XXV. *The Minute Anatomy of the Thymus.*

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The following research was begun in the year 1876, and has been carried on at intervals since that time.

We will first give the result of this research in a brief preliminary statement; secondly, the history of the subject; and finally, a detailed account.

Preliminary Statement.

I.—*The cortex is the more important and essential part of the follicle of the thymus. In the cortex there are two kinds of retiform tissue—one (with small meshes), which we call a reticulum, formed of fine fibres with thickened nodal points; and the other, which we call a network, composed of branched connective tissue corpuscles.*

II.—*The formation of connective tissue and of new vessels occurs chiefly by the agency of granular cells; these granular cells arise from connective tissue corpuscles, and there is great similarity between the formation of the connective tissue in the thymus, and in pathological new formations.*

III.—*A concentric corpuscle usually arises, partially from the granular cells, and partially from the epithelioid connective tissue corpuscles; and the giant cells from either one or other of these sources. The concentric corpuscles are transformed into fibrous tissue.*

IV.—*The connective tissue corpuscles in the thymus of the Dog can undergo certain changes, which finally transform them into ciliated epithelial cells.*

V.—*In involution, the gland, diminished in size, though with enlarged blood-vessels, is transformed into connective tissue, and in Mammals is buried in fat.*

VI.—*The thymus arises, in the embryo, in connective tissue.*

VII.—*There are present in the lymph issuing from the thymus, cells containing coloured blood corpuscles and hæmoglobin granules; and in the lymphatics of the thymus there are more colourless cells than in the lymphatics of the neck.*

History.

An account of the knowledge and speculations of the old writers is given very fully by Haugsted (1),* Simon (2), and Friedleben (3); consequently this part of the history is dealt with very shortly in this paper.

* See the references, p. 1119.

RUFUS OF EPHESUS (4) first mentioned the thymus, and noticed that it cannot be found in all bodies.

GALEN (5) said that the organ has attained its greatest size in newly born animals, and diminishes after birth.

This view, that it decreases very rapidly after birth, seems to have been held from this time until the latter half of the seventeenth century; although MÖBIUS (6) noticed a thymus in the post-mortem examination of a man thirty years old.

GLISSON (7), 1671, found that it is large in children.

MANGETUS (8), 1717, said that the gland is very large in newly born children, but decreases during childhood.

VERHEYEN (9), 1726, was the first who definitely presented the fact that the thymus grows after birth. He said that it is larger in children some years old, than in those newly born.

HEWSON (10), 1777, said that the gland enlarges to the end of the first year; and since his time it has been generally accepted, that the growth of the gland is not terminated by the duration of fœtal life.

It was in the end of the seventeenth century that two anatomical statements were put forward, both of which delayed for a long time a more extended knowledge of this organ. One statement was as fruitful a source of physiological error as the other was of anatomical misconception.

In 1670, VELSCH (11), in the Alpine Marmot, confounded the fat glands and the thymus. This confusion between fat glands and thymus, which was a very natural one, was continued by HARDER (12), SCHEUCHZER (13), PALLAS (14), MECKEL (15), PRUNELLE (16), and TIEDEMANN (17). It was in consequence of this error that PALLAS (14) in 1778 compared hibernation to fœtal life. CUVIER (18) noticed that the thymus and other glands diminish the capacity of the chest in hibernating animals. In 1817, however, JACOBSON (19) showed that the glands in the thorax, which enlarge in the winter sleep, are not thymus; and that the thymus behaves in animals which hibernate, as in other animals; and maintained that the thymus has nothing in common with the peculiar glands lying in its neighbourhood, either in its development, appearance, or secretion. He was followed by RUDOLPHI (20) and HAUGSTED (1), the latter giving drawings of the two organs at various periods of life; and the facts were further confirmed by BARKOW (21) and others. SIMON (2), however, accepted the older doctrine, holding that the thymus is very large in hibernating animals, and he partially founded upon this supposed fact his view of the function of the organ.

The second error arose, as has been stated, about the same time. In 1673, BARTHOLINUS (22) asserted that the thymus contains a cavity; and a great part of many subsequent anatomical researches were taken up with the various accounts of this cavity, the openings into it, and other supposed facts about it. The existence of a cavity was accepted by HUGO (23), who worked with HALLER, by LUCAE (24), by

ASTLEY COOPER (25), and indeed by almost all anatomists, with the exception of BICHAT (26), BERRES (27), BISCHOFF (28), and GOODSIR (29), until we come to quite recent times, when the methods of hardening the tissue had so improved, that JENDRASSIK (30), and FRIEDLEBEN (3) had grave doubts of its existence; and BERLIN (31), KLEIN (32), and AFANASSIEW (33), asserted that the thymus contains no cavity.

WHARTON (34), 1659, noticed that in young Oxen which were put to the plough, the thymus disappears much sooner than in those at rest.

HALLER (35), 1766, thought that the thymus is not entirely changed into fat, but lost in fat. *"In adipe circumfuso sepelitur."*

HEWSON (10), 1777, first described the thymic corpuscles, and found that in size and shape they exactly resemble the central particles in the vesicles of the blood; he attributed to them the destiny of becoming nuclei for the vesicles of the blood. He tied the lymphatics of the thymus of the Calf and the Dog, and found that they contain a great number of small colourless solid particles, such as are found in the fluid of the lymphatic glands. He suspected that the lymphatic vessels were possibly the excretory ducts of the thymus, and that the structure and uses of this organ are similar to those of the lymphatic glands, to which it may be considered an appendage.

BICHAT (26), 1803, said that the thymus is composed of a mass of little vesicles.

LUCAE (24), 1811, described the gland as divided into lobes, lobules, and alveoli (follicles). He noticed that the alveoli, when seen from the surface, have a polygonal area.

Sir A. COOPER (25), 1832, gave drawings of the lobes of the Calf's thymus, with the communicating vessel. (See his fig. I.) He found that the thymus consists of ropes, which can be unravelled, and which are disposed in a spiral manner; he thought he recognised two large absorbent vessels, which run down the cervical portions and terminate in the innominate vein.

HAUGSTED (1), 1832, confirmed JACOBSON'S (19) observation as to the difference between the fat glands and the thymus, and demonstrated most clearly the increase of size in the thymus after birth; giving drawings proving both facts. He noticed that if thin layers of the thymus of infants are viewed by transmitted light, the central part of the follicles is more pellucid. He found the supposed cavity in the thymus to be hardly present in health.

GULLIVER (36), 1842, noticed a somewhat similar fact to that which had been related by WHARTON (34), as he saw that, in overdriven Lambs, the thymus shrinks; but that if the animals are afterwards well fed, the gland fills out again. GULLIVER followed HEWSON (10) in considering that this organ provides germs for the tissues of the blood.

BISCHOFF (28), 1842, also considered that the function of the thymus is to form blood corpuscles.

OESTERLIN (37), 1843, first noticed that there are cells containing pigment in the thymus.

SIMON (2), 1845, wrote an elaborate essay, which obtained the ASTLEY COOPER prize ; he dissected many rare animals, having access to the collection of the Royal College of Surgeons. He gave careful and accurate accounts of the position of the thymus in many Mammals, and described its position for the first time in Birds, Reptiles, and some Amphibia, incorrectly, however, in the Frog. SIMON rejected the theory of HEWSON (10), and considered that "the presence of the gland is co-extensive with pulmonary respiration;" "that it secretes into a closed cavity;" that in most animals the secreted matter "presents itself in a fluid form;" in some animals in "the solid form of fat;" and that the gland "fulfils its use as a sinking fund of nourishment in the service of respiration."

BARKOW (21), 1846, in a monograph on hibernation, pointed out in his sixteenth chapter that it was known to ARISTOTLE and to MARTIAL, that hibernating animals are very fat. BARKOW maintained the difference between the thymus and fat glands, and gave a very accurate description of the position of the latter.

GOODSIR (29), 1846, found no cavities or reservoirs in the substance of the thymus. He asserted that the thymus consists of lobes, grouped around germinal spots, which derive material for the formation of the cells from arteries passing through them.

ROBIN (38), 1847, first noticed the thymus in the Fish.

HANDFIELD JONES (39), 1849–1852, noticed that the absorbent vessels of the thymus travel to glands in the anterior mediastinum. He found that the thymic corpuscles are not similar in appearance and structure to the colourless granular corpuscles of the blood.

HASSALL (40), 1849, said that the gland consists of a straight tube, with the follicles arranged around it in a spiral manner. He described the concentric corpuscles (which have sometimes been called the concentric corpuscles of HASSALL) as parent cells, containing several granular nuclei, each of which is surrounded by one or more concentric lamellæ.

After this time nearly every writer dwelt on the structure of the concentric corpuscles, and their opinions on that subject do not differ so very materially from those of later writers; but their views of the origin and functions of these bodies differ very widely.

