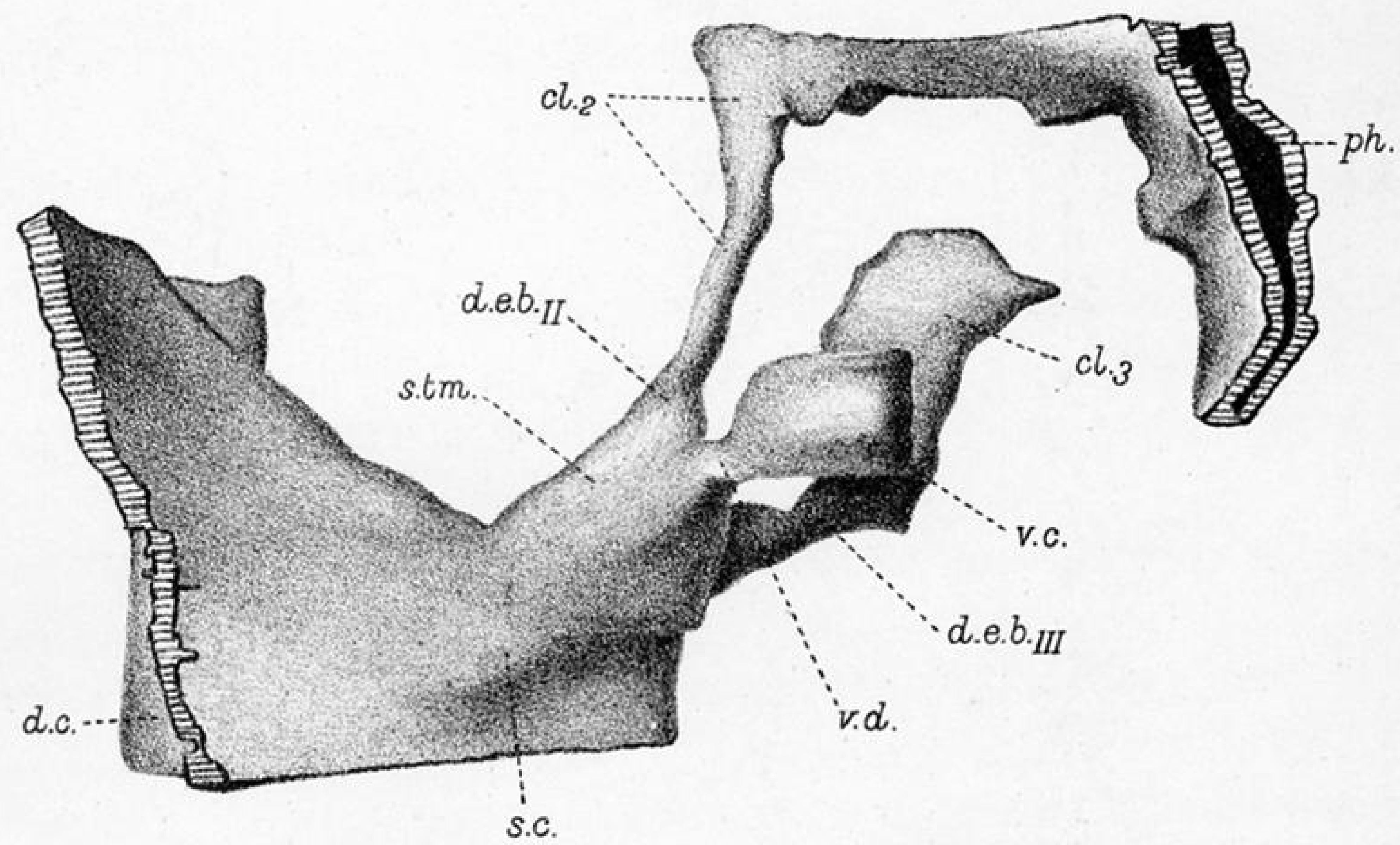

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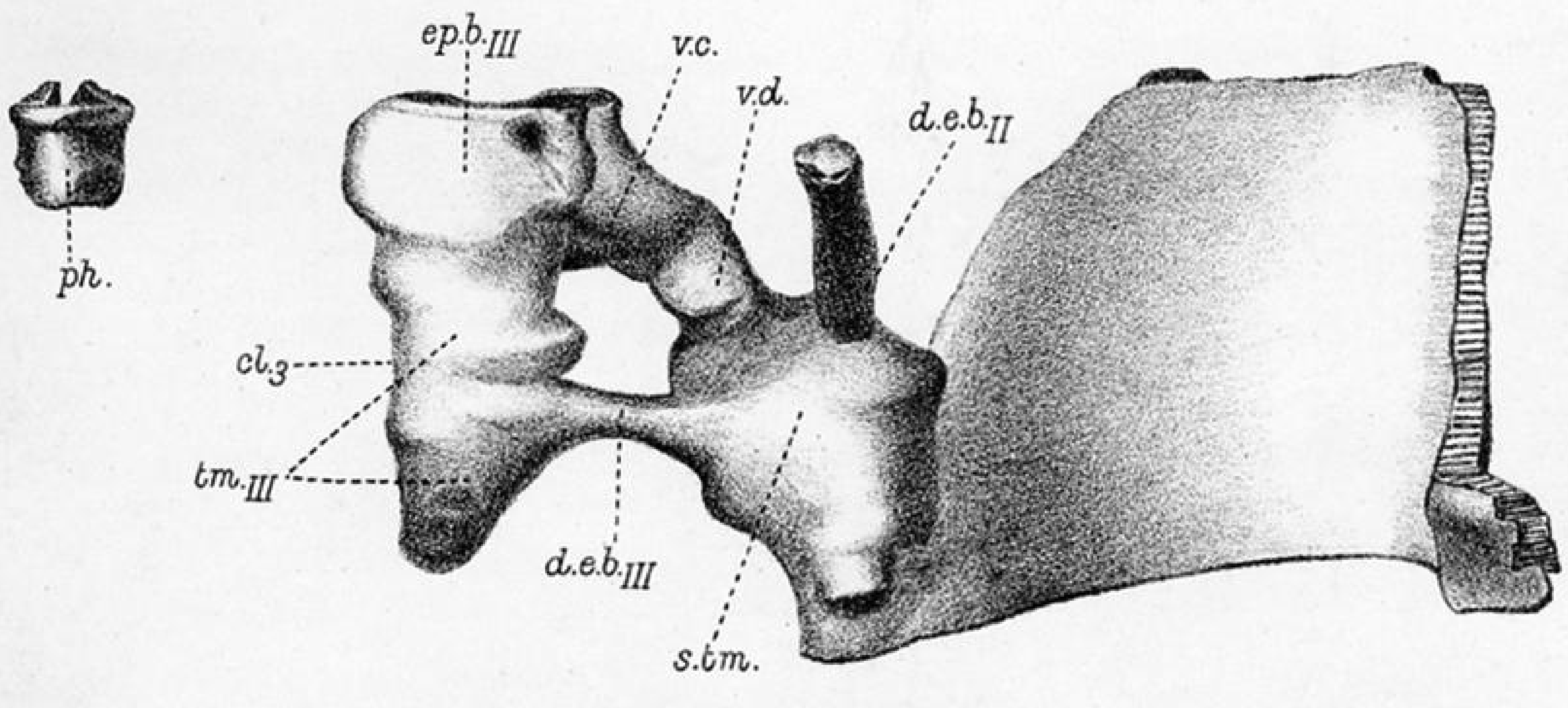

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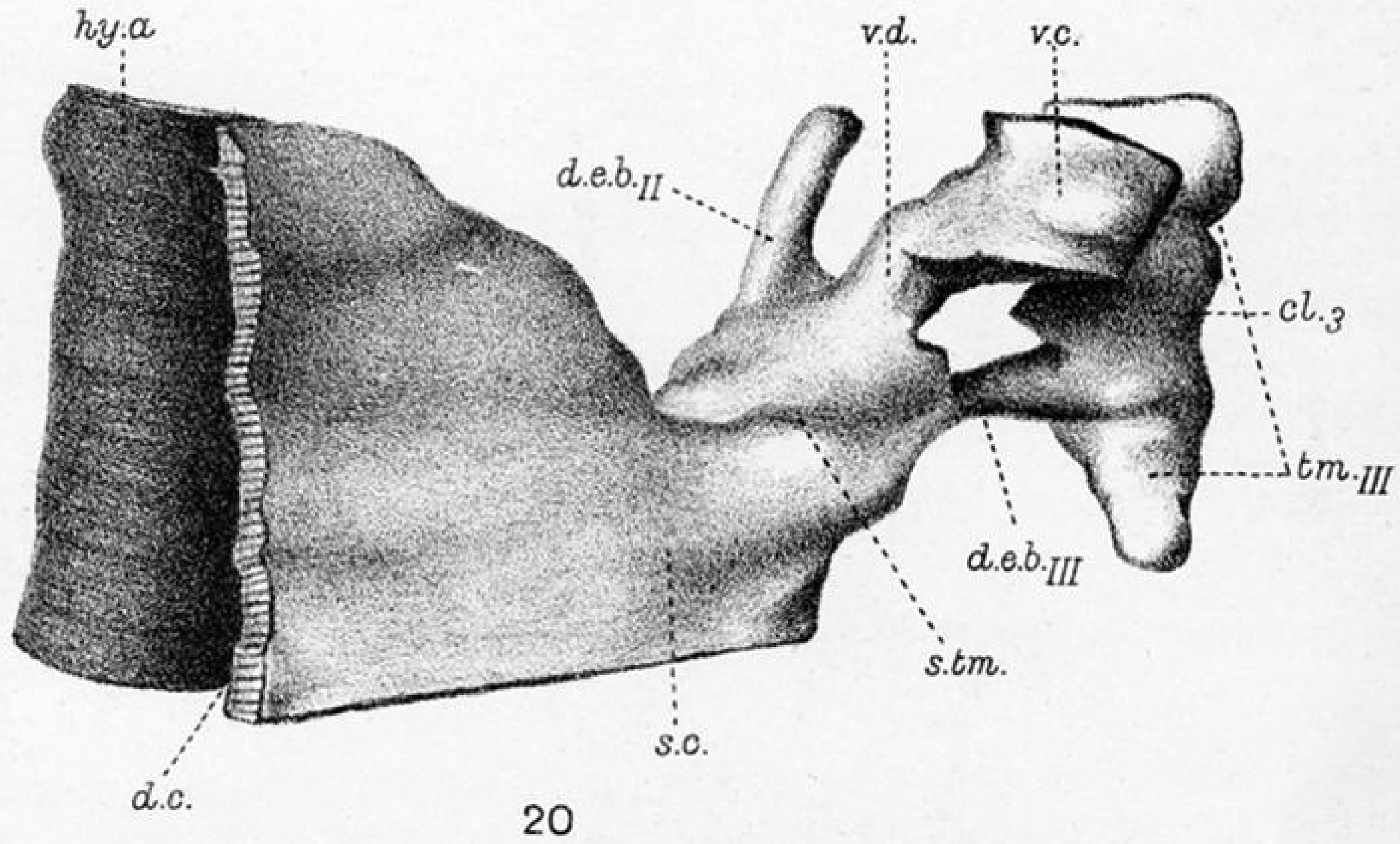

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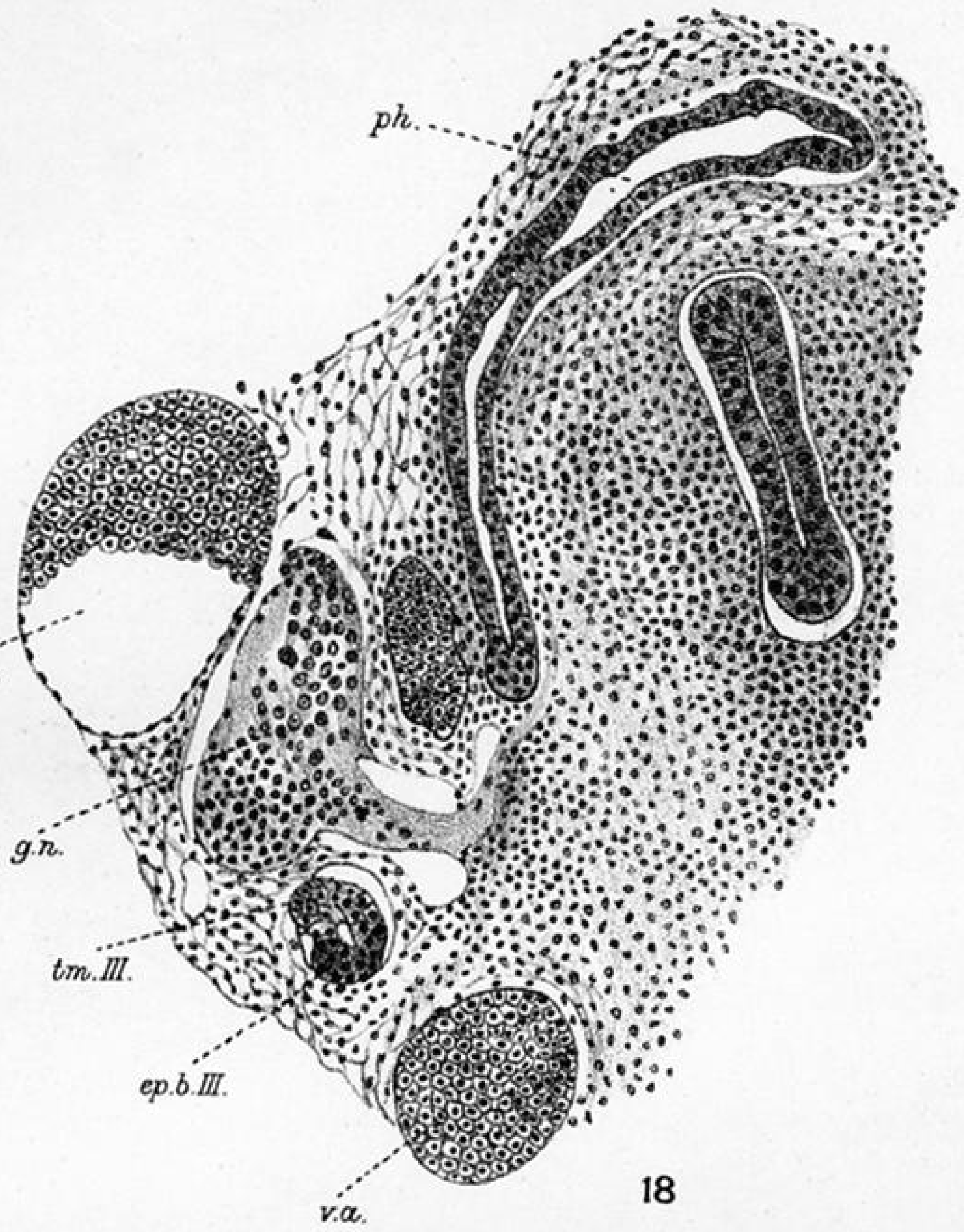

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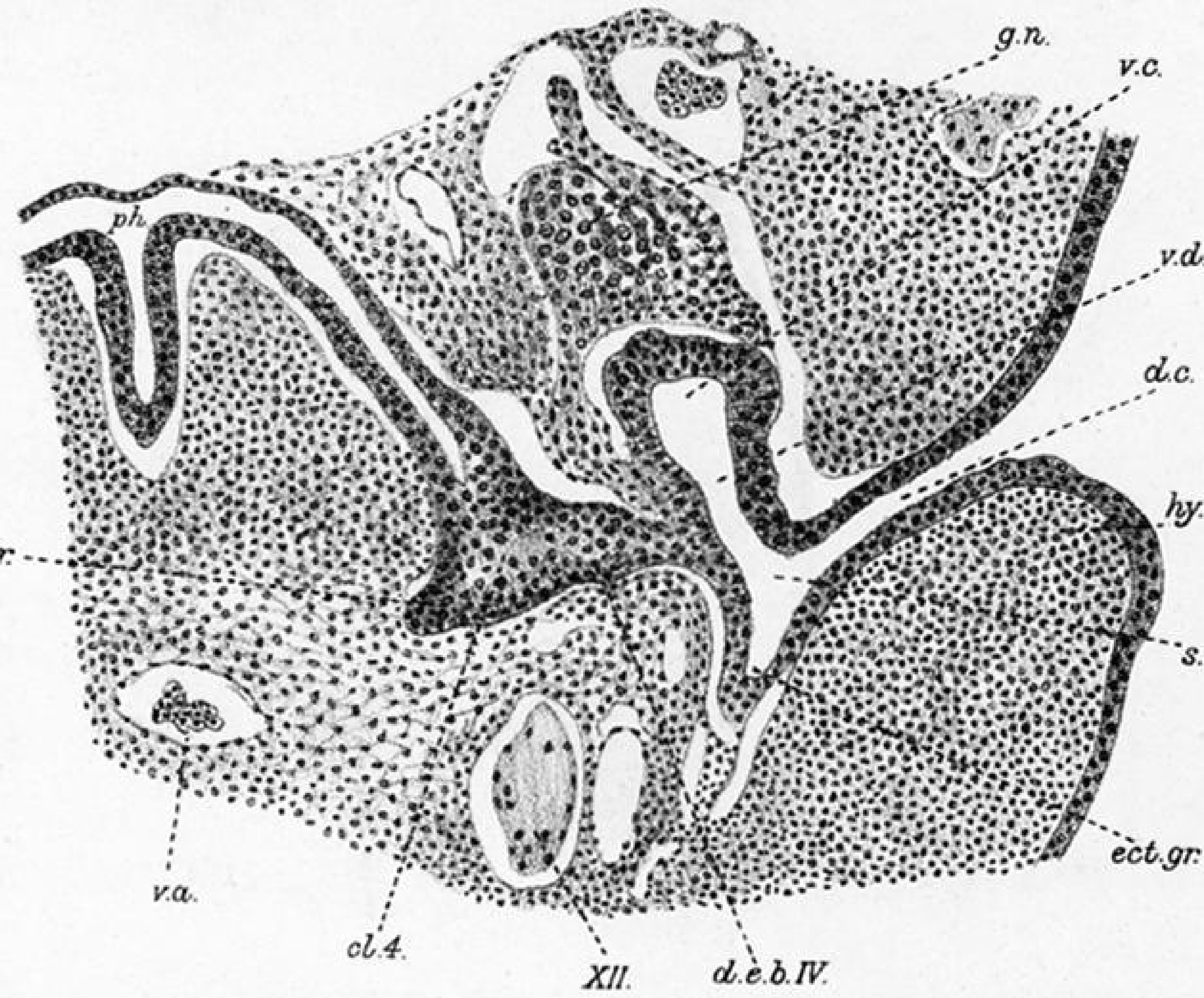

