II. *The Thyroid and Parathyroid Glands throughout Vertebrates, with Observations on some other closely related Structures.*

By F. D. Thompson.

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[Plates 10–14.]

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I. Introductory.

The main object of the investigation, the results of which are given in the present communication, is to throw light on the question as to a morphological and functional relationship between the thyroid and parathyroid glands. Incidentally it has been necessary to describe the appearances and discuss the significance of some closely allied structures, that is to say, of other tissues and bodies which are developed in the region of the mucous membrane of the fore part of the alimentary tract, such as the post-branchial body, the ventral "Kiemenrest" of anura,* the carotid body, and *pars intermedia* of the pituitary.

A large amount of work has been done upon the development of the parathyroids, thymus, and some of the less known gill cleft derivatives (especially in the lower vertebrata) such as the ventral branchial bodies in anura, and the doubtful structure

* Hereinafter to be referred to as the "Ventral Branchial Body."

known as the carotid gland. On the other hand, detailed descriptions in the adult condition accompanied by illustrations are wanting, or at any rate inaccessible. Thus, even such detailed accounts of the branchial organs as are given by GAUPP* are unaccompanied by drawings, and I am not aware of the existence of a histological illustration of the ventral branchial body in the Frog, one of the most striking organs of the cervical region of the animal, larger than thyroids and parathyroids together, and in my experience, indeed, the only one of the series which can be readily found by the ordinary methods of dissection. For these reasons it seemed that a series of drawings of these bodies in the lower vertebrates would be valuable.

In regard to the main object of this research, as indicated above, it is necessary at the outset to give a brief history of the discussion.

The parathyroids discovered by SANDSTRÖM in 1880 were considered by him to be embryonic thyroids. He stated that all the variations in their structure corresponded to different stages in thyroid development. For many years this view was pretty generally accepted, but gradually the views of workers on this subject began to change, and the climax was reached in the work of KOHN, who insisted that the parathyroid is to be considered as an organ *sui generis*.

On the physiological side, the theory of a separate and, indeed, a supreme functional importance of the parathyroid was first put forward by GLEY in 1893, but, perhaps, owes its prominence chiefly to the work of VASSALE and GENERALI. In his earlier contributions GLEY states that the parathyroids left in the rabbit after removal of the thyroid undergo a more or less complete transition into thyroid tissue. This view, subsequently abandoned by GLEY himself, has been recently revived by KISHI, and by VINCENT and JOLLY, who found that parathyroids left behind in the cat after removal of the thyroids developed into thyroid tissue, implying a close morphological and functional relationship between the two kinds of tissue. This view has been supported by FORSYTH from the standpoint of comparative anatomy, and the present communication, though offering views differing in some essentials from those of the last-named author, furnishes further evidence in the same direction.

During the time I have been occupied with this research, other workers in the laboratory have been performing extirpation experiments, and it has occurred to me that probably a collection of the known facts concerning the anatomy of the thyroid and parathyroids might be of considerable practical utility to experimenters.

The literature of the subject is enormous, and although I have striven to make myself acquainted with as many as possible of the important papers, I beg that any unintentional omissions may be pardoned.

Absolutely fresh material was fixed in Flemming's fluid (strong formula), Zenker's fluid, saturated solution of corrosive sublimate, and other recognised fixatives. It was dehydrated by gradually increasing strengths of alcohol, and embedded in paraffin of a melting point of 48° C. The saturation in paraffin did not last more

* ECKER'S 'Anatomie des Frosches.'

than an hour, so that undue exposure to heat was avoided. Various staining methods were employed.

The elasmobranch material was obtained from the Marine Biological Laboratory, Plymouth, England, and I take this opportunity of expressing my thanks to Dr. E. J. ALLEN for his kindness in dissecting out and preserving the material.

Much of the mammalian material was transferred immediately from the living animal on the operation table to the fixing fluid.

All the microscopical drawings have been made with the aid of the camera lucida.

II. THE THYROID GLAND IN ELASMOBRANCH FISHES.

1. *Historical.*

The organs arising in the neighbourhood of the gill clefts in elasmobranchs are the thyroid, the thymus, and the post-branchial body. The parathyroids have so far not been described.

Although the thyroid gland is well recognised as existing in elasmobranch fishes, the literature of this part of the subject is not voluminous, and precise descriptions are rare.

The earliest reference I have found is to SIMON, who discovered it in all classes of fishes. CH. ROBIN* studied it especially in Plagiostomes, and a few years later LEGENDRE† gives a description of the gland. The only detailed account to which I have had access is that of GUIART.‡

This author gives a careful description of the gland in *Scyllium catulus*, *Acanthias vulgaris*, *Mustelus lævis*, *Galeus canis*, *Carcharias glaucus*, as well as in *Rhina squatina* and others.

His description of the anatomy of the gland in *Scyllium catulus* is very complete. A beautiful account of the histological structure in the same species is also given, with excellent illustrations.

Modern text-books say very little about the anatomy or microscopical structure of the thyroid in elasmobranchs. Thus, BRIDGE§ is content with the following:—"In adult elasmobranchs the thyroid is represented by a moderately large compact organ, situated near the anterior end of the ventral aorta." WIEDERSHEIM‖ says "Bei Selachiern verharrt die unpaare Anlage in ihrer ursprünglichen Form, und liegt unter der Symphyse des Unterkiefers genau in der Medianlinie im Theilungswinkel des Kiemenarterienstammes.

* "Mémoire sur une Nouvelle Espèce de Glande vasculaire chez les Plagiostomes, et sur la Structure de leur Thyroide," 1847. Quoted by GUIART. 'Thèse de Paris,' 1896.

† "De la Thyroide," 'Thèse de Paris,' 1852.

‡ 'Thèse de Doctorat en Médicine,' Paris, 1896.

§ 'Cambridge Natural History,' "Fishes," London, 1904, p. 343.

‖ 'Grundriss der vergleichenden Anatomie der Wirbeltiere,' p. 364.

2. *Histological Structure.*

I have examined the histological structure in the following species :—

(a) *Scyllium canicula.*
(b) *Mustelus vulgaris.*
(c) *Acanthias vulgaris.*
(d) *Rhina squatina.*
(e) *Raja blanda.*
(f) *Raja clavata.*
(g) *Raja miraletus.*

There is a striking uniformity in the general microscopic appearances of the thyroid gland throughout vertebrates. Such differences as are found throughout vertebrates in regard to the amount of intervesicular connective tissue, intervesicular epithelial tissue, size of vesicles, and so forth, are equally to be recognised among elasmobranchs themselves. The two drawings I have made (Plate 10, figs. 1 and 2) illustrate these differences. Thus in Plate 10, fig. 2, showing the thyroid of *Scyllium canicula*, the vesicles are large and the intervesicular material is small in amount, while in Plate 10, fig. 1, taken from *Raja blanda*, the vesicles are small, arranged in lobules separated by thick septa of fibrous connective tissue. One other striking difference between these two genera may be mentioned. In Scyllium the vesicle cells are low cubical, while in *Raja blanda* they are cylindrical, though of varying heights, and presenting an irregular, crenated outline towards the cavity of the vesicle (Plate 10, fig. 1, *e. ves.*).

Perhaps the most interesting of the species I have examined is *Scyllium canicula*, for in this the thyroid contains not only the usual vesicles and connective tissue, but also several small bodies, composed of compact masses of cells. The cells are of two kinds, lymphoid and epithelial, and neither sort occupies exclusively any particular portion of the bodies (Plate 10, fig. 2, *e. interves.* and *ad. t.*). They are usually situated near the edge of the gland. So far as I know, such epithelial bodies have not previously been described in relation to the elasmobranch thyroid. The parathyroids in fishes are not known to exist. The thymus is placed considerably dorsal to the thyroid, and, so far as I am aware, no thymus nodule in the neighbourhood of the thyroid has been described. The epithelial bodies in question are multiple, but two appear to be larger than the rest. One is more deeply placed in the substance of the thyroid than the other. In some sections the epithelial bodies appear as solid thickenings of the vesicular epithelium, and are traceable, as a rule, through a series of 10 to 12 sections of a thickness of 10 μ each. Sometimes the epithelium cells are seen in the middle, with adenoid cells at the circumference (Plate 10, fig. 2, *e. interves.* and *ad. t.*) suggesting an adenoid invasion from without. In the case of some of these structures, the arrangement is reversed.

In what category are we to place these epithelial bodies? Their mixed epithelial and lymphoid nature at once suggests thymus, and this seems, on the whole, most probable. The proportion of epithelial to adenoid tissue is perhaps not greater than is found in the thymus of young birds.* Against the supposition that they are parathyroid is the fact that embryologists have not observed any parathyroid in the course of development, and also, from a general view of the comparative anatomy of the parathyroids throughout vertebrates, one would expect that in fishes they would be represented by separate structures, lying outside and independent of the thyroid gland. MAURER† describes epithelial bodies connected with the gill clefts in fishes, but these seem to have been of a different nature.

Mustelus vulgaris has the low type of cell lining the vesicles, which are in this respect almost identical with those of mammals.

In *Acanthias vulgaris* the gland is flattened and of irregular shape, and is situated towards the end of the tongue under the coraco-mandibular muscle.

On microscopical examination the cells lining its vesicles appear not cylindrical but cubical in form. There are in parts solid accumulations of epithelial cells with no connective tissue divisions. These may be homologous with the structures described in *Scyllium canicula*.

There is a capillary network between each of the secreting hollow vesicles.

Rhina squatina.—The thyroid of this genus presents, at first sight, quite a different appearance from that of the other elasmobranchs I have examined. There is much solid cellular material between the vesicles, some of which are filled with cells instead of colloid. In many cases the lining membrane shows several rows of nuclei encroaching on the cavity of the vesicle. This latter is very irregular in shape, and there is a large amount of intercellular material which stains more deeply with iron hæmatoxylin than does the vesicular lining. This intervesicular material is in part connective tissue and in part epithelial, as in mammals. Parts of it resemble parathyroid and appear identical with the material lining the vesicles.‡

In *Raja blanda* the organ is divided into lobules by thick strands of connective tissue, but there is very little of this tissue between the individual vesicles (Plate 10, fig. 1, *c. t.*). The lumen is irregular, and the height of the lining cells varies from place to place. The pavement epithelium of the capillaries is very distinct (Plate 10, fig. 1, *end.*), and these vessels are very numerous and of various sizes. In my sections there is no intervesicular cellular material. On looking at the slides with the naked eye the lobules of thyroid can be seen embedded in large quantities of connective tissue (Plate 10, fig. 1, *c. t.*).

The only striking feature in *Raja clavata* is the great variety in the size of the vesicles.

* In birds, the epithelial remains of the thymus are represented not by small, isolated, concentric corpuscles, as in mammals, but by large masses of epithelial cells, occupying the central portion of each lobule. (LEWIS, 'Journ. Anat. and Physiol.,' vol. 38.)

† MAURER, 'Hertwig's Handbuch,' vol. 2, pt. 1, p. 133.

‡ A large portion of it is, however, probably lymphoid in nature.

In *Raja miraletus* the cells lining the vesicles are strikingly columnar in shape. Many have two distinct zones, an inner granular and an outer clear, like typical glandular secreting cells. The lumen is irregular, owing to variations in the height of the lining cells. The inner granular portion of these projects in the form of a cupola into the vesicle, and when the section is tangential these cut projections appear like separate spherical objects in the vesicle. In some vesicles the inner granular zone is not distinctly marked.* The granules are probably the precursors of colloid.

III. The Thyroid Gland in Teleostean Fishes.

The earliest description I have been able to find is that of STANNIUS,† who in 1854 gave an account of the thyroid in teleostean fishes. In the conger, LEGENDRE‡ describes two posterior lobules contiguous to the trunk of the branchial artery, and following its course, while gradually diminishing in volume. In the carp and the tench the two lobules have about the volume of a pea. According to MAURER,§ the thyroid of teleosts consists of a mass of follicles more or less separated, which surround the trunk of the branchial artery from the heart to its extremity. GUIART quotes the descriptions of other writers, but offers no new observations.

MACKENZIE,‖ in 1884, gives the following: "In Amiurus this organ occupies the exact position described for it by STANNIUS in the Ganoids and many Teleosts, viz., beneath the cupolæ of the branchial arches and surrounding the anterior end of the branchial artery. It is an impair structure extending in the medial line from the origin of the vessels at the first pair of gill arches to a short distance behind the origin of the single stem for the third and fourth pair of arches. . . . The framework of the organ consists of loose connective tissue which does not form a lining membrane, but simply passes over into the like tissue sheathing the adjacent parts and the vessel which it surrounds. The usual vesicles of the thyroid are scattered throughout this connective tissue, showing a tendency to arrange themselves in short rows. They vary in size from 15 μ to 210 μ in diameter, and are filled with the usual colloid substance. A few, however, contain a granular substance, with nuclei showing nucleoli scattered through it, while others are part filled with the granular and part with the colloid matter. . . . The wall of the vesicle consists of a single layer of columnar epithelium, resting on a basement membrane formed from the surrounding connective tissue. The epithelium is readily made out in the young fish. In the

* This form of cell has been noted in other animals and in other tissues. It has been described in the epididymis by MYERS-WARD ('Journ. Anat. and Physiol.,' vol. 32), and also in the ducts of the pancreas of elasmobranch fishes. (DIAMARE, 'Internat. Monatsschr. f. Anat. u. Physiol.,' 1899, vol. 16, parts 7/8.)

† 'Lehrbuch der vergleich. Anat. Handbuch der Anat. der Wirbelth.,' vol. 1, "die Fische," 1854; 'Lehrbuch der Zootomie,' 1854, vol. 1, p. 255.

‡ "De la Thyroïde," 'Thèse de Paris,' 1852.

§ "Schildrüse u. Thymus der Teleostier," 'Morph. Jahrb.,' 1885, vol. 11.

‖ 'Proc. Canad. Inst.,' 1884, p. 434.

youngest specimens (15 mm. long), of which I have sections, the gland is very small, and the connective tissue is unattached to any of the neighbouring structures. The vesicles are confined to a few spots, and form only a single row."

I have little new to add to MACKENZIE'S description, at any rate as far as concerns the gross anatomy. I have examined *Amiurus nigricans*, the same species as that examined by him (Plate 10, fig. 3). The connective tissue in which the vesicles appear in my specimens is very compact, and not "loose," as in his (Plate 10, fig. 3, *c. t.*). It is often difficult to recognise the epithelium lining the vesicles (Plate 10, fig. 3, *e. ves.*). In none of my slides is the epithelium columnar, nor can I verify the statement that the cells of the vesicles rest upon a basement membrane. In a specimen of the embryo sent me by Prof. RAMSAY WRIGHT, the oval vesicles are not very distinct, and are hollow. The space occupied in the adult by colloid is filled up with some material full of nuclei (epithelial or adenoid tissue ?).

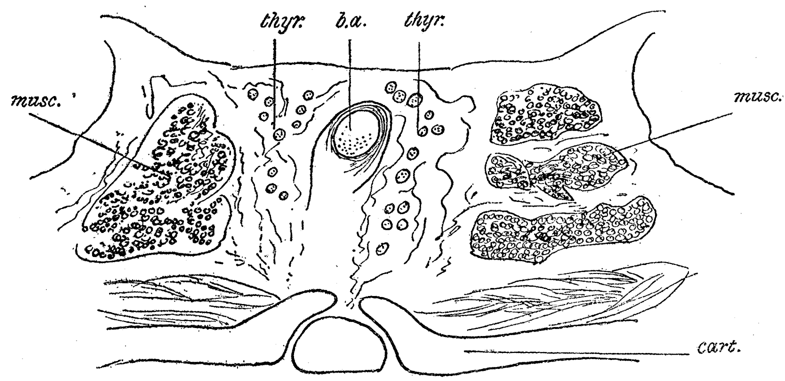

FIG. 1.—Transverse vertical section of embryo *Amiurus*, showing the thyroid as scattered groups of vesicles on either side of the branchial artery. *Thyr.* = thyroid; *b. a.* = branchial artery; *musc.* = muscle; *cart.* = cartilage.

IV. AMPHIBIANS.

A. *Urodela.*

The thyroid in the Urodela occupies a more superficial position than in the Anura. The development has been worked out in Triton, Siredon, and Necturus. The gland arises from a median rudiment, and subsequently becomes paired.

The only species I have so far examined is *Spelerpes ruber*. The thyroid vesicles are approximately of the same size as in the frog, but in my sections they have never numbered more than a dozen. There is less connective tissue than in the frog, and the vesicles are therefore more closely packed together. The colloid contents are of the same character as in vertebrates generally. The gland is, however, distinctly more vascular than in the frog; but this appearance may be due to an accidental engorgement of the blood-vessels at the time the animal was killed. Since I am not acquainted with any histological drawing of the thyroid in adult Urodela, I have appended one to show the chief features, and for comparison with the post-branchial body (Plate 10, fig. 4).

In *Triton*, there appear to be two or even three parathyroids developed on either side. In *Spelerpes ruber* I have found only one. The general histological features appear somewhat different from the corresponding structure in the frog (*cf.* Plate 10, fig. 6, and Plate 11, fig. 8, *pthyr.*). This body is of extremely small dimensions. I could not find it by a naked eye dissection. Cut in serial sections, it has the appearance shown in Plate 10, fig. 6. There are large blood capillaries in the body, and at first sight it bears more resemblance to the ventral branchial body of Anura (Plate 11, fig. 8, *v. kr.*) than to the parathyroïd of that group (Plate 11, fig. 8, *pthyr.*). It is encapsuled, but its constituent cells do not possess the whorl arrangement so characteristic of the parathyroid of the frog (Plate 11, fig. 8, *pthyr.*).

The *post-branchial body* occupies a corresponding position to that of the frog. It consists of about eight vesicles in my sections (Plate 10, fig. 5). These have a taller epithelium (Plate 10, fig. 5, *c. pb. b.*) than the thyroid vesicles, and contain no colloid (Plate 10, fig. 5).

B. *Anura.*

1. *Anatomy of the Thyroid.*—

A full account is given in some of the text-books, notably by GAUPP.*

In the frog the thyroid is by no means easily found by dissection. I have only searched for it in winter frogs, and in only one of them have I been able to find it without recourse to the microscope. The frog possesses two thyroid lobes, a right and a left, quite separate from each other in the adult, although originally derived from a median unpaired rudiment. The gland of each side is an oval corpuscle, placed ventrally to the root of the processus postero-medialis of the hyoid cartilage, and occupies a deep, concealed position. GAUPP confesses that it is difficult to find, but states that he has frequently removed it from the living animal. He further observes: "Die chemische Diagnose bestätigte, dass nicht irgend etwas Anderes, Muskelfasern und dergl., fälschlich für die Schildrüse genommen war." It would appear much more satisfactory if this diagnosis had been made by histological instead of chemical examination. It seems more than probable that the ventral branchial body has often been removed in mistake for the thyroid.

By cutting serial sections through the cervical region I have been able to study the histology of the organ, which measures in its largest dimensions 1·5 mm. by 0·5 mm. (Plate 11, fig. 7).

2. *Histology of the Thyroid.*—

Like the thyroid of all animals, that of the frog consists of a number of closed vesicles, the walls of which are composed of a single layer of epithelial cells. These vesicles are small as compared, for example, with those of *Scyllium canicula*, though individual vesicles vary considerably in size. The cells lining the vesicles are cubical but small, corresponding with the small size of the vesicles of the whole

* ECKER—WIEDERSHEIM, 'Anat. des Frosches,' Braunschweig, 1901, 3te Abth., 1 Hälfte, S. 205.

gland. The intervesicular tissue, instead of being cellular as in mammals, and to some extent also in elasmobranch fishes (*e.g. Scyllium canicula*), is formed of fibrous connective tissue with scattered nuclei and blood-vessels, and corresponds with the arrangement in teleosts (*Amiurus nigricans*) and some elasmobranchs (*e.g. Raja blanda*). The colloid contents of the vesicles call for no special notice (Plate 11, fig. 7, *c. ves.*).

3. *Development of the Thyroid.*—

According to MÜLLER and MAURER the thyroid of the frog arises as an unpaired median evagination of the ventral pharyngeal epithelium at the level of the second branchial cleft. This, at first hollow, soon becomes solid, and then separates itself off from the mother tissue, and finally divides into two parts which become quite separate and travel caudalwards, along with the heart and truncus arteriosus.

Whatever may be the relationship of the post-branchial body to the thyroid in mammals, in Anura the former never contains colloid, and never unites with the latter.

4. *Accessory Thyroids.*—

I have been fully able to confirm the existence of these. Their microscopical structure is that of the main thyroid.

5. *Parathyroids.*—

a. Literature.—GAUPP says that the parathyroids "haben mit der Schildrüse nichts zu thun." In the frog, to be sure, there does not appear to be any connection except such as seems to unite many of the branchial cleft organs. The connection between thyroid and parathyroid in higher vertebrates will be discussed in later portions of this paper. In regard to this question there appears to be an interesting analogy between thyroid and parathyroids on the one hand, and cortex and medulla of the suprarenal on the other. In lower vertebrata the two latter bodies are quite separate and distinct, but come together in the higher groups. Whether in this case there is any physiological connection is at present doubtful. This point will be referred to again later.

Parathyroids in the frog are first mentioned by ECKER,* who considered them as representatives of the thymus, and later by LEYDIG,† who considered that they, together with the ventral branchial body, represent the thyroid. That they are very different from the thyroid in their structure LEYDIG himself stated. The suggestion that one of the bodies described by LEYDIG was the ventral branchial body and the other the parathyroid is made by GAUPP,‡ and on referring to LEYDIG's monograph and looking at his plate, it seems clear that this was the

* 'Wagner'schen Handwörterbuch der Physiol.,' vol. 4.

† 'Anat. Hist. Untersuch. über Fische u. Reptilien,' Berlin, 1853.

‡ ECKER, 'Wiedersheim,' 1901.

case. After the work of Toldt* the bodies were called for some years "Nebenschildrüsen," a term which has led to much confusion with true accessory thyroids.

The matter was finally made clear by Maurer,† who recognised the homology of these organs with the "glandulæ parathyroideæ," which were discovered in higher animals by Sandström in 1880,‡ and independently by Baber,§ Horsley,|| and Gley.¶

β. *Anatomy.*—The anatomical position of these bodies has been described in sufficient detail by previous authors. I have been able to see them with the naked eye in the frog, but have studied them chiefly by means of serial sections (Plate 11, fig. 8, *pthyr.*).

The parathyroids are usually two small oval or rounded corpuscles on each side of the body. They lie in front of the common carotid artery very near to the ventral branchial body. There are sometimes three parathyroids on each side.

γ. *Histology.*—Gaupp describes the tough fibrous capsule (Plate 11, fig. 8, *cap.*) that surrounds each glandule and the compact structure of the organ, but gives no drawings. Closely-placed, elliptical, spindle-formed nuclei are seen which stain deeply (Plate 11, fig. 8, *pthyr.*). The cells are longish, and so disposed that they describe spiral turns. The cell outlines are distinct, even under a low power of the microscope; some of the nuclei are rounded, and others distinctly elongated. Some of the cells are vacuolated, probably due to fat removed in the process of preparation. In some sections the disposition of the central part of the organ presents the appearance of having been subjected to torsion stresses in different directions. In the regions where the nuclei are oval, the long axis is directed along the path of the whorl (Plate 11, fig. 8, *pthyr.*). The cells vary greatly in shape. They may be oval, cubical, pentagonal, spheroidal, or elongated.

δ. *Development.*—According to Maurer the parathyroids are formed at the time of the development of the internal gills. They arise as solid epithelial processes from the ventral ends of the third and fourth gill clefts. They are quickly separated off, and come nearer together.

6. *The Ventral Branchial Body in the Frog.*—

α. *Literature.*—The ventral branchial body was drawn and described by C. G. Carus** in 1818. This observer thought, however, that it was the thyroid.

* 'Sitzungsber. d. K. Akad. d. Wissensch., Wien. Mathemat.-naturw. Cl.,' vol. 58, Sect. II, 1868.

† 'Morph. Jahrb.,' vol. 13, 1888.

‡ 'Läkareförenings Förhandlingar,' vol. 15, 1880.