We may distinguish three opinions as to the origin of the concentric corpuscles. (1) That they arise from the cells of the thymus, (*a*) by endogenous formation, HASSALL (40), WEDL (41), GÜNSBERG (42), BERLIN (31): (*b*) as a retrograde process, BRUCH (43): (*c*) in a similar manner to cancroids, VIRCHOW (44), VERNEIUL (45), and HIS (46), 1859 : (*d*) arising by a fatty metamorphosis of the thymic corpuscles, ECHER (47): (*e*) from the gland cells, with a super-imposition of amorphous substance, KÖLLIKER (48), 1854, and JENDRASSIK (30): (*f*) from the gland cells, after passing through a stage of epithelial cells, PAULIZKY (49). (2) That they arise from the blood vessels,

(*a*) in the same manner as the angiolithic sarcoma, CORNIL and RANVIER (50), or (*b*) from the endothelium of the vessels, AFANASSIEW (51 and 33). (3) From the remains of the epithelium, from which the thymus is originally developed, HIS (52), 1880, and STIEDA (53). KÖLLIKER (54), in 1863, said that they do not arise from gland cells. Their attachment to vessels was noticed by BERLIN (31), HIS (46), and PAULIZKY (49).

BRUCH (43), 1850, noticed that the outer cells of the concentric corpuscles are epithelioid in character. He did not believe that the gland cells are changed into fat cells, as SIMON (2) and many other authors had done; but found fat cells in the connective tissue surrounding the follicles.

ECKER (47), 1853, in a long paper, propounded the most definite and elaborate statements concerning the supposed cavity, comparing the thymus to an acinus gland. He thought that the gland consists of a central canal, closed at either end, into which, during its spiral course, many cavities open. He said that the vessels are outside the gland membrane. In describing involution, he found that points or streaks of fat pierce the gland tissue, while in the surrounding connective tissue the fat increases; that certain cells contain fat granules, and that there are intermediate forms between these cells and the concentric corpuscles, which he described as arising by fatty metamorphosis of thymic corpuscles. He noticed the occurrence of pigment in the thymus of the Tortoise. He proved that the organ discovered in the Fish by ROBIN (38) is the thymus. At nearly the same time as LEYDIG (55) he described the position of the thymus in the Frog. He failed to find any difference between the fluid in the lymphatic vessels of the thymus and in those of other parts of the body.

GERLACH (56), 1854, adhered to the view that cavities exist in the interior of the gland. He noticed that the vessel network is not so rich as had been imagined, and also that extravasations often occur in the central part of the follicle.

WEDL (41), 1854, thought that the concentric corpuscles are endogenous formations, and gave good drawings of the large granular cells.

KÖLLIKER (48), 1854, described the thymus as being formed of lobes, connected by a canal which runs spirally in the interior of the gland. On the inner side of this canal he found openings, each of which leads into a lobule. He stated that the acini are solid (the acini in his drawings are, however, the cortical parts of the follicles). He noticed vessels penetrating the alveoli. He did not think it probable that there is a direct formation of blood corpuscles from thymic corpuscles, as HEWSON (10) thought.

REMAK (57), 1855, described and figured ciliated cysts in intimate connexion with the upper part of the thymus of the young Cat. He compared them to the ciliated bladders of the mesogastrium of the Frog and the mesometrium of the Rabbit. He noticed a distinction between the cortical and medullary parts of the follicle. (See his plate 8, figs. 10*a*, 10*b*.)

LEYDIG (55), 1857, also described the position of the thymus in the Fish; he classed

the thymus with the lymphatic glands, and said that it contains a network like that of the PEYER'S patches.

JENDRASSIK (30), 1857, considered that the lobules are solid, for though he noticed in some cases a hollow running through the gland, he also found portions removed from the rest, in which there was no canal. He thought that the hollows arise by a softening process, and agreed with KÖLLIKER (48) that the vessels penetrate the follicile, as he noticed large veins in their centre. He concluded that the concentric corpuscles compress and obliterate the vessels, and that they are thus concerned in involution. He observed extravasations of blood, of which some were recent and some degenerated; and that degenerated blood corpuscles are found in the concentric corpuscles.

BERLIN (31), 1857, doubted if the concentric corpuscles are concerned in involution; he noticed that they are situated in the neighbourhood of the vessels, and thought the central cavity an artificial product, and that there is no change of gland cells to fat cells; he said that chromatin crystals are often found in the gland.

GÜNSBERG (42), 1857, found crystals of hæmatoidin in the thymus, and cells containing blood corpuscles identical with those that are met with in the spleen.

FUNKE (58), 1858, came to the same conclusion as HEWSON (11) and BISCHOFF (29) in regard to the function of the thymus, considering it an organ for the restoration of the morphological elements of the blood. He concluded that some of the gland cells are transformed into fat cells.

FRIEDLEBEN (3), 1858, who is the anthor of a valuable monograph, the labour of many years, found, in the thymus of the Calf, a central string in each cervical portion. He thought that there is no duct, and that the organ consists of closed follicles. In a postscript, however, he described hollows. He noticed that the richness of the vessels had been greatly over-estimated. He gave weights of the thymus during various periods of life, to prove that it increases up to the end of the second year. He noticed concentric corpuscles in the thymus of the fœtus, but did not consider them important factors in involution; he concluded that involution partly arises from the connective tissue pressing on the follicular wall, and partly from a fatty change of the contained tissue. In involution he noticed an increase in the size of the coats of the vessels; and imagined that this is due to a change in the nerves. FRIEDLEBEN quoted and confirmed RESTELLI'S (59) observation that the blood of the thymic vein, in Calves three to four months old, contains numerous elements of the thymus; and that the blood coming from the thymus has a marble-like appearance. He failed to notice any difference between the contents of the lymphatic vessels, and of the lymph vessels of other parts; and stated that the number of lymphatics is much exceeded by that of the veins. He removed the thymus in young animals as RESTELLI (59) had previously done, and found that the animals lived and increased in weight very rapidly, and that in the blood of these animals there were more colourless blood corpuscles than usual.

HIS (46), 1859, described, and gave very good figures of, the connective-tissue-

corpuscles, and the long threads forming the network. He considered that the thymus has a central thread, to which the lobules are attached; this thread consisting of artery, vein, lymphatic vessels, and central canal; that each acinus has a small hollow, and that all the hollows are in communication with a central canal. He gave figures showing the difference, in the follicle, between the cortical and medullary portions, drawing the latter as a dark round or oval space in the centre of the follicle; he concluded that the dark spaces are the central hollows. (See his figs. 20 and 17.) He said that all the lymphoid corpuscles show a ring of protoplasm around the nucleus, if they are treated with five per cent. phosphate of soda. HIS noticed that there are cells with pigment granules and with great red spheres like blood corpuscles, and that the concentric corpuscles are connected with the small vessels, often surround them completely, or rest on their points of division. He noted that the lymphatic vessels are in close approximation to the wall of the follicle. He tied these vessels as they leave the thymus and concluded that the corpuscles travel by these paths, although he had never seen any communication between the central cavity and the lymphatic vessels. He considers that the thymic corpuscles are changed into blood corpuscles; in describing the circulation he gave drawings of the thymus after it had been injected from the arteries and the veins, and found that the arteries run into the centre of the follicles, and ramify outwards, and that the larger veins are on the outside.

MELCHIOR (60), 1859, in his dissertation dealt chiefly with the pathology of the thymus.

TURNER (61), 1860, noticed a thymus in an adult Porpoise and in an adult Antelope.

HIRZEL and FREY (62), 1863, wrote on the hibernating gland. They noticed the fact that if these glands are exposed to the air they assume a dark red-brown colour.

KÖLLIKER (54), 1863, adhered in great measure to his former view. He described the star-shaped cell network in the follicles, and noticed large cells with multiple nuclei. He confirmed the fact observed by HEWSON (10) and HIS (46), that the lymphatic vessels contain very many corpscules, similar to those of the thymus, and described the simple concentric corpuscles as having a granular mass in their interior; he did not think that they arise from the gland cells.

PAULIZKY (49), 1863, compared the concentric corpuscles to the corpora amylacea. He adhered to the view that the elements undergo fatty degeneration. PAULIZKY'S drawings of the concentric corpuscles and of the granular cells are very good. He noticed, as REMAK (57) and JENDRASSIK (30) had previously done, that the concentric corpuscles are found in the central parts of the follicles; he thought that they are pathological formations, arising from epithelial cells; these epithelial cells taking their origin from small round cells. He described and figured the vacuolation of the granular cells.

TOLDT (63), 1868, examined the thymus of Amphibia; he gave drawings of perivascular spaces around the vessels in the thymus of the Salamander.

KLEIN (32), 1870, noticed cellular elements in the capsule. He stated that there

are wide lymphatic spaces which invest the follicles; these communicate, by means of finer vessels, with the central part of the follicle. He gave the last blow to the idea that there are cavities in the thymus, and he found the individual follicles either entirely encapsulated or at times united. He described three kinds of networks in the gland: one, composed of anastomosing cells; a second, a narrow network with greater breadth of trabeculæ; and a third, formed of strong elongated fibres stretched between adjoining vessels. The cells enclosed in the network are small cells, similar to lymphatic corpuscles, large coarsely granular spheroidal bodies with one or more nuclei, and concentric corpuscles.

FLEISCH (64), 1870, in writing about the thymus of Amphibia, described and figured so-called ganglion cells; these were the granular cells already described by KÖLLIKER (54), and PAULIZKY (49), and figured by the latter.

HENLE (65), 1873, described the thymus, and appeared rather to lean to the older view, that the follicles contain cavities.