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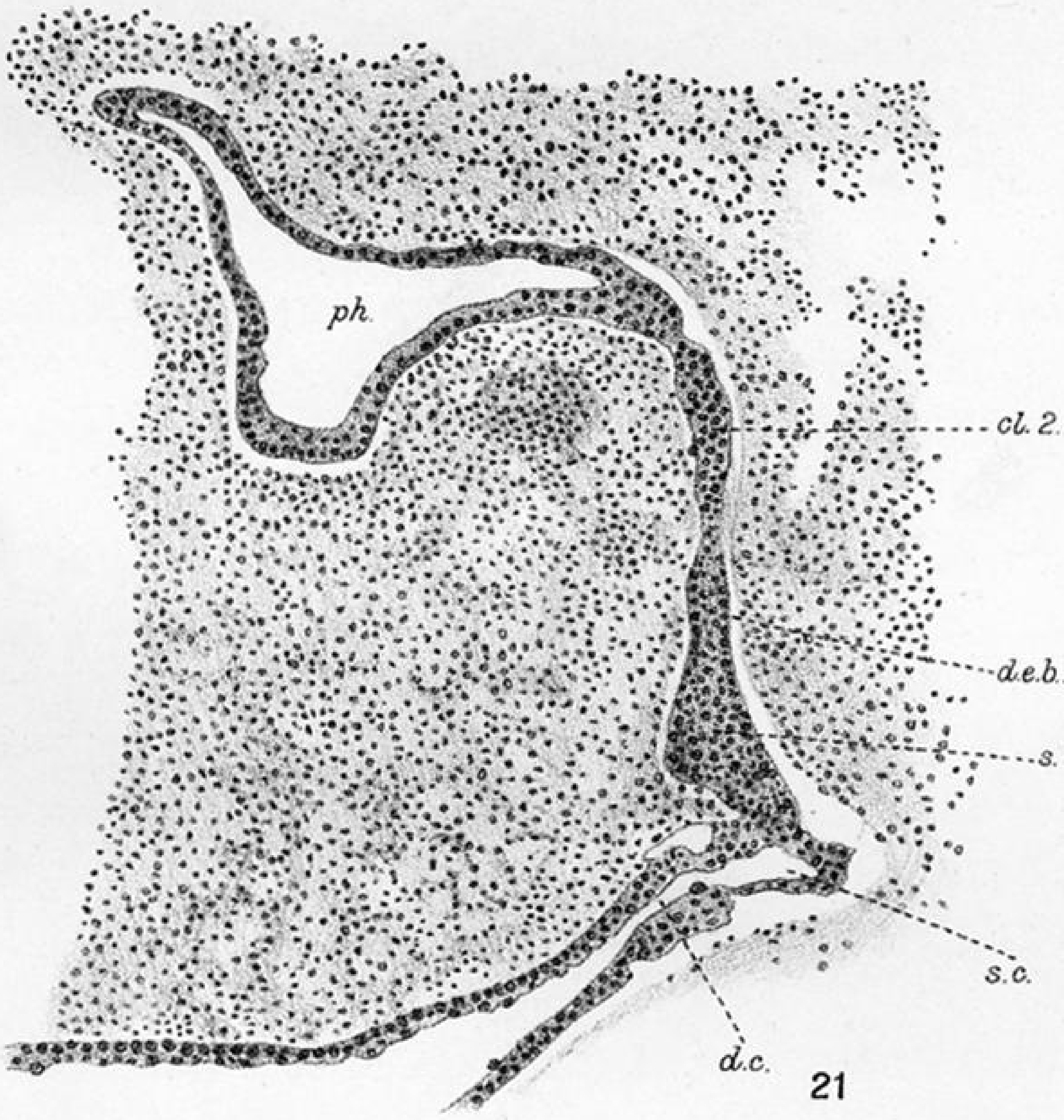

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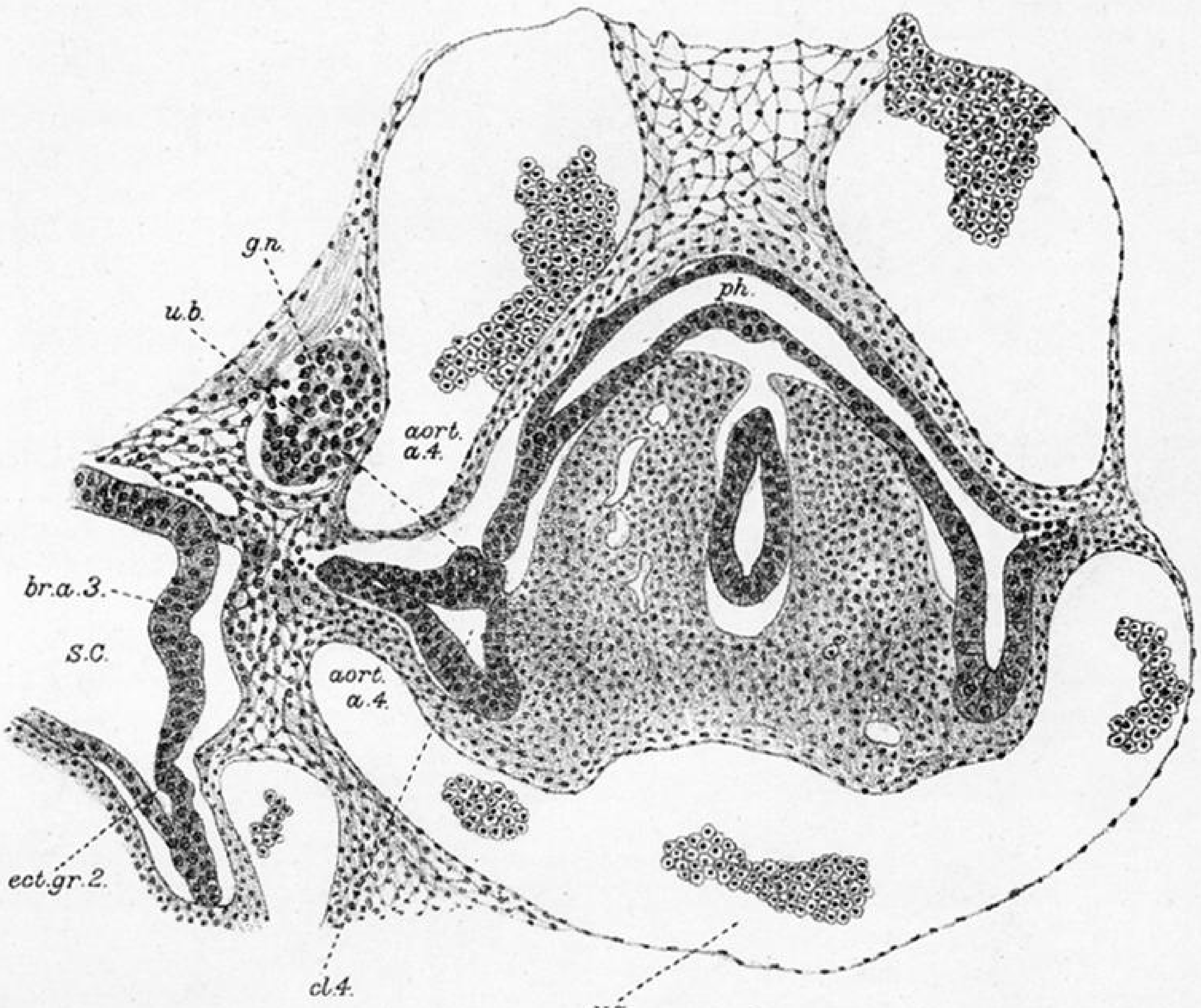

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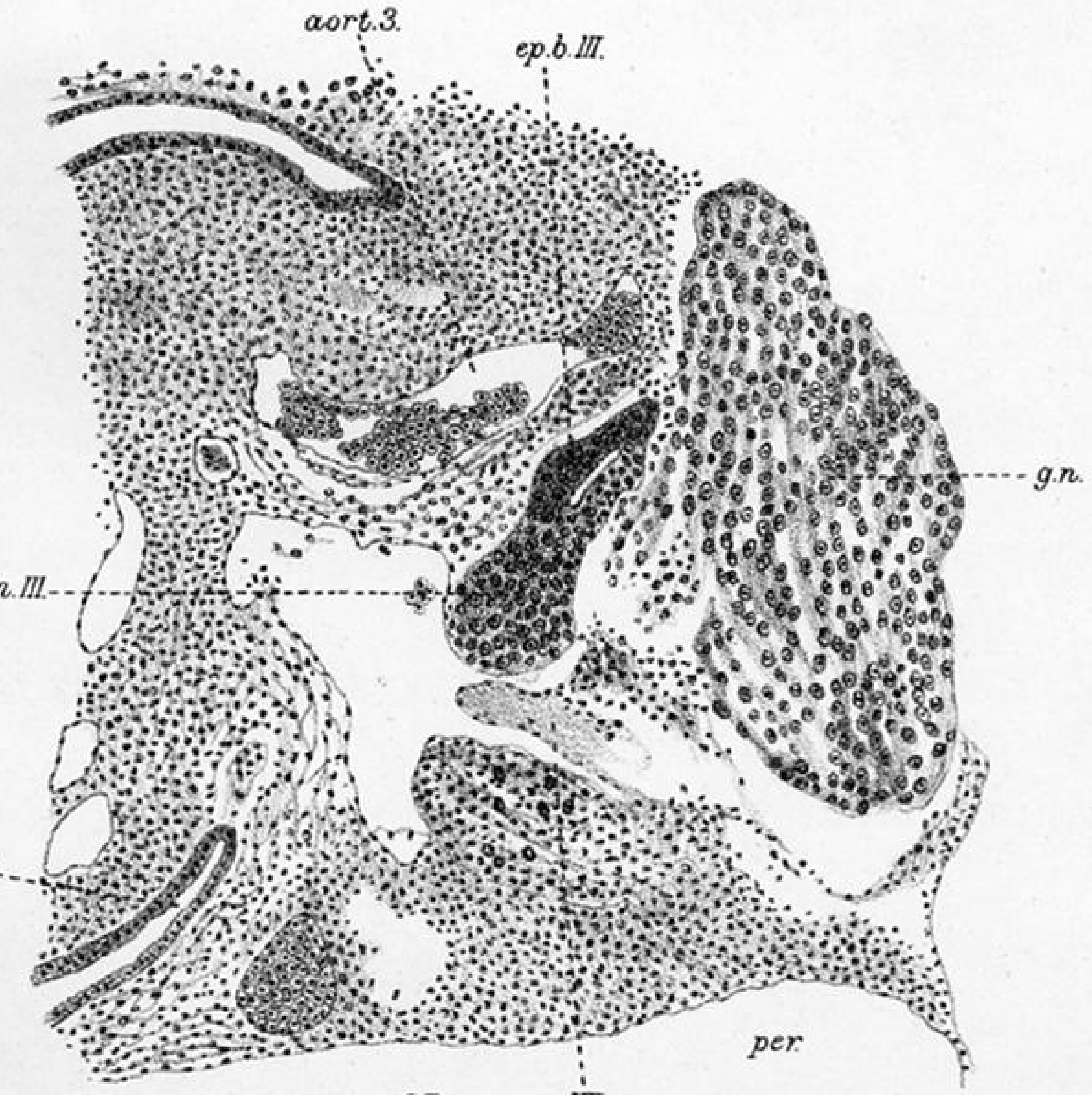

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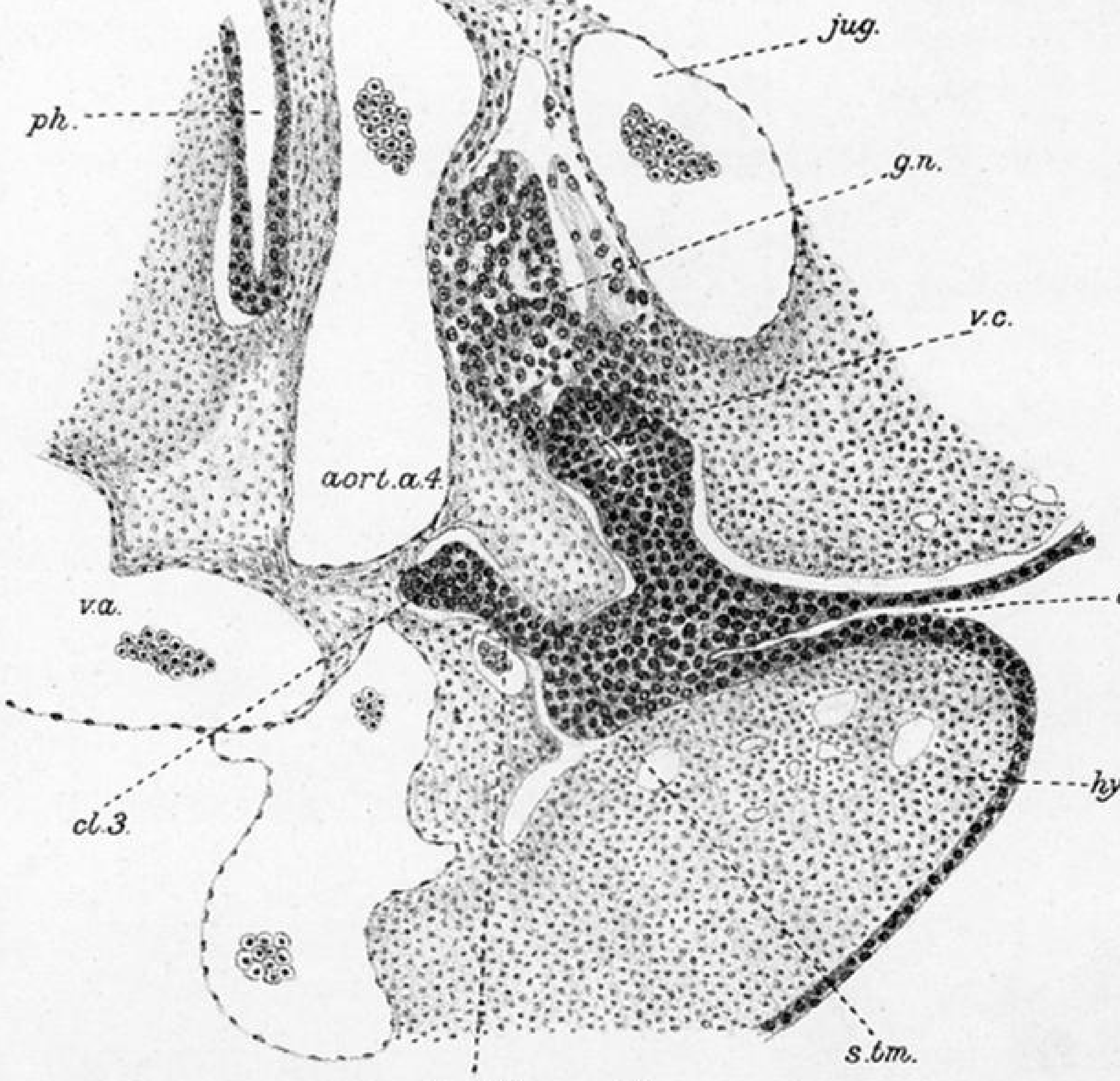

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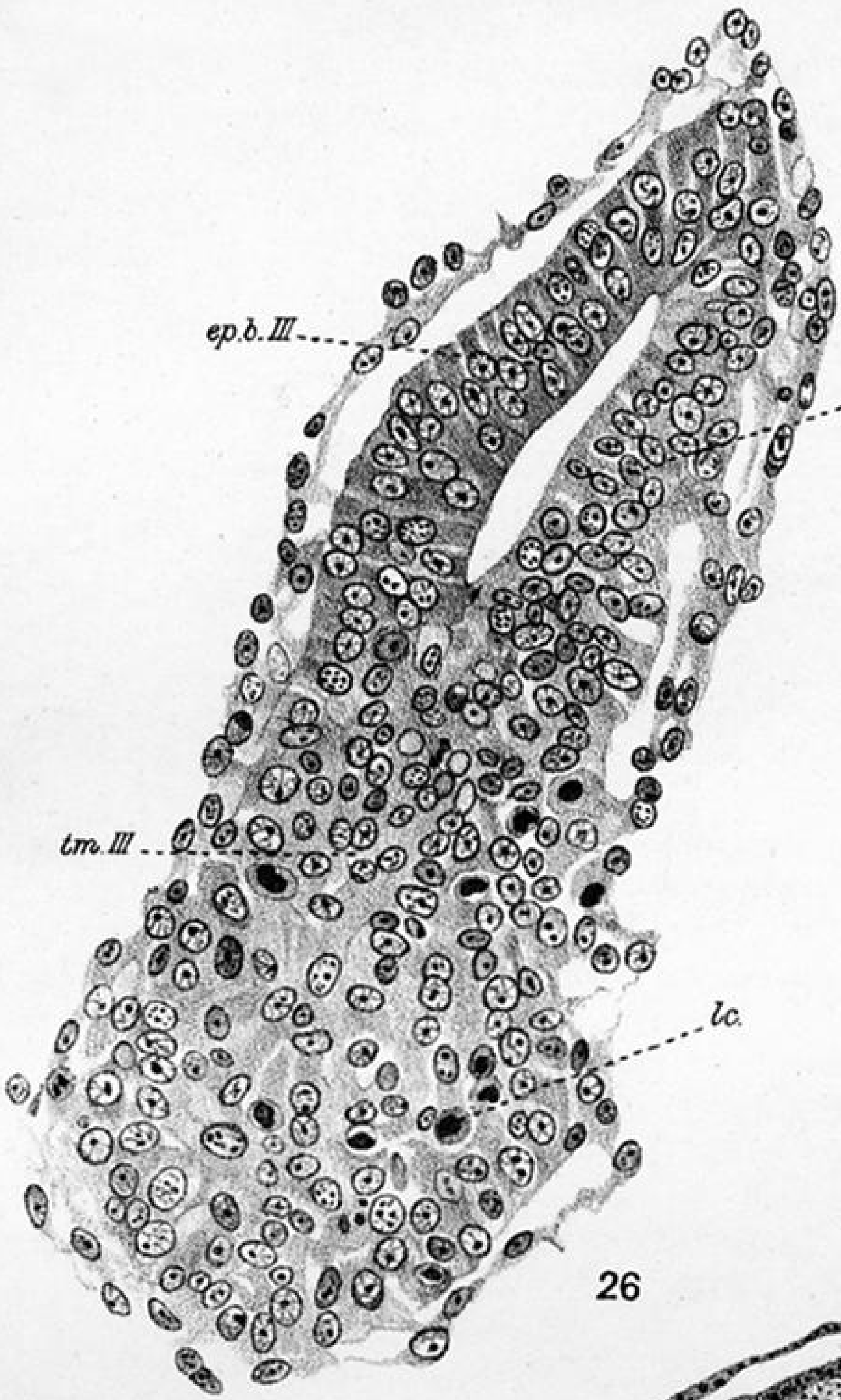