'Phil. Trans.,' 1881, part 3, p. 600.

|| 'Brit. Med. Journ.,' January, 1885; 'Lancet,' December, 1886.

¶ 'Comptes R. de la Soc. de Biol.,' 1891.

** 'Lehrbuch der Zootomie,' Leipzig, 1818.

HUSCHKE* was inclined to the same opinion, but was the first to make the suggestion that it represents gill remains. The structure and development of the organ have been more fully worked out by LEYDIG,† FLEISCHL,‡ TOLDT,§ MAURER,|| and MAYER.¶

β. Anatomy.—The ventral branchial body is a comparatively large and striking gland (Plate 11, fig. 8, *v. kr.*), and, with the possible exception of the propericardial body, is the only glandular structure in this region of the body which a dissector is likely to detect with the naked eye. It is placed in a niche behind the omohyoid muscle, in the angle which this makes with the sternohyoid. Its length is 1·7 mm., and breadth 0·75 mm. It is usually reddish, but varies in tint in different specimens. It has sulci and appears superficially lobulated. There is an abundant development of blood-vessels in its neighbourhood.

γ. Histology.—The organ is enclosed by a capsule (Plate 11, fig. 8, *v. kr.*) which is covered on the exterior by an endothelium, in the region where it looks into the sinus sternalis. The interior is made up of a network of wide blood-vessels, whose endothelium cells are distinctly seen in all sections, and meshes, composed of solid cords of cells. The general appearance is that of a lymphatic gland, or, perhaps, more correctly, a hæmolymph gland such as is found in the ox, sheep, or rat.** It may be compared also with the degenerated "head kidney" of teleostean fishes.†† The cells forming the cords separating the blood spaces are of two kinds: (1) epithelial, with large rounded or oval nuclei; (2) lymphoid, consisting of smaller rounded darkly staining nuclei with a narrow rim of protoplasm (Plate 11, fig. 8, *v. kr.*). These two varieties are seen clearly throughout the whole of the organ, but the adenoid cells are frequently more numerous in the peripheral regions, suggesting a leucocytal invasion from the exterior.‡‡ Thus the organ as it exists in the adult frog is to be looked upon as an epithelial gland which has suffered an adenoid invasion of the same character, though not to the same extent, as the thymus.§§

* 'Isis, von Oken.,' 1826, vol. 18, and 1827, vol. 20.

† 'Frorieps Tagesber. über d. Fortschr. in d. Natur. u. Heilkunde; Abth. f. Zool. u. Paläontol.,' vol. 2, 1852.

‡ 'Sitzungsber. d. K. Akad. d. Wissensch. Wien. Mathem.-naturw. Cl.,' vol. 60, Sect. II (Jahrg. 1869), Wien, 1870.

§ 'Sitzungsber. d. K. Akad. d. Wissensch., Mathem.-naturw. Cl.,' vol. 58, Sect. II, 1868, Wien.

|| 'Morph. Jahrb.,' vol. 13, 1888.

¶ 'Anat. Anz.,' 3 Jahrg., 1888.

** See VINCENT and HARRISON, 'Journ. Anat. and Physiol.,' January, 1897.

†† See VINCENT, 'Trans. Zool.,' 1897.

‡‡ This is not the case in the particular section from which the figure was drawn.

§§ It is, of course, a disputed point, in the case of the thymus, as to whether there has been an invasion of leucocytes, or an actual transformation of the original epithelial cells. The former was the older view, but BEARD ('Anat. Anz.,' vol. 9, 1894) and NUSBAUM and PRYMAK ('Anat. Anz.,' vol. 19, 1901) insist that the lymph cells of the thymus, at any rate in teleostean fishes, arise for the greater part, if not exclusively, direct from the epithelial cells.

It seems probable that the ventral branchial body has some important function in the frog, and the suggestion which lies nearest to hand is that it functions as a lymph gland. Now the only certainly known function of a lymph gland is the manufacture of white blood corpuscles. S. MAYER has suggested that the body may have some function also in relation to the red corpuscles. No signs of alterations in the red cells can, however, be detected such as are readily recognised in the hæmolymph series of organs.

7. *Post-branchial Body.*—

α. *Literature.*—The post-branchial body is of considerable importance in any discussion of the development of the thyroid. DE MEURON* was the first to find the body in the frog and the toad, and to describe its development. He considered the structure to be homologous with the "suprapericardial body," which had been described by VAN BEMMELEN† in elasmobranchs. MAURER has supported this view, and introduced the name "post-branchial body" to express its relation to the gill clefts. VAN BEMMELEN looked upon his "suprapericardial bodies" as homologous with gill clefts, but MAURER considers them to be of a different nature, because in all vertebrates where they occur they arise immediately behind the last gill cleft, whether this be the fourth, fifth, or sixth. The post-branchial body has so far been discovered in all craniata except cyclostomes and teleosts, but in many forms it appears only on one side.

β. *Anatomy.*—The post-branchial body is a tiny structure which lies at the side of the aditus laryngis.

γ. *Histology.*—The organ consists of three or four small vesicles lined with cylindrical epithelium. MAURER says that these cells sometimes carry cilia. This I have not been able to observe in the frog. The vesicles contain a coagulated albuminous substance and *débris*, but no colloid.

δ. *Development.*—MAURER states that the post-branchial body of the frog arises somewhat later than the thyroid as an evagination of the ventral pharyngeal wall behind the fifth gill cleft at the side of the aditus laryngis, and quickly separates itself off, remaining close under the epithelium. At the metamorphosis there is no change in the structure and position.

8. *Carotid Gland.*—

The nature and homology of the carotid gland in the frog are very doubtful. It is a spongy, cavernous body, and it is a question whether any structures other than those of the blood-vessels enter into it. MAURER believes that the carotid gland of Rana arises as a solid epithelial process from the first gill arch, and is homologous with the carotid gland of higher vertebrates. Other authors, especially KOHN, are strongly opposed to this view (Plate 11, fig. 8, *car. b.*).

* 'Recueil Zool. Suisse,' III, 1886.

† 'Mitt. a. d. zool. Stat. zu Neapel.,' vol. 7, 2, 1885.

V. Reptiles.

Among reptiles I have been able to examine the following species:—

Chelonia—
- *Chrysemys picta.*
- *Pseudemys scripta.*
- *Kinosternon pennsylvanicum.*

Ophidia—
- *Tropodonotus natrix.*
- *Natrix fasciata sipedon.*

Lacertilia—
- *Anolis velifer.*

In reptiles there is no very intimate connection between thyroids and parathyroids, and the mysterious post-branchial body is more in evidence than in any other group of vertebrates, with the exception, perhaps, of the birds. Moreover, the parathyroid is somewhat exceptional in its histological features.

The development of the thyroid in these animals is analogous to that in other vertebrates. It arises from an unpaired rudiment, and remains unpaired in some families (Ophidia and Chelonia), while in Lacertilia the organ is bilobed in young specimens, paired in older. The organ lies immediately in front of the pericardium. The parathyroid and post-branchial body are intimately united, paired, and placed anteriorly to the thyroid. Their precise anatomy differs in different groups.

a. *Chrysemys picta.*

α. *Thyroid.*—The vesicles are lined with low cubical cells with distinctly granular protoplasm. There is very little intervesicular material, and this is mostly connective tissue. The colloid contents of the vesicles appear to be composed of two substances showing different staining reaction. The droplets stain dark in Flemming preparations, double stained with Heidenhain's iron-hæmatoxylin and eosin, while the rest of the colloid substance stains faintly with eosin.

β. *Parathyroid.*—The parathyroid is a compact organ of moderate size, having a loose capsule, and delicate trabeculæ of connective tissue bearing an abundant capillary plexus. This divides the whole organ into lobules, having the general form of glandular alveoli or acini. Some of the cells are extremely elongated and are of two kinds, some staining darkly and some lightly. Some appear shorter or even rounded. In some parts of the organ, especially at its periphery, the cells are arranged in a radiate fashion round small blood-vessels, so that the general appearance is as if the vessel were the lumen of a secreting tubule. In other cases, however, the lumen does not contain blood corpuscles, and has no lining epithelium, and is therefore a true lumen to the parathyroid alveolus. These, however, in the specimens I have so far examined, do not contain colloid.* The protoplasm of the cell is distinctly but finely granular. The whole appearance is strikingly like cortical adrenal tissue in lower vertebrates, except as to the appearance of a lumen.

γ. *Post-branchial Body.*—This is in close relation to the parathyroid. It consists of a number of vesicles of varying size and shape, though they tend to be spherical. The vesicles are of two distinct types: some large, with very low epithelium staining very deeply (Flemming, Heidenhain's hæmatoxylin and eosin), others smaller, with cylindrical epithelium. Some of the vesicles 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. Some of the vesicles lying closest to the parathyroid are composed of cells of the same character as those of the latter body. Of such it is indeed difficult to say whether they belong to the parathyroid or to the post-branchial body. In this species, then, we have very intimate relationships between the two latter bodies, and the occasional presence of colloid in the vesicles of the post-branchial body is not without significance.

b. *Pseudemys scripta.*

In Pseudemys the parathyroid and post-branchial body present features of special interest (Plate 11, fig. 9, *pthyr. pb. b.*). The parathyroid, fixed in $HgCl_2$, and stained with hæmatoxylin and eosin, presents a very beautiful picture (Plate 11, fig. 9, *pthyr.*). It is composed of masses of cells of irregular size and shape, but mostly elongated or sausage shaped, separated by a rich capillary plexus, and *each one possessing a small distinct lumen.*

The post-branchial body (Plate 11, fig. 9, *pb. b.*), as in *Chrysemys picta*, is in close relation with the parathyroid, and consists of a number of vesicles varying in size. Some of these possess only a very small lumen, and are almost indistinguishable from the corresponding columns of the parathyroid. Again, a small number of them undoubtedly contain colloid material (not shown in the figure). In parts of the gland small thymus nodules are seen (Plate 11, fig. 9, *thym.*).

c. *Kinosternon pennsylvanicum.*

In this species the chief point of interest is that the parathyroid contains lumina (Plate 11, fig. 10, *l.*) as distinct as in *Pseudemys scripta.* There is the same relation with the post-branchial body, and in the centre of the parathyroid is a group of cells, differing in character from the rest, more lightly staining and larger, looking remarkably like islets of Langerhans among the tubules of the pancreas.

d. *Natrix fasciata sipedon.*

In this reptile the *thyroid* calls for no special description. 'Wiedersheim' and other text-books say that in snakes the gland is bilobed. This, in my

* In some cases what appears to be colloid is seen in the lymphatics.

specimens, has not been found to be the case. It is a median, unpaired spherical body.

On microscopical examination, I have found a *parathyroid* encapsuled in the head of the thymus. Its cells are arranged in a whorl, as in the frog, whose parathyroid it resembles more closely than the corresponding organ of Chelonia, from which it differs especially in that it shows no lumina. There are in the parathyroid arrangements of cells like concentric corpuscles, and in the thymus many cells like unaltered parathyroid.

There are numerous other interesting histological details which concern the thyroid, parathyroid, thymus, and post-branchial body in reptiles, but as the significance of these is very problematic, and as I have not yet worked through the whole of my material, it would be well to hold these over for a future communication.*

VI. Birds.

The general histological features and the mode of development of the thyroid are the same as in reptiles. The adult thyroid is a paired organ, placed near the large blood-vessels of the neck.

The third and fourth clefts each give rise to a parathyroid. Sometimes there is another from the fifth cleft. The two bodies from the third cleft are in relation to the thyroid; the derivative of the fourth cleft is in close contact with the post-branchial body.

The post-branchial body of birds is described as consisting of three parts. The first is composed of compact epithelial cords; the second of spherical vesicles, lined with cubical epithelium, which may be ciliated; and the third of true parathyroid tissue and thymus.

Van Bemmelen† says that the post-branchial body of birds is not strictly homologous with that of lower vertebrates, but has a more complicated significance.

a. *Pigeon.*

α. Thyroid.—The vesicles are for the most part small and irregular in shape. The intervesicular material is large in amount and in certain regions, and in certain specimens forms large areas of solid tissue which is indistinguishable from parathyroid. This state of affairs in the thyroid of the bird has been emphasised by Forsyth;‡ but he seems to have found much more extensive areas of this tissue than I have.

* It will give a hint of the curious findings among these structures if I state my belief that these epitheliogenous cells are the remains of the original epithelium of the thymus nodule which is very regularly found in the parathyroid of the Chelonia. Thus, in *Pseudemys scripta* both elements of the thymus are plainly seen, the lymphoid cells and the remains of the original epithelium forming an island in its midst (Plate 11, fig. 9, *thym.*).

† 'Zool. Anz.,' 1888.

‡ 'Journ. Anat. and Physiol.,' vol. 42, 1908.

From the very wide variations found in different specimens of the same species, and from the feeding experiments described below, we must conclude that the proportion between vesicular tissue and intervesicular tissue varies under different physiological conditions.

β. *Parathyroid.*—The parathyroid in the pigeon differs strikingly in its general appearance from the corresponding structure in other animals. But this difference appears to be simply due to the fact that the epithelial cells contain an abundance of fat, and that they become extensively vacuolated during the process of preparation for the microscope. Unlike the parathyroids of reptiles, those of birds appear to have no lumen in the masses of cells (Plate 12, fig. 11, *pthyr.*).

γ. *Post-branchial body.*—In close relationship with, and in the same region as, the parathyroid we find a body having an extraordinarily complicated structure. It is obviously of epithelial origin and nature. It is composed largely of structures which at first sight resemble small arteries, but whose walls are made up entirely of concentrically placed spindle-shaped cells (Plate 12, fig. 11, *c.c.*), and projecting into the lumen are irregular cells, lining the tubules. The rest of this body appears to be built of structures identical with the various well-known forms of HASSALL's corpuscles of the thymus. There is a mass of this tissue in the centre of the parathyroid, and small portions of it in other regions of the same glandule (Plate 12, fig. 11, *c.c.*). There are also true thymus nodules in the neighbourhood.

Thus, the structure which is commonly called post-branchial body in the pigeon (a yellowish-white body some little distance posterior to the thyroid) is composed, not only of post-branchial tissue, but also of parathyroid and thymus.

b. *The Fowl.*

α. *Thyroid.*—In the thyroid of the hens that I have examined there is a larger amount of intervesicular material than in the pigeon. This occupies chiefly the central portion of the gland. A large part of the solid looking material is found on examination with the high power to contain small vesicles, but some of it is entirely devoid of them.

β. *The Parathyroid.*—The parathyroid presents the same general features as in the pigeon, except that the vacuolated part is found more particularly in the centre.

γ. *The Post-branchial Body.*—The post-branchial body is represented by a group of eight to ten vesicles, lined with a low cubical epithelium, embedded in a constricted off portion of the elongated thymus. In the thymus nodule there is also a structure which must be put in the same category. This is a much infolded vesicle of large size, lined with columnar ciliated epithelium.

Thus, in the fowl we have the same intimate relation of parathyroid, post-branchial body, and thymus as in the pigeon.

c. *Sylvia bachmanii.*

The thyroid is very small, and no external parathyroids can be seen with the naked eye. On cutting sections a parathyroid was found on each side, closely adjacent to the posterior end of the thyroid, but entirely separated from it by a very small strand of connective tissue. The whole of each lobe of the thyroid measures 1 mm. by 2 mm. The thyroid is composed of very small vesicles, very round, and very even in size, filled with colloid. Their average size is 1/25 mm. The parathyroid has two sorts of cells, epithelial and adenoid, and resembles that of the fowl. The post-branchial body resembles that of the pigeon, but is not so intimately mingled with the parathyroid tissue.

While the birds illustrate fairly well what has been insisted upon frequently in regard to other groups, namely, an intimate relationship and anatomical continuity between thyroid, post-branchial body, and parathyroid, it must be admitted that as regards the essential relationship between thyroid and parathyroid the evidence is not so convincing as in mammals. Although a parathyroid is derived both from the third and fourth clefts, yet the one derived from the latter does not become enclosed by thyroid tissue as is the case in mammals. Apparently as a consequence of this we do not meet with the transition forms between the two kinds of tissue which I have described (*vide infra*), and depicted, in mammals.

FORSYTH has largely employed birds to support his main thesis, and although the results of my own investigation fully support his conclusions in mammals, I am inclined to suspect that he has been somewhat hasty in placing thyroid tissue with few and small vesicles in the category of parathyroid. It may seem inconsistent to use the arguments put forward under another section (*vide* Mammals, *infra*) as applied to mammals, and refuse to admit the same arguments in birds; but it seems, in fact, that the intimate physiological and anatomical connection obtaining in mammals has not yet been established in the class *aves.**

VII. MAMMALS.

1. *Gross Anatomy in Man and other Mammals.*

The anatomy of the thyroid gland itself is too well known, both in the human subject and in the majority of laboratory animals, to require any detailed description.

* FORSYTH says ('Thyroid and Parathyroids in Mammals and Birds,' p. 313) "Thyroids normal." Has there yet been enough observation and research to establish what is normal? He does not mention the thymus. Is he not aware that there is a nodule of thymus within the thyroid as well as a large body of it lying along a good part of the length of the trachea? Perhaps what he refers to as "lymphoid" really is thymus. FORSYTH'S material was obtained from the Zoological Gardens, London, and, strictly speaking, we doubt whether any of it was normal. Much of it must have been pathological, and, as he does not tell us how fresh the specimens were, it is possible that there may also have been *post-mortem* changes. He mentions that some of the birds had been skinned, which shows that they had passed through other hands, and probably they had been dead some time before he received them.

It seemed to me, however, that it would serve a useful purpose to describe in a series of mammals the probable number and the usual position of the parathyroids in relation to the thyroid. Although this is described under the head of gross anatomy, it must be borne in mind that the "internal" parathyroid (parathyroid IV) is frequently almost, or quite, surrounded by thyroid tissue, so as to escape detection except by slicing or serially sectioning the organ. Further, in some cases where I have indicated the position of a parathyroid, it has been necessary to examine it microscopically in order to be sure that it was not accessory thyroid, or thymus, or other tissue.

In the following account my observations have been practically confined to the more usual laboratory animals, namely, the dog, cat, rabbit, and guinea-pig, and some few observations upon rats, wolves, and badgers. In the case of other animals which are included for the sake of completeness, I have depended on information from various sources which are acknowledged in their place.

The parathyroids of mammals are usually four in number. They are small oval or spherical bodies, in most cases of a distinctly lighter tint than the thyroid tissue, and occupy very variable positions, not only in different species but in different individuals. On either side of the median line of the body there are typically two of these glandules, which are referred to at the present time either as external and internal, or as parathyroid III and parathyroid IV respectively, the Roman numeral indicating the number of the gill cleft from whose epithelium the gland was originally formed. The latter mode of signification is by far the most precise, but most observers prefer to refer to an external and internal glandule on either side. The terms external and internal appear, however, to be used by different authors in a different sense. KOHN'S* original definition of the terms was given in the following words:—"Das eine lag in der Regel der Aussenfläche der Seitenlappen lose an, das andere innerhalb derselben. Ersteres wurde 'äusseres' letzteres 'inneres' Epithelkörperchen gennant." By "external" and "internal" here is implied "on the surface of" and "in the interior of" respectively; but SCHÄFER† interprets the terms differently, thus: "That there is one parathyroid ('outer epithelial body') constantly to be met with in mammals, on the lateral surface of each lobe of the thyroid, and another on the mesial surface of each lateral lobe ('inner epithelial body')." So also FORSYTH.‡ Despite this confusion in terminology, for most animals with which I am acquainted the terms external and internal are suitable for designating parathyroids III and IV, because it *happens* that the parathyroid which lies on the surface of the gland lies also in the majority of cases on the lateral aspect of the lobe, and the one which is buried in thyroid substance is nearer the tracheal surface of the lobe.

* 'Ergebnisse der Anat. und Entwickelungsgeschichte,' vol. 9, 1899.

† QUAIN'S 'Anatomy,' vol. 3, part 4, p. 314, 1896.

‡ 'Journ. of Anat. and Physiol.,' vol. 42, p. 142, 1908.

Man.—The human thyroid belongs to the group with an isthmus. There are points of interest, embryological and surgical, connected with some common variations, but there will not be space to treat of these in the present communication.

The *parathyroids*, according to most observers, are four in number, two on each side. Their average dimensions are about 6–7 mm. in length, 3 or 4 mm. in breadth, and 1·5 or 2 mm. in thickness. The length is very variable, while the thickness is fairly constant. In shape they are oval or pyriform, and may be connected by a stalk, in which run the parathyroid vessels, to the thyroid gland. The average weight is 0·035 gramme. There seems to be no relation between the weight of the parathyroids and that of the thyroids. The parathyroids are of a lighter colour than the thyroids, and yellowish, owing to the presence of fat. The surface is smooth and soft.

The two glands on each side are described under the names of the *posterior superior parathyroid* and the *anterior inferior parathyroid*, the names indicating their relation to each other. The posterior superior parathyroid is more constant in position than the anterior inferior. It lies usually on the posterior wall of the œsophagus or pharynx, at the level of the lower edge of the cricoid cartilage, immediately internal to the posterior margin of the lateral thyroid lobe, and in front of the prevertebral division of the cervical fascia. The parathyroid is usually separated from the thyroid by a septum of connective tissue.

The anterior inferior parathyroids are very inconstant in position and relations. Sometimes their position is more anterior, sometimes more posterior, and they may, especially in the former case, be placed very low down, even at the level of the tenth tracheal ring.*

Monkey.—So far as I am aware, there is no description of the parathyroid in the anthropoid apes. In the species of monkey usually employed in the laboratory for operations, the arrangement of the parathyroids is quite different from that in the human subject. VINCENT and JOLLY† found in the monkey that the thyroid lobes are sometimes united by an isthmus, sometimes unconnected. These authors specially mention a well-developed isthmus in two specimens of *Macacus rhesus*. They state that the parathyroids are four in number, two on each side, and are always, so far as they have seen, more or less imbedded in the substance of the thyroid.

Dog.—The *thyroid* consists of two distinct lobes. In only one of a large number of dogs that I have examined have I found an isthmus. ELLENBERGER and BAUM,‡ however, state that the thyroid consists of two lateral lobes and an isthmus, which isthmus is wanting in small dogs and present in large ones, while in dogs of medium size it is sometimes present. The lateral lobes are elongated oval, and taper slightly

* WELSH, 'Journ. of Anat. and Physiol.,' 1898, p. 401; FUSARI, 'R. Accad. di Med. di Torino, February, 1899; CHANTEMESSE et MARIE, 'Société des Hôpitaux,' Séance du 17 mars, 1893.

† 'Journal of Physiology,' vol. 34, 1906.

‡ 'Anatomie des Hundes,' Berlin, 1891.

at oral and aboral ends. They are placed at the side of and towards the dorsal aspect of the trachea, immediately aboral from the larynx.

The rule as to the number of *parathyroids* is fairly well kept in the dog, but there may be as many as five and sometimes it is not possible to see more than three with the unaided eye. The external parathyroids are as a rule very easily found. Sometimes they are at some distance from the lobe, while at other times they are more or less embedded in the substance of the thyroid, though never so deeply as is the internal parathyroid. Occasionally they are quite separated from the thyroid lobe, and their blood supply is such as to permit of their being left behind in thyroidectomy (see text-fig. 6). This, however, is rare. The internal parathyroid, on the contrary, is small, deep in the thyroid substance, and very variable in position, so that in the living animal the experimenter has frequently to abandon the attempt to find it, while even *post-mortem* it sometimes cannot be revealed except by serial sections. VINCENT and JOLLY state that it is very rarely found that the internal parathyroids of both sides can be seen.

Some of the variations which I have found are illustrated in the following six drawings :—

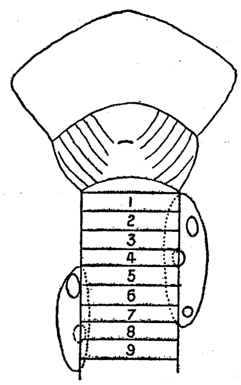

FIG. 2.

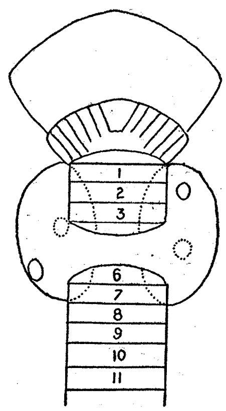

FIG. 3.