CORNIL and RANVIER (50), 1873, said that concentric bodies, calcified or otherwise, are often found in the thymus; these bodies hang from the vascular walls, and have the same origin as the angiolithic sarcoma—*i.e.*, they arise as hollow buds, which communicate with the lumen of the vessel, and growing, become pedunculated. The cellular elements are flattened, and arranged in concentric layers upon the wall of the vessel.

RAINEY (66), 1875, put forward some peculiar views as to the physiology of the thymus.

KRAUSE (67), 1876, described long spaces as existing in the gland, connected with one another: they are not canals, but connective-tissue spaces, filled by arteries, veins, lymphatic vessels, and nerves. The follicles are completely penetrated by blood vessels. The external vessels are radiating.

AFANASSIEW (51), 1877, said that the concentric corpuscles arise from the endothelium of the veins and capillaries; the endothelial cells increase by division, and fill the lumen. He found vessels in which the lumen was stopped up by the increase, and others where the endothelium was concentrically arranged. He noticed blood corpuscles in the interior of the concentric corpuscles; and also said that the walls of the vessels are often thickened, and can beget the capsule-like formations. He quoted the monograph on the development of cancer by KÖSTER, who said that concentric corpuscles in carcinoma are derived from the endothelium of the lymphatic vessels.

In a *second paper*, AFANASSIEW (33) found that the periphery of the follicles is clearly bordered, and that the central parts run into one another. In describing the network, he said that it is not formed of cells, except in the embryo; but that flat connective-tissue cells lie on the nodal points of a reticulum. There are lymphatic vessels in the interfollicular tissue, and they spread out into the follicle, in the direction of the blood vessels. The lymphatic vessels, leaving the thymus, run to lymphatic glands in the mediastinum and in the neck. He found that coloured and colourless

blood corpuscles escape from the vessels, and thus an increase of connective-tissue is set up; the new tissue presses on the concentric corpuscles, which gradually fade away, and thus few of them remain in the later stages. He injected the concentric corpuscles in five cases, and said that the smallest are in size and form similar to sympathetic nerve ganglia. Involution is produced by the decay of the vessels; yet the presence of the concentric corpuscles is an expression of regressive metamorphosis. He found much pigment in the thymus of the Hedgehog; and in certain Mammals, round cells containing one or more coloured blood corpuscles. There is a fatty granular formation in the glandular elements; and fat arises in the pigmented cells, which are divided from the rest of the thymus by the bundles of connective-tissue running into the follicle; the pigmented cells are very like those of the hibernating gland.

DAHMS (68), 1877, noticed a difference, in stained sections, between the outer and inner parts of the follicles, in animals of all ages; but thought the difference due to condensation of the glandular elements at the periphery of the follicle. She considered that the centres of the concentric corpuscles are filled by two or three spherical cells, but that they are formed by lymphoid cells; and she found that there are more concentric corpuscles during involution than at other times.

WATNEY (69), 1878, in a short note, showed that the follicles consist of two parts, which differ in the character of their network, and of the cells contained in their meshes, and in the arrangement of the blood vessels. He described granular cells, which help to form, partly by a process of vacuolation, the concentric corpuscles. These granular cells are attached to the blood vessels, and to the trabeculæ. He found giant cells in the medulla, and stated that the concentric corpuscles are concerned in the formation of vessels and trabeculæ; and that in fresh preparations colourless cells are seen, which contain granules and spherules of hæmoglobin.

KLEIN (70), 1879, confirmed the fact of the existence of a cortical and medullary portion in the follicle. He said that in the medulla there are large endothelial cells, each of which fills up a mesh of reticulum; and there are transition forms between these and the granular cells, and between these last and giant cells.

KLEIN (71), 1881, found that the thymus does not much vary in the young and in the adult Guinea Pig.

WATNEY (72), 1881, in a second short note, stated that there is an increase of connective tissue during involution, inside and outside the follicle; that the cortical part of the follicle attains its greatest size at the period of the greatest activity of the gland; and that the granular cells are actively concerned in the formation of connective tissue. A network of connective tissue corpuscles and a reticulum were described as both existing in the cortical portion.

WATNEY (73), 1881, in a third short note, stated that the lymphatic vessels issuing from the thymus contain more colourless corpuscles than the lymphatic vessels of the neck; and that in the thymus of the Dog ciliated epithelium can be found, if the animal be over a certain age.

History of the views concerning the development of the thymus.

This part of the subject has been given separately.

HAUGSTED (1), 1832, found that the thymus appears in the ninth or tenth week in the human embryo, as a double organ.

ARNOLD (74), 1831 and 1837, thought that the thymus is developed from the mucous membrane of the respiratory tract, and that it arises nearly in common with the larynx and thyroid.

BISCHOFF (28), 1842, noticed the gland as early as the eighth week in the Mammalian embryo; he considered that it arises in connexion with the thyroid.

SIMON (2), 1845, described and figured the thymus as commencing as a simple hollow tube; the tube bulges at certain points, and gives origin to diverticula or follicles, and by the extension of this process of follicular growth, the thymus attains its bulk and complexity of structure.

ECKER, 1851–1859, in the 'Icones Physiologicæ,' gave drawings of the position of the thymus in the Chick on the nineteenth day of incubation, and in the embryo of *Squatina vulgaris.*

REMAK (57), 1855, said that the thymus is developed from part of the pharyngeal wall, and arises between the arches of the aorta; that in the front of the neck of the Chick there is a gland which disappears very rapidly. He found that it has near relations to the thymus, although the one is not developed from the other; he accepted ECKER's view of the position of the thymus in the neck of the Chick.

FRIEDLEBEN (3), 1858, found that the gland is not formed originally as a tube, but that it appears as a connective-tissue stroma, in which round nuclei are imbedded. This stroma multiplies on all sides; the capsule then shows traces of blood vessels.

ROBIN (75), 1874–1875, said that by the successive invaginations of the internal folds (? of the hypoblast) the epithelium of the pharynx, of the œsophagus, of the trachæa, and of the lungs is formed; and that the thymus and the thyroid are produced in the same manner.

AFANASSIEW (33), 1877, found that the thymus is developed in the Chick at the end of the fifth or sixth day of incubation in the reticular connective-tissue, which lies behind and outside the vessels, as masses of indifferent cells. In a fœtal Rabbit, one-fifth of an inch in length, he saw the commencing thymus in the connective-tissue in front of the carotid artery, as a heaping up of indifferent cells.

DAHMS (68), 1877, thought that the thymus arises as a mass of agglomerate little rounded bodies around a clearer part; that in some cases there is a canal in the very early stage; and that there is an invagination of the mucous membrane of the respiratory tract.

KÖLLIKER (76), 1879, said that it arises, as an epithelial organ, from the branchial clefts; he gave a drawing of a cross-section of the gland, in its earliest stage of development, showing a central canal. The canal is lined by many layers of epithelial cells.

The cells become gradually smaller and less distinct, until at length they look like round nuclei, and have lost their epithelial character; at the same time there is an ingrowth of vessels and connective-tissue in the thick wall of the organ. As regards the further development of the gland, KÖLLIKER agreed with the views of SIMON (2).

Besides the thymus, he found in embryoes of fifteen, sixteen, and seventeen days, an accessory thymus as a double organ between the œsophagus and the trachæa; this organ showed hollow spaces and vessels in the embryo of seventeen days old. In an embryo of fourteen days he found another organ like a thymus before the first arch of the aorta. In an embryo of sixteen days, he found the lateral part of the thyroid consisted of two parts—one was in its usual place, the other on the side of the carotid, and behind the upper end of the thymus.

HIS (52), 1880, gave drawings of closed rings of epithelium, which he said probably form the thymus. In a footnote he said that the acinous form of the gland is thus explained; that the adenoid tissue arises from the surrounding connective-tissue, and that the concentric corpuscles are the remains of the epithelium.

STIEDA (53), 1881, examined the thymus of many young Mammalian embryoes; he demonstrated and figured the thymus as arising from one of the branchial clefts (probably the third) as a hollow epithelial tube; around this tube there is a connective-tissue envelope, and between these two adenoid tissue is developed. He found it impossible to trace the epithelial elements; but he thought that the concentric corpuscles and the large cells are the remains of the original epithelial layer.

Opinions of various authors concerning the so-called plasma cells.

WALDEYER (77), in 1875, described cells with coarse granules, which are often found near the blood vessels; they are easily transformed into fat cells; he called them plasma cells.

FLEMMING (78), in 1876, found that plasma cells are more numerous in some animals than in others; he did not deny that they form fat cells, but he thought that they much resemble atrophied fat cells.

EHRLICH (79), 1877, used an aniline dye, *dahlia,* to trace out the plasma cells; he found that they do not contain fat; he noticed them, among other places, in the thymus of the Calf, where they have the form of lymphoid cells.

LÖWE (80), 1878, considered that the granules in the plasma cells are not fat granules, but the precursors of fat.

EHRLICH (81), 1879, showed that the cells, all classed by WALDEYER as plasma cells, are probably not all of a similar nature; he considered that certain of these cells should be classed separately; they are characterised by their containing granules which are very readily stained by aniline dyes.