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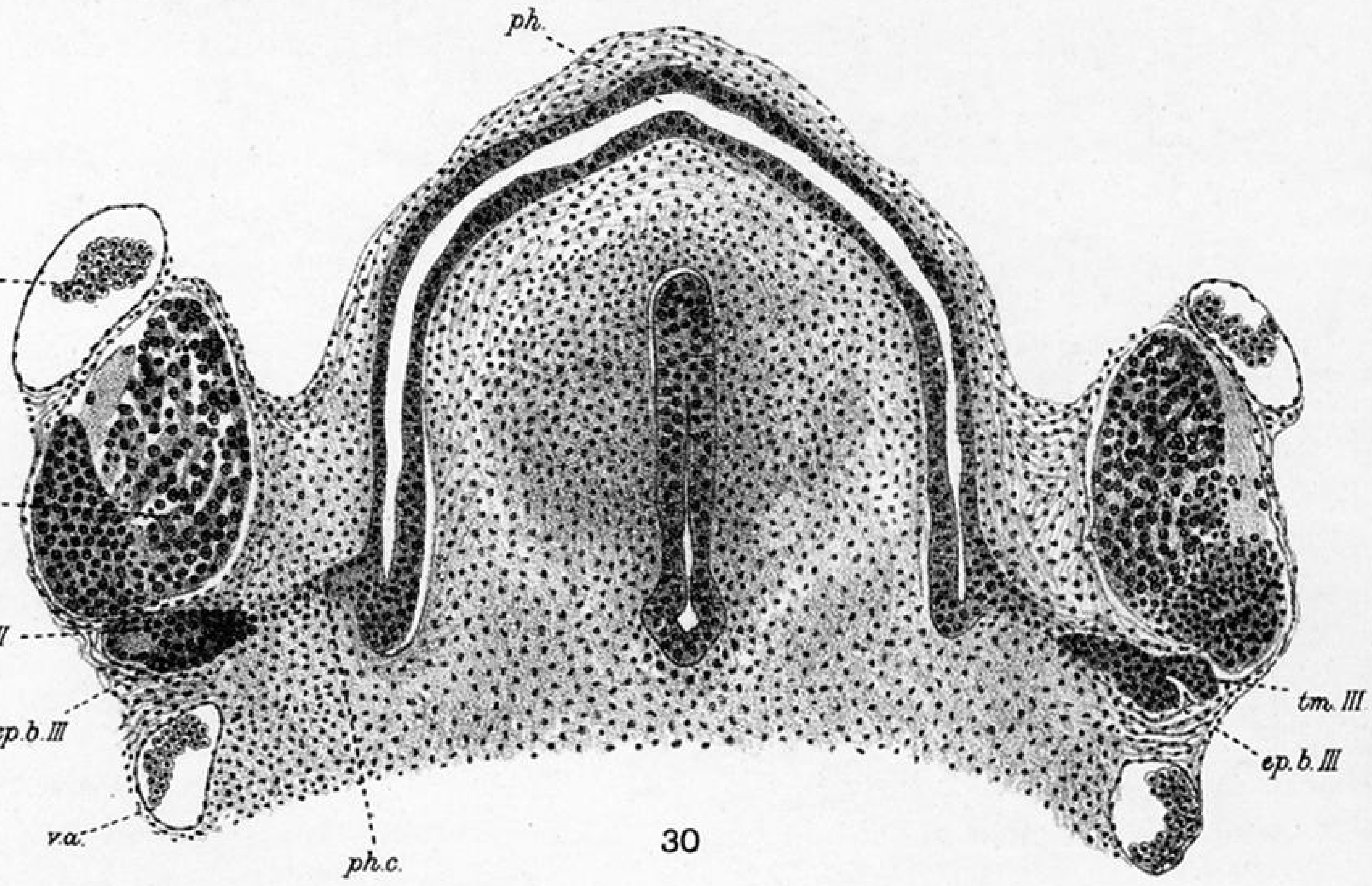

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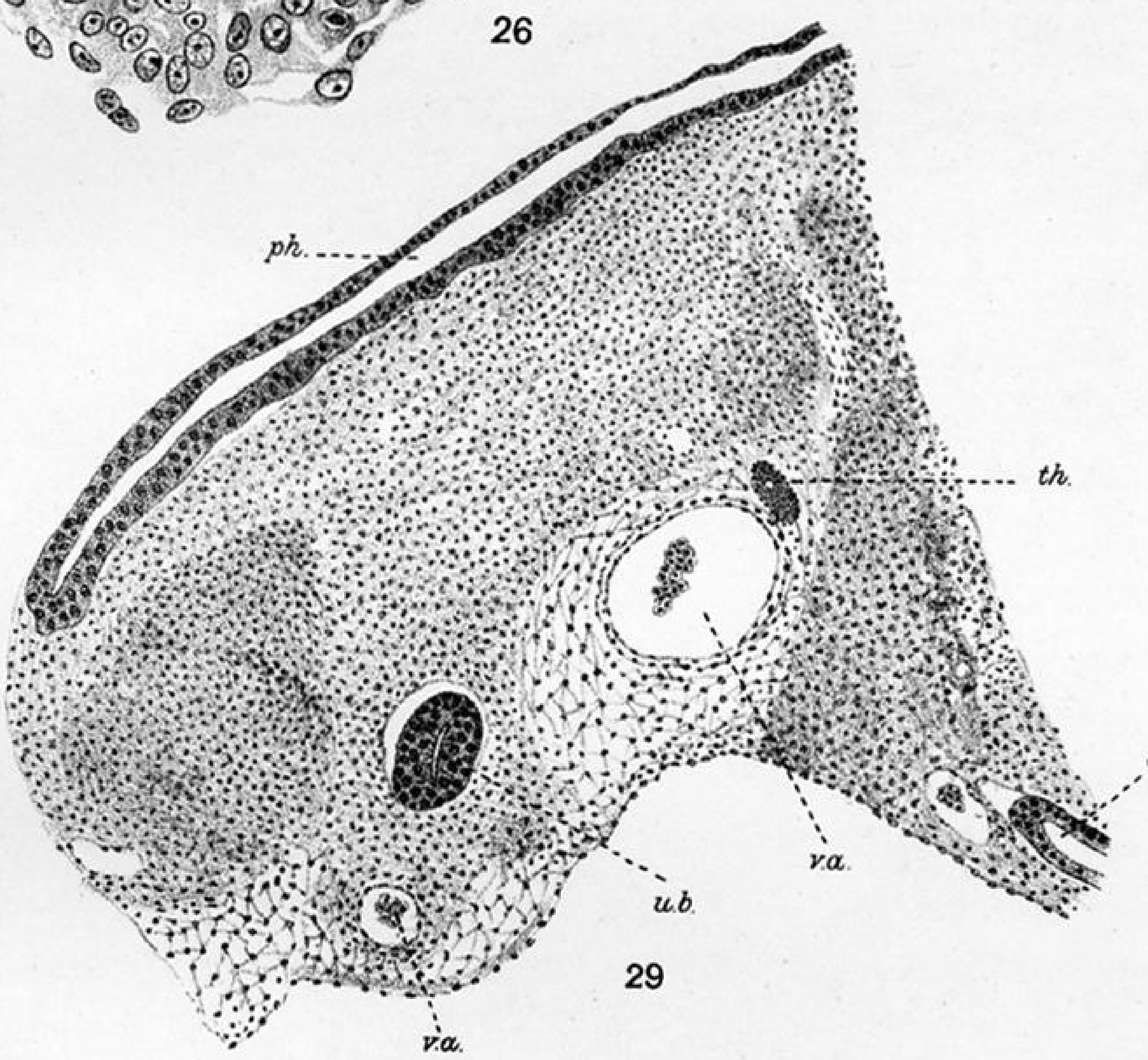

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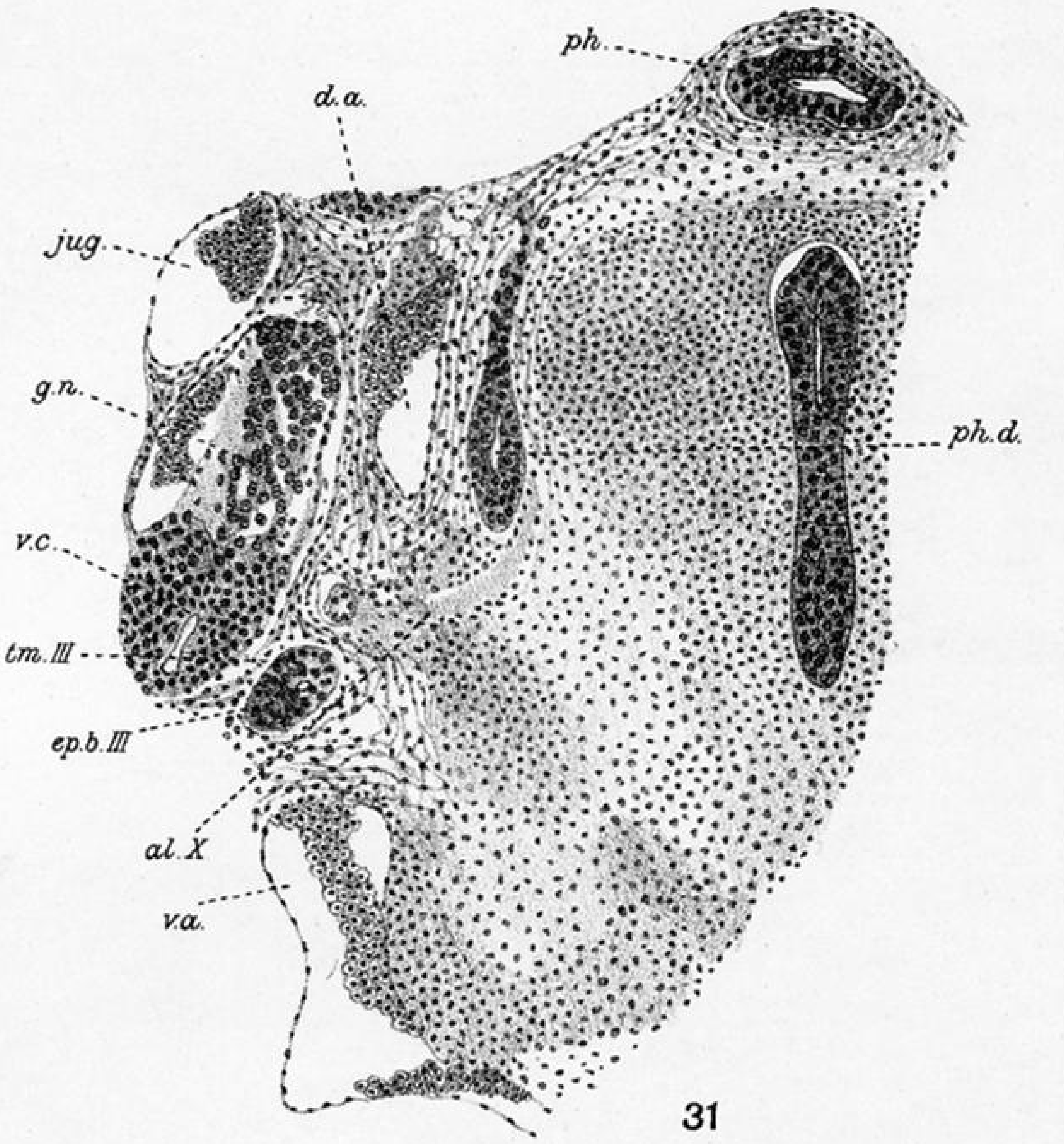

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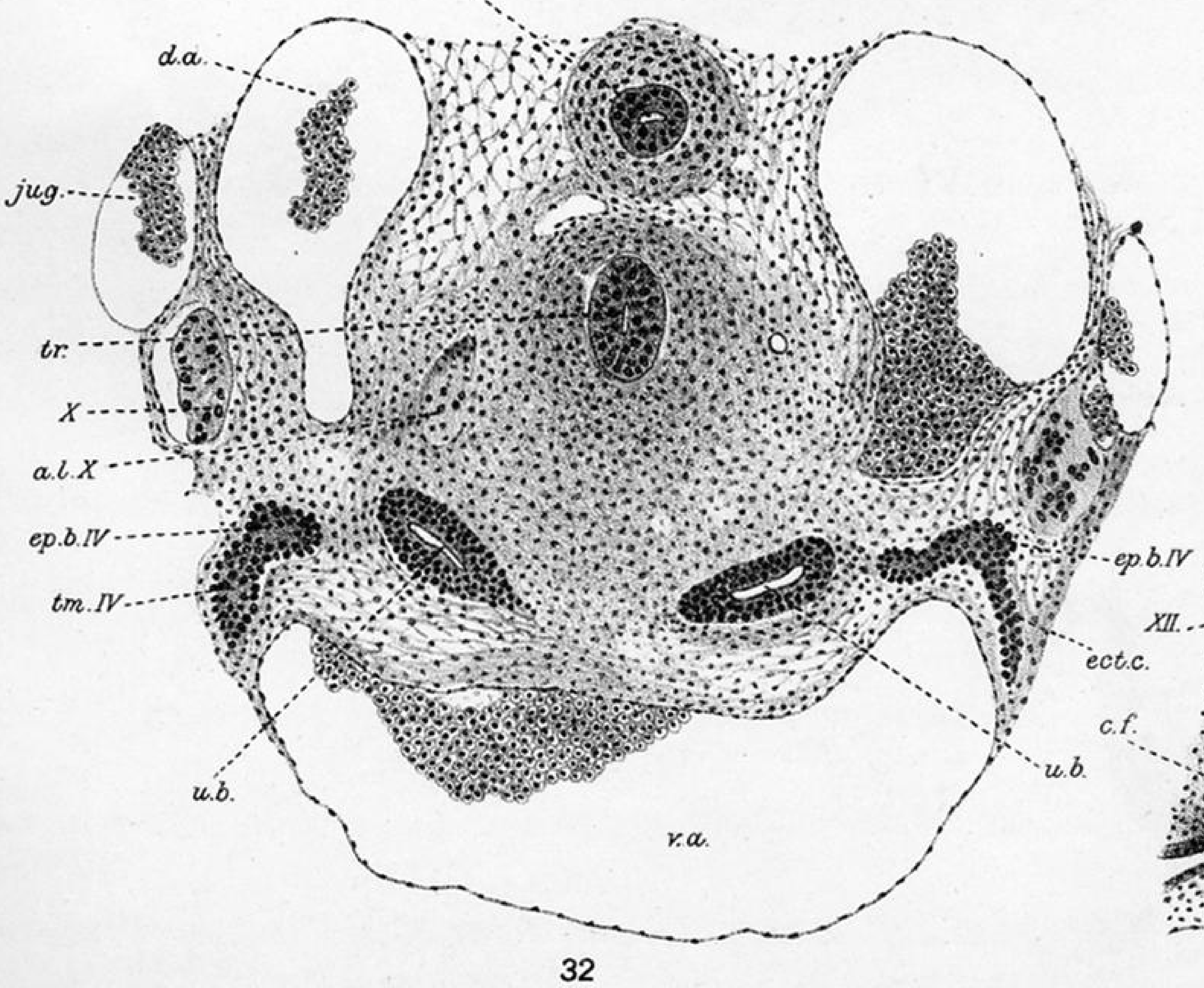

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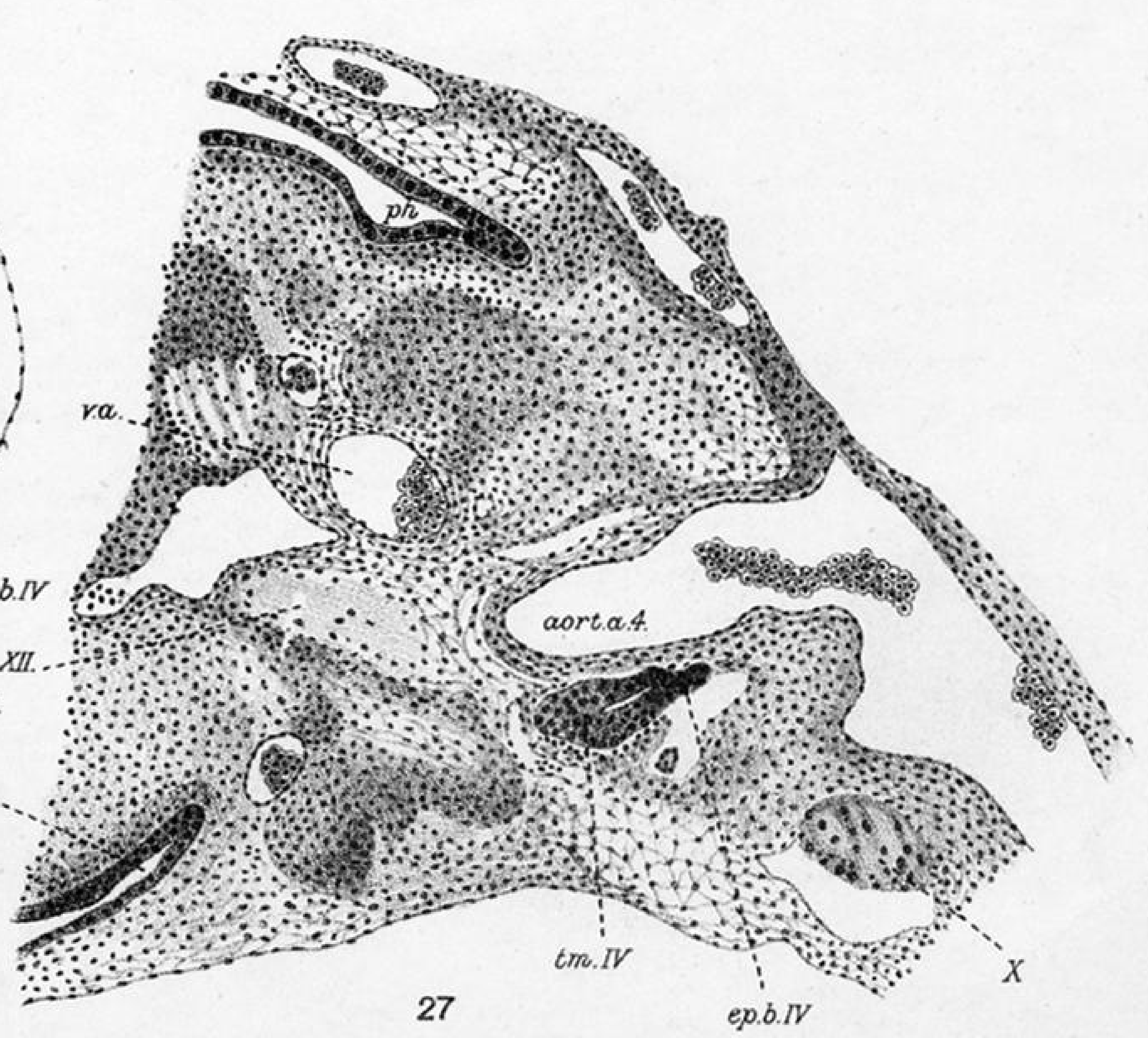

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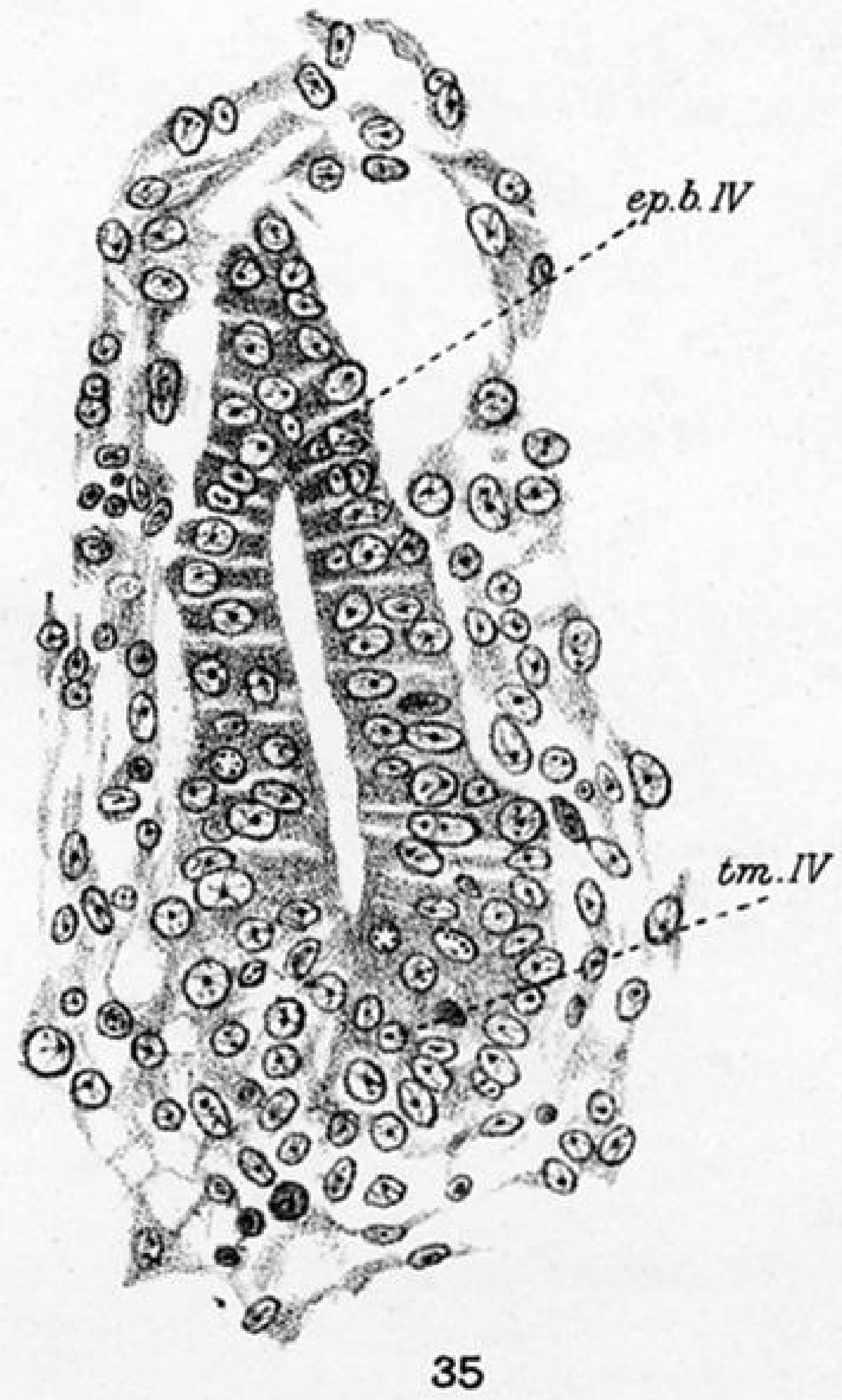