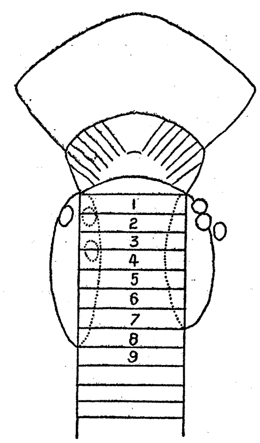

FIG. 4.

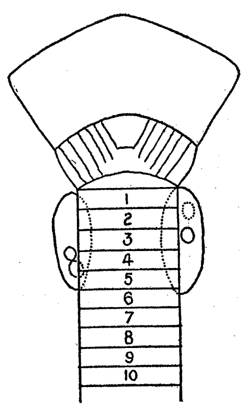

FIG. 5.

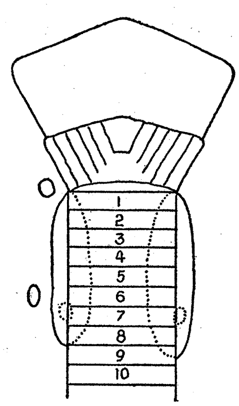

FIG. 6.

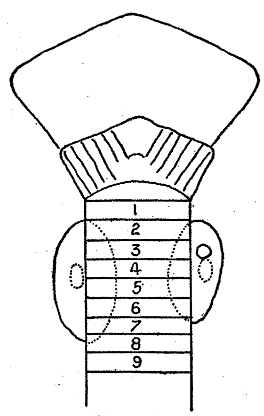

FIG. 7.

FIGS. 2 to 7.—Semi-diagrammatic Sketches showing the Position of the Parathyroids, the Thyroid, and the Trachea in the Dog. The parathyroids in dotted lines are "internal."

Cat.—As is most usual throughout mammals, there are four parathyroids, two internal and two external, as shown in the accompanying figure :—

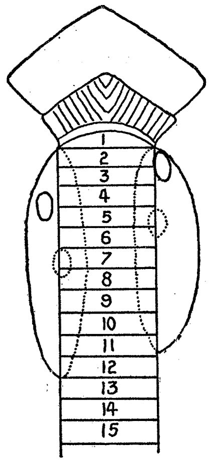

FIG. 8.—Shows the Relative Positions of the Parathyroids, Thyroid, and Trachea in the Cat. This may be described as an average condition of affairs. The "internal" parathyroids are in dotted outline.

Rabbit.—There are usually four parathyroids in the rabbit, but the peculiarity about this animal is that the external parathyroids are very uniformly placed at a considerable distance from the thyroid lobe. For this reason, in the earlier extirpation experiments they were left behind at the time of the operation. The following series of drawings illustrates some of the positions in which I have found the external parathyroid. The internal is not represented in these drawings, for the reason that I have never observed it except after cutting sections.

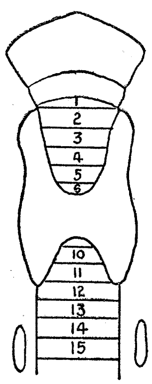

FIG. 9.

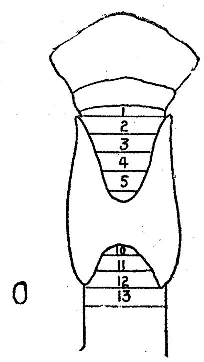

FIG. 10.

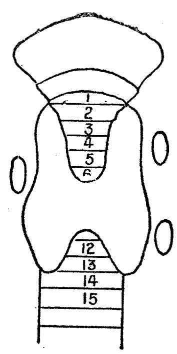

FIG. 11.

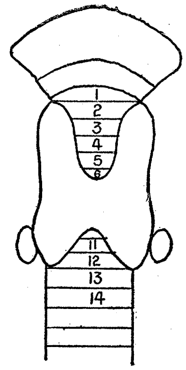

FIG. 12.

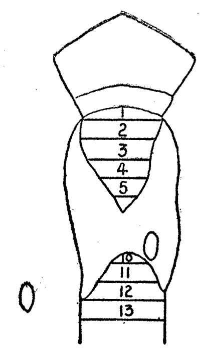

FIG. 13.

FIGS. 9 to 13 are semi-diagrammatic, and show the Relationship of the Thyroid, External Parathyroids, and Trachea in a series of Rabbits. The "internal" parathyroid is not shown in any case, as it was found only microscopically.

Guinea-pig.—The distinction between internal and external parathyroids seems largely to break down in this species. There are usually four, sometimes three, or even only two. The following drawings represent the position in which I have found the glandules. In one specimen I found an isthmus :—

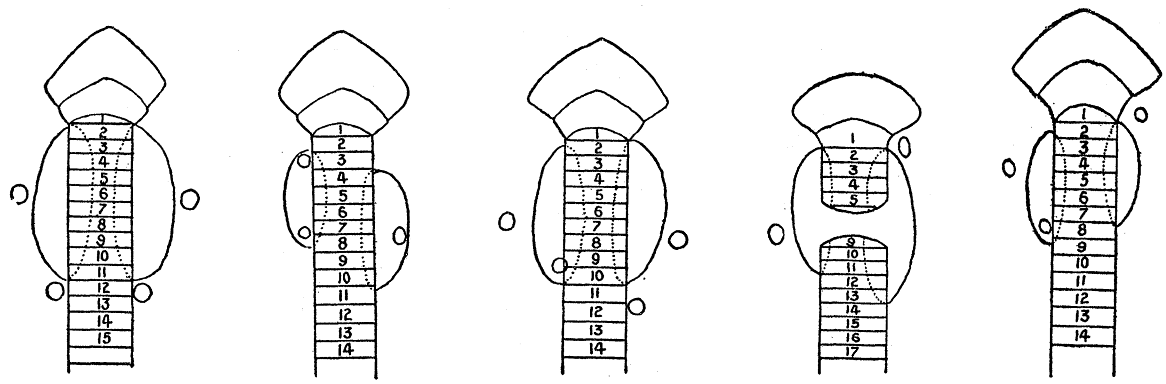

FIG. 14. FIG. 15. FIG. 16. FIG. 17. FIG. 18.

FIGS. 14 to 18.—Parathyroids in the Guinea-pig. The extreme variability in number and position is shown. In none of this series were any true "internal" parathyroids seen with the naked eye.

Rat.—The thyroid in the rat consists of two lobes united by an isthmus. It is stated by VINCENT and JOLLY that there is only one parathyroid in connection with each thyroid lobe. They dissected several specimens and found that the parathyroid lies on the surface of the thyroid lobe, and seems to correspond to the external parathyroid of the cat. They state that it is easily accessible, and can be cauterised without difficulty.

In the *Prairie Wolf* and *Badger* there are four parathyroids whose precise location does not call for any observation.

In the *Pig* the internal parathyroid is stated by ELLENBERGER to be absent. In ruminants and the pig the external parathyroid is not close to the thyroid, but is in connection with the thymus.

In the *Horse* the anatomy of the parathyroids is not fully worked out.

In a recent paper, W. L. ESTES* states that the external gland of the horse is found close to the upper end of the thyroid, or in the perithyroid areolar tissue. The internal parathyroid occurs in the thyroid tissue, "sometimes superficially placed, sometimes more deeply, sometimes near the upper pole, sometimes near the lower." He concludes, "The horse has four parathyroids, two on each side. One parathyroid is found at the superior pole of the thyroid in relation to the branching of the thyroid artery. The other is found variously placed beneath the capsule of the thyroid, usually near its upper pole. The external gland is much the larger."

In *Sheep* and *Goats*† there are two parathyroids embedded, or partly embedded, in the thymus, one on each side, on the level of the thyroid cartilage of the larynx, and just in front of the carotid and vagus nerve. These are the external parathyroids.

* 'Johns Hopkins Hospital Bulletin,' vol. 18, No. 198, 1907.

† MACCALLUM, THOMSON, and MURPHY, 'Johns Hopkins Hospital Bulletin,' vol. 18, No. 198, September, 1907.

They are visible as bright red, rounded, smooth bodies, 3 to 5 mm. in diameter, lying in a pale cream coloured thymus. "The thyroid consists of a rather small lobe on each side, united across the front of the trachea by a delicate band or isthmus. Embedded in each of these lobes is the remaining parathyroid. These masses which we have found in the thyroid in every case cannot be clearly seen in the living animals, and we have found it necessary, in order to secure their extirpation, to remove the whole thyroid lobe each time. In hardened tissue, however, they stand out fairly plainly on section from the surrounding thyroid tissue. They are not furnished with any capsule, but come into very intimate relation with the thyroid tissue. No very definite statement can be made as to their exact position in the thyroid, because this seems to vary considerably."

2. *Intervesicular Cellular Tissue.*

In many lobules, in addition to the vesicles, solid cords and nests of epithelium cells are found, and these are more numerous in the young and developing thyroid. It is desirable to call particular attention to this intervesicular material. Its structure and morphology are of supreme importance as bearing on the inter-relationship of thyroid and parathyroids.

SCHÄFER* gives no drawing to show this tissue, though he says in the text: "In the interstitial connective tissue of the gland there occur a number of cells, similar to the 'plasma cells' of WALDEYER ('parenchyma cells,' BABER)."

VON EBNER† gives drawings from human subjects, in some of which the inter-vesicular tissue is well shown, and in some it appears to be absent.

STÖHR‡ gives a drawing of the human thyroid in which, so far as I can understand, no tissue is represented apart from that of the vesicles and connective tissue. More-over, this drawing gives the appearance of a very pronounced *Membrana propria* to the vesicles.

ELLENBERGER§ states "zwischen den Follikeln finden sich hier und da unregel-mässig verteilt mehr oder weniger grosse Nester von Zellen, die in ihrem Aussehen durchaus den Follikelepithelien gleichen (interfollikuläres Epithel, HÜRTHLE) sie sind zwar weder zu Drüsenbläschen angeordnet, noch enthalten sie Colloid, doch ist nicht ausgeschlossen, dass in der wachsenden Drüse an diesen Stellen die Neubildung des Parenchymgewebes einsetzt."

VINCENT and JOLLY|| call attention to this intervesicular tissue, and state that "in many thyroids there are solid masses of cells, not, however, so distinctly marked

* QUAIN'S 'Anatomy,' vol. 3, part 4, p. 312, 1896.

† KÖLLIKER'S 'Handbuch,' vol. 3, pp. 317–319, 1902.

‡ 'Text-book of Histology,' trans. BILSTEIN, Philadelphia, 1901.

§ 'Handbuch der vergleich. mikr. Anat. der Haustiere,' Berlin, 1908, p. 286.

|| 'Journal of Physiology,' vol. 34, 1906, p. 304.

off as the parathyroids proper, which are practically identical in structure with the latter bodies.

The amount of this material varies within very wide limits in the thyroid of different species of mammals, in different individuals of the same species, and to some extent also in different regions of the same thyroid gland. It is not rare to find a pair of vesicles in close juxtaposition to each other, so that the colloid of one is separated from the colloid of the other by nothing but the two rows of vesicular cells. In other cases there is a certain amount of connective tissue separating the vesicles. But, speaking for mammals generally, it is more usual to find, separating the colloid-containing vesicles, a variable mass, composed of cells which are almost identical in size, cytoplasm and nucleus, with those lining the colloid vesicles. This intervesicular cellular tissue is proportionately greater in amount where the vesicles are small, as is strikingly the case in the rabbit, and also in young animals generally.

In the monkey, also, the amount of intervesicular tissue is proportionately great, and it is not possible to determine any fundamental differences between its cells and those of the vesicles.

There is, as a rule, no basement membrane to the cells lining the vesicles, but in the rabbit there is a delicate band of fibrous connective tissue in the position of the basement membrane of other glands.

In the human thyroid some portions of the gland show a large amount of intervesicular tissue, some almost none. In some regions there is as much of the intervesicular as there is of the vesicular material.

In the intervesicular tissue there is a rich plexus of blood-vessels, which is striking in proportion to the amount of vascular engorgement which was present at the time of the death of the animal.

3. *Histology of the Parathyroids in Man and other Mammals.*

The parathyroids in man are built up of closely packed polygonal cells, which are divided up, by connective tissue septa, into masses and cords of varying size and shape. The glandules are usually surrounded by their own capsule, but in the case of those placed on the surface of the thyroid, the connective tissue sheath is seen to be derived from and continuous with that of the thyroid lobe. The capsule sends in septa into the interior of the organ, which septa convey blood-vessels and nerves destined for the supply of the gland substance.

The protoplasm of the cells often appears to be homogeneous, it does not stain well with eosin, and is vacuolated. The nuclei are rounded, and about $4\,\mu$ in diameter, and frequently show a chromatin network.

Permeating the whole glandule, and even separating the individual cells in many places, is a delicate network of fine fibres which appear to be of a distinct nature from ordinary connective tissue.* It is stained by eosin and faintly also

* KÖLLIKER, 'Handbuch der Gewebelehre,' vol. 3, p. 326.

by orcein. Near the periphery of the organ the cells are smaller and lack this special sheath.

In man and other mammals KOHN* distinguishes three different arrangements of the epithelium cells which may be met with: (1) a compact cell mass; (2) a lobular conformation; (3) a retiform structure. These different arrangements are not characteristic of any species or age, but may be found side by side in the same glandule.

In the cat the internal parathyroid has a peripheral layer of cylindrical cells, and there appear to be other differences in structure between this body and the external parathyroid.† Thus, the cells are not so closely packed in the internal as in the external gland, and their outlines are more easily distinguished. Further, the cell nuclei of the internal parathyroid do not stain so deeply as those of the external body. This last difference, however, can be detected only in adult animals. In some animals, as the rabbit, the internal parathyroid is intimately connected with a "central canal" (post-branchial body) and with the thyroid tissue itself. In close contact with each of the parathyroids we may find a thymus nodule, and occasionally the central portion of this last is seen to be directly continuous with the tissue of the parathyroid. Again, parathyroids may be found either in the cortex or medulla of the thymus.

When we bear in mind the development of these various organs, such intimate anatomical connections, and occasionally even apparent confusions, are not astonishing.

4. *Histology of the Thyroid and Parathyroids, considered as one Tissue.*

At first sight, the histological features of thyroid and parathyroid appear to be so strikingly different that the majority of authors, at any rate in recent years, have looked upon the two as totally distinct organs. This was the emphatic view of KOHN, whose account is referred to above, and it has been shared with more or less modification by nearly all experimental physiologists and pathologists. A careful examination of the glands throughout a series of mammals reveals the fact that the fundamental histological features of the two tissues are, if not identical, very significantly similar. Some stress has already been laid on the wide-spread occurrence of intervesicular cell masses in the thyroid, whose cells are of the same character as those lining the vesicles. Now it must have occurred to many students of thyroid histology that this thyroid intervesicular material is very like the parathyroid. More detailed histological investigation seems entirely to support the view that the essential elements of thyroid and parathyroid are the same. This becomes clear only when a large number of animals is studied. Occasionally a parathyroid, or a portion of a parathyroid, is seen, which from its degree of compactness, staining reaction, and

* 'Arch. f. mikr. Anat.,' vol. 42, 1895, p. 377.

† KOHN, 'Arch. f. mikr. Anat.,' vol. 44, 1895.

encapsulation, presents an appearance markedly different from the parenchyma of the thyroid. Sometimes the parathyroid nuclei are slightly smaller than those of the thyroid tissue, sometimes they are slightly larger. Again, in some instances they appear more closely packed than in the thyroid, while in others they are less closely packed. These differences are, however, not fundamental, and there are abundant instances where it is almost impossible to distinguish the parathyroid from the intervesicular tissue of the thyroid. This is especially true in the case of the internal glandule, which, as admitted by KOHN, is often in direct continuity with the thyroid, and which I have frequently observed to show every kind of transition to the colloid vesicle formation of the latter. This transition of thyroid into parathyroid is sometimes very distinctly seen in the rabbit's gland, and is shown in Plate 12, fig. 15, *tr. t.*, and Plate 13, fig. 16, *tr. t.* In the right-hand portion of Plate 13, fig. 16, is shown the small vesicled thyroid tissue proper, while, as one passes further and further towards the left-hand portion of the figure, the colloid vesicles become fewer and smaller, and finally disappear. Even when colloid can no longer be seen, there are still traces of the vesicular formation. Finally this disappears also, and in the extreme left of the drawing typical parathyroid tissue is shown.

In the external parathyroid of the ox can sometimes be seen all stages between undoubted thyroid and typical parathyroid (Plate 13, fig. 18). A most striking illustration of the identity of parathyroid tissue with intervesicular thyroid is afforded by the badger (Plate 13, fig. 17). There is here, so far as I can perceive, no kind of difference as regards size and shape of nuclei, or their staining reaction, in compactness, or general arrangement between the two tissues. The impression given is that the only difference consists in the presence of colloid in the thyroid. If, indeed, in any part of the parathyroid, a spherical droplet of colloid were to be formed among the cells, this portion of the glandule would have to be called thyroid, and the circlet of cells immediately surrounding the colloid would be considered as the lining epithelium of the thyroid vesicle (Plate 13, fig. 17, *c. ves.*). This development of colloid in what was originally parathyroid actually occurs under certain circumstances. In Plate 12, fig. 12, is depicted what topographically is, or, to be more correct, was, parathyroid. But it will be seen (Plate 12, figs. 13 and 14, *c.v.*) that many parts of the substance are studded with colloid vesicles.

The specimen is from the human subject, and was probably pathological.

5. *Functional Changes in the Thyroid.*

In a dog which had been subjected to a few days' inanition, the thyroid (hardened in strong Flemming's fluid) appears very different from the normal (Plate 13, fig. 19, *cf.* fig. 20). The cells appear swollen, rather than proliferated, and in some cases vesicles are filled with cells. The vesicles are shrunk so as to assume various shapes, and much intervesicular material appears. The general appearance is as if the gland had been roughly squeezed, so that the vesicles are any shape but spherical. The change wrought by inanition seems to make the structure of the gland tend towards that of parathyroid (Plate 13, fig. 19, *e. interves.*).

In two experiments: (1) of feeding a dog exclusively on meat for one month, and (2) exclusively on cereals for the same period, there was little difference found in the two glands on microscopical examination. The one that was cereal fed seemed to tend to some extent towards the appearance caused by inanition, and during the period of dieting the dog reduced in weight from 8 kilos. to 7·5 kilos.

The thyroid of the meat-fed dog differed in no way from the normal.

An experiment which I made with the object of comparing the thyroids of meat-fed pigeons with those of grain-fed was unsuccessful, for the pigeons refused the meat diet. Probably the experiment would succeed better in the fowl. CHALMERS WATSON* describes a very marked hypertrophy of thyroid and parathyroid in the fowl after an exclusively meat diet. He further found, in the second generation of meat-fed rats, entire absence of colloid, and little or no attempt at vesicle formation. The results obtained, he admits, were very variable, but he considers that they show that an excessive meat diet induces structural changes in the thyroid gland. It is reasonable to suppose that such would be the case, but the author's observations by no means prove it, for, as pointed out by FORSYTH,† there is great variation in the thyroids of the same species of birds. I would suggest, further, that many of the changes described by CHALMERS WATSON as being due to an excessive proteïn diet are in reality due to inanition, the structural effects of which I have described above.

6. *Changes in the Thyroid after Parathyroidectomy.*

EDMUNDS‡ describes certain changes in the thyroid after parathyroidectomy. These histological changes, he states, are identical with those described as "compensatory hypertrophy," but the thyroid as a whole does not appear to enlarge; on the contrary, sometimes it becomes smaller.

A cat from which the thyroid lobe on one side, including its parathyroids, and three parathyroids only on the other side had been removed, was allowed to live nearly a month. At the end of this period it was sacrificed, and the remaining thyroid lobe examined. The thyroid had atrophied; and on histological examination very little true thyroid tissue was found to have persisted. There were vesicles in some parts of the tissue, but few and far between. There was a large amount of tissue indistinguishable from normal parathyroid, and a still larger amount of which it would be impossible to state to which category it belonged. Of course, in this instance one cannot state definitely that no parathyroid tissue was left behind at the operation, but this doubt does not affect the certainty that a large amount of thyroid

* 'Journal of Physiology,' vol. 31, No. 2, May 3, 1904; vol. 34, June 2, 1906.

† *Loc. cit.*

‡ "Erasmus Wilson Lectures," 'Lancet,' May 11, 18, 25, 1901.

which was left *in situ* was found at the time of the *post-mortem* examination to have undergone extensive structural alterations.

It is to be noted that this cat showed no symptoms.

In another cat in which an analogous operation had been performed, but which died with typical symptoms within five days, still more extensive structural changes were found in the thyroid at the *post-mortem*.

These observations would tend to support the view of VINCENT and JOLLY,* that in the operation of parathyroidectomy it is the concomitant injury to the thyroid which is the cause of severe symptoms and death.†

VIII. A DISCUSSION OF THE RELATIONSHIP BETWEEN THYROID AND PARATHYROIDS.

The question of the relationship between thyroid and parathyroids naturally arose only with the discovery of the parathyroids.

This sketch will therefore begin with a history of the discovery of, and the views concerning, these bodies.

REMAK‡ appears to have been the first to notice the parathyroids. He found at the upper end of the thymus in new-born cats small bodies of peculiar appearance which he called "Wimperblasen der Thymus."

Ten years later VIRCHOW§ describes small rounded bodies about the size of a pea in the neighbourhood of the thyroid, but thought they were accessory thyroids, or lymph glands. From the marked constancy with which VIRCHOW'S bodies occur, it is practically certain they are parathyroids. These observations were entirely forgotten, or overlooked.

It was not till 1880 that the parathyroids were definitely discovered and distinguished from "accessory thyroids." In this year SANDSTRÖM|| described them in man and several animals. It is to this observer that we owe the name "Glandulæ parathyreoideæ." He found the glandules constantly present in fifty human subjects examined by him. So far as can be gathered from an abstract by RETZIUS,¶ only the external glandule was noted. In situation, size, form, and colour, they exhibited great variety.

* *Loc. cit.*

† In the second experiment above quoted there were many signs of inflammatory new connective tissue, but apart from this, what was left of the thyroid was scarcely distinguishable from parathyroid. What few vesicles could be observed were undergoing suppression.

‡ 'Untersuchungen über die Entwickelung der Wirbeltiere,' Berlin, 1855.

§ 'Die krankhaften Geschwülste,' vol. 3, p. 13, Berlin, 1864–5.

|| 'Om en ny körtel hos menniskan och åtskilliga daggdjur. Upsala, Läkareförenings Förhandlingar,' vol. 15, 1880. ("Ueber eine neue Drüse des Menschen und einiger Säugetiere.") Ref. in SCHMIDT'S 'Jahresb.,' 1880; HOFMANN-SCHWALBE'S 'Jahresber.,' 1881; VIRCHOW u. HIRSCH, 'Jahresber.,' 1880.

¶ HOFMANN-SCHWALBE'S 'Jahresb.,' vol. 9, 1881, p. 224.

Among mammals, the dog, cat, horse, ox, and rabbit were investigated, and in all was the gland constantly found. All the variations in their structure corresponded to different stages of thyroid development, and he pronounced them to be embryonic material destined to form thyroid tissue.

In the same year, BABER,* unaware of SANDSTRÖM's work, in his second memoir upon the thyroid, devotes a special section to what he calls "undeveloped portions," in the dog, kitten, sheep, seal, rook, and pigeon, and says: "In the thyroid gland of the dog, however, it is remarkable that although these bodies are of frequent occurrence, there is usually, in dogs aged three months and upwards, no evidence to show that they are undergoing further development."

HORSLEY,† who was also unacquainted with SANDSTRÖM's discovery, re-investigated the "embryonic tissue" described by BABER, and emphasised the doubt as to its embryonic nature.

WÖLFLER‡ and ROGOWITCH§ described "embryonic" cell masses in the thyroid, but the work of SANDSTRÖM, BABER, and HORSLEY fell into almost complete oblivion.||

In 1891, GLEY,¶ in his preliminary note on the effects of extirpation of the thyroid in the rabbit, describes the bodies under the name of "Glandules thyroïdiennes." His observations were confirmed and extended by CRISTIANI** and NICOLAS.†† This last author found in *Vesperugo pipistrellus* that there are always two parathyroids on each side.