There have been two other papers on these subjects by WESTPHAL (82) and SCHWARZE (83), neither of which I have been able to obtain. The last author said

that certain granular cells occur in the blood and in the organs which form the blood; and that the granules in these cells are neither fat nor hæmoglobin.

The Methods used.

(*a*). To tease up the tissue in saline solution, either in the fresh state, or after leaving small pieces some hours in $\frac{1}{10}$ per cent. osmic acid; another method is to immerse small portions in a dilute solution of bichromate of potash, to which a considerable quantity of watery solution of eosin has been added; the pieces were usually left in the solution from twenty-four to forty-eight hours, at times from one to three weeks; and were then teased in saline solution and mounted.

(*b*). To make sections of the thymus. For this purpose the tissues were hardened in one of the following ways: (1) for ten days in $\frac{1}{6}$ to $\frac{1}{4}$ per cent. chromic acid, and then in 50 per cent. alcohol for two days, and afterwards placed in strong methylated alcohol; (2) in 2 per cent. bichromate of potash for weeks or months, and then in alcohol; (3) in chloride of gold for some hours, and then in chromic acid, and subsequently in alcohol; (4) in equal parts of $\frac{1}{2}$ per cent. osmic acid, and $\frac{1}{5}$ per cent. chromic acid, from ten to fifteen days, and then transferred to alcohol; (5) in methylated alcohol.

The sections were, except in a few instances, stained in hæmatoxylin, and mounted in Canada balsam; some of them were shaken in a test tube, from twenty minutes to four of five hours, before being mounted.

It was found that to shake out the smaller cells, a two rigid hardening of the tissue was Preudicial.

Staining by means of hæmatoxylin extract.

It has long been known to those who have used a watery solution of extract of hæmatoxylin and alum (one part of the extract to three of alum, as recommended by Professor Arnold (84) and Dr. Klein (85)) that in certain cases the resulting fluid is purple, at other times blue, and occasionally red. The red solution gives a disagreeable colour to the sections, and also stains very slowly.

In working with various microscopical specimens of the thymus, it was found, how[illegible] tissues were well stained by the red solutions, and others readily by the blue. It has been my custom in many cases to double stain the specimens, using first a red solution of the colour of Plate 86, fig. 22, *c*, and deepening the staining of the specimen, and making parts of it purple-blue by a solution of the colour of Plate 86, fig. 22, *e*.

The method adopted is to leave them in a rather strong solution of *c*, from sixteen to eighteen hours. They are then washed and placed in a weak blue solution, from four to twenty-four hours. It is necessary to use the red fluid of such a strength that it will not change to blue, even during three or four days' exposure; and to insure this it is better to use it rather strong, as all weak solutions are more liable to turn

blue. It is also better to keep the red solution very strong, and to filter a few drops of it into a watch-glass of water to the required strength each time it is used, as all filtering tends to turn the solution blue, especially if a clean dry filter-paper is used; and the filtering of weak solutions is prejudicial to the red colour. The blue solution is used with more water, because the weaker the colour the bluer the specimen.

Specimens of thymus treated in this way will, in most cases, show double staining; the difference of colour, it is true, is not much marked, but still is quite sufficient to clearly distinguish the cortical from the medullary part of the follicle (see Plate 83, figs. 1, 2; and Plate 84, fig. 3), or to stain the granular cells of the thymus, and the surrounding protoplasm, of two distinct colours (see Plate 85, fig. 8).

The red hæmatoxylin stains the connective-tissue, and the protoplasm of the connective-tissue-corpuscles and of the granular cells, and the walls of the vessels; while the blue deeply stains mucus, almost all nuclei, the reticulum, and the lymphoid corpuscles.*

As a rule, if only a single staining is used, the solutions which are of a purple colour are much the best; the red hæmatoxylin solutions do not stain deeply enough, though specimens stained by them bear high powers well. The blue solutions leave the protoplasm of the cells almost uncoloured; and the dark colour of the nuclei, and of the lymphoid cells, prevents the other features of the specimen from being wellseen, in fact such specimens are very unsatisfactory.

The difference in colour of the hæmatoxylin solutions depends almost entirely on the alum which is used in making them. It is true that the different woods give a slightly different extract, but the variation between the extracts, whether they are made from Campeachy or Jamaica, Honduras or St. Domingo woods, is so slight as not to be of any real importance. The alum by keeping becomes more acid, and acid, as is well known to chemists, turns the blue colour of hæmatoxylin, red. The most intensely blue colour is obtained by using freshly-prepared dried alum, while old powdered crystals of alum (potash alum) give a most decided red or even a yellow colour. The proportion of alum to the hæmatoxylin extract is also somewhat important. If the proportion sinks below three of alum to one of extract, the red colour will probably be seen; but, in that case, the staining properties will not be so good. Any amount of alum, above three of alum to one of extract, appears to [illegible] little difference to the colour. To show the difference between the solutions when different alums are used, see Plate 86, fig. 22. The solutions whose colours are represented by *a*, *b*, *d*, *e*, *f*, were all made with the same extract of hæmatoxylin, on the same day, and with the same proportion of alum to extract, one of the latter to three of the former.

* The words "lymphoid corpuscles" are used in this paper in reference only to the smaller thymic corpuscles, such as are figured in Plate 92, figs. 72, 73, 74, 75, and 76, as the

Staining by means of extract of Brazil wood.

This extract is treated with alum, in the same manner as that from hæmatoxylin woods. The colour is very beautiful, and varies from dull red to carmine, according to the character of the alum used in making the solution. The extract stains in much the same manner as hæmatoxylin, and can be used with it as a double staining. There are three kinds of wood in the English market called Brazil wood, *i.e.*, Lima chips, Sappan wood, and Brazil wood. They all contain a staining substance: Brasilin, which changes from yellow to red, as hæmatoxylin changes from yellow to blue.*†

GENERAL OBSERVATIONS.

The thymus was examined in the human fœtus and the Child, and in the following animals: the Hedgehog, the Cat, the Dog, the Lamb, the Calf, the Ox, the Alpine-Marmot, the Rat, the Guinea Pig, the Rabbit, the Pelican, the Turkey, the Pigeon, the Chick, the Alligator, the Snake, the Tortoise, the Frog, the Axolotl, the Cod-fish, and the Ray-fish.

The thymus first appears in early embryonic life. It increases rapidly in size during the life of the embryo, and during the early part of the growth of the animal. The time at which it ceases to enlarge, and the duration of its involution, differ considerably in the different classes of Vertebrates, and in the different species. In Mammals it decreases slowly, does not get much smaller until adult life, and does not finally disappear until some period of adult life has passed.‡ In Birds it has in most instances disappeared before adult life, and the same is true of the thymus of the Frog. In the Tortoise and the Ray-fish the thymus is very large in large specimens, as in a Ray three feet five inches wide; however, in the large Rays the thymus has been in a great measure transformed into connective tissue.

The involution has been traced in the Ox, Cat, Dog, Guinea Pig,§ Bird, Tortoise, and Ray-fish.

The position of the thymus varies much in different animals, and has been carefully described by SIMON (2), LEYDIG (55), AFANASSIEW (33), and others; so that there is no need to say any more, than that in Mammals it is found either in the thorax on the pericardium, as in the Dog; or in the neck, as in the Guinea Pig where the follicles are contiguous to the salivary gland; or extending from the pericardium to the thyoid, as in the Child; or even nearly to the angle of the jaw, as in the Calf. In Birds, it

* See FLÜCKIGER and HANBURY 'Pharmacographia,' p. 216, 2nd edit., 1879.

† I have to thank Messrs. HEARON and SQUIRE, and Messrs. LESCHER and EVANS, for taking considerable trouble to procure me the various hæmatoxylin and Brazil woods.

‡ It is in consequence of the want of this knowledge that it has been described by many observers as being permanent. I have seen a thymus in a man fifty years old.

§ There is some difficulty in obtaining old Guinea Pigs, as it is difficult to ascertain the ages of the animals; and the breeders usually have no knowledge of the age of any given animal.

is found on each side of the neck, at the back of the jugular vein (see Plate 87, fig. 29); in the Reptile, lying on the vessels near the base of the heart, as in the Alligator or the Snake; or situated near the carotid artery, as in the Tortoise; in Amphibia, at the back of the angle of the jaw; in the Ray-fish, lying behind the spout cavity, and between the gills and the muscles of the back (see Plate 84, fig. 5, *Th.*).

Its appearance in Mammals is always the same—*i.e.*, a grey white mass divided up into lobules and follicles. In the Bird, it appears as an elongated mass, which to the naked eye contains a central band, on which the follicles are arranged; in the Reptile, as a small oval pale yellow mass, a little whiter than the fat of the animal; in Amphibia, as a white oval body; in the Ray-fish, as a grey-white triangular mass, very soft in texture, but in the adult animal showing the individual follicles to the naked eye.

In the following pages, the thymus, as it is found in the Mammal, will be described; and afterwards the various differences and points of agreement between the thymus of the Mammal and that of other Vertebrates will be pointed out.

The thymus is surrounded by a connective-tissue envelope; this covering sends in membranous projections, which penetrate between the separate lobes, and to a very great extent between the lobules; and penetrating into the lobules, mark out the division into follicles (see Plate 83, fig. 1). In the connective-tissue run the blood and lymphatic vessels, and a few nerves.