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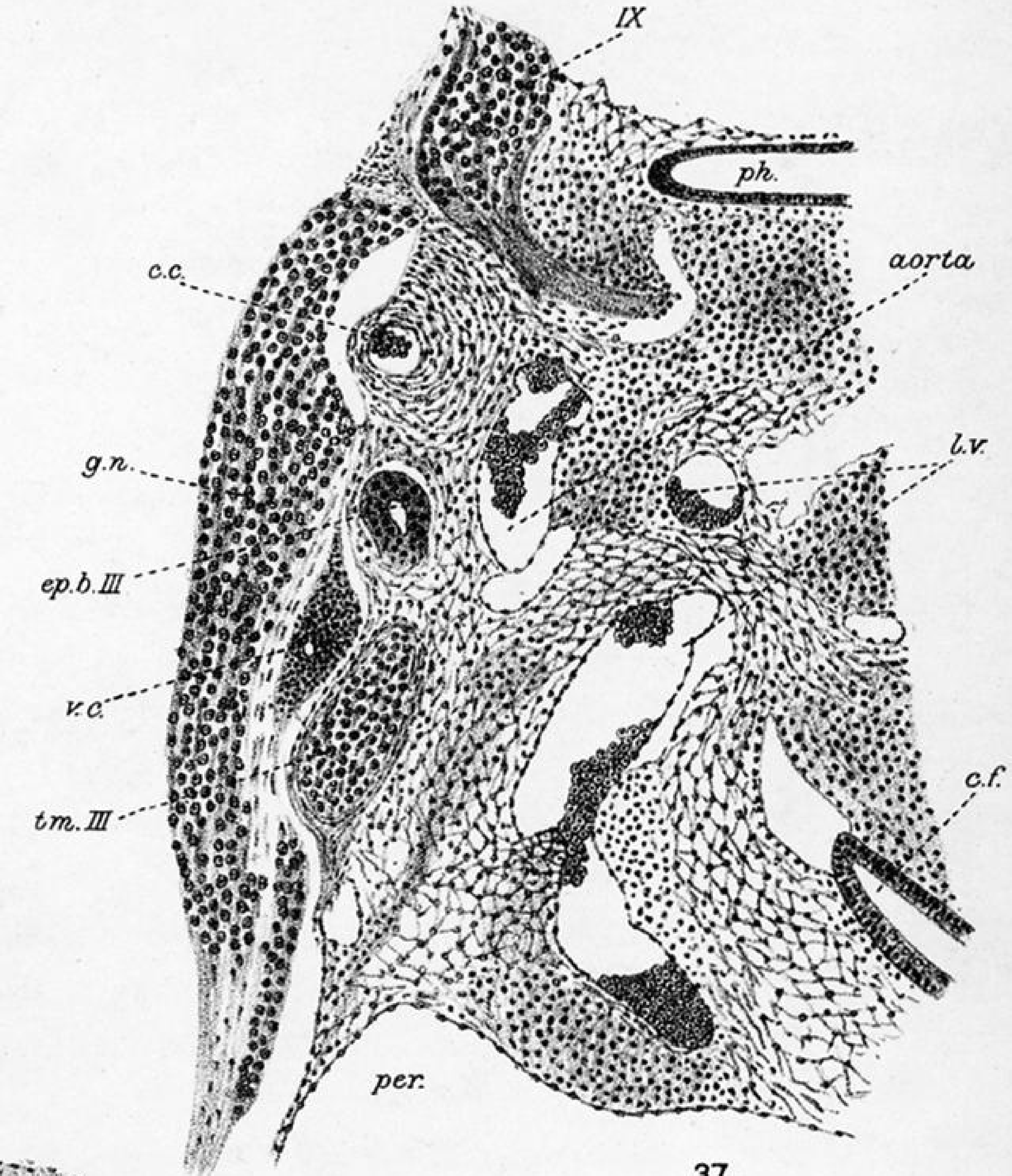

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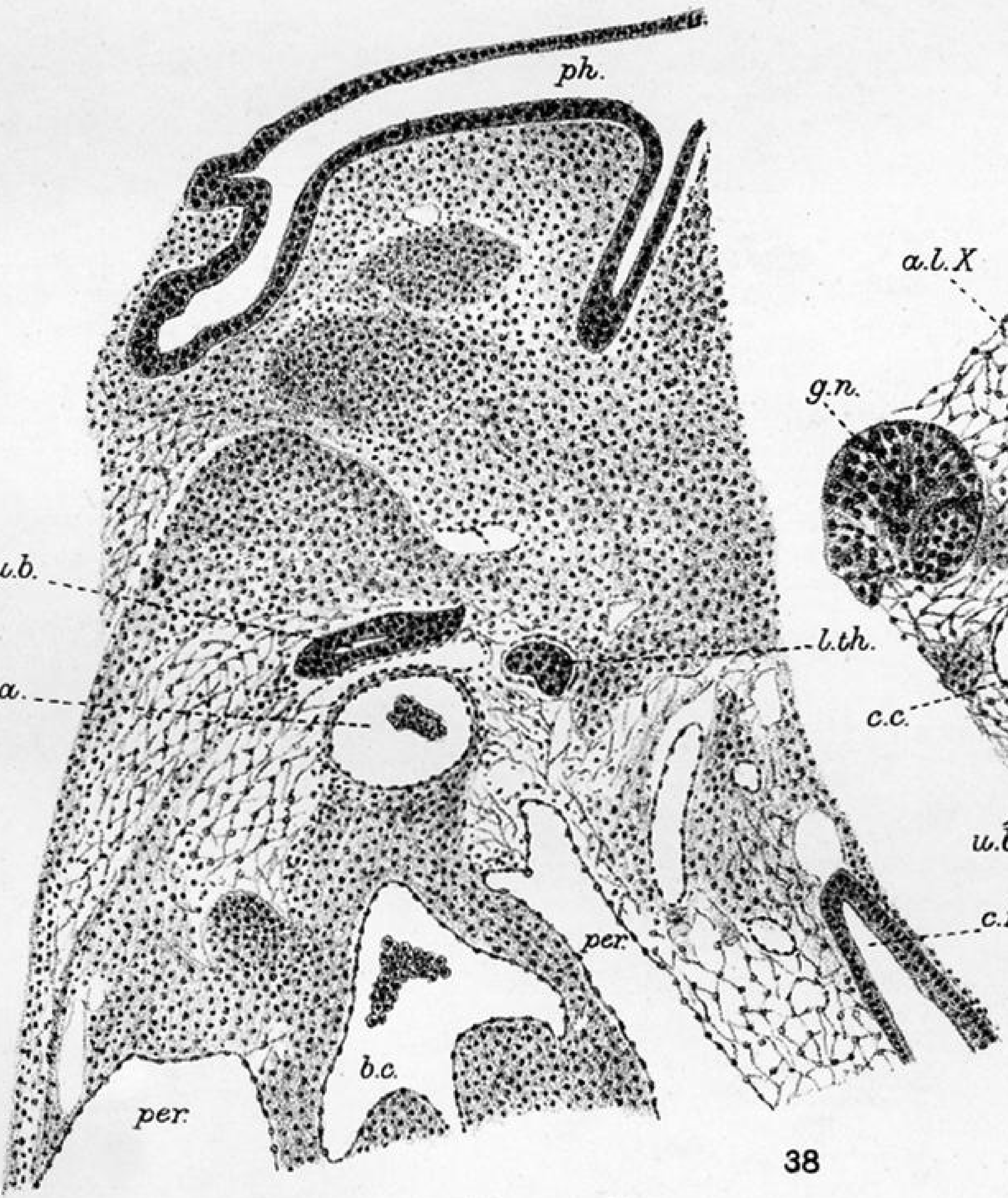

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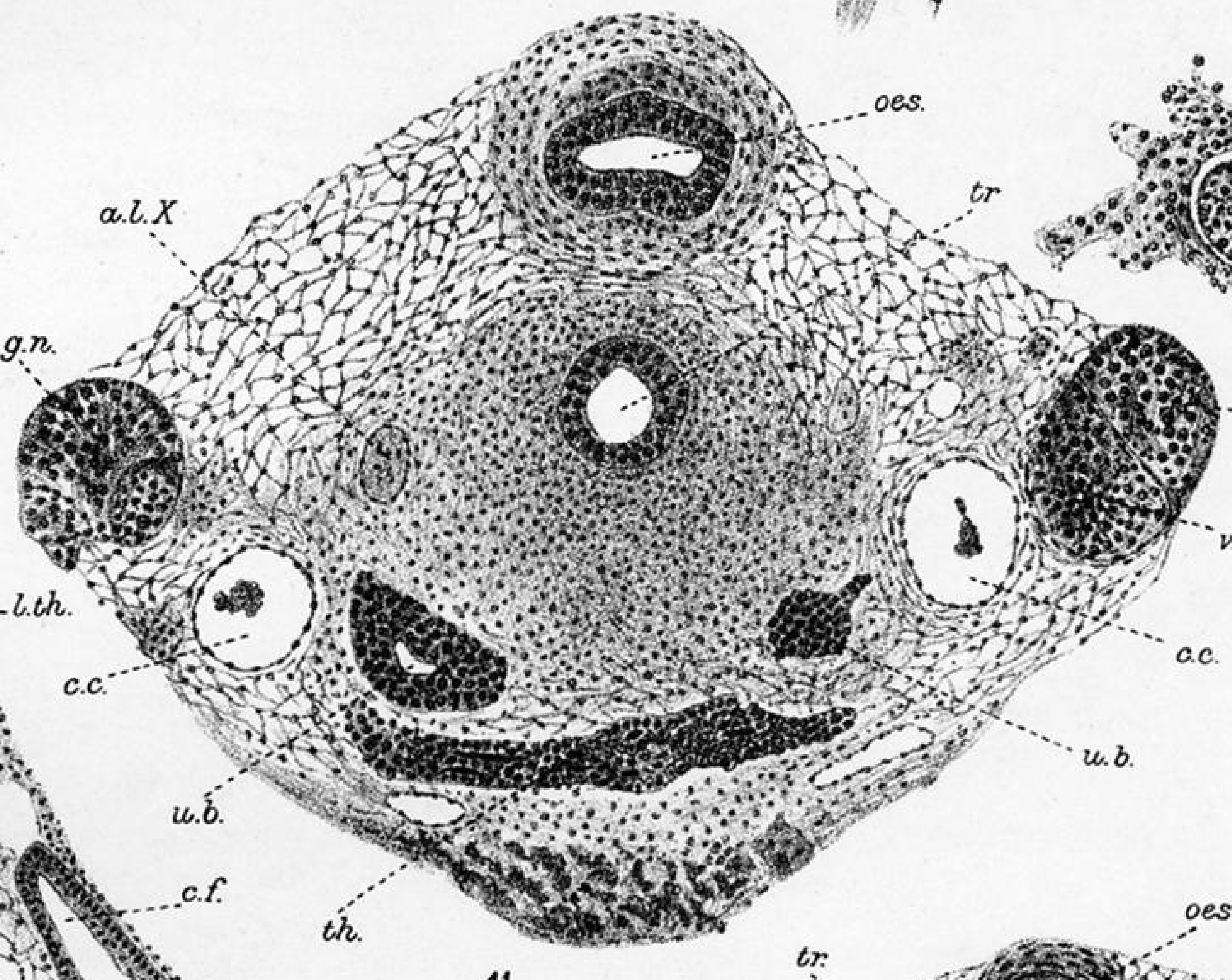

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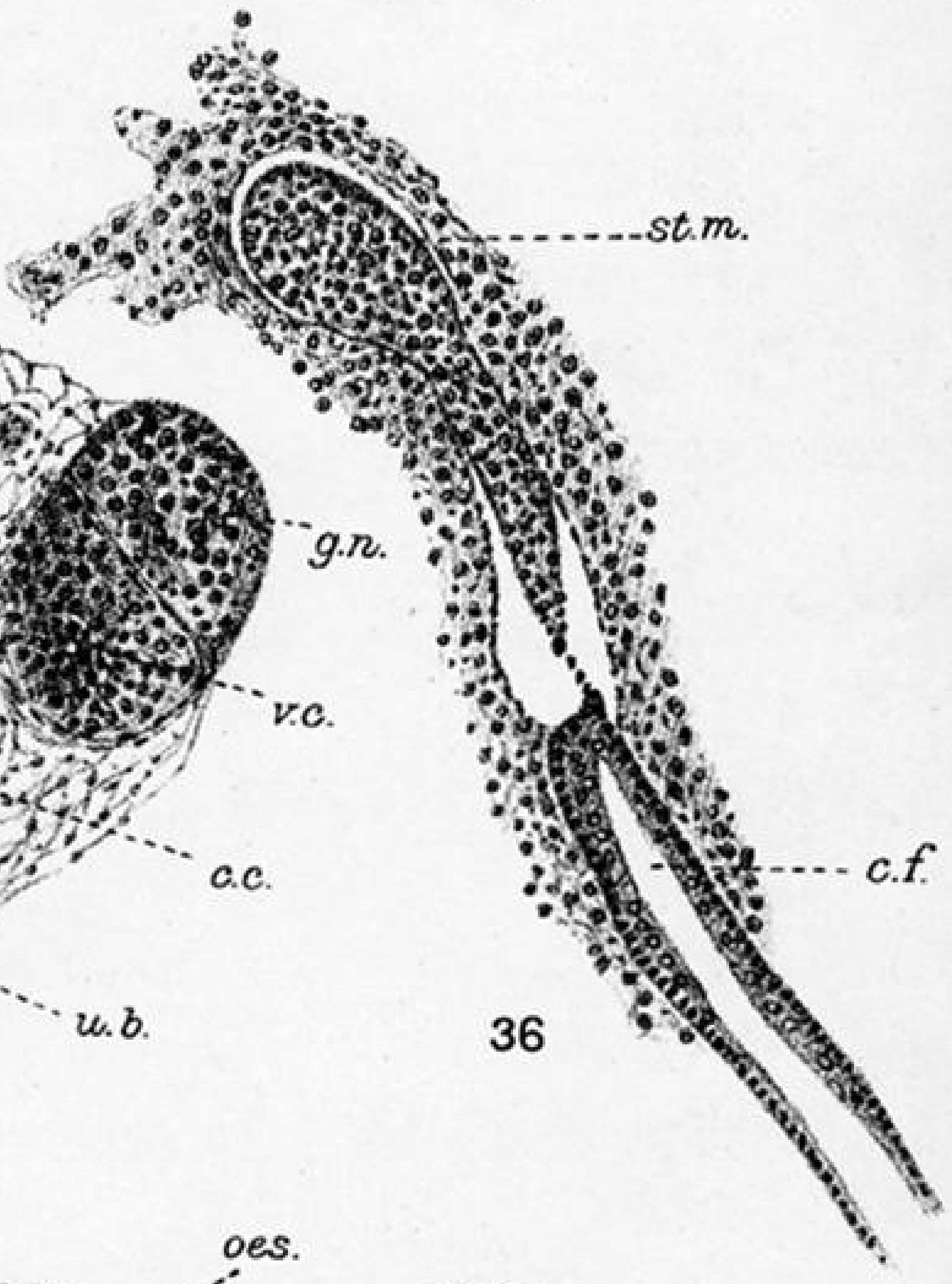

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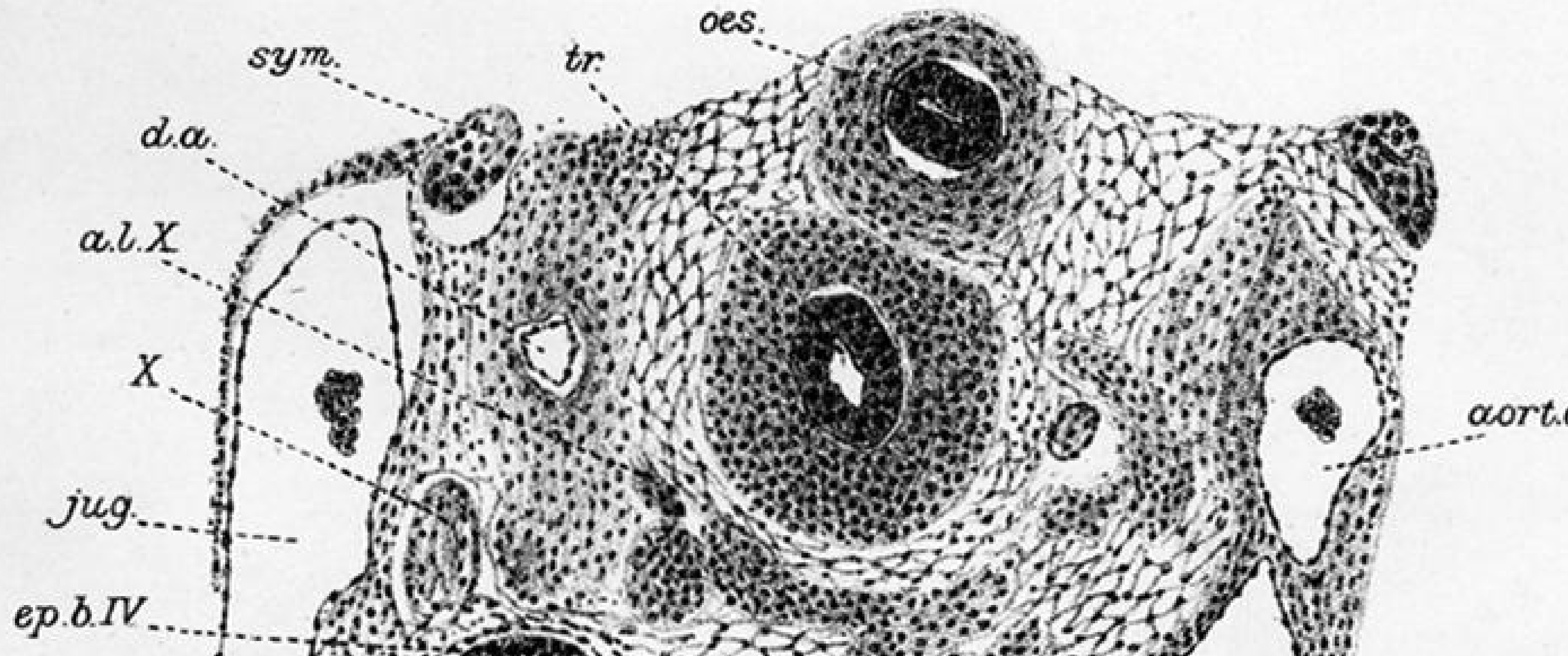