KOHN‡‡ was one of the first to oppose the view that parathyroids are embryonic remains of thyroid tissue, and his attitude was supported by the experimental results of VASSALE and GENERALI,§§ who urged the separate functional importance of the parathyroids.

GLEY, in 1901,|||| put forward a theory of a functional relationship between thyroids and parathyroids based on chemical, physiological, and histological grounds. This was supported by JEANDELIZE.¶¶

VINCENT and JOLLY*** found, on microscopical examination of parathyroids left

* 'Phil. Trans.,' 1881, part 3, p. 600 (received November 25, 1880).

† 'Lancet,' December 18, 1886, vol. 2, p. 1163.

‡ 'Arch. f. klin. Chir.,' vol. 29, p. 17, 1883.

§ 'Arch. de Physiol. norm. et pathol.,' 1888, p. 419.

|| KRAUSE describes the glandules, after SANDSTRÖM, in 'Nachträge zur allgemeinen u. mikr. Anat. Hanover,' 1881, p. 71.

¶ 'C. R. Soc. Biol.,' 1891, p. 843.

** 'C. R. Soc. Biol.,' 1892, p. 798; 'Arch. de Physiol. norm et path.,' 1893, vol. 25, p. 164; 'C. R. Soc. Biol.,' 1893, p. 4.

†† 'Bullet. des Séances de la Soc. des Sciences de Nancy,' 1893.

‡‡ *Loc. cit.*

§§ 'Arch. ital. de Biol.,' 1896, vol. 25, p. 464.

|||| Congrès Internal. de Physiol., Turin, 1901.

¶¶ 'Insuffisance Thyroïdienne et Parathyroïdienne,' Paris, 1903.

*** 'Journ. of Physiol.,' vol. 32, No. 1, December 30, 1904; *ibid.*, vol. 34, Nos. 4 and 5, August 10, 1906.

in situ after removal of the thyroid, that these exhibit conspicuous alteration in structure. This presented itself to them at first as a difficulty in recognising whether small bodies which had been left behind were thyroid or parathyroid. Later, they became convinced that these are intermediate between the two. They are now compelled to adopt the view that parathyroid tissue, when left behind, approximates in appearance to ordinary thyroid tissue, so that the final product in some cases cannot be distinguished from the latter.

HALPENNY* performed the following experiment on a dog: Both thyroid lobes and the two internal parathyroids were removed, leaving behind the external parathyroid on each side. These were typical in appearance, rounded, paler in colour than the thyroid, and having a separate and distinct blood supply.

The animal lived without showing any symptoms for eighty-three days, when a second operation was performed, and the two remaining parathyroids were removed. These were found to have hypertrophied, and showed on microscopic examination the appearance depicted in Plate 14, fig. 21.

The parathyroids have to all intents and purposes become converted into thyroid. There is still a comparatively large amount of intervesicular tissue which is identical with that of the solid columns forming the normal parathyroid. The vesicles are irregular in shape, though each is surrounded with a regular row of epithelial cells. Colloid is scarce in these vesicles, though it is undoubtedly present in some of them (see Plate 14, fig. 21, *e. ves.* and *c.*). The most noticeable feature about the thyroid tissue which has developed from parathyroid is the irregular shape of the vesicles, but the appearance thus presented is strikingly similar to that which is found in the thyroid after parathyroidectomy (Plate 14, fig. 22). What VINCENT and JOLLY found in the cat has thus been confirmed in the dog. The general conclusions of VINCENT and JOLLY are that when the thyroid is removed the parathyroids appear capable of replacing it to a certain extent, and the histological structure of the latter bodies changes accordingly. They lay great stress upon the difficulties of the operation of parathyroidectomy, and consider that when this proves fatal it is probably due to the severe damage simultaneously done to the thyroid. Thyroid and parathyroids are looked upon as a single physiological apparatus, the two kinds of tissue being intimately associated embryologically and working together physiologically.

In a later paper VINCENT† lays stress upon the fact that the two structures are derived from very similar sources, and even in their fully developed state there is no fundamental difference between their constituent cells.

FORSYTH‡ looks upon the parathyroids as essentially thyroidal in nature, possessing no peculiar function, but engaged in the active secretion of the same substance as the

* HALPENNY and THOMPSON, 'Anat. Anz.,' vol. 34, 1909, p. 376.

† 'Lancet,' August, 1906.

‡ 'Quarterly Journal of Médicine,' January, 1908, vol. 1, No. 2; 'Journ. Anat. and Physiol.,' vol. 42, June, 1908.

thyroid. He describes also transitions and intermediate types. FORSYTH'S views largely agree with my own, but I am not prepared to go so far as to admit that the parathyroids "are part of the main thyroid gland, which have assumed functional activity but have not yet formed vesicles." To admit this conclusion would be to disregard in an unwarrantable manner the patient and brilliant work of VERDUN,* MAURER,† and other embryologists.

It has been pointed out in previous paragraphs that the parenchyma of the thyroid is by no means entirely made up of the colloid vesicles, but there is a large though variable amount of intervesicular, cellular material, whose constituent cells do not differ in any important respects from those lining the vesicles. It has further been demonstrated that this tissue is, to all intents and purposes, identical with that of parathyroid; and instances of tissue continuity, and gradual transitions and intermediate types have been described in the text and drawn in the figures.

In, perhaps, the majority of cases, the transition forms are best seen between thyroid and internal parathyroid; but in the case of the ox, such a transition is shown between thyroid and external parathyroid (Plate 13, fig. 18); and in the case of the human gland shown in Plate 12, figs. 12, 13, 14, it is the *external* parathyroid which contains typical colloid vesicles. Further, it was the external parathyroids in the experiments of VINCENT and JOLLY which, after removal of the thyroid, became converted into a tissue resembling the latter. So that, although some authors have been inclined to look upon external and internal parathyroids as separate and distinct organs, the present series of observations does not lend any support to the view that either one is less intimately connected with the thyroid than the other.

The nature of this relationship is, however, by no means clear. As stated above, the facts of embryology cannot be ignored. It seems to be well ascertained that the parathyroids are developed from the epithelium of the third and fourth gill-clefts, while the thyroid is derived from the median rudiment on the ventral wall of the embryonic pharynx. Moreover, the two structures do not arise at the same time, and many embryologists believe that parathyroids only secondarily enter into relation with the thyroid. It is not, however, to be imagined that the primitive epithelial outgrowths, constituting the buds of thyroid, parathyroid, thymus, and other branchial cleft organs, can be very different from each other. Thus the material of the thymus, when first laid down, is indistinguishable from that of the parathyroid, and if, for any reason, in any particular species, the usual lymphatic metamorphosis did not occur, I imagine that the tissue would be looked upon as parathyroid, that is, if its point of origin were not definitely known.

However this may be, there seems to be no escape from the conclusion that in mammals the thyroid and parathyroid tissues are related to each other, and that the connections are not only physiological but anatomical.

* 'C. R. Soc. Biol.,' 1897.

† 'Jenaische Zeitschr.,' VI; 'Semon Zool. Forschungsreisen,' III, 1899.

Although the embryonic theory more closely coincides with the truth than do the others, yet the precise form in which the true relationship probably obtains has not been previously stated. In the lower vertebrates, thyroids and parathyroids appear to be separate and distinct, developed separately and at different periods, and never coming into intimate relation with each other, either anatomically or (so far as our present knowledge goes) physiologically. But in mammals the parathyroids enter into a peculiar relationship with the thyroid. They lie in close contact with it, or, indeed, actually in its substance, and their solid epithelial columns tend, especially in the case of the internal glandule, to merge gradually into the tissue surrounding its colloid vesicles. Moreover, when the thyroid is removed, the remaining parathyroids may take on its function and change their structure accordingly.

IX. Physiology of the Thyroid and Parathyroids.

It is universally recognised that the thyroid apparatus plays a very important part in the animal economy. It is further certain that this apparatus is of special importance in regard to the general development and nutrition of the young animal, though precisely what *rôle* it plays has not yet been ascertained. In extirpation experiments, apart from the symptoms of mal-development and mal-nutrition, others of a nervous character are manifested, grouped under the name of "tetany." It has become the fashion of late years, following the lead of Vassale and Generali, to ascribe the latter to deficiency of the parathyroids, while the former are attributed to insufficiency of the thyroid proper. The orthodox view may be represented somewhat as follows: That thyroid and parathyroids are separate and distinct organs, having no connection with each other embryologically, anatomically, or physiologically. Or, rather, that if there is an anatomical relationship, this is distinctly of a secondary character. Absence or insufficiency of the thyroid gives rise to chronic symptoms of cachexia of a cretinoid or myxœdematous nature, while absence or insufficiency of the parathyroids gives rise to acute symptoms of a nervous character, called tetany, which are typically exemplified in the case of an animal experimentally deprived of its parathyroids.

This view has been widely accepted, both in Europe and America, and has been adopted, among others, by MacCallum.* It has, at any rate, the merit of simplicity, but it is, in my opinion, not supported by the facts at our disposal. From the physiological standpoint, the independence of thyroid and parathyroid has been challenged by Vincent and Jolly.† Forsyth, more recently, has strongly

* See MacCallum and Davidson, 'New York Medical News,' April 8, 1905. These authors have been unable to verify the statements of Vassale and Generali and, later, Lusena, that the effects of parathyroidectomy come on more suddenly, and are more violent, than those of thyroparathyroidectomy, and oppose, on the basis of their own experiments, the theory of Lusena that the thyroid is a gland in which toxic substances are collected from the blood, and, under the influence of the parathyroids, converted into the innocuous colloid.

† *Loc. cit.*

inclined to the same view, from his work in comparative anatomy and histology. This view also seems to be gaining ground in England.*

My investigations have convinced me that the parathyroids cannot be looked upon as totally independent of the thyroids. As to the nature of the physiological relationship, I have no views to offer, but there can be no doubt that some such relationship actually exists.†

X. Relationship of Thyroid and Parathyroids to the other Ductless Glands, and in particular to the Pituitary.

From the earliest times of anatomy and physiology there has been a tendency to look upon the ductless glands as related to each other, so far, at any rate, as concerns their functional significance. Many of the suggestions are of an *a priori* character. Cyon‡ has elaborated a complicated theory respecting pituitary and thyroid, and regards the former as a centre from which the vascular supply of the brain is influenced through the latter. Sajous§ believes in a physiological relationship between the various ductless glands, whose functions dominate most of the activities of the body, normal and pathological.

Rogowitsch,‖ in 1889, stated that the pituitary acts vicariously for the thyroid, and that in rabbits and other animals which can survive thyroidectomy the function of the thyroid is taken over and maintained by increased activity of the pituitary. Other observers¶ have found changes in the pituitary consequent on removal or

* In a letter to the 'Lancet,' October 31, 1908, Mr. J. Berry, in discussing a paper on "Endemic Cretinism in the Chitral and Gilgit Valleys," read by Captain R. McCarrison, I.M.S., "deplored the fact that for the last few years an immense amount of teaching had been spread abroad alleging that the parathyroids were special glands with a special function distinct from the thyroid."

Although many English pathologists accept the view put forward by Vincent and Jolly, and supported, with some modifications, by Forsyth, yet others, notably Edmunds ('Lancet,' November 14, 1908), hold firmly to the theory that the parathyroids have a function distinct from that of the thyroid. In a publication of an earlier date ('Erasmus Wilson Lectures,' Edinburgh and London, 1901) Edmunds says: "It is not easy to identify the parathyroid glands in the human subject, because some of the minute outlying nodules are found to consist of ordinary thyroid tissue, and to be, therefore, accessory thyroid glands: only those that consist mainly or exclusively of cells are to be regarded as parathyroid glands." I presume that Dr. Edmunds would insist that the structure drawn in Plate 12, fig. 14, is a thyroid, and that all the instances of intermediate structures in the body of this paper are thyroid also, because they do not consist exclusively of cells.

† Further references on the physiological aspects of the question will be found in the papers of Vincent and Jolly ('Journ. of Physiol.,' vol. 32, No. 1, 1904; vol. 34, Nos. 4 and 5, 1906), Vincent ('Lancet,' 1906), MacCallum ('New York Medical News,' October 1, 1903), Forsyth (*loc. cit.*).

‡ Pflüger's 'Archiv,' various papers, 1898 to 1902.

§ 'The Internal Secretions and the Principles of Medicine,' Philadelphia, 1903.

‖ 'Ziegler's 'Beiträge zur patholog. Anat.,' vol. 4, p. 453, 1889.

¶ Hofmeister, "Zur Physiologie der Schildrüse," 'Fortschritte der Medicin,' p. 81, 1892; Gley, "Recherches sur la fonction de la glande Thyroide," 'Arch. de Physiol. nor. et path.,' p. 311, 1892;

disease of the thyroid. HERRING* has recently reinvestigated this subject and finds that after thyroidectomy there is increased activity of the cells of the *pars intermedia.* The most striking changes, he states, are manifested in the nervous part of the posterior lobe, and in the laminæ forming the floor of the third ventricle. In these situations, granular, hyaline, or colloid bodies become very numerous. They appear to be, in part at least, of a cellular nature, and to find their way between the ependyma cells into the infundibular recess, and ventricles of the brain. The colloid appears to arise from the epithelial cells of the *pars intermedia.*

Changes in the Pituitary Body after Parathyroidectomy.

In view of the close relationship existing between thyroid and parathyroid it occurred to me to investigate whether, after parathyroidectomy, any changes could be observed in the pituitary, corresponding to those which have been recorded after thyroidectomy. Accordingly the pituitary body, removed *post mortem* from a dog which had died some weeks after parathyroidectomy, was preserved in Flemming's fluid and microscopically examined. The difference between this pituitary and that of a normal dog preserved in the same way, especially as regards the *pars intermedia,* is striking. The layer of epithelial cells reflected over the nervous portion of the gland is hypertrophied and *contains numerous colloid vesicles, in all respects resembling those found in the thyroid gland, and occasionally, as I have fully pointed out, in the parathyroid also* (see Plate 14, fig. 23, *c. ves.*, *e. ves.*).

It thus appears that removal of the parathyroids produces the same compensatory changes in the pituitary as does removal of the thyroid itself, and this, I submit, affords additional evidence of the intimate relationship subsisting between thyroid and parathyroids.

But the appearance of these groups of colloid vesicles in the *pars intermedia* of the pituitary body, especially after operation upon the thyroid, has a probable much wider significance. The occurrence in the pituitary body of a substance resembling the colloid of the thyroid has long been known, and even definite vesicles have been described and drawn. But, so far as I am aware, no adequate stress has been laid upon their extraordinary resemblance, nay, identity in all essential points, with the colloid vesicles of the thyroid gland. HERRING† says: "The epithelial cells do not show the regular arrangement which is so characteristic of the thyroid vesicles; the walls are irregular and may be composed of one or several layers of cells." This description apparently applies to the pituitary body of the cat, and is, I admit, true in some cases for the *normal* pituitary of the dog, but is far from being the case in

PISENTI et VIOLA, "Beitrag zur normalen und pathologischen Histologie der Hypophysis und bezüglich der Verhältnisse zwischen Hirnanhang und Schildrüse," 'Centralbl. f. die med. Wissensch.,' p. 459, 1890; SCHÖNEMANN, "Hypophysis und Thyreoidea," VIRCHOW'S 'Arch.,' vol. 129, p. 310, 1892.

* 'Quart. Jour. Exper. Physiol.,' 1908.

† 'Quart. Jour. Exper. Physiol.,' 1908, p. 138.

the pituitary of the dog which died after parathyroidectomy (see Plate 14, fig. 23). In this case the vesicles are lined with a regular circle of epithelial cells precisely as is the case with the thyroid. The colloid material appears to be of the same character as in the thyroid (*cf.* Plate 14, fig. 23; Plate 12, figs. 14 and 15) and, so far as my investigations at present show, appear to give the same microchemical reaction.

The hypothesis seems a tempting one that a third component is to be added to the thyroid apparatus, and I am inclined to believe that thyroid, parathyroid, and *pars intermedia* of the pituitary form together an apparatus whose parts not only work together physiologically but are closely related developmentally.*

XI. Summary of Chief Conclusions.

1. The organs recognised as arising in the regions of the gilt-clefts in elasmobranchs are thyroid, thymus, and post-branchial body. The parathyroid and carotid glandules have not yet been discovered in these animals.

2. Within the thyroid gland of elasmobranchs are small, solid masses of cells, partly epithelial, partly adenoid. These have not, so far as I am aware, been previously described. One is tempted to suppose that these are homologous either with parathyroid or thymus. In the latter case it would correspond with thymus IV of mammals. (It has not been suggested that the thymus derivative of the fourth cleft furnishes isolated nodules in the thyroid of elasmobranchs.)

3. In Teleosts the only organs of the series are the thyroid and the thymus. The parathyroid has never been described in this group, and it is doubtful whether there is any trace of post-branchial body. The thyroid in *Amiurus* consists of a few scattered vesicles embedded in the connective tissue matrix. The cells lining the vesicles are very low columnar, and in some cases almost flat.

4. In Urodela the branchial cleft organs are thyroid, thymus, parathyroid, and post-branchial body. The thyroid is fairly superficial, and there is no intimate relation with the parathyroid.

* I am aware that many embryologists regard the anterior (epithelial) portion of the pituitary as derived from Rathké's pouch, and as therefore of purely ectodermal origin. This, if true, would tend to discount any views implying any kind of embryological community between thyroid and pituitary. But Kupffer ('Sitzber. der Gesellschaft f. Morpholog. u. Physiolog. in München,' p. 59, July, 1894) stated that part of the epithelial lobe is derived from Rathké's pouch, and part from the anterior end of the foregut. Nusbaum ('Anat. Anz.,' vol. 12, pp. 161–167, 1896) found that in dog embryos of 9 mm., Seesel's pouch is well developed, and its anterior extremity abuts against the posterior wall of Rathké's pouch. In 80 per cent. of older embryos examined it gives rise to a column of cells, which unites with the epithelium of Rathké's pouch. What further part, if any, in the formation of the anterior lobe of the pituitary is played by these cells Nusbaum did not determine. Other authors, Saint-Remy ('C. R. de la Soc. de Biol.,' p. 423, Paris, 1895), Dohrn ('Mittheil. der Zoolog. Stat. zu Neapel,' III, p. 252), Valenti ('Anat. Anz.,' vol. 10, p. 538, 1895), have also described a part or the whole of the anterior lobe as derived from the foregut. I am not in a position to discuss from my own work these embryological observations, but it appears to me to be not out of the question that the *pars intermedia* of the pituitary body is derived from a blastema not very different from that which gives rise to thyroid and parathyroid.

5. In Anura, the branchial organs are in addition to thyroid and parathyroid, thymus, post-branchial body, ventral branchial body and carotid gland. The thyroid is very small and deeply placed. The parathyroid has not yet entered into intimate relations with the thyroid. The ventral branchial body is a large striking looking organ which must have been frequently mistaken for the thyroid, and appears to be a hæmolymph organ. The arrangement of the cells in the parathyroid is somewhat characteristic, and is described in the text.

6. In reptiles, thyroids and parathyroids are still anatomically separate organs, but the parathyroid in some instances possesses distinct lumina, and in this the fundamental distinction between thyroid and parathyroid is at once broken down. Moreover, in this group there are clear indications that the post-branchial body secretes colloid.

7. In birds, we frequently find large areas of the thyroid either devoid of colloid vesicles or having these in a compressed, crowded condition. But the parathyroids are still separate and distinct organs. The post-branchial body presents certain peculiar features, described in the text, among these being an accumulation of concentric corpuscles such as is found in the epithelial part of the thymus.

8. In mammals, there is much more intimate relationship between the parts of the thyroid apparatus than in lower animals. The cells lining the vesicles are practically of the same character as those accumulated in varying amount between the vesicles, and do not differ in any essential respect from those forming the parathyroid glandules.

Many of the masses of intervesicular cells are indistinguishable from parathyroids. The internal parathyroid is frequently in direct tissue continuity with the thyroid, and every kind of transition form exists. Parathyroid has only, indeed, to have colloid spaces in its interior to constitute itself thyroid, and this occurs in the human subject under certain pathological conditions.

Parathyroids left behind after removal of the thyroid develop colloid vesicles, and become practically converted into thyroid. Moreover, the changes in the thyroid, after removal of the parathyroids, may be interpreted as the reverse change of thyroid into parathyroid tissue. The experimental evidence as to a separate function for parathyroids is inconclusive.

9. Thyroid and parathyroids are to be looked upon as structures of somewhat different embryological origin, which are anatomically separate and distinct in the lower vertebrata, but which come into very intimate anatomical and physiological relationships with each other in the mammalia. In this latter group they are, in fact, to be looked upon as constituting one apparatus.*

* It is interesting to note that each of the three "ductless glands," suprarenal, thyroid-parathyroid, and pituitary body, consists of portions derived originally from quite separate sources, which come into intimate relationship in the higher vertebrata. In the case of the suprarenal capsules there is never, however, any commingling of the constituent cells, nor even a true anatomical continuity, and no

10. Parathyroidectomy, like thyroidectomy, causes compensatory changes in the pituitary body. These consist in a notable increase of the colloid vesicles in the *pars intermedia*.

This observation confirms the general view that thyroid and parathyroid are very intimately related to each other. The colloid vesicles of the *pars intermedia* of the pituitary resemble in all respects those of the thyroid and of the parathyroid (where such occur), and it is probable that the intermediate portion of the pituitary is to be looked upon as an integral part of the thyroid-parathyroid apparatus.

[The expenses of this work have been defrayed by a grant of money from the British Association for the Advancement of Science.]

XII.—EXPLANATION OF PLATES.

Lettering common to all Figures.

a.	= artery.
ad. t.	= adenoid tissue.
bld. c.	= blood corpuscles.
bld. cap.	= blood capillaries.
c.	= colloid.
cap.	= capsule.
car. b.	= carotid body.
cart.	= cartilage.
c. c.	= concentric corpuscles.
c. pb. b.	= cells lining vesicles of post-branchial body.
c. t.	= connective tissue.
c. ves.	= colloid vesicle.
e. interves.	= intervesicular epithelium cells.
end.	= endothelium.
e. ves.	= epithelium of colloid vesicles.
l.	= lumen.
n.	= nerve.

relationship between the functions of the two parts has ever been traced. In the case of the pituitary the same is probably true.

An illustration of another kind of relationship is that between the secreting tubule and islet of LANGERHANS in the pancreas. Both are derived from the same blastema and have only an apparent or temporary separation from each other. (See VINCENT and THOMPSON, 'Internat. Monatsschr. f. Anat. u. Physiol.,' 1907, vol. 24, parts 1, 3; LAGUESSE, 'Journ. de l'Anat. et de la Physiol., XXXIIe Année, 1896, No. 3, May—June; 'Archives d'Anat. micr.,' vol. 4, parts II and III, 1901; *ibid.*, vol. 5, part III, 1902; 'C. R. Soc. Biol.,' August 4, 1900.)

pb. b.	= post-branchial body.
p. c.	= pigment cells.
p. inter.	= pars intermedia of pituitary.
pthyr.	= parathyroid.
thym.	= thymus.
thyr.	= thyroid.
tr. t.	= transition tissue between thyroid and parathyroid.
v.	= vein.
v. pb. b.	= vesicles of post-branchial body.
v. kr.	= ventral branchial body.

Plate 10.

Fig. 1.—Section of the thyroid gland of *Raja blanda*, fixed in Flemming's fluid (strong formula). Sections stained with gentian violet and orange G. Drawn with Leitz camera lucida. As seen under a magnification of 400 diameters, showing thick septa of connective tissue between the lobules of vesicles, and cylindrical cells lining the vesicles.

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 2.—Section of the thyroid gland of *Scyllium canicula*, fixed in corrosive sublimate. Sections stained with hæmatoxylin and eosin. Drawn with Leitz camera lucida. As seen under a magnification of 400 diameters, showing small body composed of lymphoid and epithelial cells (*e. interves.* and *ad. t.*).