If we attempt with the scalpel and forceps to divide up the thymus, and select the thymus of the Calf, as being from its great size the easiest to deal with, it will be found that we can easily separate the gland into lobes, and these again into smaller lobes. In the lobes, the lobules are marked out to the naked eye, especially in portions of the gland which have been allowed to lie for some hours in 2 per cent. bichromate of potash. They are generally four-sided, and somewhat pyramidal in form (see Plate 87, fig. 24). The attempt to separate the lobes into lobules is not however always successful, as though some lobules are unconnected, in most cases they are attached to one another or to a central string which runs up the cervical portion of the thymus, as was known and depicted by various authors including Sir A. COOPER (25). This central string consists of connective-tissue and of blood vessels. The lobules are seen by the naked eye to be composed of follicles, but it is not possible to separate the individual follicles, as they are almost always attached to one another (see Plate 83, figs. 1, 2; and Plate 84, fig. 3).

ANATOMY OF THE FOLLICLE AS A WHOLE.

The follicles are, in the fully-developed thymus, chiefly of a polygonal form (see Plate 83, fig. 1). As, however, they are usually attached to one another, their forms are somewhat various. In some cases, compound branched follicles are met with (see Plate 83, figs. 1, 2; and Plate 84, fig. 3).

The follicles, except in earliest embryonic life, are composed of two parts, a cortex and medulla, which, as we shall see, differ very materially in structure. The difference between the two parts can be seen by the naked eye in a thymus which has been left for two or three weeks in bichromate of potash or monochromate of ammonia. In sections made from hardened tissues and stained in hæmatoxylin, this difference is easily seen (see Plate 83, figs. 1, 2; and Plate 84, fig. 3), and depends on two main facts: the first, that the concentric corpuscles, the giant cells, the granular cells, the numerous endothelial connective-tissue-corpuscles (together with the large vessels and fibrous-tissue met with in certain states of involution) are found, with few exceptions, in the medulla, and that therefore there are necessarily much fewer lymphoid corpuscles in that part of the follicle; the second fact is, that the reticulum is but rarely met with in the medulla, while it surrounds nearly every lymphoid corpuscle in the cortex; and the preponderating presence of these two deeply staining bodies, the lymphoid corpuscles and the nodal points of the reticulum, causes the cortex to assume a much darker and bluer colour in preparations stained by logwood. In some follicles there are seen to be two or even three medullary portions (see Plate 83, fig. 1, *c*).

The follicles are sometimes united by cortical-tissue (see Plate 83, figs. 1 and 2, *a*), and at other times by medullary-tissue (see Plate 83, figs. 1, 2; and Plate 84, fig. 3, *b*). These follicles, when united by medullary-tissue, may sometimes be spoken of as compound follicles (see Plate 84, fig. 3, *b*).

It will be noticed that processes of the connective-tissue penetrate the follicle in a radiating manner (see Plate 83, figs. 1 and 2, *c′t′*). These processes often contain somewhat large vessels (see Plate 85, fig. 6, V′), and thus the medulla is in contact with the surrounding connective-tissue and vessels; and it is not necessary for the vessels to pass through the cortical lymphoid tissue in order to reach the medulla.

In the embryonic state, the upper part of each half of the thymus may be said to consist of one follicle (see Plate 87, fig. 23). This is not at first differentiated into cortex and medulla, and the differentiation does not occur until the follicle is divided up by connective-tissue, as will now be described. The blood vessels penetrating into the follicle from the outside, pass in, surrounded by connective-tissue; and by the ingrowth of this connective-tissue, the original follicle is divided into a considerable number of follicles (see Plate 86, fig. 11).* The follicles increase in size, and are each divided, and thus the thymus is formed of a large number of follicles, partially or wholly separated from one another; these follicles forming lobules, which are often united. During the ingrowth of this connective-tissue, the blood vessels increase in size. This process goes on during the whole growth of the thymus, and the follicles increase in size and in number. Although the connective-tissue is constantly ingrowing, the bands of connective-tissue, in the fully-developed thymus, are very thin (see Plate 83, fig. 1).

* This description applies to the development of the thymus, except in its very earliest stage; this will be described under the head of "Development."

The very same process by which the thymus is separated into follicles, and by which the follicles are multiplied in number, is also at work during involution; only then, although the connective-tissue penetrates further into the follicles, and the blood vessels enlarge, the follicles do not increase in size; on the contrary, they diminish, and thus the follicles are split up and surrounded by connective-tissue (see Plate 86, fig. 10); and the connective-tissue increasing, the follicles are finally left as islands imbedded in it (see Plate 84, fig. 4).

On examination of Plate 83, figs. 1 and 2, and Plate 84, figs. 3 and 4 (representing tissues treated exactly in the same manner and magnified to the same number of diameters) which are made specially to point out the appearances of the follicles at various stages of development and involution, it will be seen that the foregoing description is quite correct; for while in Plate 83, fig. 1, the ingrowing processes of connective tissue are quite fine, in Plate 83, fig. 2, the cortex is divided by broader bands. These bands in Plate 84, fig. 3, are still larger, and the cortical portions are still further separated from one another; and it will be also seen that the follicles have, during the process of involution, become considerably smaller; and this in two ways, one of which is only indicated in the drawings, namely, by the invasion of the medulla by connective-tissue, while the other is clearly shown, by the great shrinking both in breadth and thickness of the cortex. It will be seen in Plate 84, fig. 4, that finally the medulla becomes converted almost entirely into connective-tissue, and the cortex shrinks to thin lines of tissue.

In Mammalia this connective-tissue surrounding the follicles, and even that penetrating them, becomes, during involution, a bed for the deposit of fat cells, as will be described further on (see Plate 83, fig. 2; and Plate 84, figs. 3 and 4); but this deposit of fat does not occur in the other classes of Vertebrates, and therefore should not be insisted on as a main factor in the involution of the follicle, as has been done by so many authors; indeed, in the Bird, where the thymus disappears so early, there is no formation of fat.

The cortical part of the follicle is, as has been already stated, not differentiated from the rest of the follicle at an early period of the existence of the organ (see Plate 87, fig. 23); and when first differentiated in the fœtal thymus is not of very great extent (see Plate 86, fig. 11). In the fully-developed thymus (as in Plate 83, fig. 1) the cortex is seen to be at least twice the size of the medulla. On the other hand, as the follicle undergoes involution, the cortex shrinks more rapidly than the medulla (see Plate 84, fig. 3). The cortical part of the follicle consists in a very large measure of lymphoid cells, and it will be shown afterwards that these cells leave the thymus by the lymphatics. Although the medulla contains some lymphoid cells, it also contains other elements not peculiar to the thymus (or the lymphoid tissues), as the granular cells, giant cells, and fibrous tissue.

Briefly stated, the cortex is much larger in the fully-developed organ, and undergoes involution more rapidly than the medulla. It is composed almost entirely of

lymphoid cells, such as are found in the lymphatics. These considerations point out that *the cortex of the follicle is the more important and essential part of the thymus.*

The Lymphatics of the Thymus.

The capsule of the follicle surrounds the cortical portion, separating the cortical-tissue from the projections of interfollicular-tissue, such as are shown at *c′t′*, in Plate 83, figs. 1 and 2 and Plate 86, fig. 10. In sections of the thymus, the capsule is seen to be composed of endothelial cells; blood vessels penetrate it obliquely, and, supported by it, enter the follicle (see Plate 87, fig. 25). The capsule in certain stages of involution contains much fibrous tissue and some cells; but in the majority of cases it appears as a double membrane, whose outer wall is also the wall of a lymphatic space. These lymphatic spaces contain many thymic corpuscles. It is however possible that some of these cells have passed into the lymphatic spaces in making the specimen.

It was not found possible to discover any lymphatic vessels in the follicles, and none can be shown to exist in the cortex of the follicle during the period of the full development of the gland; as no lymphatic vessels can be seen in sections, and there are no perivascular sheaths to the vessels (see Plate 87, figs. 25 and 26). In the medulla many of the vessels, even in the early stages of the growth of the thymus, have perivascular sheaths; and during involution almost all the vessels of the medullary portion (see Plate 94, fig. 96) and many even of the vessels of the cortex, are surrounded by perivascular spaces. These spaces may act as lymphatic vessels. It is seen from the foregoing description that the cortical part of the follicles—the more important part—has nothing which can serve as a lymphatic vessel, during its greatest development, except the lymphatic space on the outer side of the capsule.

The course of the lymphatics issuing from the thymus was traced in the Calf. The young animals were killed by chloroform, and, as soon as dead, a small quantity of a saturated solution of indigo-carmine was injected by puncture into the thymus, the small wound in the skin was closed up, and the animals were left for half-an-hour. It was found that the indigo-carmine solution passed into the lymphatic vessels, travelled along them, and marked them out, so that they could be easily followed by careful dissection.

In the neck part of the thymus the blue fluid is seen to leave the organ by a number of small vessels running by the side of the minute veins. These small lymphatic vessels form the afferent vessels of small glands lying in the neck on each side of the thymus; from these glands the efferent lymph-vessel runs down the neck, not far from the large lymphatic trunk, but never joins it, and can be traced to two other lymphatic glands lying on the trachea, close to its point of entrance into the thorax. It will be noticed that the lymphatic vessels do not run longitudinally in the gland, and that there is no large lymphatic vessel running at the back of the isthmus of the thymus, as described by His (46).