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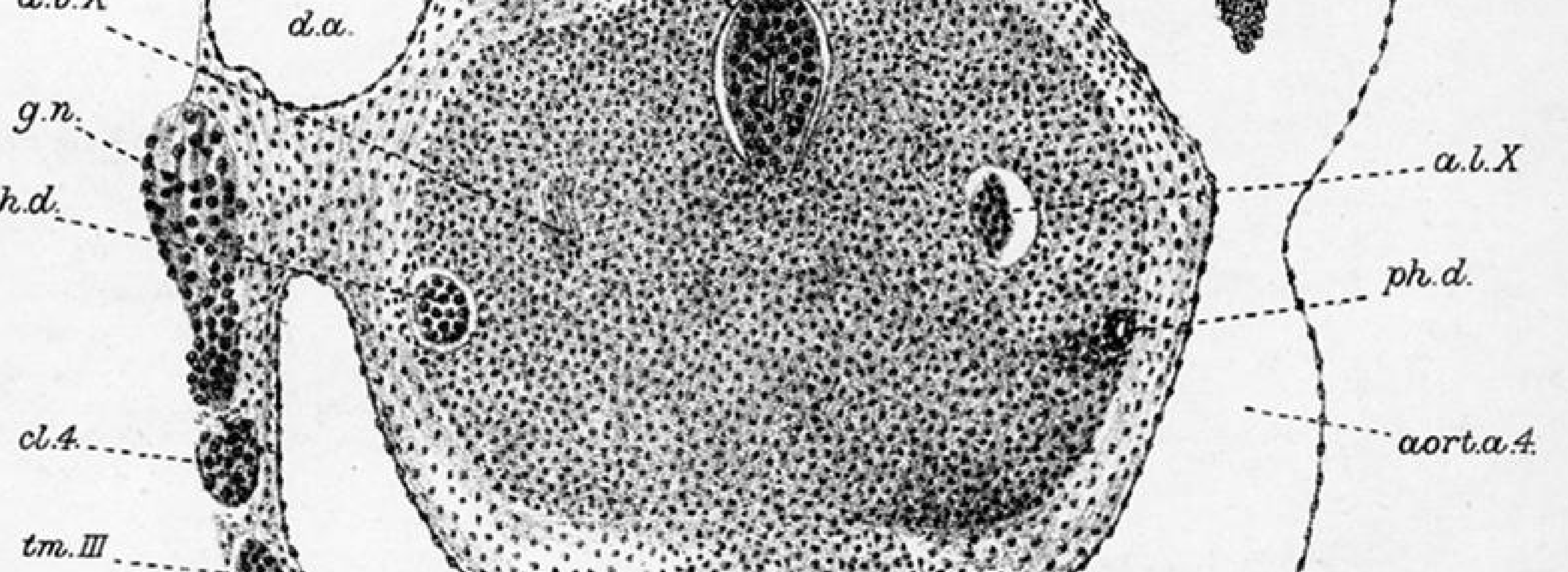

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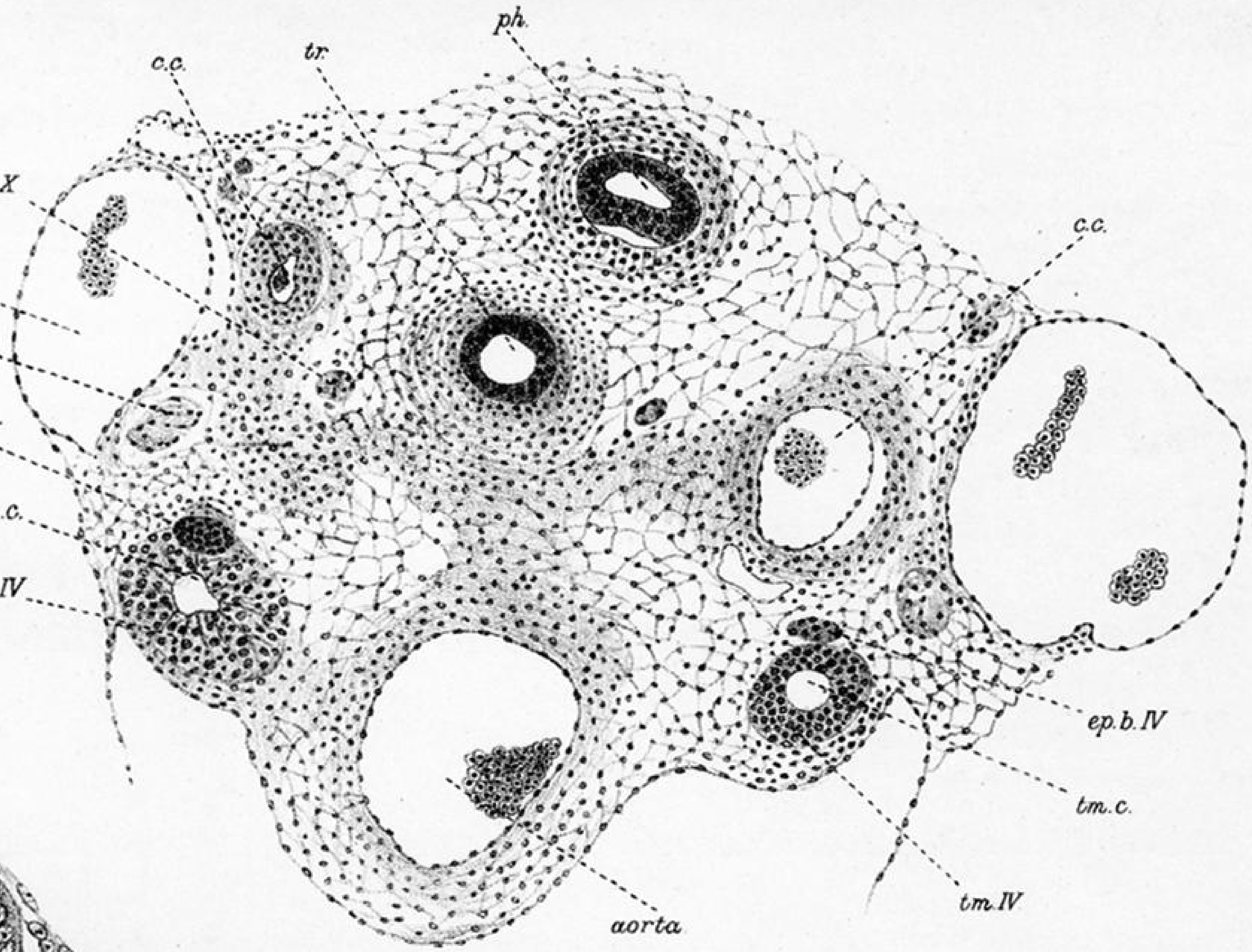

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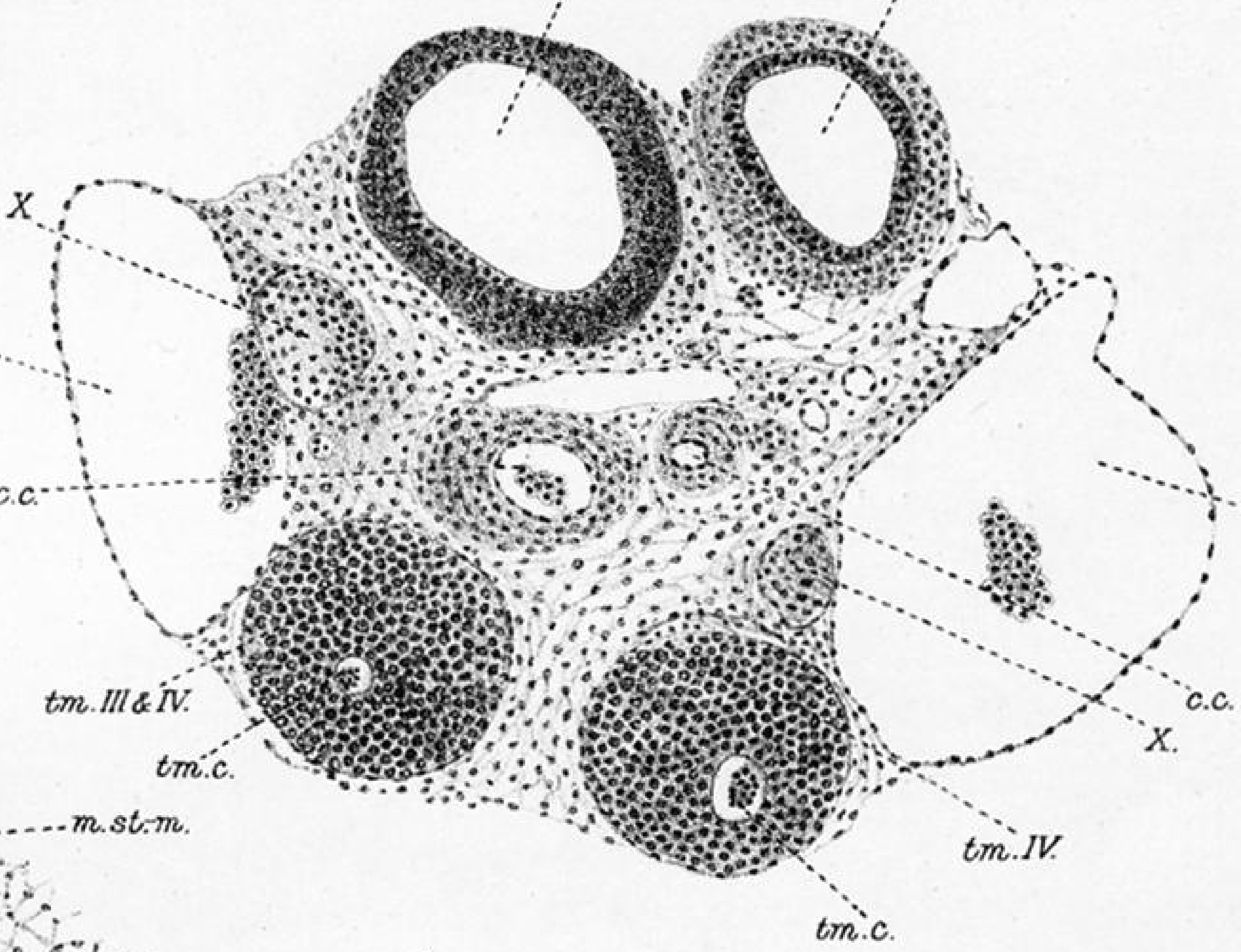

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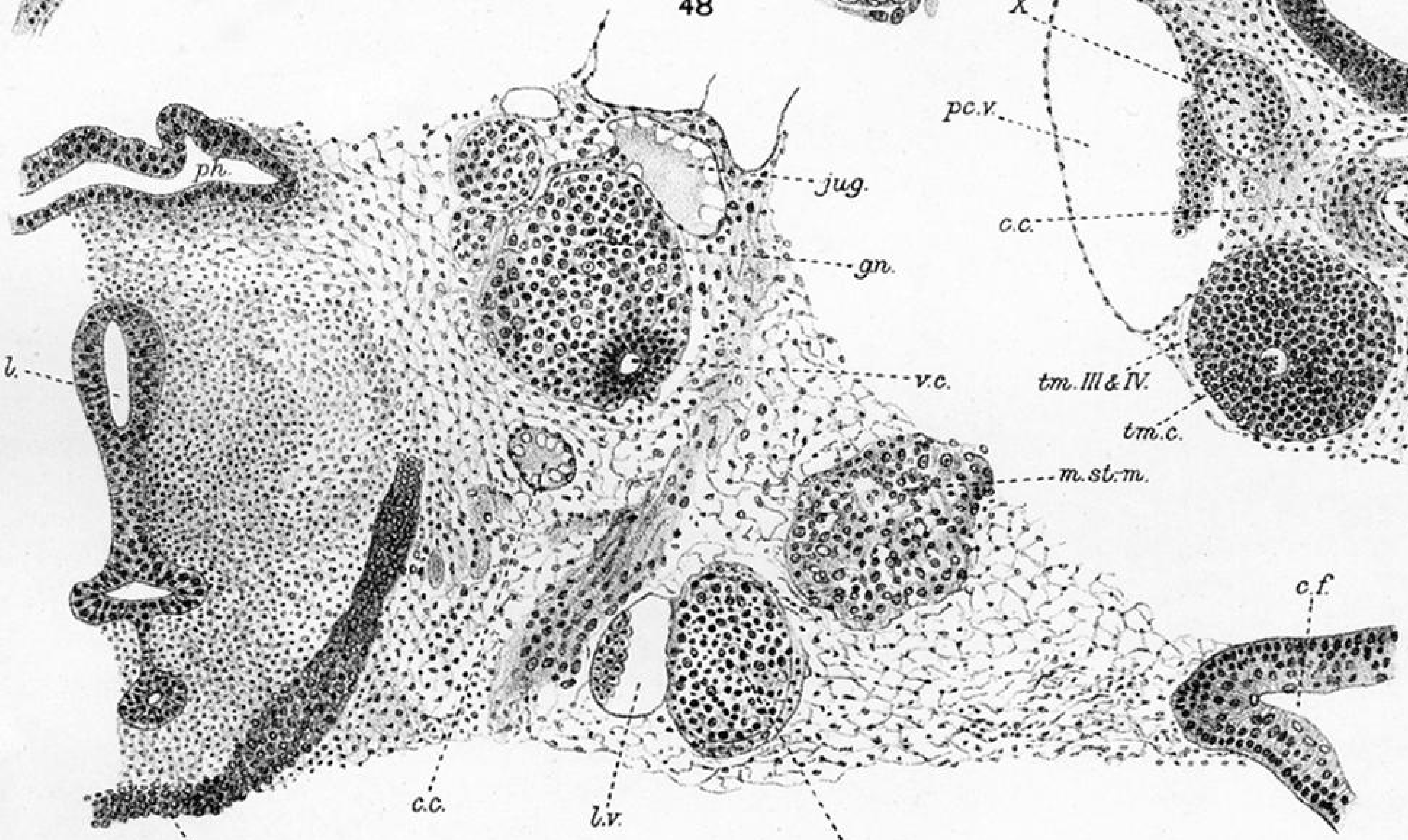

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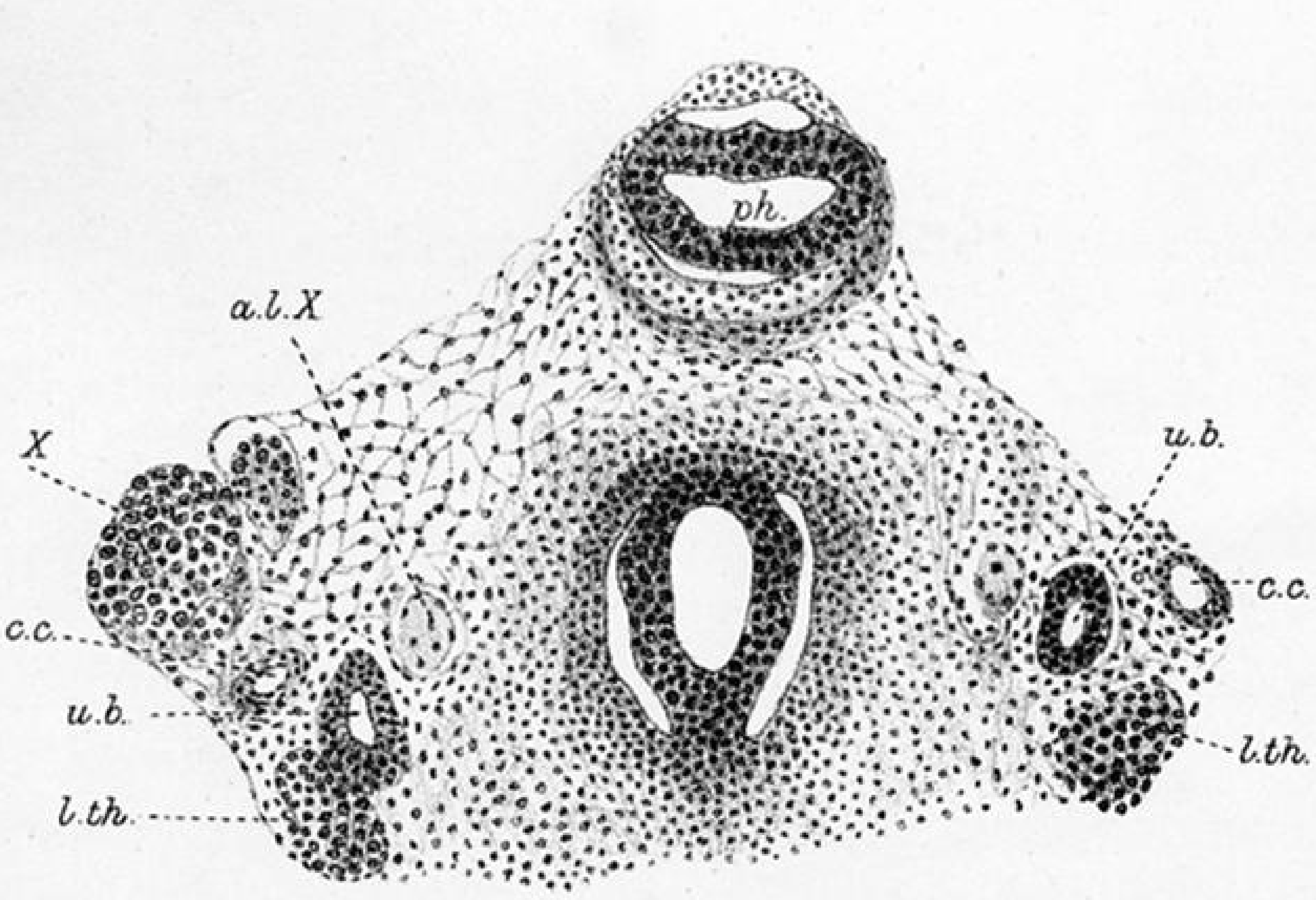