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 3.—Thyroid of *Amiurus nigricans*. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; as seen under a low power. Note the large amount of connective tissue and the few scattered vesicles, and the fact that the epithelium lining the vesicles is very low, and sometimes absent.

Fig. 4.—*Spelerpes ruber*. Thyroid; Flemming's fluid, iron hæmatoxylin, and eosin; camera lucida; low power.

Fig. 5.—*Spelerpes ruber*. Post-branchial body; $HgCl_2$, hæmatoxylin, and eosin; camera lucida; low power. Shows a group of vesicles lined with columnar epithelium. Note the difference in the position of the nuclei in these vesicles and in those of the thyroid, *e.g.*, in fig. 1.

Fig. 6.—*Spelerpes ruber*. Parathyroid; fixed in $HgCl_2$, and stained with hæmatoxylin and eosin; low power; camera lucida. The glandule has wide capillaries and is formed of solid columns of cells, sometimes one cell deep, sometimes consisting of several rows.

PLATE 11.

Fig. 7.—Thyroid of the frog. Corrosive sublimate, hæmatoxylin, and eosin. Camera lucida; ×400. Shows colloid vesicles, with intervesicular connective tissue, and epithelium, and indicates the close apposition of the body to the hyoid cartilage.

Fig. 8.—This drawing represents the parathyroid, ventral branchial body, and carotid gland of the frog. Corrosive sublimate, hæmatoxylin; camera lucida; low power. The ventral branchial body is seen to be a comparatively large body, made up of columns of cells, separated by blood capillaries. The cells of the columns are of two kinds. The parathyroid shows the characteristic whorl arrangement referred to in the text. The carotid body consists of a number of cavernous spaces, separated by a tissue resembling that of the wall of the blood-vessels. The section shows also the large blood-vessels of the neck and the vagus nerve.

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 9.—*Pseudemys scripta.* Parathyroid and post-branchial body. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; low power. Part of the nodule of parathyroid is occupied by thymus tissue, in whose centre is the remains of the original epithelium cells of the thymus.

Note that some of the vesicles of the parathyroid approach in structure those of the post-branchial body, while many of the groups of cells in the region of the post-branchial body resemble those cell-columns of the parathyroid which are without a lumen. There is here clearly a close relationship between parathyroid and post-branchial body.

Fig. 10.—*Kinosternon pennsylvanicum.* Section of the parathyroid showing lumina and a granular inner zone to the lining cells; corrosive, hæmatoxylin, and eosin; camera lucida; low power.

PLATE 12.

Fig. 11.—Pigeon. Portions of post-branchial body (on the left) and parathyroid (on the right), separated by a connective tissue septum. Note the presence in both of structures identical with HASSALL's corpuscles of the thymus. These are numerous in the post-branchial body, and few in the parathyroid. In both, these concentric bodies frequently show a lumen

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 12.—Human. A drawing, as seen under a simple lens, of a portion of the thyroid and a parathyroid which is considerably hypertrophied and otherwise modified. The specimen is pathological, but I have been unable to trace any record of the patient. The object of this figure is to show that the structure (*pthyr.*) is morphologically a parathyroid.

Drawing reduced to $\frac{1}{2}$ of original size.

Fig. 13.—From the same preparation as fig. 12. A portion of the thyroid and neighbouring parathyroid, with a fairly thick connective tissue partition; low power; camera lucida. On the right we see the colloid vesicles of the thyroid; on the left the parathyroid, which is of a typical parathyroid structure, near the connective tissue septum; but which shows several undoubted colloid vesicles in the left-hand portion of the drawing.

Fig. 14.—From the same preparation as figs. 12 and 13. A small portion of the parathyroid shown in the last two figures. This section is from a part of the parathyroid somewhat further removed from the thyroid than any part of fig. 13. The drawing was made with a camera lucida, high power. It is seen that, although the vesicles are small, they are typically thyroidal in character. They may be compared with those from the rabbit, shown in the next figure.

Drawing reduced to $\frac{1}{2}$ of original size.

Fig. 15.—Rabbit. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; high power.

The figure shows an undoubted transition between thyroid (upper part of figure) and internal parathyroid (lower part of figure).

Drawing reduced to $\frac{1}{2}$ of original size.

Plate 13.

Fig. 16.—Shows a similar appearance in the same animal under a low power.

Fig. 17.—Badger. Internal parathyroid. Corrosive sublimate, hæmatoxylin, and eosin. The section is taken through that portion of the parathyroid which becomes continuous with thyroid. It is evident from the drawing that there is no line of demarcation between the two organs, and, further, that the details of the structure gradually change as we pass from one to the other.

Fig. 18.—Parathyroid of the ox. This preparation was made from a nodule of glandular tissue lying outside the thyroid gland in the position where the external parathyroids are usually found. It is obvious that the structure is of a mixed nature, revealing every kind of intermediate formation between thyroid and parathyroid.

Fig. 19.—Thyroid of dog, killed after a few days' inanition; compare with fig. 20, taken from a normal dog. In the inanition thyroid there is a marked increase of intervesicular tissue, and a distortion, shrinkage, and occlusion of the colloid vesicles.

Plate 14.

Fig. 20.—Thyroid of normal dog. Preparation the same as fig. 19, viz., Flemming, iron hæmatoxylin.

Fig. 21.—Parathyroid of a dog, 83 days after thyroidectomy, showing vesicles, some of which contain colloid. $\times 120$.

Fig. 22.—Thyroid of a dog, 32 days after removal of all four parathyroids. The vesicles have become very irregular in shape, and there seems to be an increase in the intervesicular epithelial tissue. $\times 120$.

Fig. 23.—Small portion of the *pars intermedia* of the pituitary of a dog, which died some weeks after parathyroidectomy. The structure is practically indistinguishable from thyroid. Flemming; iron hæmatoxylin; high power; camera lucida.

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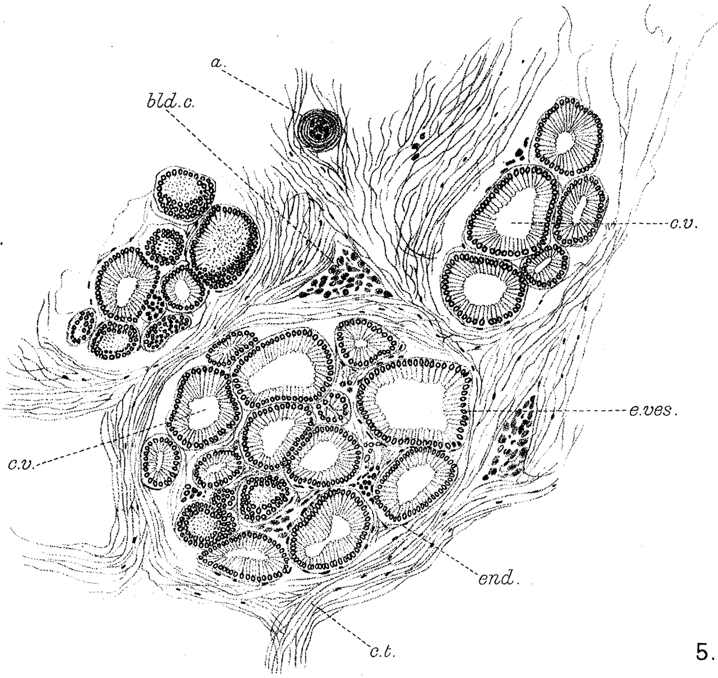
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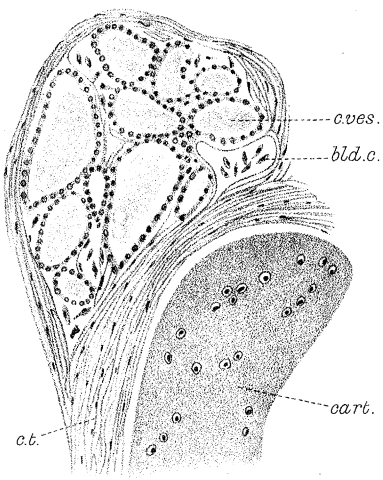
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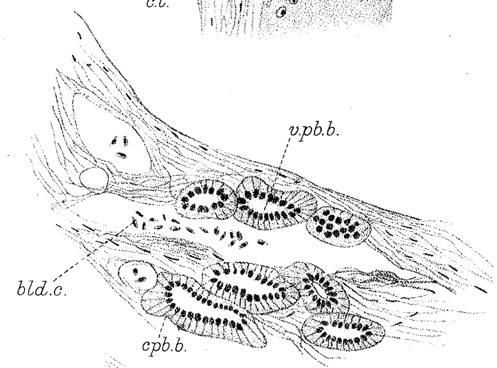
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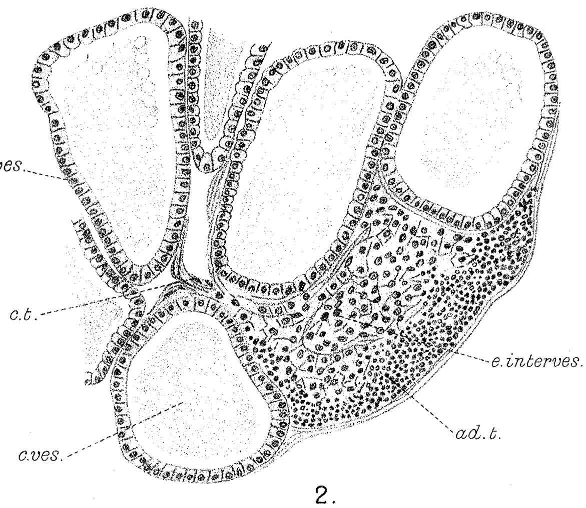
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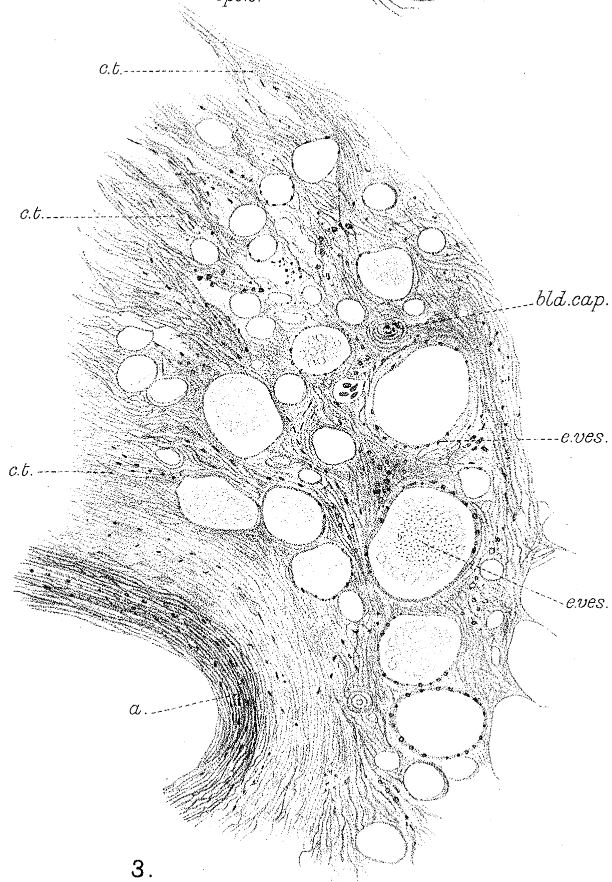
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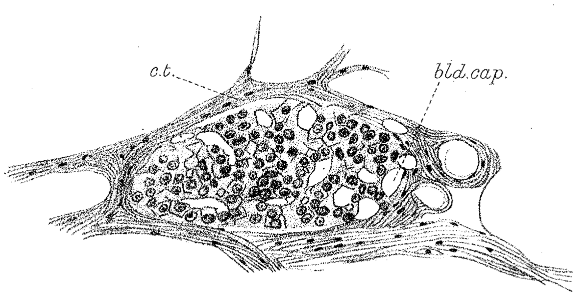
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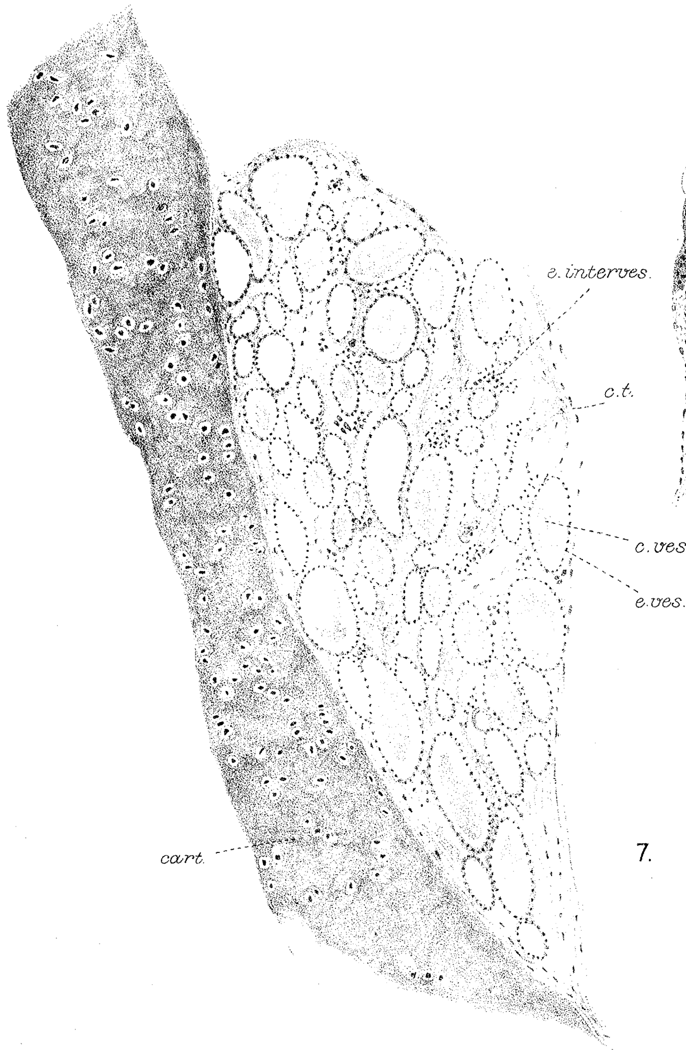

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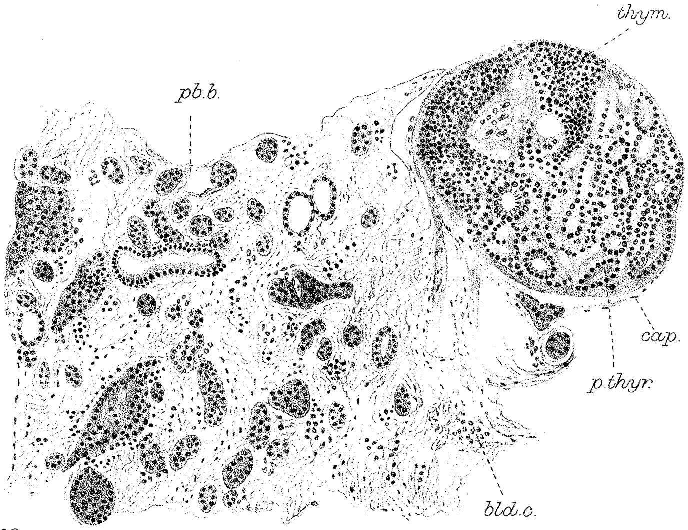

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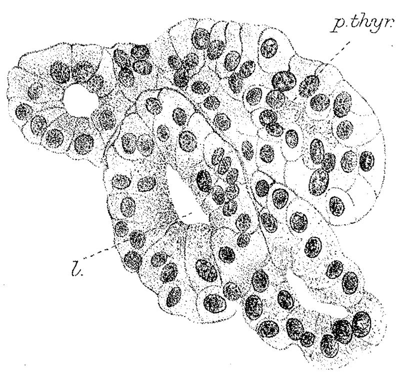

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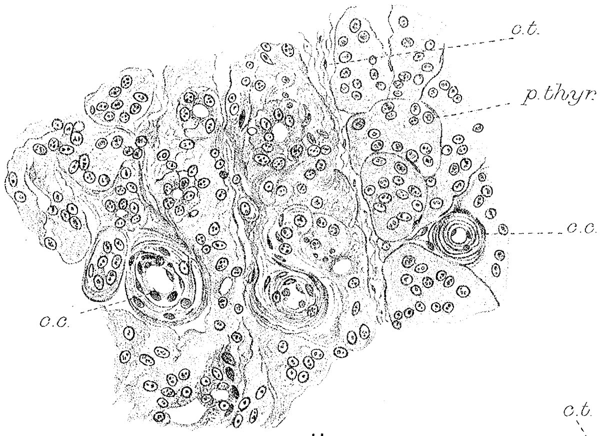

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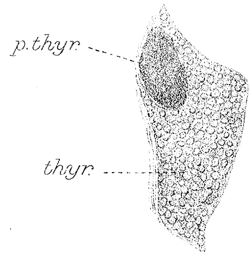

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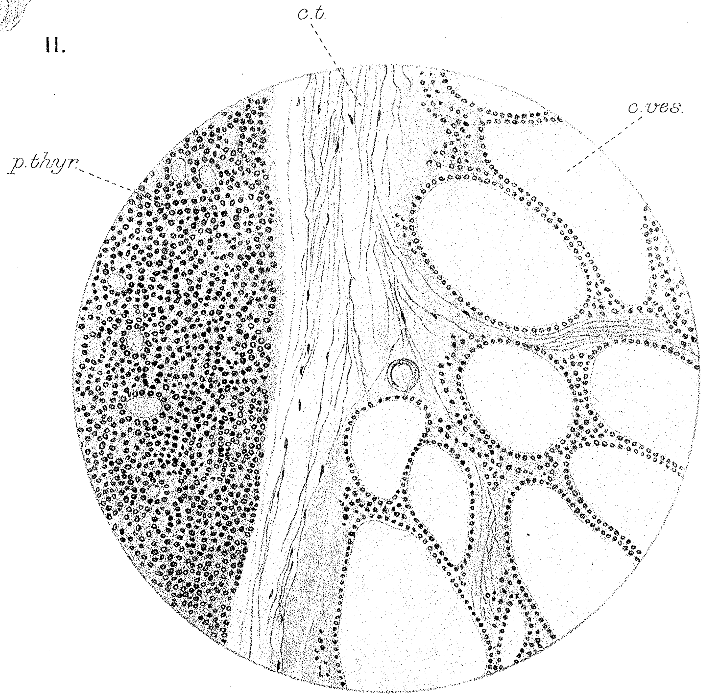

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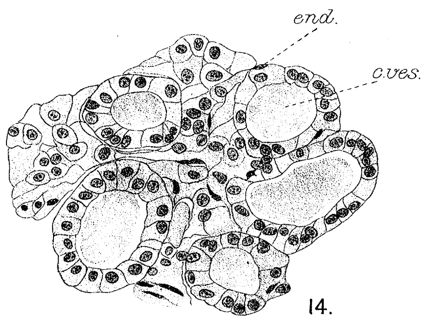

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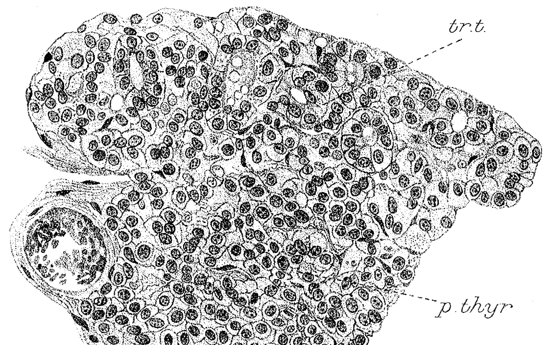

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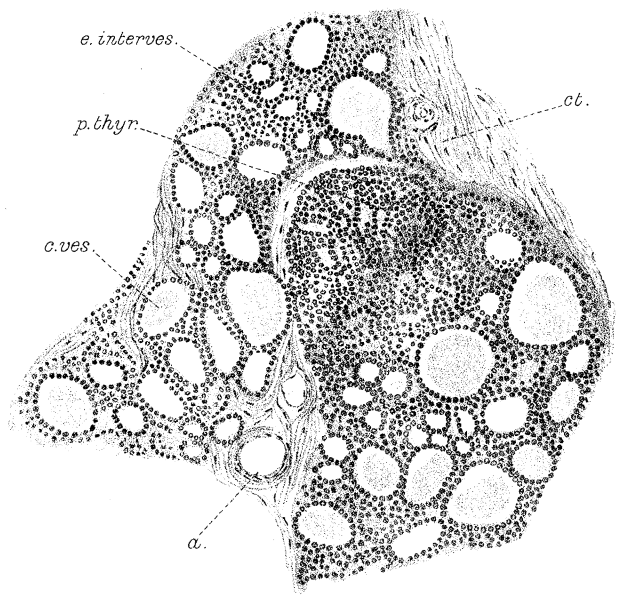

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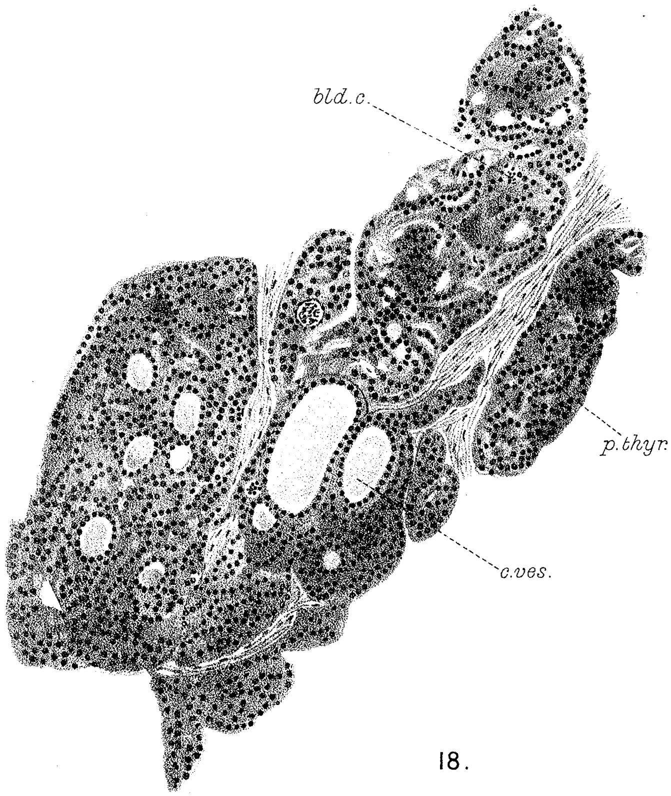

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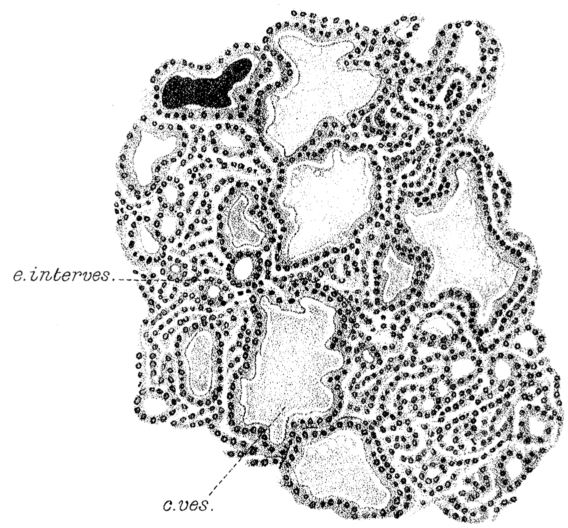