The indigo-carmine solution, if injected into the thoracic portion of the thymus, can be traced to lymphatic glands lying in the thorax, generally to one gland lying on the arch of the aorta, and from thence to the large veins on the left side. There seems to be no intercommunication between the lymphatics of the thorax and of the neck.

The Blood Vessels.

The most noticeable fact about the blood vessels of the thymus, in an injected specimen (see Plate 85, fig. 6), is the disposition of the large vessels in two rings :—(1) They, to a great measure, surround the follicle, more so, usually, than in Plate 85, fig. 6 ; and (2) form nearly a complete circle on the margin of the medullary portion of the follicle. This latter circle is not, however, outside the medulla, but situated within it, or just on its borders. This disposition of the vessels is true of all cases where the follicle is polygonal, and contains one medullary centre. Where there are two medullary portions there are two central rings of vessels, or if the medulla be in the form of long processes, the surrounding vessels run longitudinally. The ring of vessels surrounding the follicle is composed of arteries and veins, which give off or receive branches from two neighbouring follicles. The inner circle, or circles, is also composed of arteries and veins, but chiefly of the latter. The cortex is thus surrounded by large vessels running parallel to its inner and outer surfaces, and is chiefly supplied with arterial blood from the outer circle of vessels, while the inner circle collects the venous blood from the cortex and from the medulla. In the cortical portion fine capillary vessels are met with, the majority of which run in a radiating manner from the exterior inwards. There are, however, a few vessels penetrating the cortex from the arteries in the medulla, and sometimes vessels from outside run in loops, and join the veins on the outside.

The medulla, in injected specimens of the thymus, is more vascular than the cortex, on account of the ring of large vessels which it contains. The blood supply of the interior of the medullary portion varies as follows : When the thymus is in a state of growth, or during full development, the vessels in the interior of the medulla are few and fine, there being often one or more small central arteries; those parts of the medulla which contain the granular cells and the concentric corpuscles have very few and only small vessels (see Plate 85, fig. 6). In the thymus during involution, on the contrary, the vessels of the medulla are numerous and very large, often surrounded by connective tissue, and have perivascular sheaths. The large veins of the medulla, as has been described, pass out of the follicle in the bands of connective tissue which invade the cortex (see Plate 83, figs. 1 and 2; and Plate 85, fig. 6, V′), and help to form the large veins running between the follicles.

Extravasations take place in injected specimens if the pressure used is at all high. These extravasations occur only in the medullary portion; and the fluid, if it be carmine and gelatine, is found, as a coloured reticulum, between the cells.

In the early stage of development of the thymus, the blood vessels are quite small, and are found in the follicle and on its border (see Plate 87, fig. 23).

The relation of the blood vessels to the granular cells, concentric corpuscles, and network will be spoken of in treating of those tissues.

The Tissues composing the Cortical portion of the Follicle.

In thin sections of the cortex, the first feature which strikes the eye is the very great number of lymphoid corpuscles, which lie closely packed from the capsule to the edge of the medulla. They are seen to be supported by a delicate reticulum, that is, by a closely-meshed web, which is broadened at the nodal points. The meshes are very close, so that as a rule they are only large enough to enclose one lymphoid corpuscle (see Plate 85, fig. 9; and Plate 87, figs. 27 and 28). This reticulum encloses all the other tissues met with in the cortex, and thus resembles that which I have described in the mucous membrane of the intestine (see reference No. 86).

In specimens which are stained by hæmatoxylin, the difference in colour between the irregularly-shaped nodal points of the reticulum and the lymphoid corpuscles is not very great (see Plate 87, fig. 27), although the refractive powers of the two are very different. A great difference between the lymphoid cells and the nodal points is, however, noticed in specimens stained in indigo-carmine and carmine (see reference No. 87); for in this case the nodal points are stained of a blue-green colour, and the contained lymphoid corpuscles, red (see Plate 85, fig. 9).

In sections of the cortex which have been shaken, and in which the lymphoid cells and the reticulum have been washed away, we have, stretching from the capsule of endothelial cells, a network (1) of connective-tissue threads (see Plate 87, figs. 25 and 26, *th*), (2) of capillary blood vessels, and between these vessels and threads, but attached to both, a delicate but widely-meshed network, composed (3) of branching cells with long fine delicate processes (see Plate 87, fig. 25). This cell network forms an adventitia to the vessels (see Plate 87, figs. 25 and 26), and the connective-tissue threads with the network of branching cells form only one network.

This network of cells differs in two respects from that found in any other lymphoid tissues of the body. In the first place, it is a permanent network of cells—*i.e.*, it is not like that found in the follicles of the lymphatic gland (only a network of cells during very early life, to be replaced afterwards by a non-nucleated reticulum), for it exists as long as the thymus, and can be found in shaken specimens of the thymus of adult animals, as for instance, in an Ox four years old. Secondly, the network is unlike any other network, the cells with their very fine branching processes being peculiar to, and characteristic of, the cortex of the thymus gland.

It will be seen that this network is not a reticulum of threads on which epithelioid cells lie, but that the processes of the connective-tissue-corpuscles, with the cell bodies, form the greater part of the network of the cortex. If the specimen be roughly shaken,

most of the cells and their processes will be shaken away (as in Plate 87, fig. 26), only those remaining which are attached to the blood vessels, and thus have a firm support.

The nuclei of the connective-tissue-corpuscles, forming the network, and of the endothelial cells of the blood vessels (see Plate 87, figs. 28 and 25) and the nuclei of the cells forming the capsule, are all similar in size and appearance; and in specimens stained in indigo-carmine and carmine, the branched connective-tissue-corpuscles, the blood vessels, and the connective-tissue threads, all stain of a red colour, and not like the reticulum, of a blue-green.

It will be seen from the foregoing description, and from Plate 87, figs. 25 and 27, *that in the cortex there are two kinds of retiform-tissue; one (with small meshes) which we have called a reticulum, formed of fine fibres with thickened nodal points; and the other, which we have called a network, composed of branched connective-tissue-corpuscles.* These are not to be considered as identical, nor as arising the one from the other, but are two distinct meshes lying one within the other.

The Tissues composing the Medullary portion of the Follicle.

The network of branched connective-tissue-corpuscles of the cortex is continuous with a network of branched cells in the medulla, but there is a considerable difference in the two networks (compare Plate 87, fig. 25, with Plate 86, fig. 18, and Plate 93, fig. 78). In Plate 86, fig. 18, the cells are larger than in Plate 87, fig. 25; they are joined together, not by very delicate, but by coarse, sharply-defined cell processes; and the body of the cell is also much thicker. Again, the spaces enclosed by the cell processes are not of an indefinite polygonal area, but are sharply defined, and nearly spherical (see Plate 93, fig. 78).

The connective-tissue-corpuscles forming the network are not, however, always met with as branching cells, but at times are close together, and then they have no processes, but lie side by side like an endothelium (see Plate 88, fig. 30, *c′t′*, and Plate 89, fig. 45 A, B, C). These latter will be called epithelioid cells. Further, in some places, the cells are so closely approximated that no trace of cell-division can be seen; and here we find masses of protoplasm, containing three, four, or numerous nuclei, not differentiated into cells (see Plate 88, fig. 30; and Plate 90, fig. 54).

The reticulum, which is so marked a feature of the cortex, is also found to a slight extent in the medulla (see Plate 88, fig. 31; and Plate 93, fig. 83), but in this part of the follicle it does not enclose all the other tissues in its meshes. It is only seen here and there, and gives the impression which would be made if the cells which it originally enclosed had multiplied, the reticulum itself not having increased; so that the reticulum is only seen at intervals, among the connective-tissue-corpuscles or the epithelioid cells.

The medulla, therefore, contains a network, formed either (1) of branched connective-

tissue-corpuscles, or (2) of epithelioid cells, or (3) of protoplasmic masses not differentiated into cells: and also contains a reticulum, which only occurs at rare intervals.

Besides these, there are many granular cells, giant cells, and concentric corpuscles, found in the medulla, each of which will now be considered.

Granular cells.

During the latter part of fœtal life, the medulla is studded in places with granular cells (see Plate 90, fig. 49), and during the remaining period of growth and involution these cells are present (see Plate 88, fig. 31). However, there are many more during the first period of involution than at any other time. They are more numerous in the Calf than in other Mammals, but they are found in all classes of Vertebrates, and in much greater number in the Mammalia and in the Frog, than in the Bird, Reptile, or Fish. They are easily recognised, in sections made from tissue hardened in bichromate, and stained in hæmatoxylin, as yellow masses with somewhat coarse granules; they are often found lying close together, arranged in bands, or in masses lying over one another in great numbers. They are not readily stained by the ordinary hæmatoxylin solutions, or by carmine, if the tissue has been hardened by chromic acid and alcohol. They are, however, stained very readily if the tissue has been hardened in osmic acid (see Plate 90, fig. 49), and are deeply stained by red hæmatoxylin solutions (see Plate 85, fig. 8).