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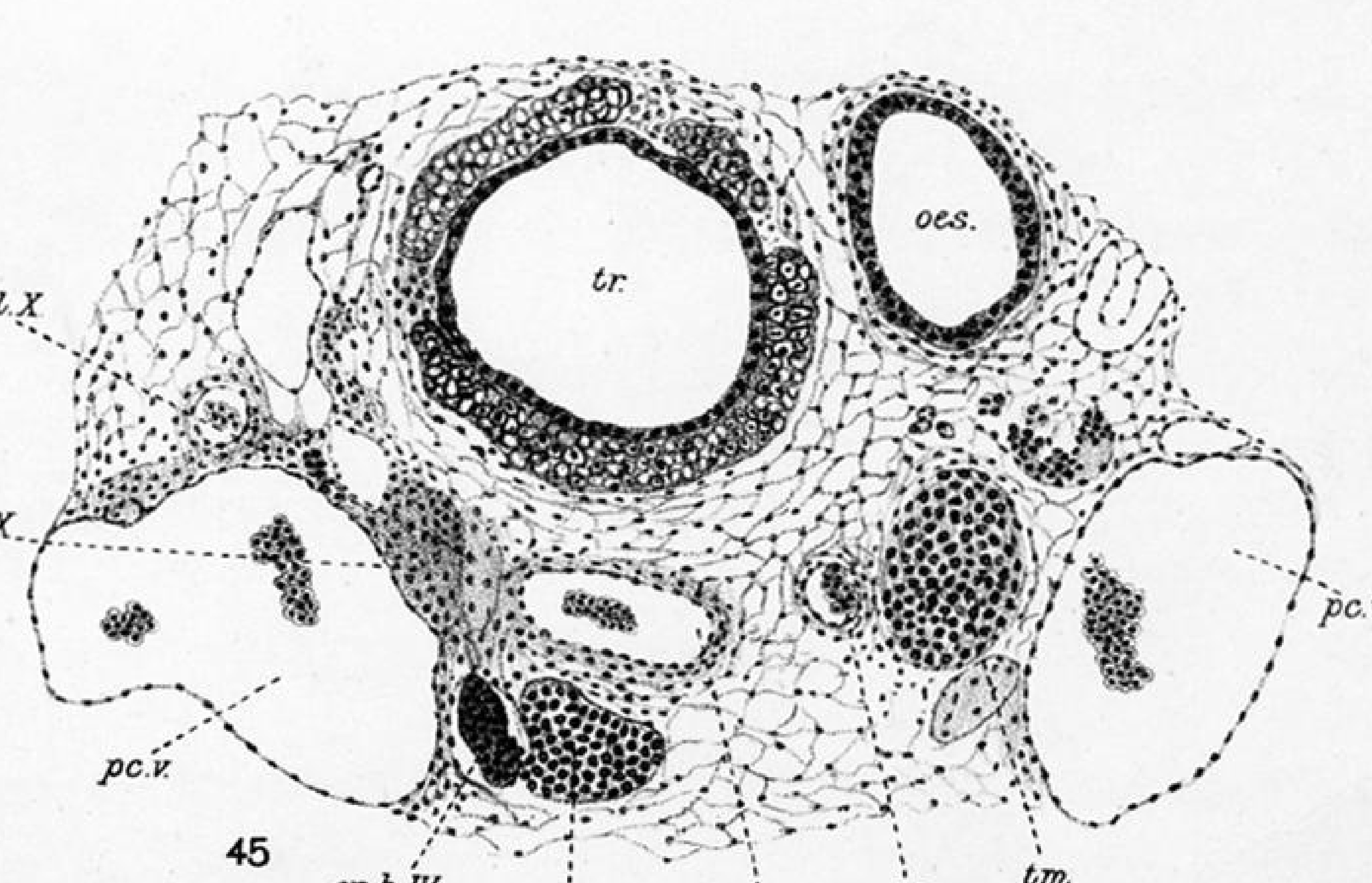

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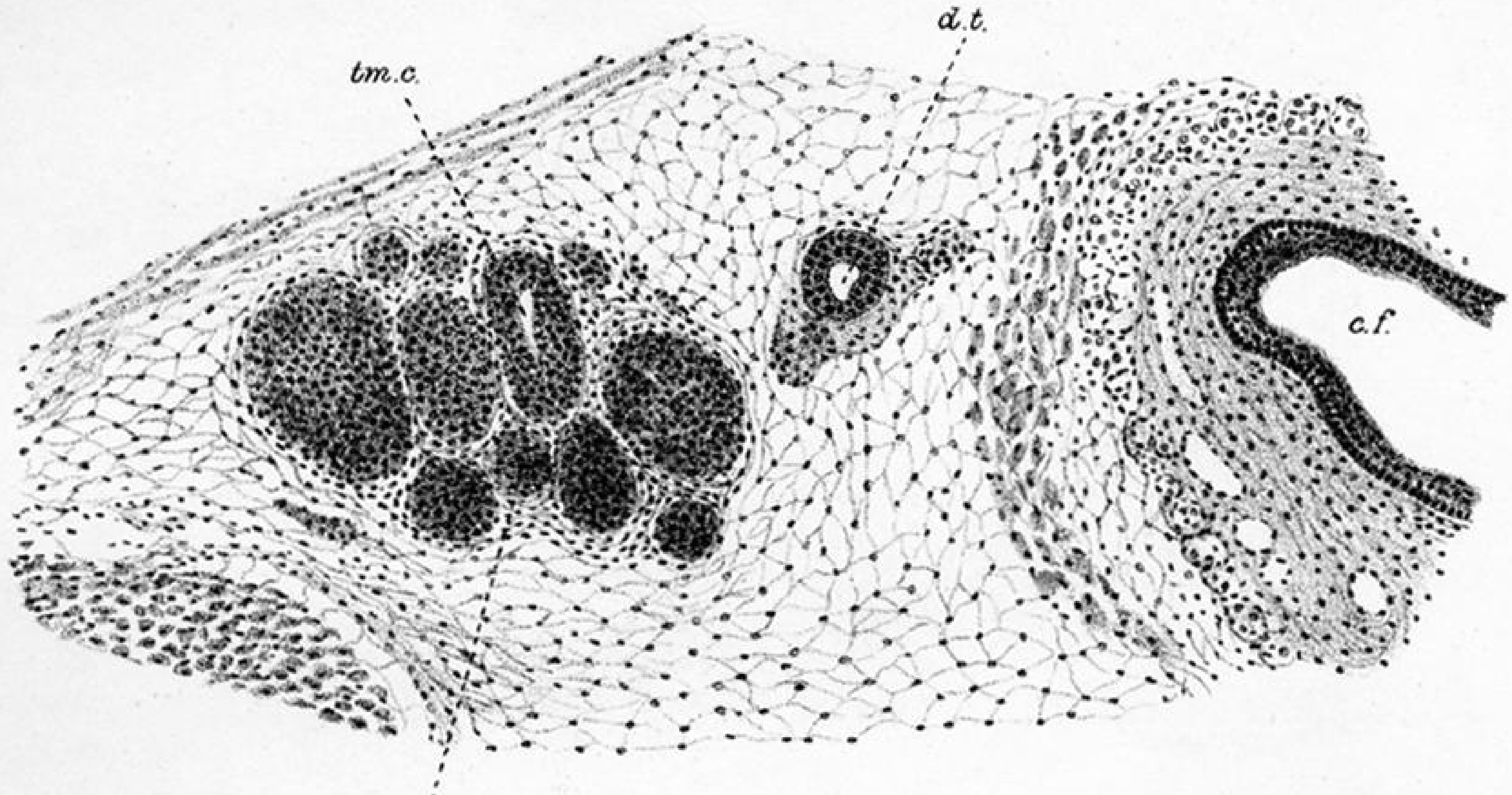

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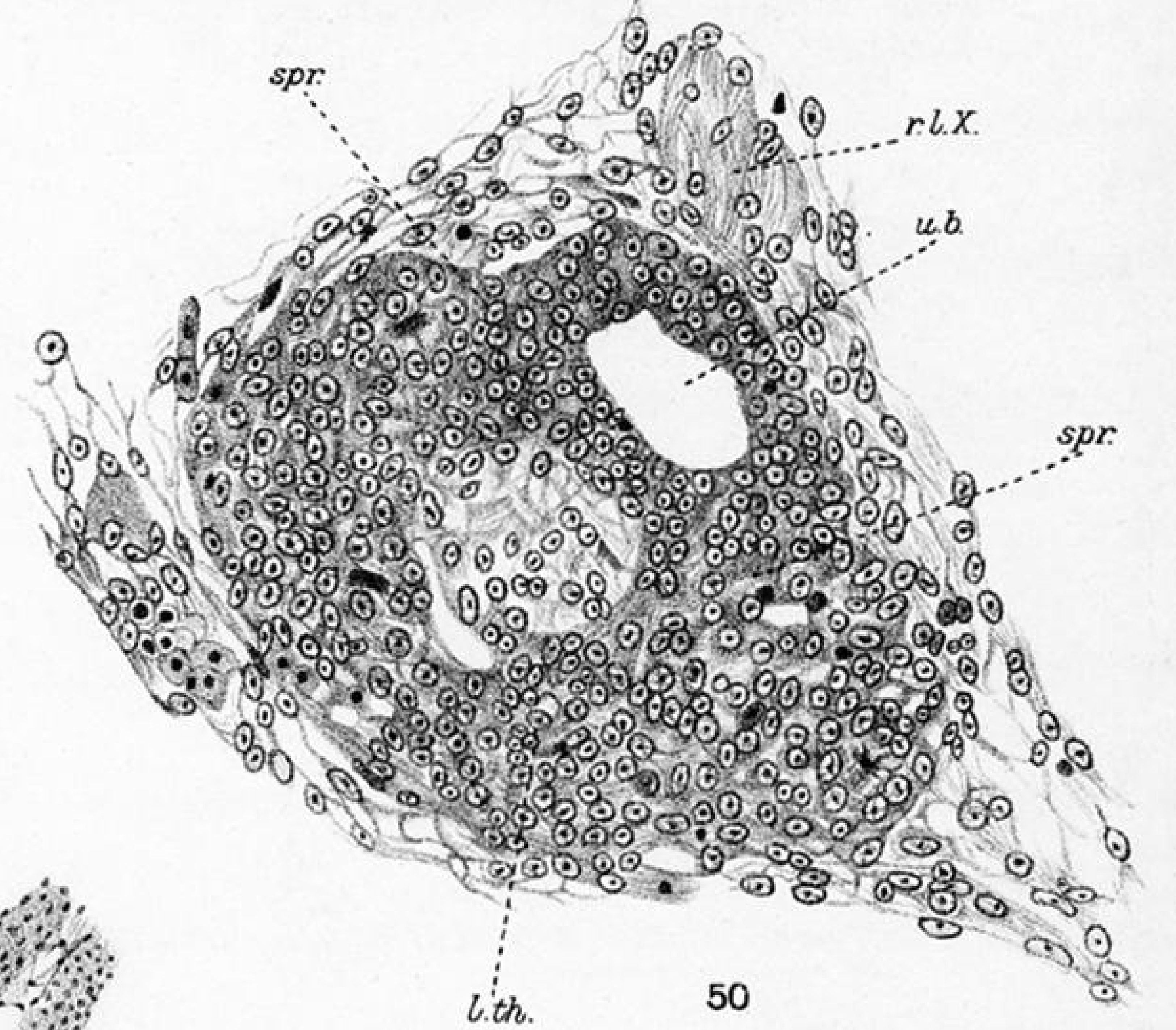

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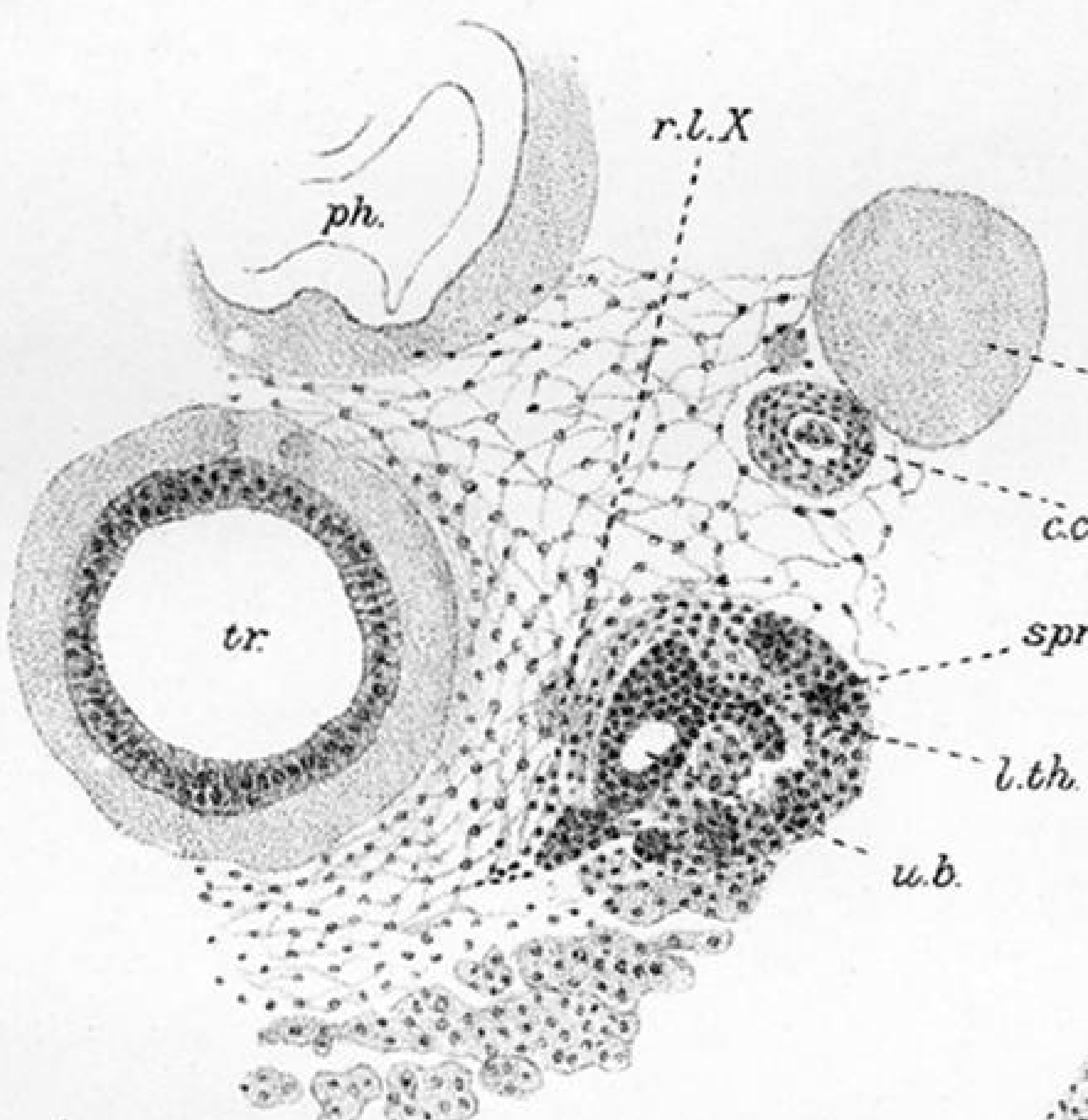

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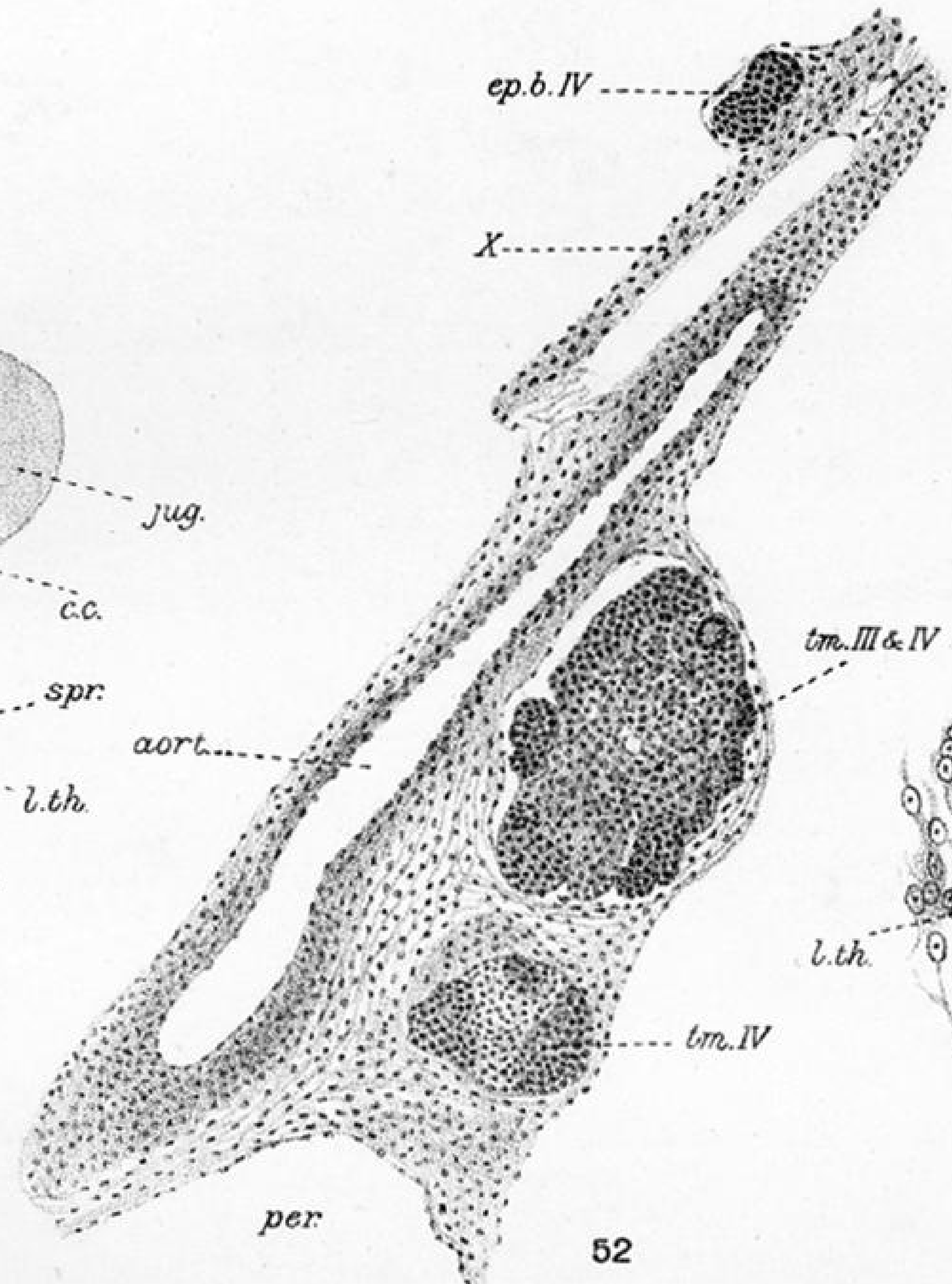

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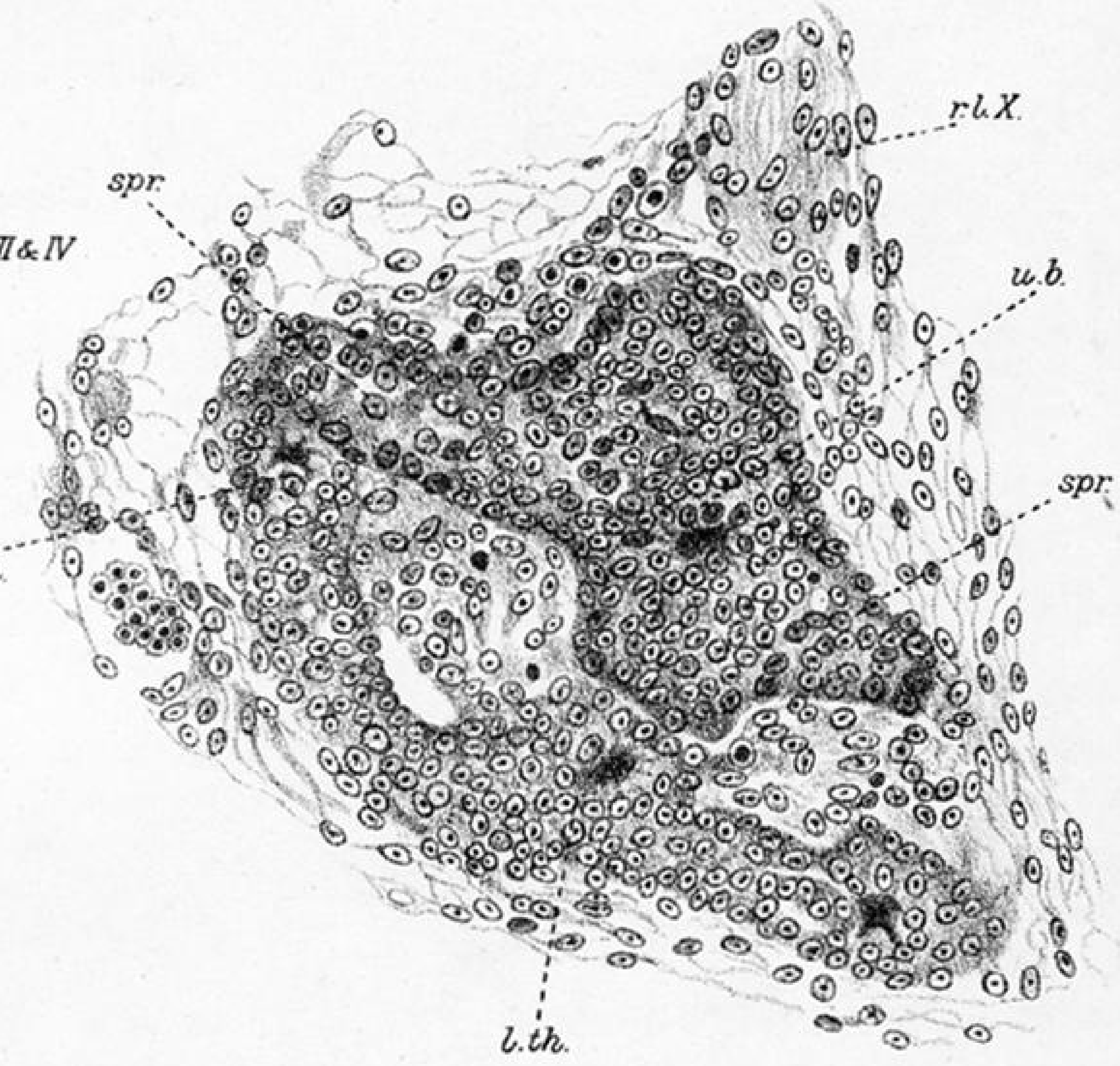