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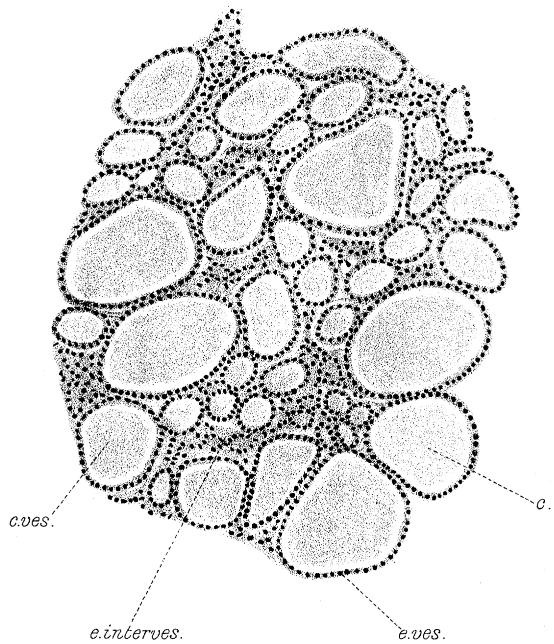
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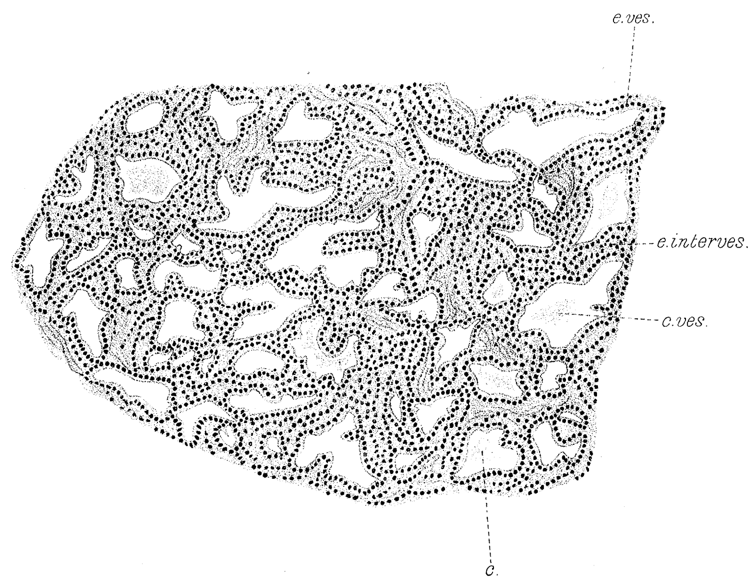
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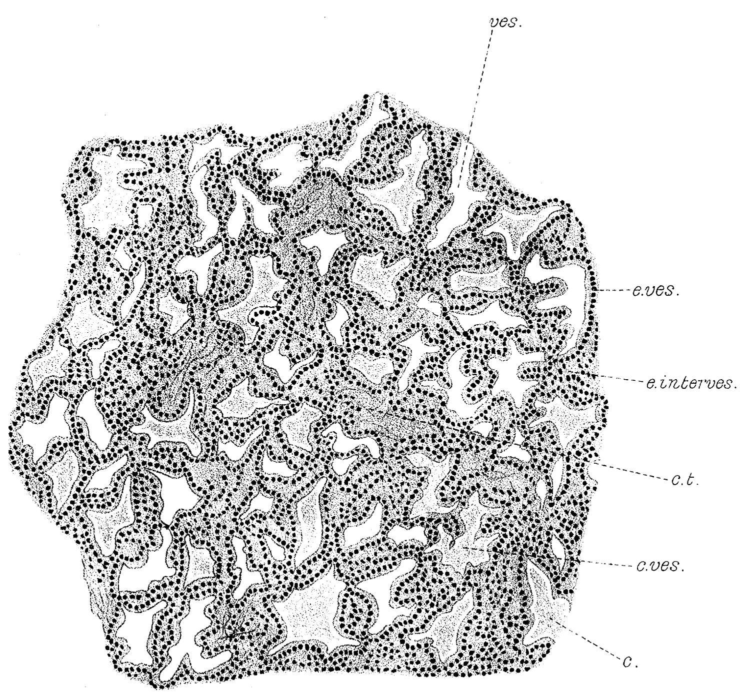
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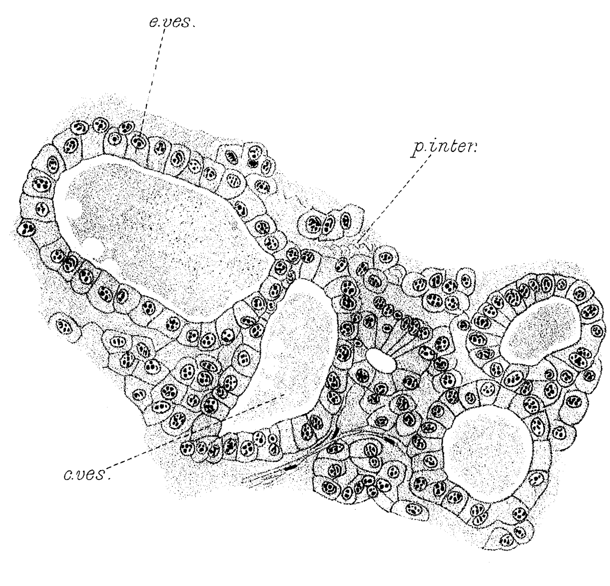
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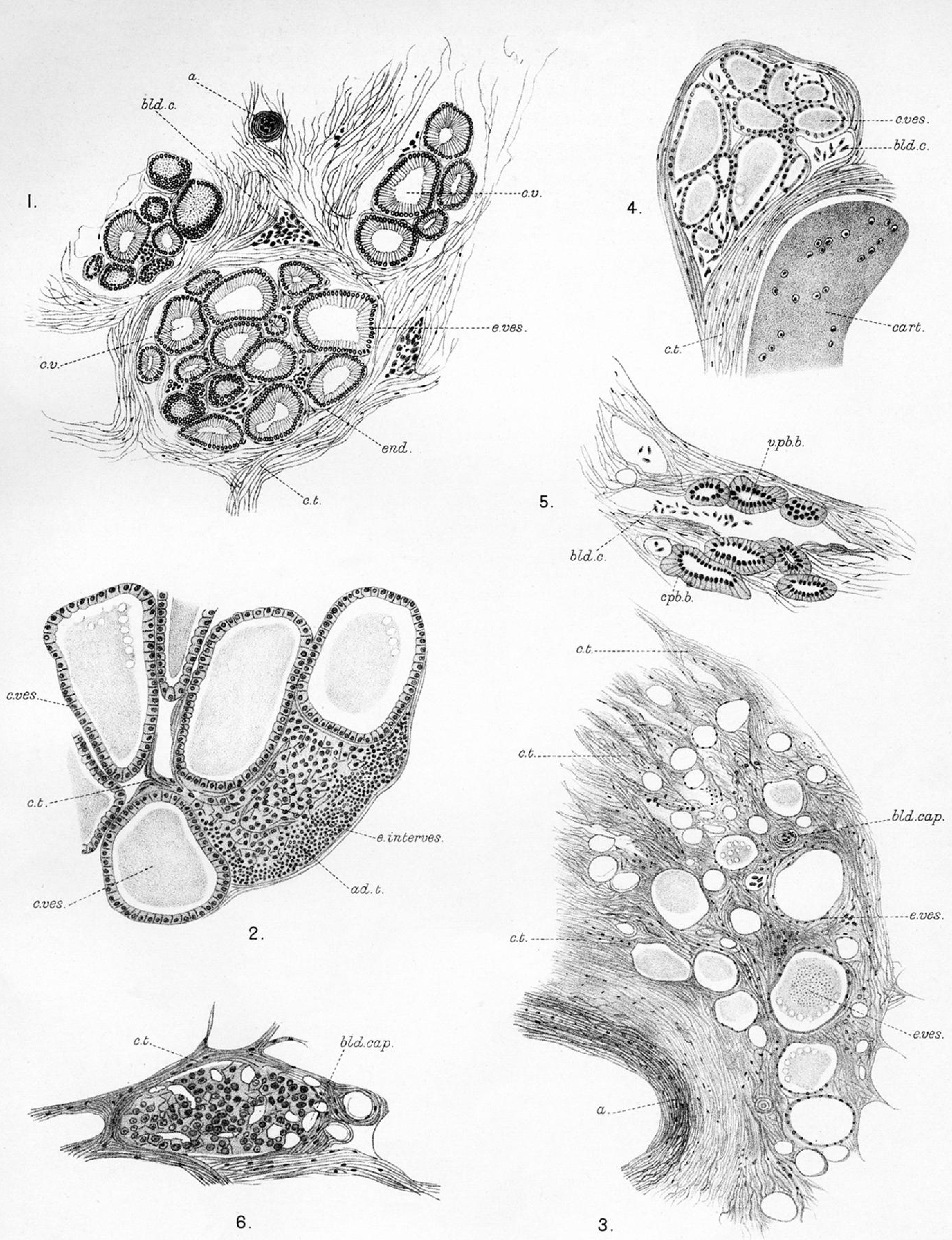


PLATE 10.

Fig. 1.—Section of the thyroid gland of *Raja blanda*, fixed in Flemming's fluid (strong formula). Sections stained with gentian violet and orange G. Drawn with Leitz camera lucida. As seen under a magnification of 400 diameters, showing thick septa of connective tissue between the lobules of vesicles, and cylindrical cells lining the vesicles.

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 2.—Section of the thyroid gland of *Scyllium canicula*, fixed in corrosive sublimate. Sections stained with hæmatoxylin and eosin. Drawn with Leitz camera lucida. As seen under a magnification of 400 diameters, showing small body composed of lymphoid and epithelial cells (*e. interves.* and *ad. t.*).

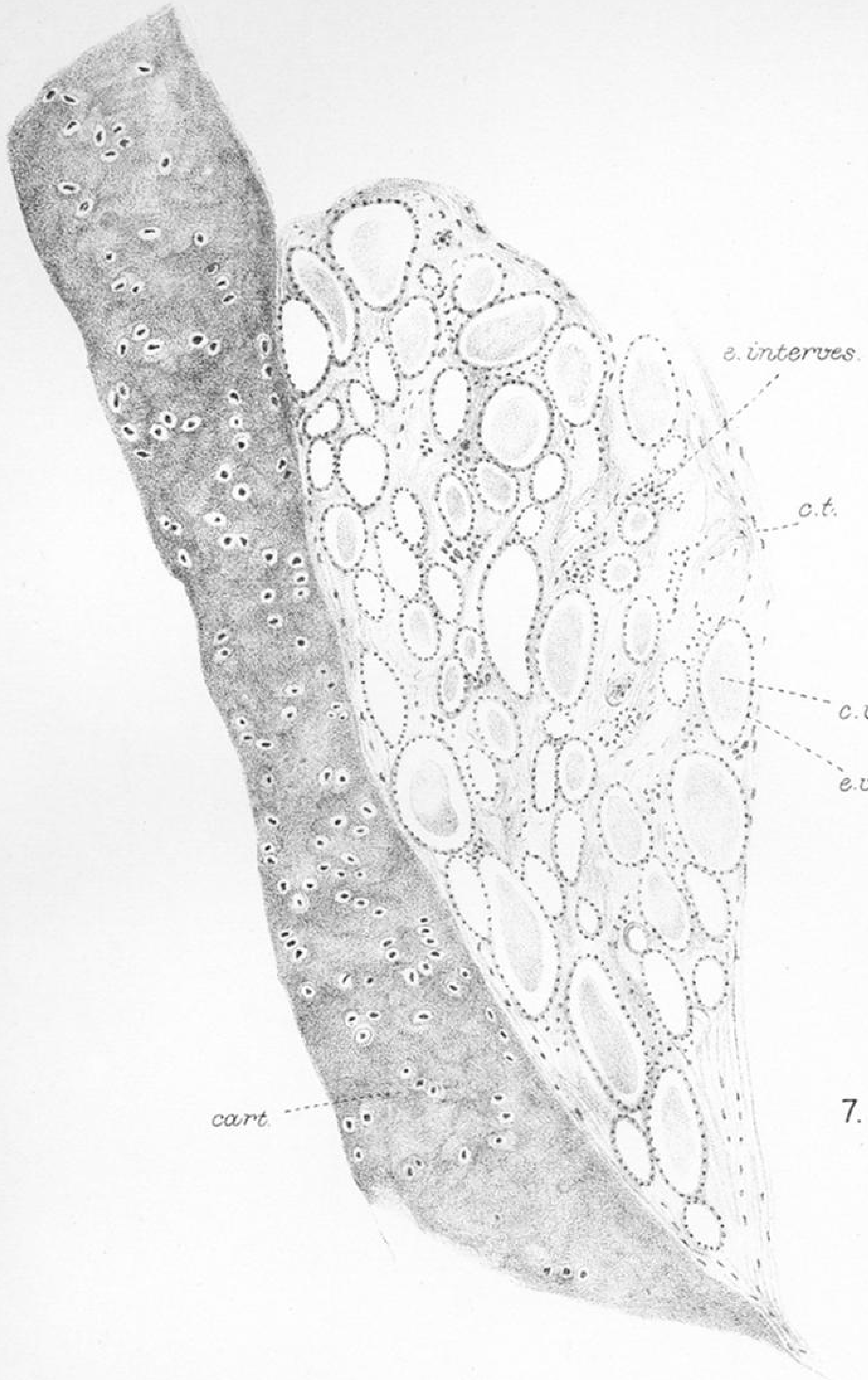
Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 3.—Thyroid of *Amiurus nigricans*. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; as seen under a low power. Note the large amount of connective tissue and the few scattered vesicles, and the fact that the epithelium lining the vesicles is very low, and sometimes absent.

Fig. 4.—*Spelerpes ruber*. Thyroid; Flemming's fluid, iron hæmatoxylin, and eosin; camera lucida; low power.

Fig. 5.—*Spelerpes ruber*. Post-branchial body; $HgCl_2$, hæmatoxylin, and eosin; camera lucida; low power. Shows a group of vesicles lined with columnar epithelium. Note the difference in the position of the nuclei in these vesicles and in those of the thyroid, *e.g.*, in fig. 1.

Fig. 6.—*Spelerpes ruber*. Parathyroid; fixed in $HgCl_2$, and stained with hæmatoxylin and eosin; low power; camera lucida. The glandule has wide capillaries and is formed of solid columns of cells, sometimes one cell deep, sometimes consisting of several rows.



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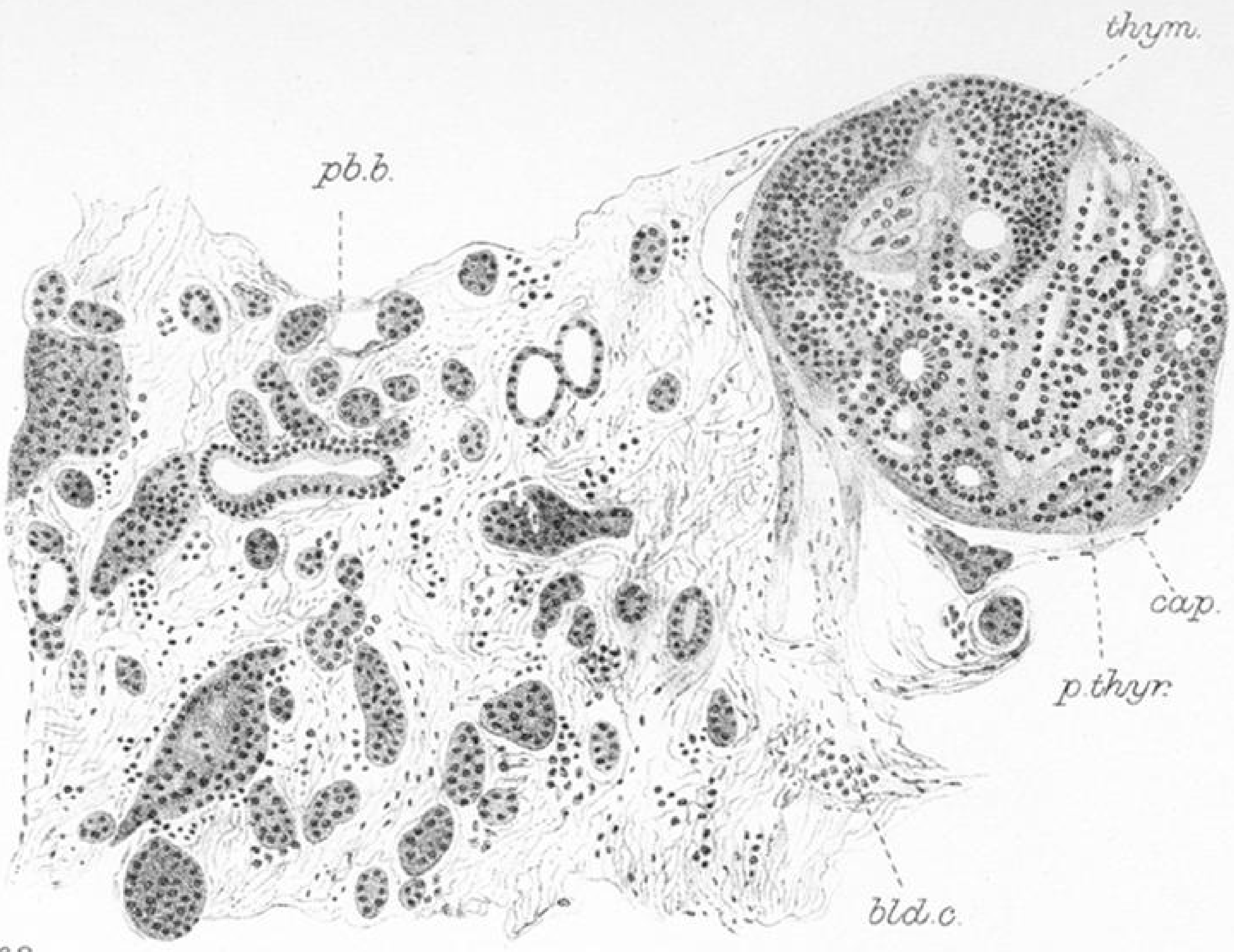

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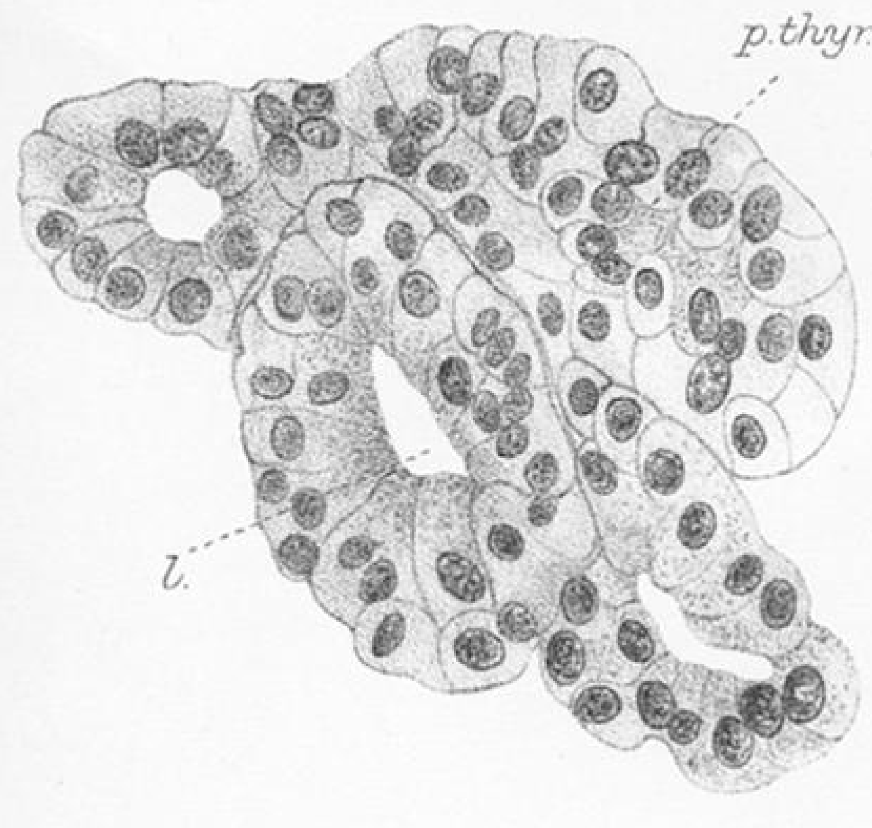

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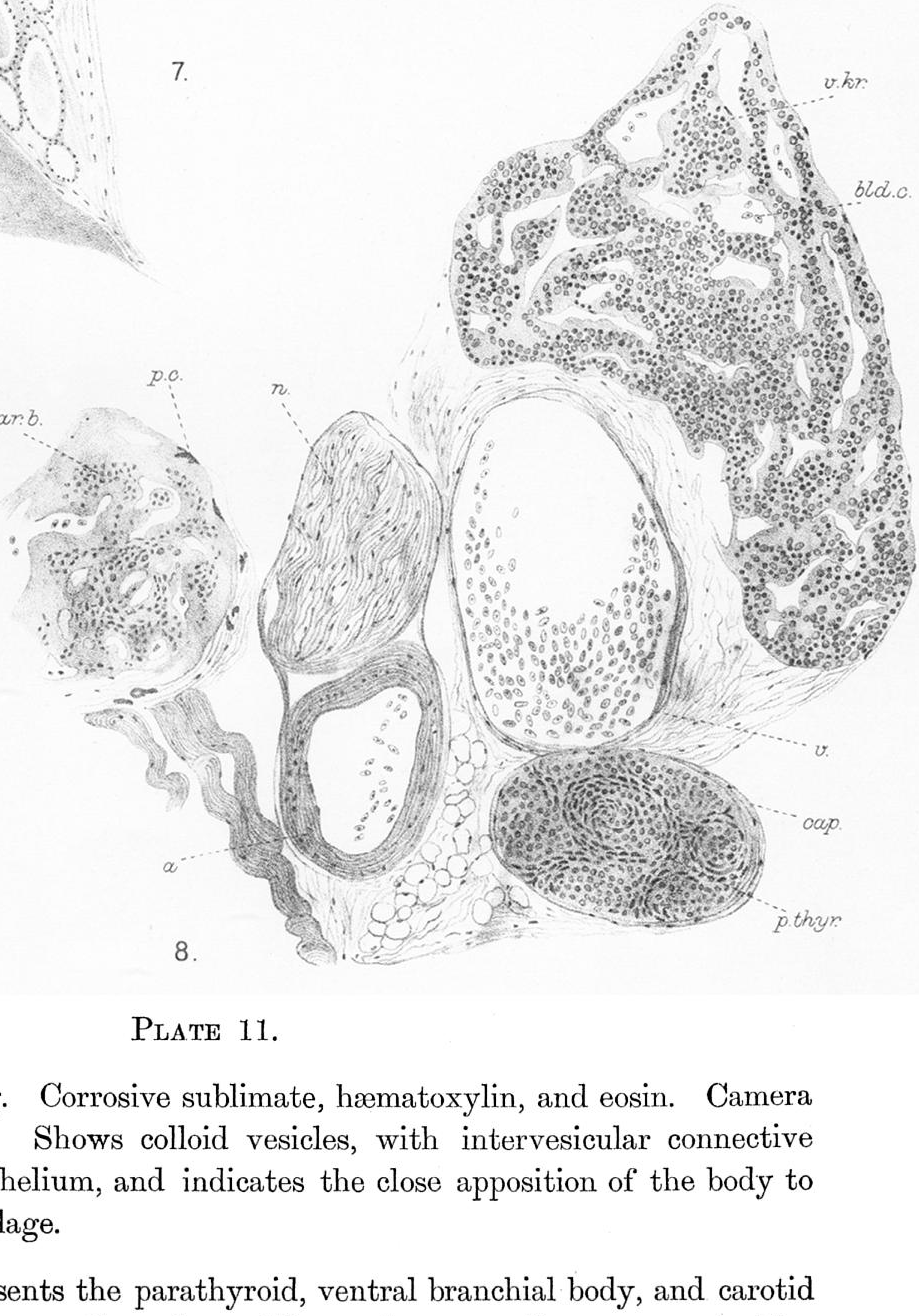

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PLATE 11.

Fig. 7.—Thyroid of the frog. Corrosive sublimate, hæmatoxylin, and eosin. Camera lucida; ×400. Shows colloid vesicles, with intervesicular connective tissue, and epithelium, and indicates the close apposition of the body to the hyoid cartilage.