These granular cells vary considerably in size (compare Plate 93, fig. 82; and Plate 88, fig. 36). In fresh preparations, their protoplasm closely resembles in appearance that of the giant cells of medulla of bone. In sections, some cells having very coarse granules are met with, close to others with much finer granules (see Plate 88, fig. 33, and compare figs. 33 and 34).

The granular cells may be divided, for the sake of convenience, into four varieties, although it should be clearly understood that there are intermediate forms.

They are found (1) as polygonal or rounded epithelioid cells, often lying in close approximation; the central part of the cell only is granular (see Plate 88, figs. 31 and 33); (2) as vacuolated cells, in this case the mass lying in the vacuole is granular (see Plate 88, fig. 32; and Plate 89, figs. 45 B, *va*, and 45 C, *va*); or (3) as spheroidal masses lying in cavities between the branching processes of the connective-tissue-corpuscles, as in Plate 88, fig. 30, and Plate 89, fig. 46 E; or (4) as club-shaped masses, attached to blood vessels and to newly-formed connective-tissue, as in Plate 88, figs. 35, 37, and 36, 38.

We will first consider the epithelioid cells which contain granular masses. They are well seen in Plate 88, figs. 33 and 31. The granular mass in the cells varies in size from quite small spheres (as in Plate 89, figs. 44 A, 45 A, *g*, and 41) to masses which nearly fill the cell (see Plate 89, fig. 44 F). When the contained granular mass is quite small the nucleus of the cell is nearly central (see Plate 89, figs. 44 A and 41), but as it increases in size the nucleus is forced to one side (see Plate 88, fig. 31), and

the nucleus occasionally divides, as some of these cells contain several nuclei (see Plate 88, fig. 31, *g*). Sometimes, but not often, the contained granular mass is nucleated (see Plate 89, figs. 44 D and E, and 45 A, *gr*). This form of granular cell might with equal reason be described as epithelioid connective-tissue-corpuscles containing granular masses; and presently, when we come to consider the origin of the granular cells, we must lay great stress on this variety. These cells are generally situated near to one or more concentric corpuscles or to giant cells (see Plate 90, fig. 49). Traces of a reticulum can be seen among them (see Plate 88, fig. 31, *r*).

The second kind of granular cells are those which are vacuolated, and contain granular masses in their interior. They are generally polygonal or spheroidal (see Plate 88, fig. 32; and Plate 89, figs. 45 B, *va*, and 45 C, *va*), and are found in most cases close to those of the first kind, and appear to arise from them, the clear protoplasm of the cell having shrunk away from the granular mass. These vacuolated cells are found in some animals, as in the Bird (see Plate 95, fig. 98), in greater numbers and of much larger size than in Mammalia. This vacuolation of the cell, as we shall see afterwards, is a process of great importance in the formation of concentric corpuscles in some animals, and in the formation of the ciliated cysts in the Dog.

If the vacuolation of the cell proceeds further the granular mass is set free, and can assume an independent existence.

We then have the third form of granular cell, as met with in Plate 88, fig. 30, and Plate 89, figs. 46 D and E. In the two latter figures the granular mass is also vacuolated. In Plate 88, fig. 30, we find large granular masses, enclosed in a network of connective-tissue; the granular masses may be considered as separate cells. In preparations of the thymus which have been shaken, we often meet with branched networks of connective-tissue-corpuscles, from which most of the granular cells have been shaken out (see Plate 93, fig. 78).

The fourth variety of granular cells are club-shaped or rounded, and are attached to the blood vessels and the connective-tissue trabeculæ (see Plate 85, fig. 8; Plate 88, figs. 37, 38; and Plate 92, fig. 69). They are evidently not merely lying in apposition to these structures, but attached to them; as shaking for a long time (three or four hours) does not separate this connexion. Those which are attached to the vessels sometimes appear to be entirely formed of a granular mass (see Plate 92, fig. 68, and some of the cells in Plate 88, fig. 37), at other times of a clear protoplasm, nucleus, and granular mass (see Plate 88, fig. 35; and Plate 89, fig. 43); the latter stains of a different colour to the nucleus (see Plate 85, fig. 8). The lumen of the vessels appears to be quite unchanged (see Plate 85, fig. 8; and Plate 89, fig. 43), and there are no extravasations in the neighbourhood, nor any other feature to indicate that these cells have passed out from the vessel. The vessels have at times, however, a considerable thickening of the adventitia (see Plate 88, figs. 35 and 37).

The granular cells attached to the connective-tissue trabeculæ are well shown in Plate 88, figs. 36 and 37, and Plate 92, fig. 69, *gr*. In Plate 92, fig. 69, there are

indications of the cells having a surrounding zone of clear protoplasm, for the nuclei are seen outside the granular mass; but in Plate 88, figs. 36 and 38, the granular masses are nucleated and constitute the whole cell. There is some resemblance between these granular cells attached to newly-formed connective-tissue, and osteoblasts attached to the edge of newly-forming bone; and this resemblance is not a deceptive one, for the granular cells are concerned in forming fibrous tissue, their processes are often seen to be fibrillated (see Plate 88, fig. 36), and the fibrillæ are continuous with those of the connective-tissue trabeculæ (see Plate 93, fig. 82). Sometimes the whole cell is directly transformed into fibrillated connective-tissue.*

The granular cells form blood vessels. They stretch across from vessel to vessel, forming bands of granular tissue. In most cases these slender bands of tissue become fibrous-tissue. To demonstrate the formation of new vessels, it is therefore necessary to select those granular bands stretching between the vessels, where one part of the band, or newly-forming vessel, is hollow, and the other part is still formed of a granular cell (see Plate 94, fig. 94) or of granular cells (see Plate 94, fig. 93). In the former case the vessel is intra-epithelial, and in the latter it is inter-epithelial.

From what do the granular cells arise? Their position near the blood vessels, their being massed in the medulla of the follicle, where at times extravasations take place, might suggest the idea that they arise from extravasated colourless blood corpuscles. However, that is not the case; and the figures given in the plates show that they arise from the connective-tissue-corpuscles. In Plate 89, fig. 45 B, some of the cells are epithelioid connective-tissue-corpuscles, others contain a granular mass in the centre of the cell. This transition of epithelioid connective-tissue-corpuscles to granular cells can also be seen in Plate 89, figs. 45 A and C (see also figs. 41 and 45 A, *g*), where there is a very small granular mass in an epithelioid cell. The same thing is shown by the series of figs. 44 A to F, in which various epithelioid cells are seen with larger or smaller granular masses in their interior. An argument might, however, be put forth, that the drawings would be equally explained by supposing that the granular cells are the first formed, and that they are afterwards transformed into epithelioid cells. This argument is answered very completely by the thymus of the Bird, where we find very many epithelioid, and very few granular cells (see Plate 95, figs. 100 and 101). The thymus of the Tortoise also contains many epithelioid, and very few granular cells.

Another origin of the granular cells which might be suggested would be either the giant cells or the concentric corpuscles. But there are two fatal objections to the view that either of these is the forerunner of the granular cells: first, that sometimes in the inner edge of the cortex solitary granular cells are seen (see Plate 89, fig. 39), and such solitary cells could not have arisen from either of these sources; secondly, that the granular cells are found in much greater number than would be the case if they took their origin from either the concentric corpuscles or the giant cells. Again, the granular

* The papers of ZIEGLER (89) and TILLMANNS (90), who described the formation of fibrous tissue in pathological new formations, by an exactly similar process, will be referred to afterwards.

cells met with in the cortex are usually attached to the connective-tissue network (see Plate 89, fig. 39, *a* and *b*).

The giant cells.

These appear to be capable of division into two kinds, which differ somewhat in their appearance, the period of life at which they are formed, and their probable origin.

In the fœtal thymus, giant cells are found in considerable numbers (see Plate 90, fig. 50). They are large, very granular, and multinuclear; they are met with near granular cells, and appear to arise from them; for in some cases we find granular cells of very irregular size and shape (see Plate 89, figs. 40 E and F, and 39 C and D); in other cases, granular cells containing two or three nuclei (see Plate 89, fig. 48; and Plate 90, fig. 49, *gr*); finally, we meet with preparations like those in Plate 90, fig. 50, *gr*, where a granular cell with three nuclei seems to be coalescing with other granular cells to form a giant cell.

In animals, during involution, when fibrous-tissue is present in the organ, giant cells are met with close to the newly-formed tissue. They are much branched; the branches lie in several planes (see Plate 90, fig. 56; and Plate 91, fig. 57). In other specimens we find giant cells containing granular masses in their interior (see Plate 90, figs. 51, 52, and 53). Others contain cavities or gaps looking something like the lumen of a vessel (see Plate 90, figs. 51 and 55). This form of giant cell seems to arise from the network of connective-tissue-corpuscles, and we can trace the transition from masses of protoplasm containing many nuclei, to these giant cells. In Plate 88, fig. 30, at the left side of the figure, there are masses of protoplasm containing large granular cells. In Plate 90, fig. 54, is seen a newly-formed band of connective-tissue, *ct*, and at right angles to it, and above it, multinuclear masses of protoplasm containing oval gaps. These masses of protoplasm in Plate 90, fig. 54, appear to be intermediate forms between the branched network of connective-tissue-corpuscles and the giant cells, and to account for the manner in which the gaps are formed in the giant cells, and for the presence of granular cells in the giant cells.