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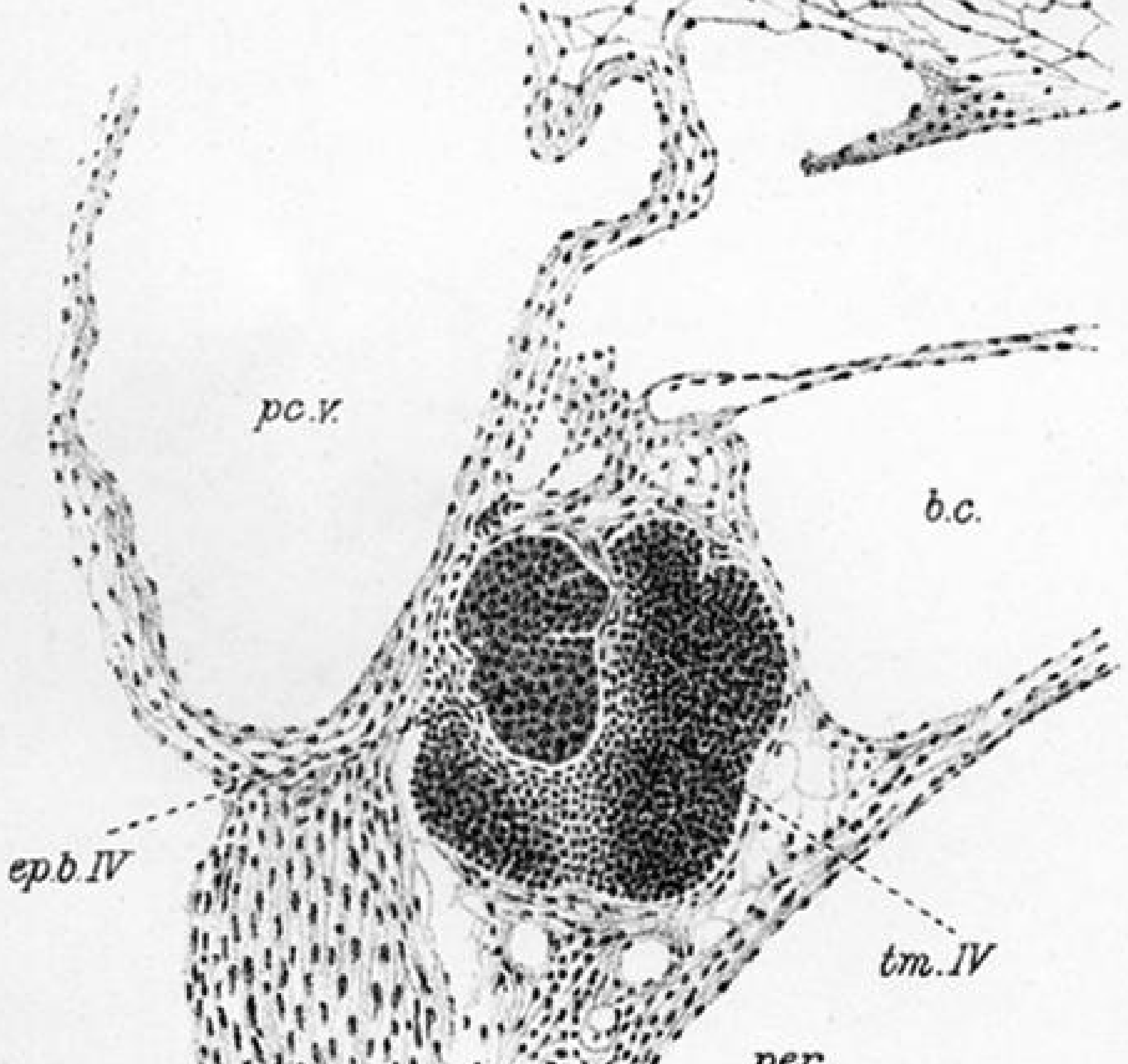

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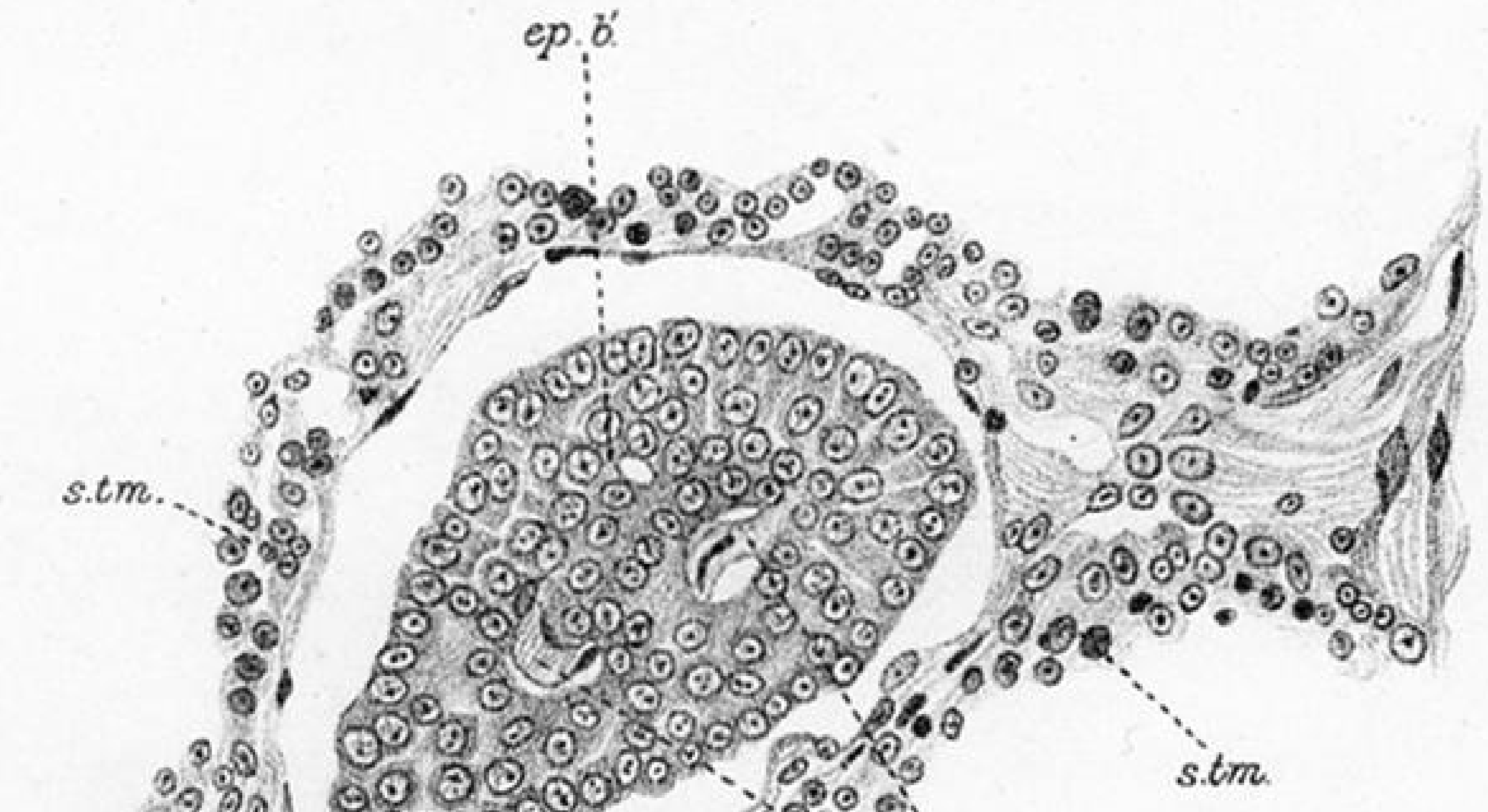

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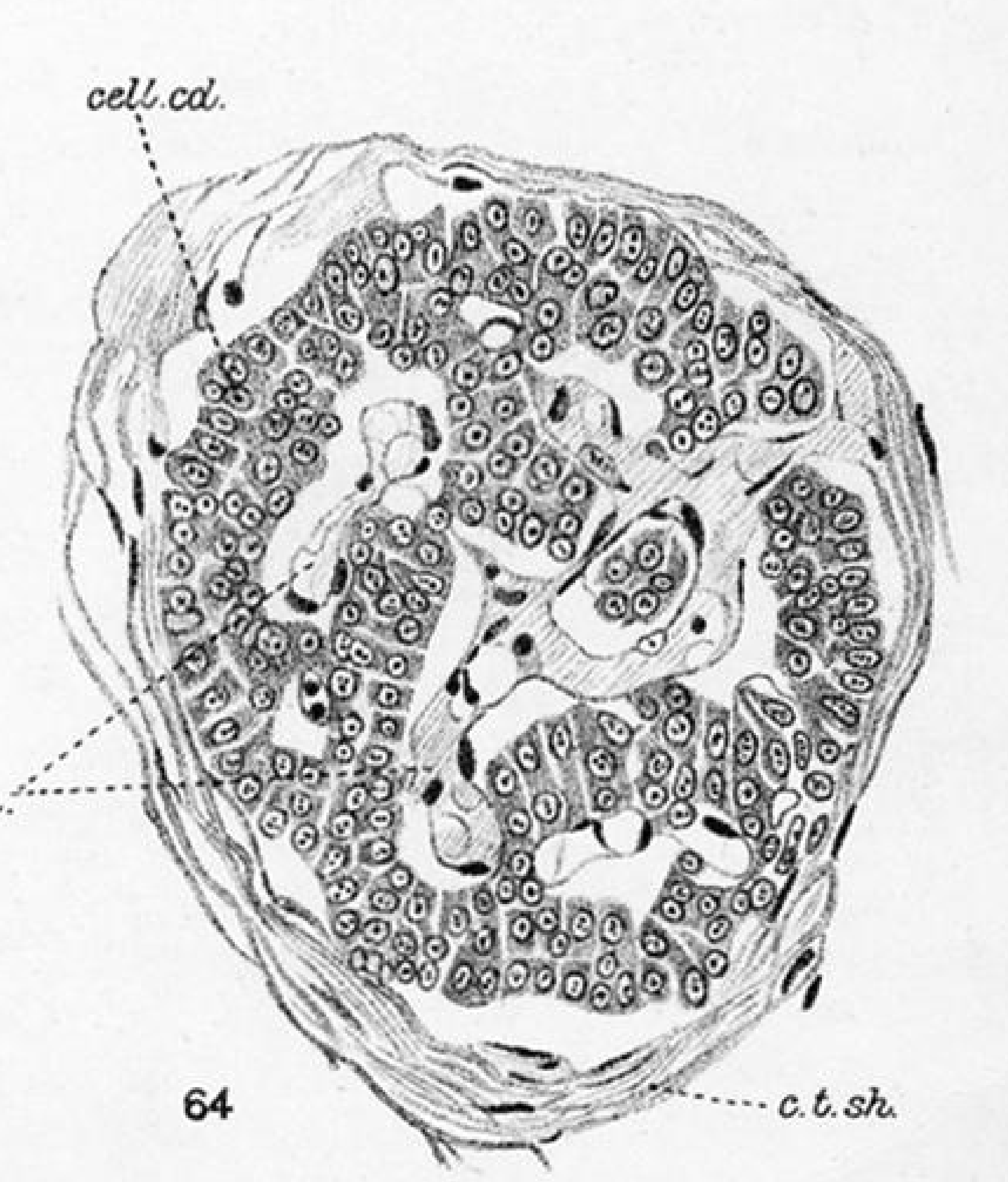

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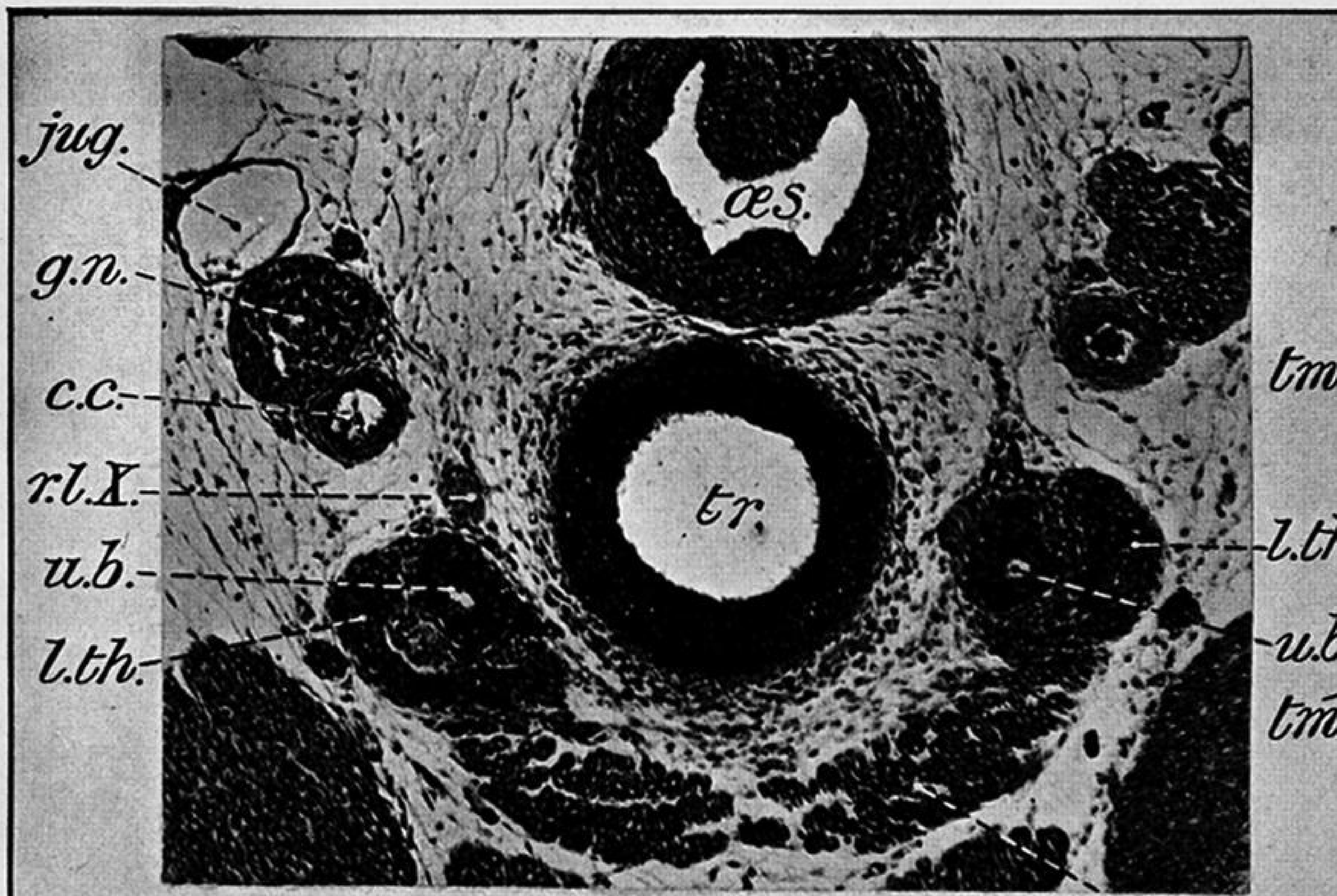

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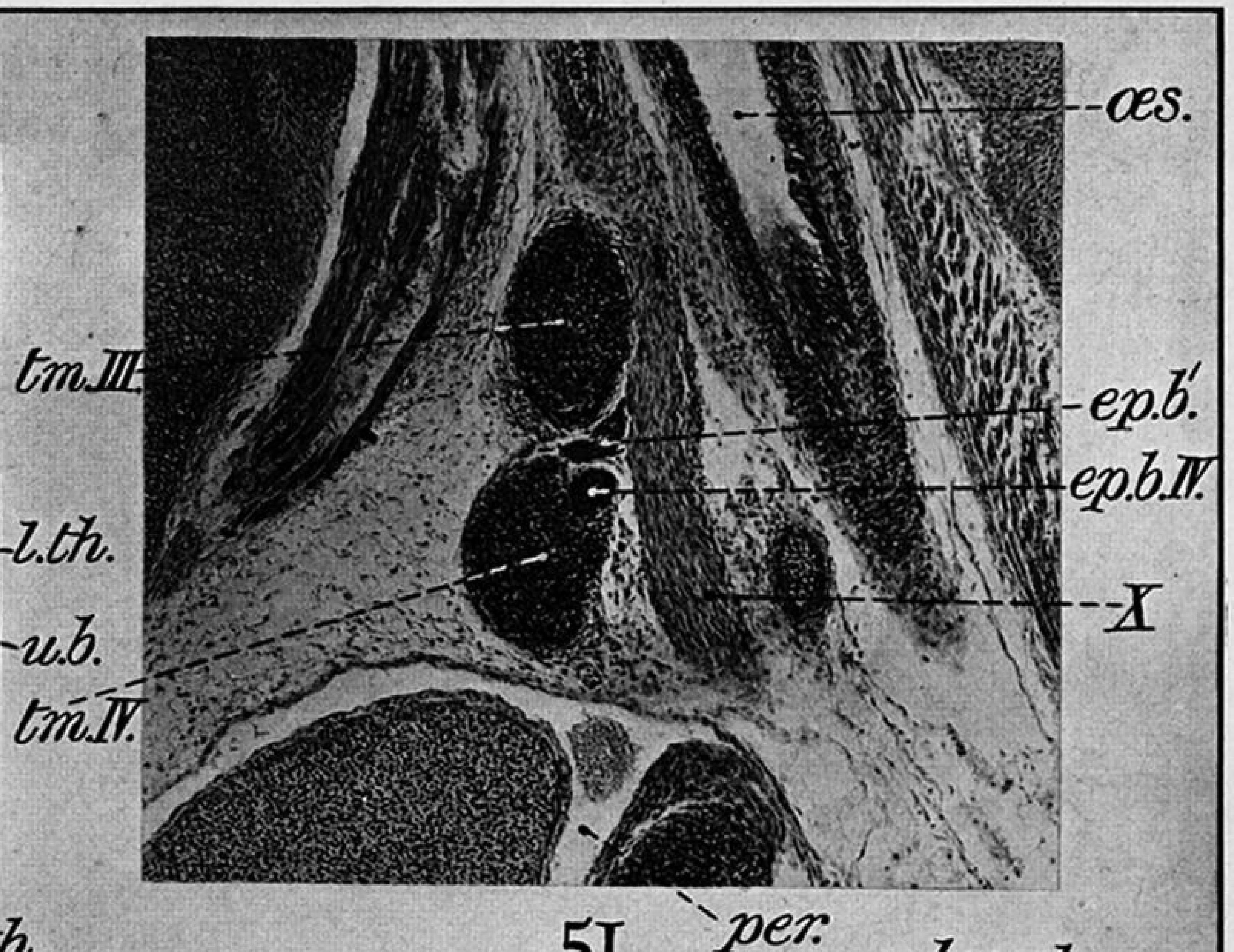