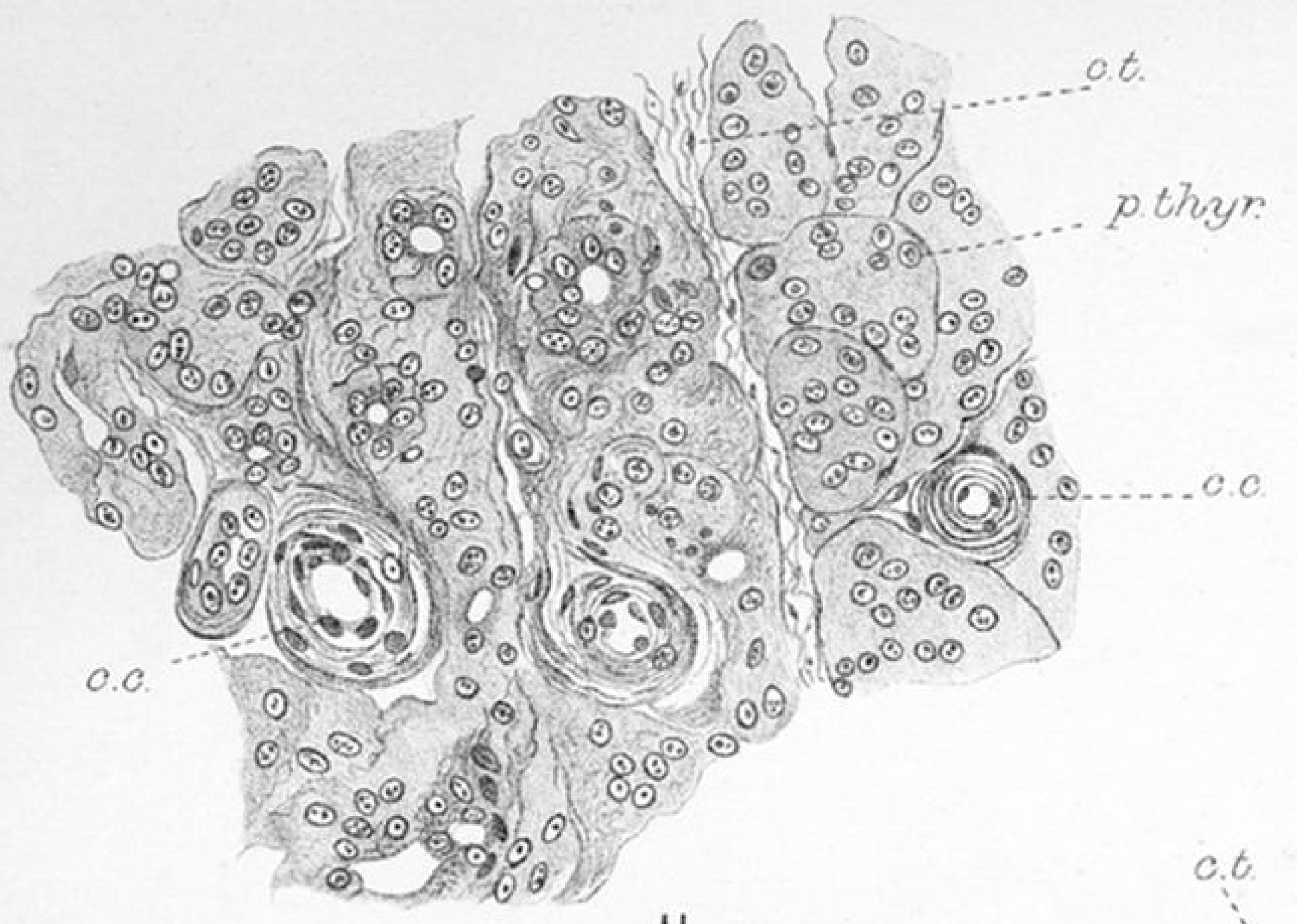
Fig. 8.—This drawing represents the parathyroid, ventral branchial body, and carotid gland of the frog. Corrosive sublimate, hæmatoxylin; camera lucida; low power. The ventral branchial body is seen to be a comparatively large body, made up of columns of cells, separated by blood capillaries. The cells of the columns are of two kinds. The parathyroid shows the characteristic whorl arrangement referred to in the text. The carotid body consists of a number of cavernous spaces, separated by a tissue resembling that of the wall of the blood-vessels. The section shows also the large blood-vessels of the neck and the vagus nerve.

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 9.—*Pseudemys scripta.* Parathyroid and post-branchial body. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; low power. Part of the nodule of parathyroid is occupied by thymus tissue, in whose centre is the remains of the original epithelium cells of the thymus.

Note that some of the vesicles of the parathyroid approach in structure those of the post-branchial body, while many of the groups of cells in the region of the post-branchial body resemble those cell-columns of the parathyroid which are without a lumen. There is here clearly a close relationship between parathyroid and post-branchial body.

Fig. 10.—*Kinosternon pennsylvanicum.* Section of the parathyroid showing lumina and a granular inner zone to the lining cells; corrosive, hæmatoxylin, and eosin; camera lucida; low power.



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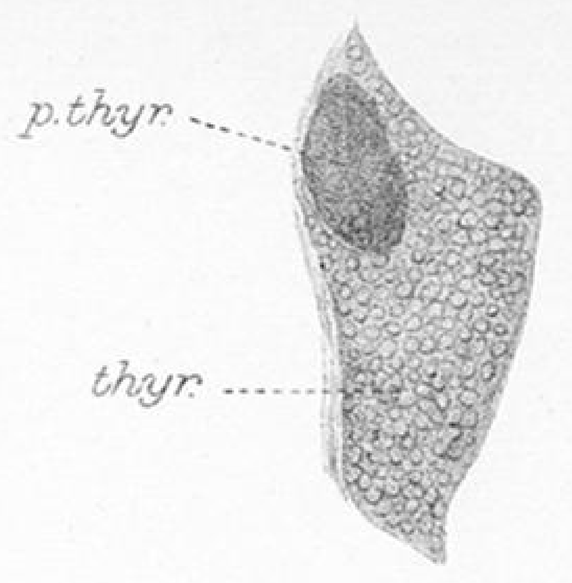

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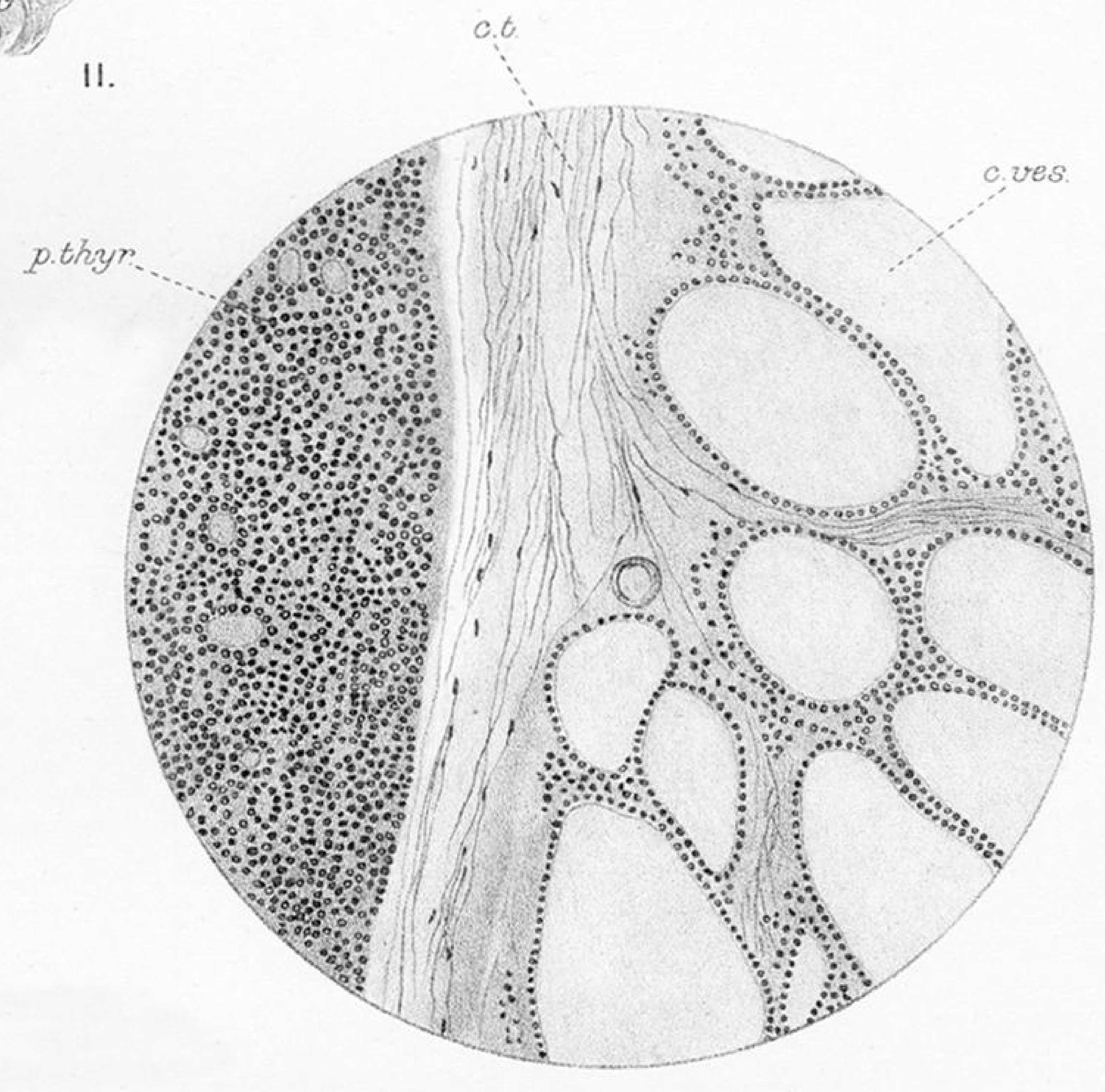

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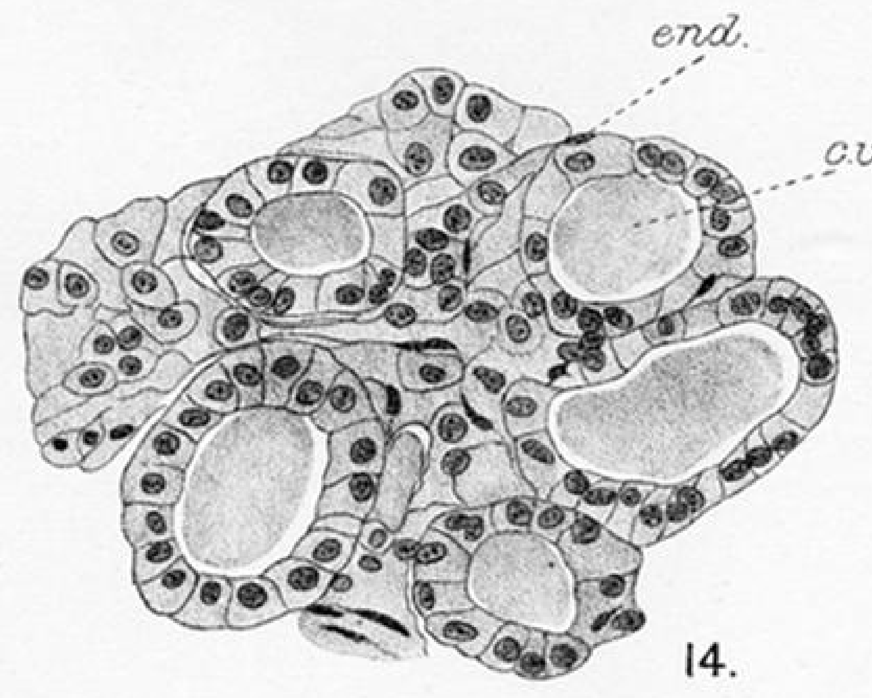

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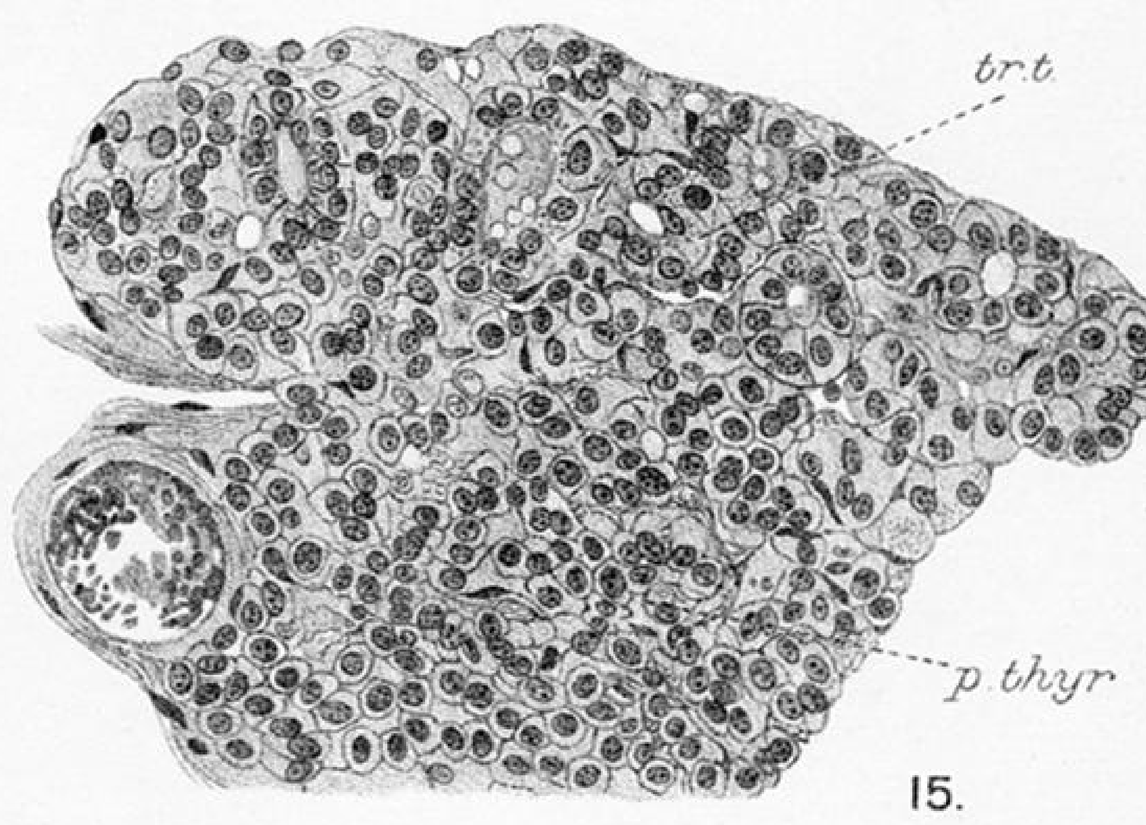

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PLATE 12.

Fig. 11.—Pigeon. Portions of post-branchial body (on the left) and parathyroid (on the right), separated by a connective tissue septum. Note the presence in both of structures identical with HASSALL'S corpuscles of the thymus. These are numerous in the post-branchial body, and few in the parathyroid. In both, these concentric bodies frequently show a lumen

Drawing reduced to $\frac{2}{3}$ of original size.

Fig. 12.—Human. A drawing, as seen under a simple lens, of a portion of the thyroid and a parathyroid which is considerably hypertrophied and otherwise modified. The specimen is pathological, but I have been unable to trace any record of the patient. The object of this figure is to show that the structure (*pthyr.*) is morphologically a parathyroid.

Drawing reduced to $\frac{1}{2}$ of original size.

Fig. 13.—From the same preparation as fig. 12. A portion of the thyroid and neighbouring parathyroid, with a fairly thick connective tissue partition; low power; camera lucida. On the right we see the colloid vesicles of the thyroid; on the left the parathyroid, which is of a typical parathyroid structure, near the connective tissue septum; but which shows several undoubted colloid vesicles in the left-hand portion of the drawing.

Fig. 14.—From the same preparation as figs. 12 and 13. A small portion of the parathyroid shown in the last two figures. This section is from a part of the parathyroid somewhat further removed from the thyroid than any part of fig. 13. The drawing was made with a camera lucida, high power. It is seen that, although the vesicles are small, they are typically thyroidal in character. They may be compared with those from the rabbit, shown in the next figure.

Drawing reduced to $\frac{1}{2}$ of original size.

Fig. 15.—Rabbit. Corrosive sublimate, hæmatoxylin, and eosin; camera lucida; high power.

The figure shows an undoubted transition between thyroid (upper part of figure) and internal parathyroid (lower part of figure).

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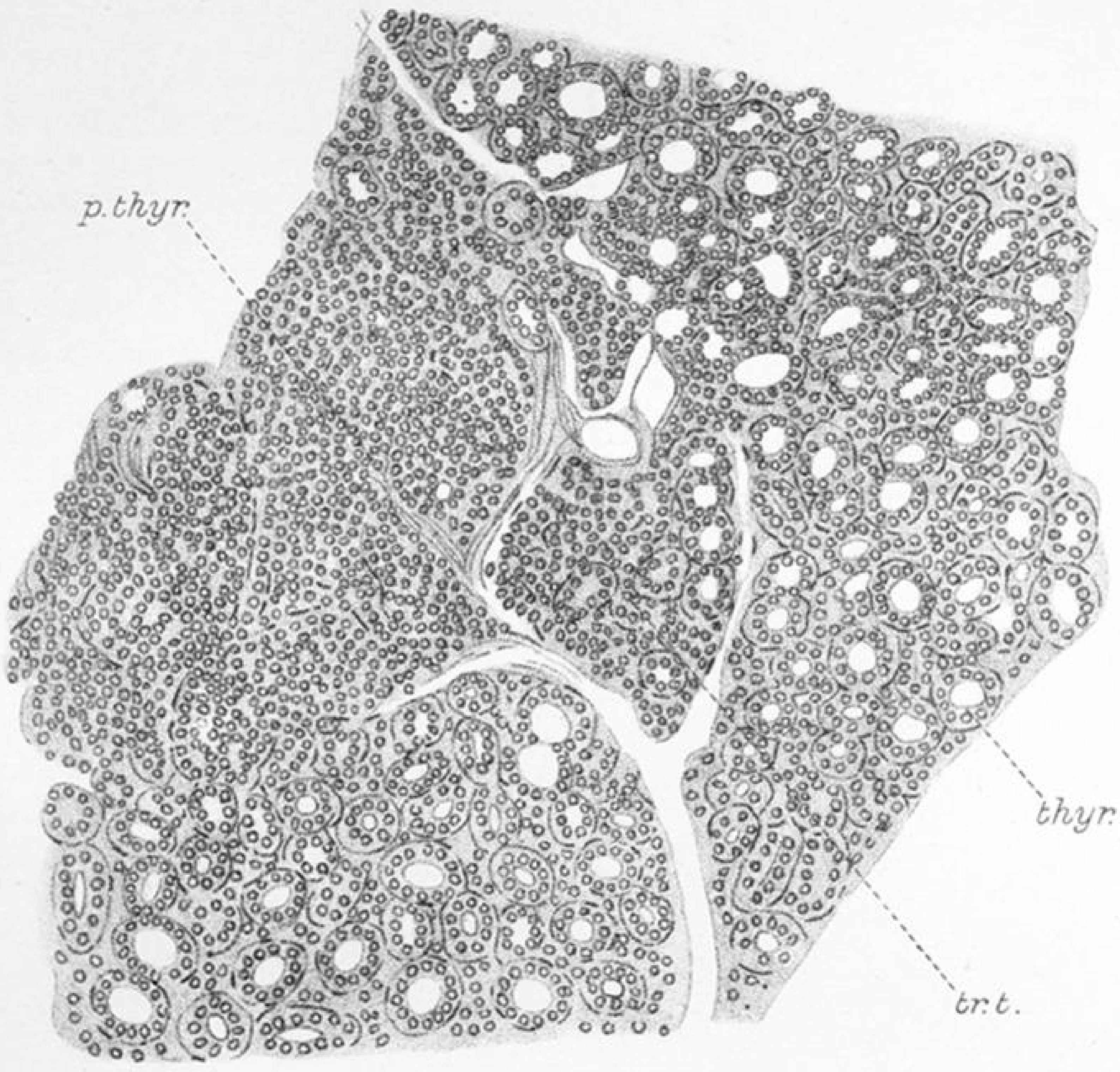

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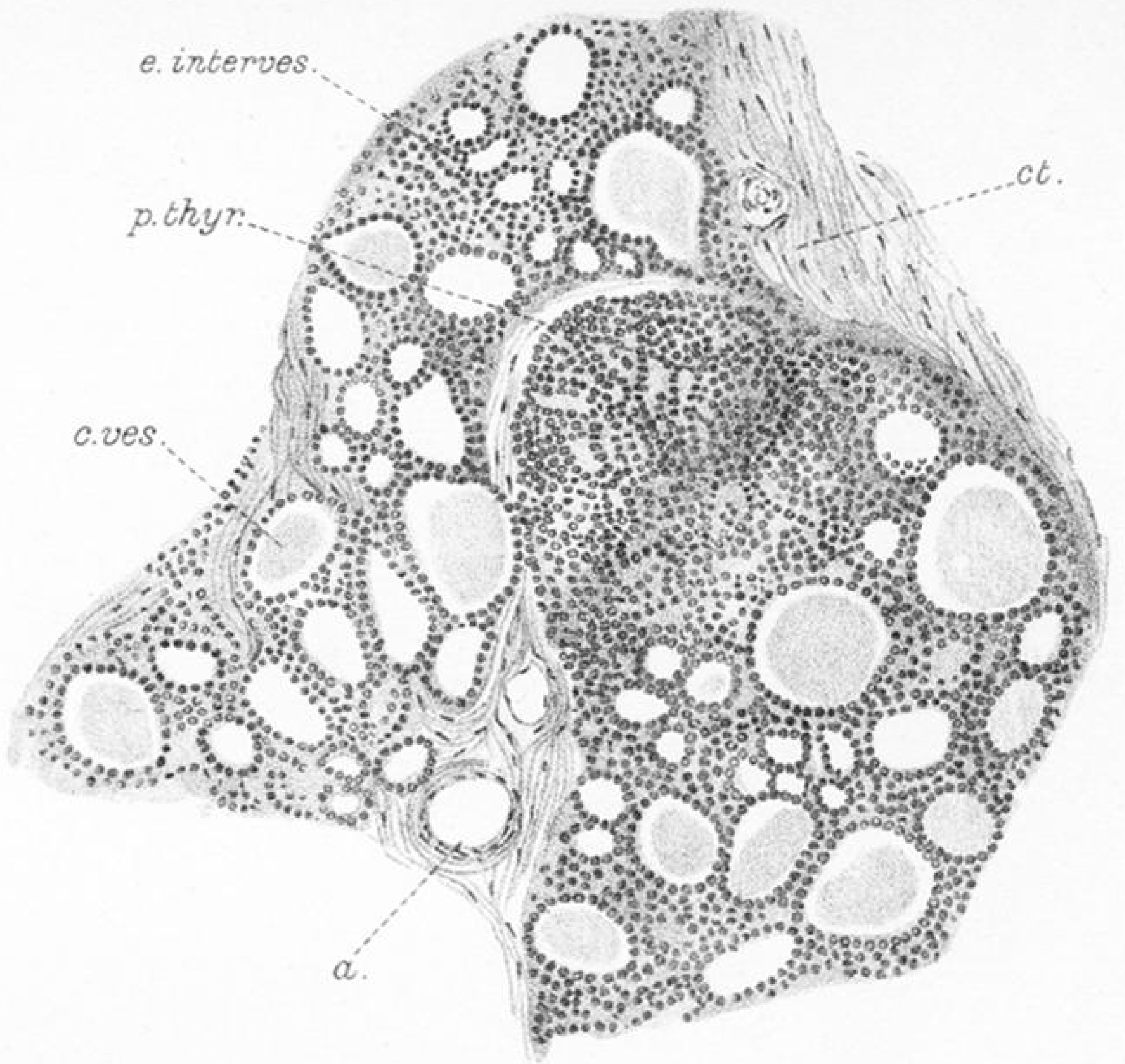

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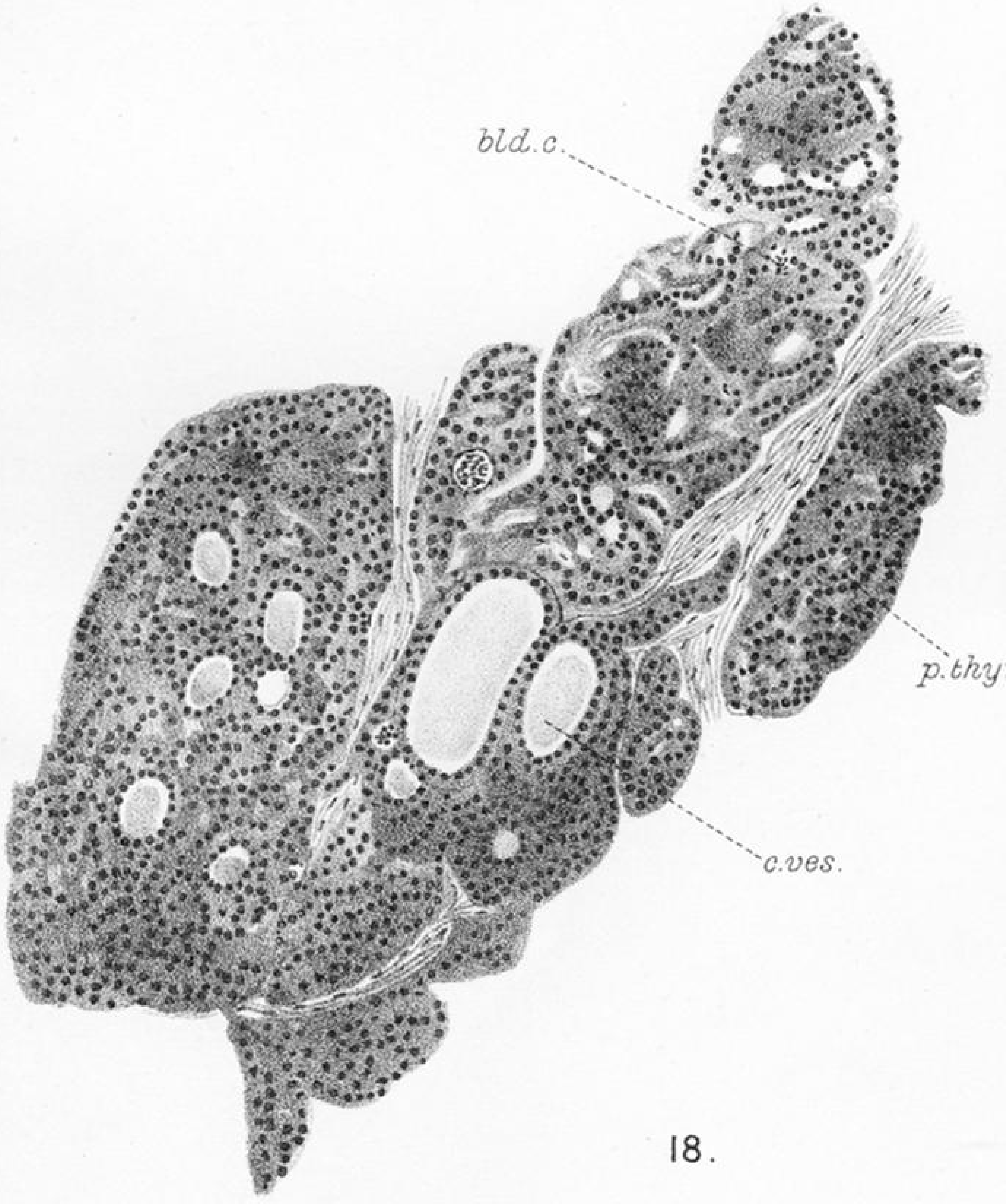

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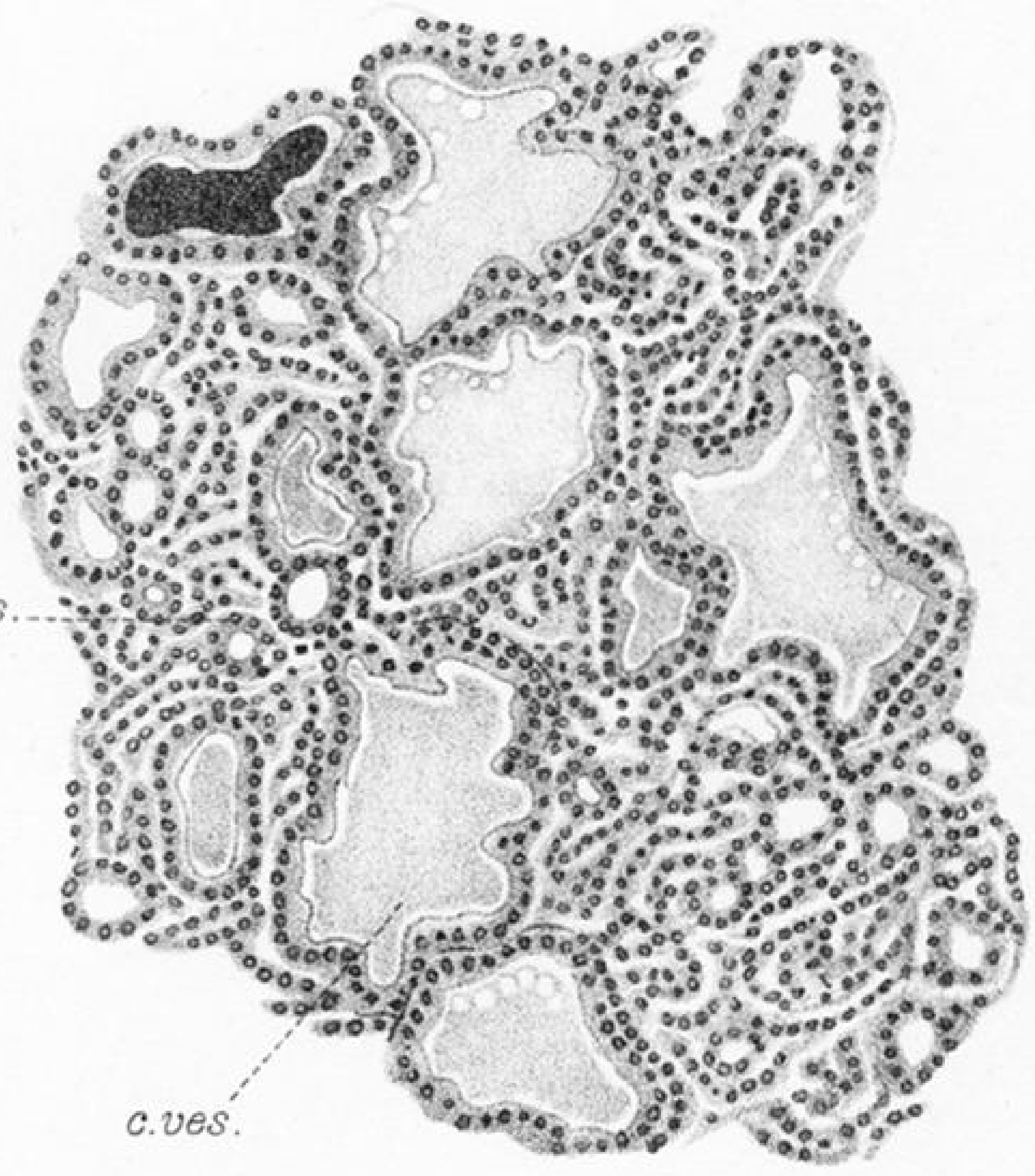


19.

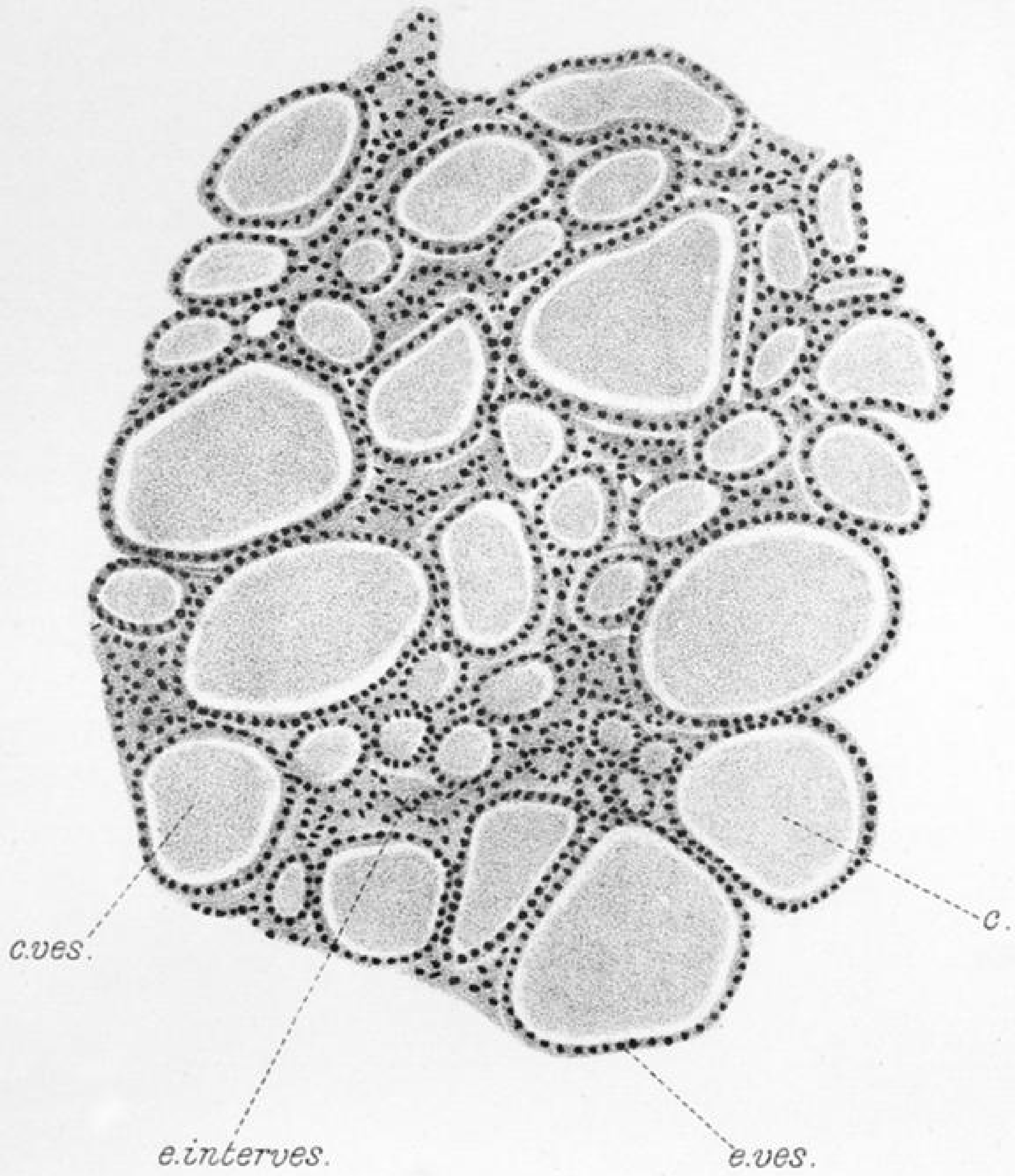
PLATE 13.

Fig. 16.—Shows a similar appearance in the same animal under a low power.

Fig. 17.—Badger. Internal parathyroid. Corrosive sublimate, hæmatoxylin, and eosin. The section is taken through that portion of the parathyroid which becomes continuous with thyroid. It is evident from the drawing that there is no line of demarcation between the two organs, and, further, that the details of the structure gradually change as we pass from one to the other.

Fig. 18.—Parathyroid of the ox. This preparation was made from a nodule of glandular tissue lying outside the thyroid gland in the position where the external parathyroids are usually found. It is obvious that the structure is of a mixed nature, revealing every kind of intermediate formation between thyroid and parathyroid.

Fig. 19.—Thyroid of dog, killed after a few days' inanition; compare with fig. 20, taken from a normal dog. In the inanition thyroid there is a marked increase of intervesicular tissue, and a distortion, shrinkage, and occlusion of the colloid vesicles.



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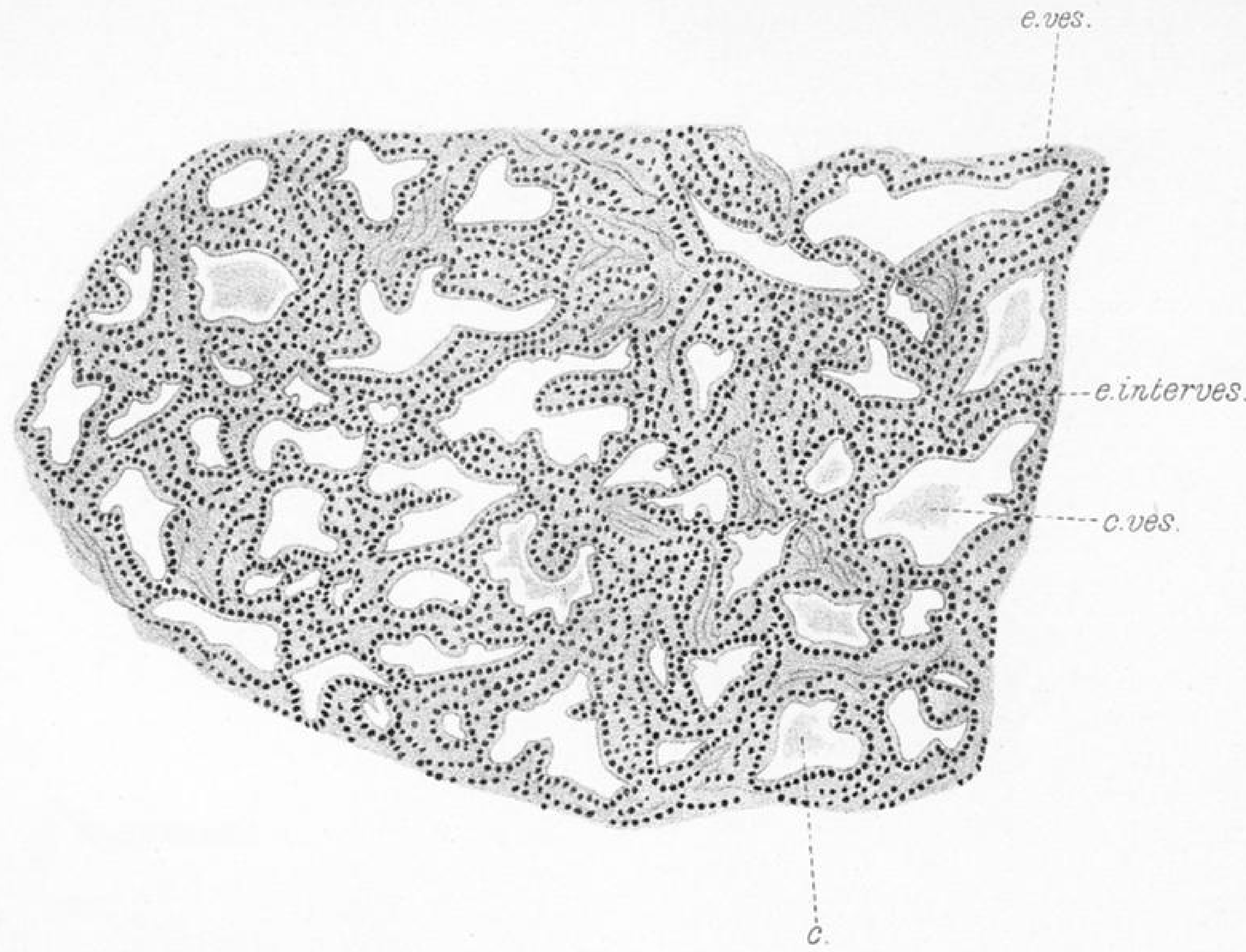

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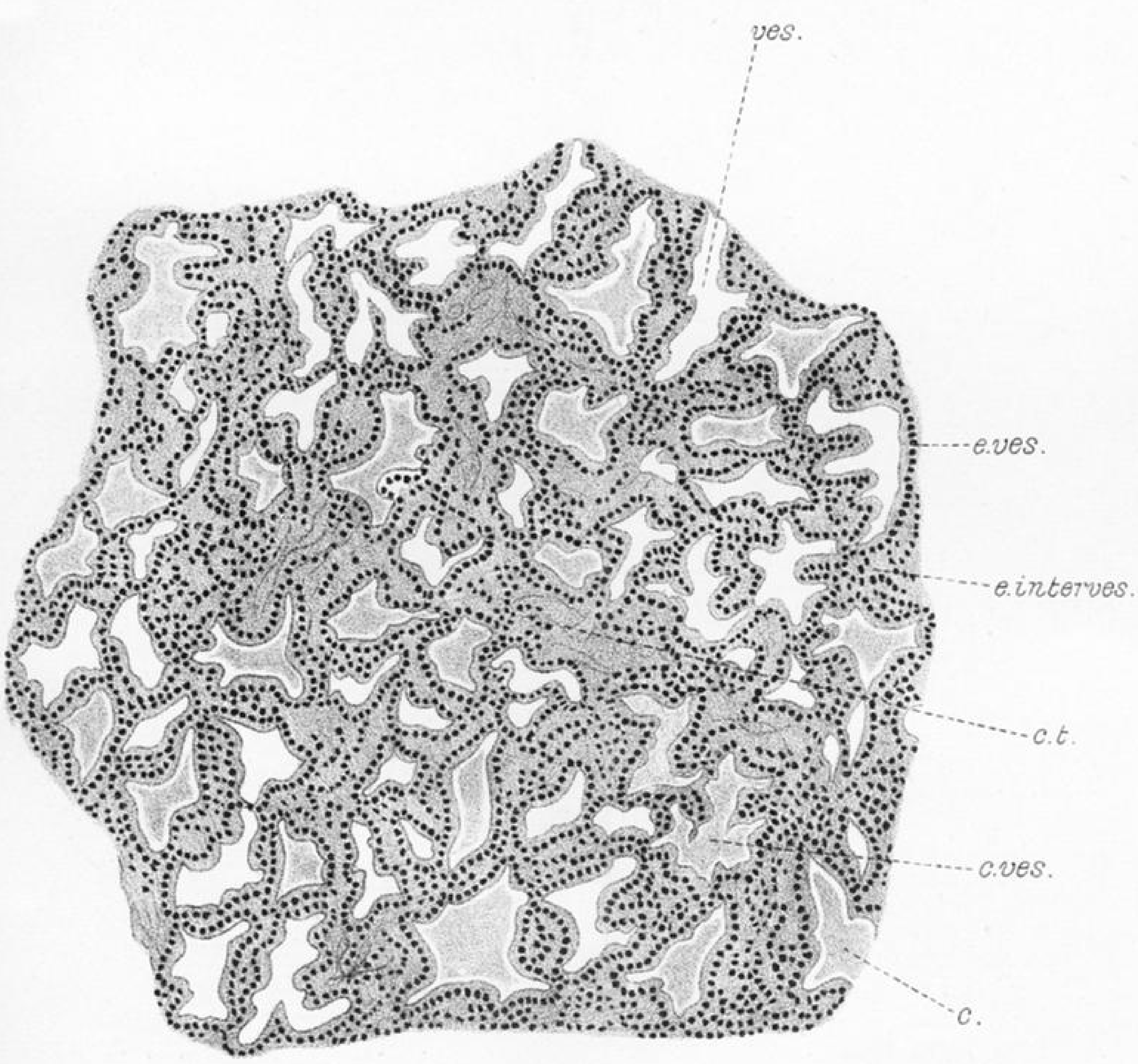

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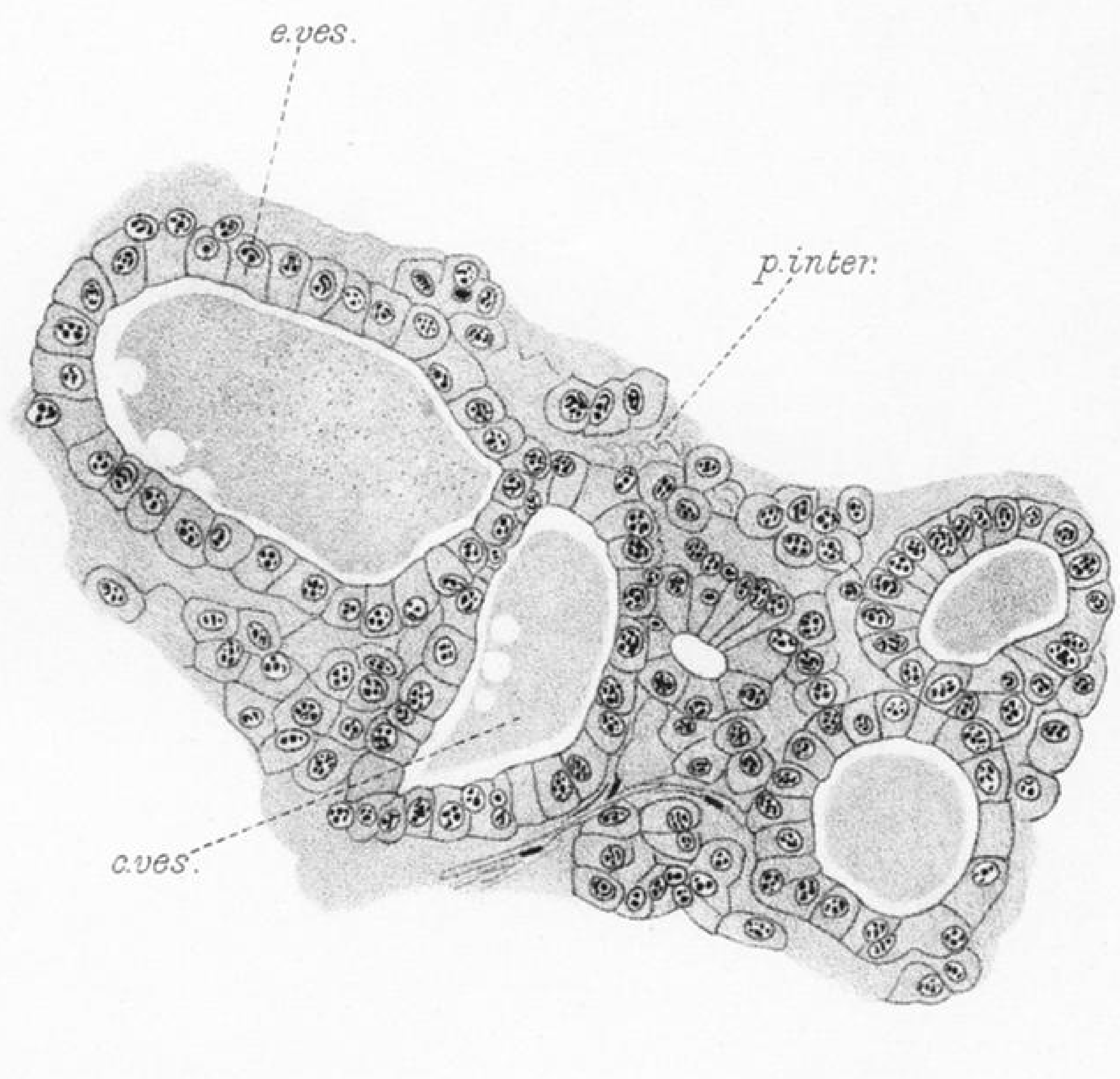

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PLATE 14.

Fig. 20.—Thyroid of normal dog. Preparation the same as fig. 19, viz., Flemming, iron hæmatoxylin.

Fig. 21.—Parathyroid of a dog, 83 days after thyroidectomy, showing vesicles, some of which contain colloid. ×120.

Fig. 22.—Thyroid of a dog, 32 days after removal of all four parathyroids. The vesicles have become very irregular in shape, and there seems to be an increase in the intervesicular epithelial tissue. ×120.

Fig. 23.—Small portion of the *pars intermedia* of the pituitary of a dog, which died some weeks after parathyroidectomy. The structure is practically indistinguishable from thyroid. Flemming; iron hæmatoxylin; high power; camera lucida.

Drawing reduced to $\frac{2}{3}$ of original size.