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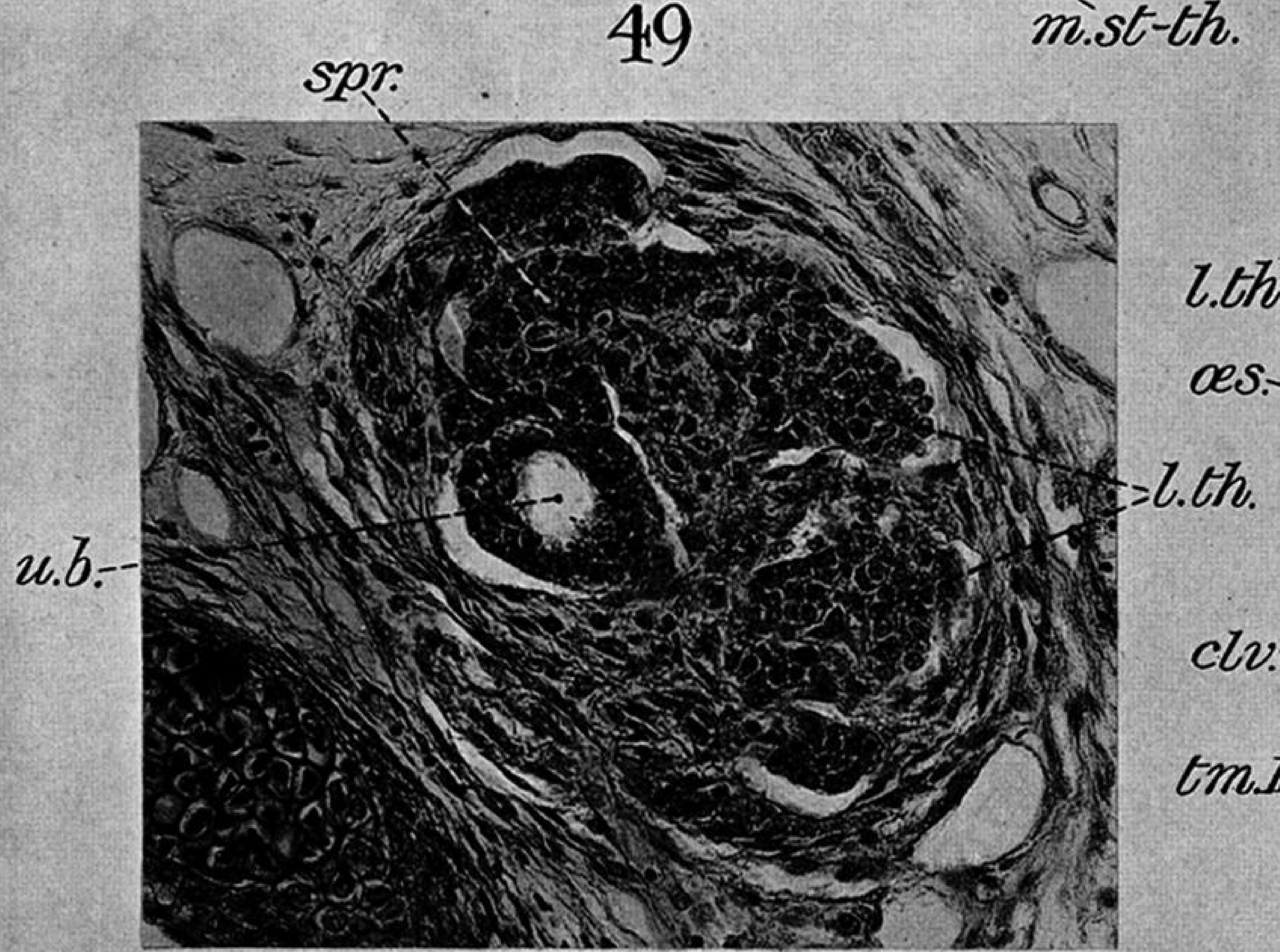

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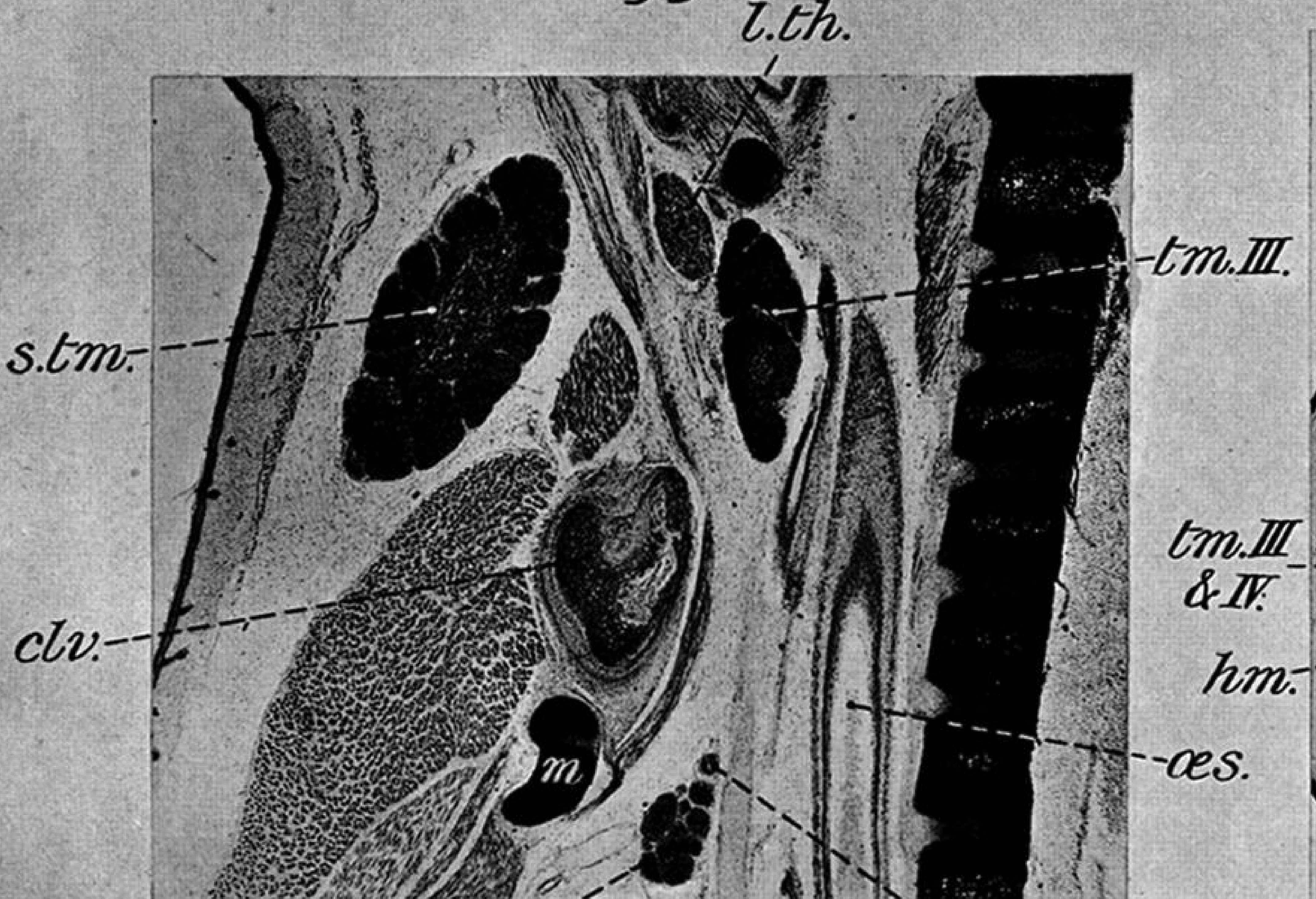

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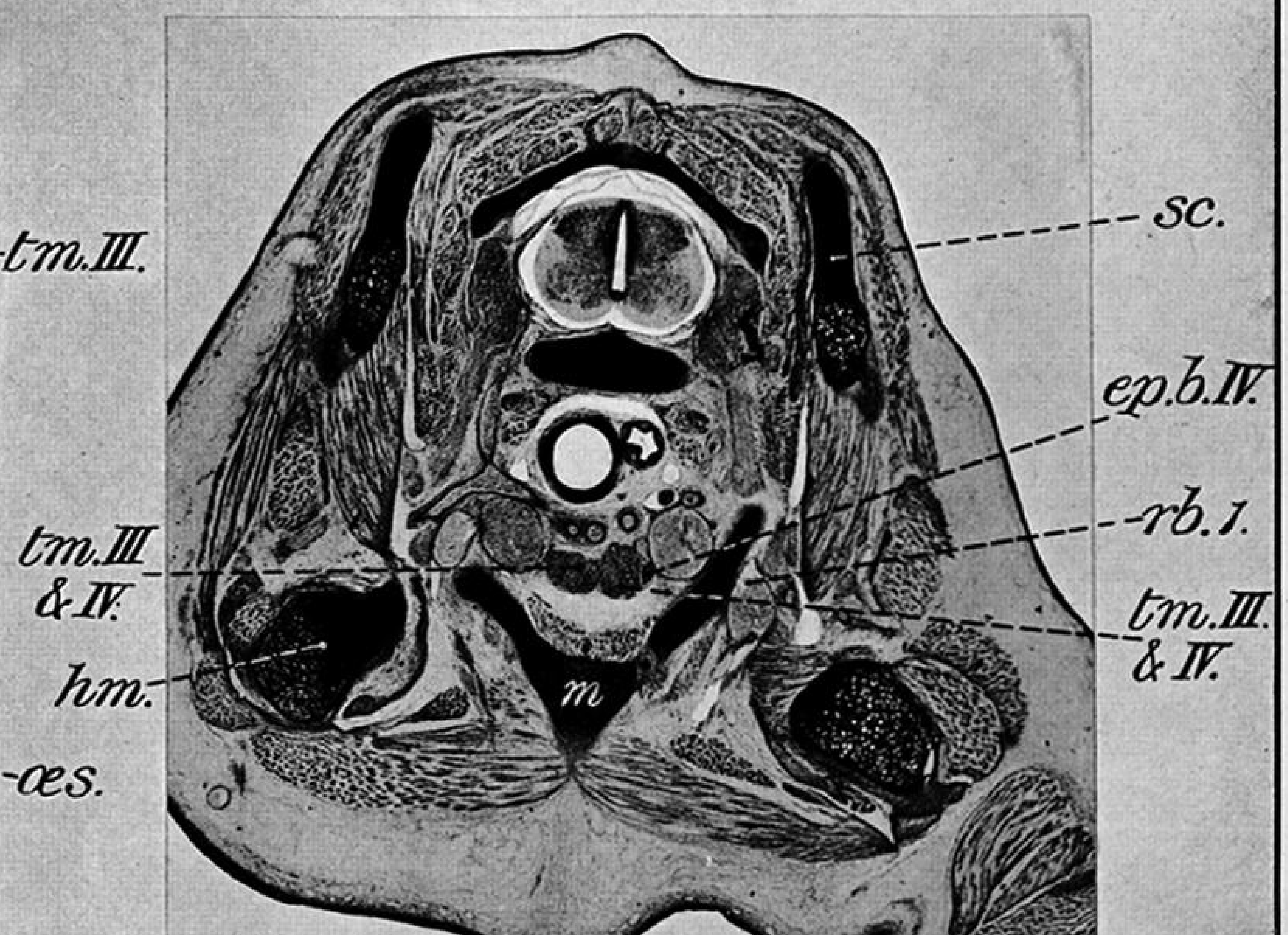

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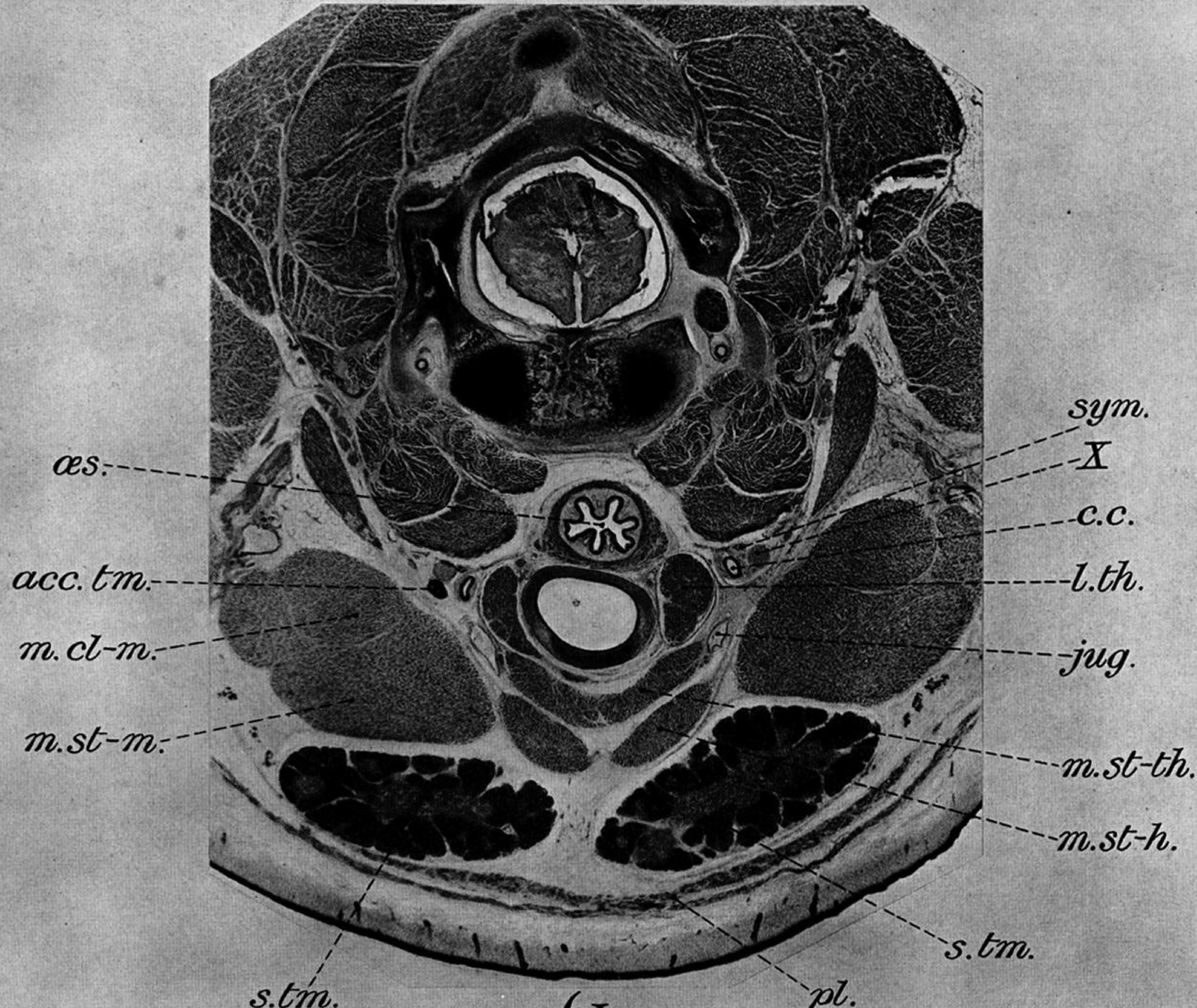
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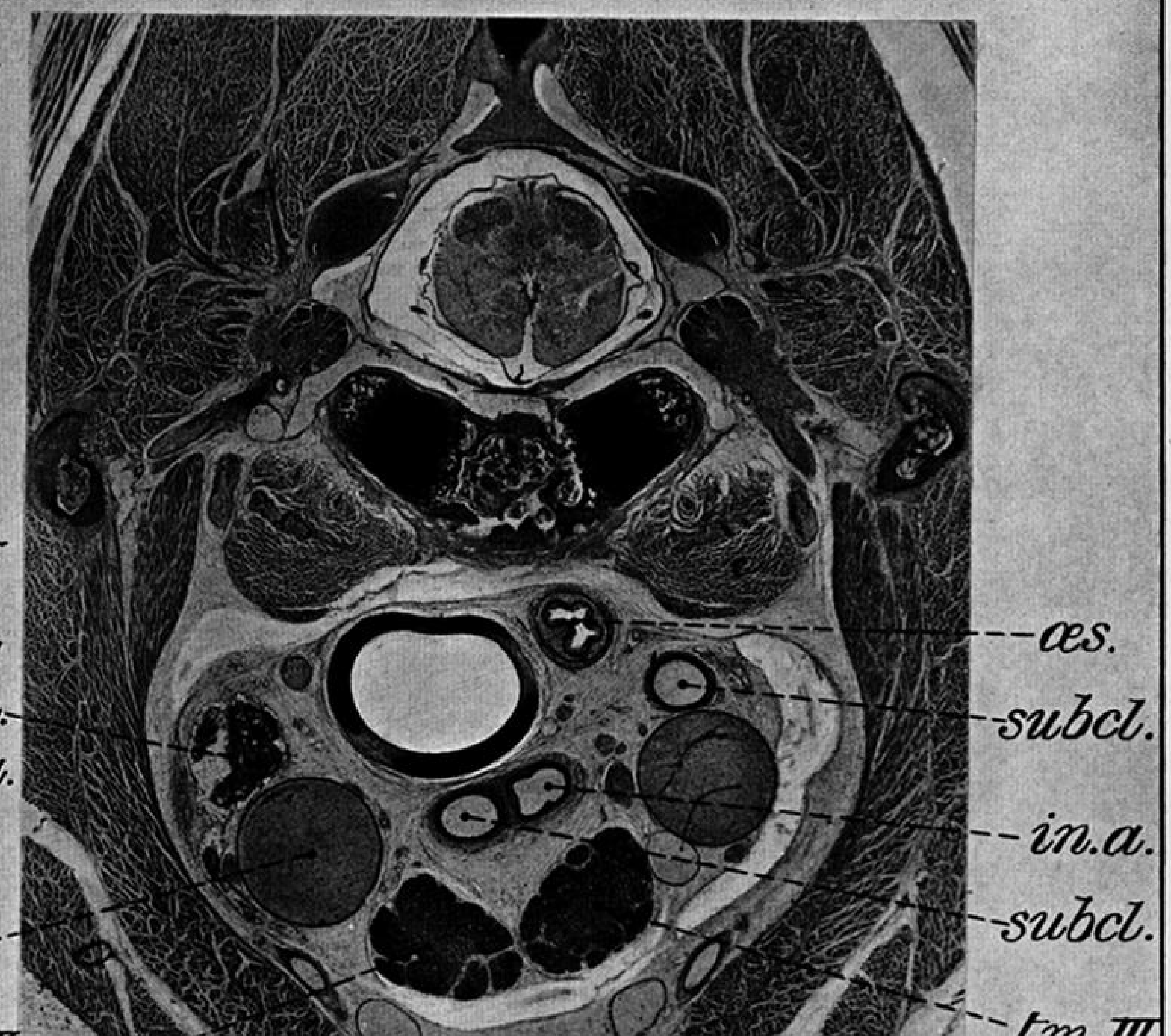
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