Concentric corpuscles.

The appearance of the concentric corpuscles, when large and fully formed, is very peculiar (see Plate 91, figs. 59, *a*, and 63). They consist of a central part and of outer layers, which latter we will for convenience call the capsule.

The central mass is composed: sometimes (1) of small cells: at other times (2) of granular masses, which have many small nuclei imbedded in them; these nuclei are concentrically arranged, as at Plate 85, fig. 7, *b*: or again (3) of a mass of fine granules, as at Plate 85, fig. 7, *g*: but in general (4) of a homogeneous and strongly refractive substance, which presents no definite structure, and consists of two, three, or more parts (see Plate 86, fig. 15; Plate 90, fig. 50; and Plate 91, fig. 63). These central masses are often of a yellow colour, and contain hæmoglobin granules (see Plate 86,

fig. 17). The central mass does not always completely fill the capsule (see Plate 91, figs. 63 and 59, *a*), the interval having been formed by the shrinking of the contained substance. The central part is sometimes found passing down the vessel-like prolongations, which are attached to the concentric corpuscles (see Plate 91, fig. 59, *a*; and Plate 85, fig. 7, *ce*).

The outer part of the concentric corpuscle, which we have called the capsule, is formed of epithelioid cells (see Plate 91, fig. 59, *b*; Plate 90, fig. 49; and Plate 85, fig. 7). These cells are flattened towards the inside of the capsule; on the outer side they are polygonal, and are anatomically continuous with the branching connective-tissue-corpuscles, which form the network of the medulla (see Plate 86, fig. 15; Plate 91, fig. 64; and Plate 92, fig. 69).

The larger concentric corpuscles, besides being connected to the network of the medulla, have often projections formed of epithelioid cells, very like vessels in appearance (see Plate 91, figs. 59, 64, and 65). Others show sharply-defined processes, formed of epithelioid cells, such as are shown in the lower part of fig. 17, Plate 86. The cells composing these processes are generally very large, and contain large nuclei; and the cells of the network to which they are attached are larger than in the other parts of the medulla. As a rule, the nearer the connective-tissue-corpuscles are to the concentric corpuscles, the larger they are, the coarser are their processes, and the larger their nuclei. Again, we often find the concentric corpuscles attached to one another, or to the surrounding network, by long coarse threads, which have nuclei embedded in them at intervals. Such are shown from teased preparations in Plate 86, fig. 15, *th*; and Plate 91, figs. 61 and 62; and from sections of the tissue in Plate 90, fig. 50, *th*; and Plate 92, fig. 69, *th*. These coarse processes often run for long distances across the medulla, and mark out the position of the future bands of connective-tissue. In other specimens the concentric corpuscles are attached to one another, or to fibrous trabeculæ, by bundles of these coarse threads (see Plate 91, fig. 60) or by bands of fibrillated-tissue (see Plate 91, figs. 58 and 63).

Having considered the structure of the concentric corpuscles, when fully formed, let us trace their origin. In Plate 90, figs. 50 and 49, where sections are made through large portions of tissue, we find the concentric corpuscles near those parts of the medulla where there are granular cells. We have also seen that the epithelioid cells, forming the capsule of the concentric corpuscles, are continuous with the epithelioid connective-tissue-corpuscles of the medulla (see Plate 90, fig. 49), and it is from these two elements, the granular cells and the epithelioid cells, that the concentric corpuscles are formed. As the granular cells take their origin primarily in the connective-tissue-corpuscles, we may say that the concentric corpuscles arise from connective-tissue-corpuscles; and we shall be able to support this latter proposition in considering the somewhat different concentric corpuscles of the Bird and the Tortoise.

In Plate 92, fig. 68, is shown a medium-sized concentric corpuscle; the central part and the capsule are not yet differentiated from one another; and therefore we are

able to perceive the tissues from which the corpuscle is formed. Nearly in the centre there is a granular cell lying in a vacuole, which has a thickened border, deeply stained by hæmatoxylin; around the vacuole are epithelioid connective-tissue-corpuscles, with many nuclei. These cells enclose two other granular cells.

In the upper part of Plate 92, fig. 69, another and smaller concentric corpuscle is shown; the structure is essentially the same. In the centre there is a granular cell, lying in a vacuole with a thickened border. The vacuole is surrounded by epithelioid connective-tissue-corpuscles, and the neighbouring cells are very large.

Plate 91, fig. 64, shows nearly the same; two small concentric corpuscles are in process of formation; the centre of each contains a granular mass, lying in a vacuole with a thickened border. The simplest concentric corpuscle of all may be seen in Plate 89, figs. 46 E and G, and Plate 91, figs. 66 and 67, where the granular mass, or in fig. 66 the three granular masses, are surrounded by protoplasm with proliferating nuclei.

It is thus seen that the concentric corpuscles and the giant cells arise from the same sources, *i.e.*, from the granular cells, and the epithelioid connective-tissue-corpuscles.

In considering the function of the concentric corpuscles, and their behaviour during involution, one point must be apparent to all, *i.e.*, that many of them disappear; for if the thymus of a very old animal be examined, very few will be found, and these as a rule will be small. It is also not difficult to prove that the greater part of most of the concentric-corpuscles, connective-tissue threads, and fibrous processes, become fibrous-tissue; the threads and processes becoming thicker, in consequence of the deposition of new tissue, by the granular cells, attached to their sides and lying between them. In these bundles of connective-tissue we find vessels which are either the pre-existing vessels enclosed by the newly-formed connective-tissue, or newly-formed vessels. Finally, the concentric corpuscles and the fibrous bands are changed into connective-tissue containing large vessels, which generally have one or two peri-vascular membranes. These changes are most easily traced in the thymus of the Calf and of the Child.

We shall find in some animals that the concentric corpuscles are transformed into cysts; this is notably the case in the Dog, Bird, and Tortoise.

Great differences will be noticed in sections of the thymus of different animals, both in the number and in the size of the concentric corpuscles. In the Child they are very numerous, and are often large and compound. In the Kitten they are still larger. In the Calf, on the other hand, they are small, and comparatively few in number. As a rule, the very large concentric corpuscles are compound; the layers of epithelioid cells, which in the single concentric corpuscle form only a capsule, are here extended over a large area, and embrace two or three, or even five concentric corpuscles (see Plate 85, fig. 7). At times we meet with abortive concentric corpuscles, where the capsule has been formed; but the central parts are composed of unchanged lymphoid cells of the connective-tissue network, and of traces of the reticulum. These abortive concentric

corpuscles are sometimes of considerable size; and here, also, the capsule is finally converted into fibrous tissue. The concentric corpuscles are not found when the thymus is first formed, but can be seen during the middle and later periods of fœtal life (see Plate 90, figs. 49 and 50). They are most numerous during the first period of involution, *e.g.*, in the Calf, when the animal is from six to eighteen months old; a few are found even in very old animals, as in the Ox, twenty years old.

It is important for us to understand the relations of the concentric corpuscles to the blood vessels, since CORNIL and RANVIER (50) and AFANASSIEW (51 and 33) have concluded that these bodies are formed from the endothelium of the vessels. It is true that they are attached to the vessels, as has been noticed by HIS (46) and other observers; the connexion of the concentric corpuscles to the network ensures their connexion to the vessels; but they have a more intimate connexion where the capsule of epithelioid cells has, in its growth, surrounded a vessel. This has partially taken place in Plate 91, fig. 63, *v*, and completely in Plate 92, fig. 69. It has already been mentioned that in that part of the medulla where the granular cells and concentric corpuscles are formed there are only a few vessels, and these are very fine. In injected specimens the vessels may be seen to pass through the large compound concentric corpuscles in every direction but one, never through the central opaque masses. This is well shown in Plate 85, fig. 7. The very large compound concentric corpuscle fills nearly one-third of the medulla; the central part of the mass has fallen out, but the remainder shows five concentric bodies. The blood vessels are found in the outer part of the compound concentric corpuscle, but do not enter the granular masses, although they may wind around them as at *d*. I have two other preparations which show very similar appearances.

Various views have been held as to the origin of the concentric corpuscles (see p. 1067). It appears to me that there can be no doubt but that they arise from the epithelioid and granular cells; the question therefore resolves itself into this—from what do the epithelioid and granular cells arise? I think I have shown in pages 1084 and 1087, that they take origin from connective-tissue-corpuscles. Another source which might be suggested, which has not been already discussed (see page 1087) would be the remains of epithelial cells, of which the thymus is supposed (by some authors) to be at first formed; this is the view of HIS (52) and STIEDA (53). They, however, do not attempt to support their view by evidence, although STIEDA says that the concentric corpuscles cannot be injected; AFANASSIEW (33) showed however that the injection penetrates the concentric corpuscles, and it has been shown in the preceding paragraph, and in Plate 85, fig. 7, that vessels undoubtedly do penetrate into these corpuscles.

The proposition that the concentric corpuscles arise from the remains of the epithelial cells presents some probability, because of the undoubted epithelioid character of the cells found in the medulla of the thymus, and of those taking part in the formation of the concentric corpuscles. This similarity to epithelial cells, however, is met with in other places, as in pathological new formations. Thus epithelioid cells

take part in the formation of tubercle, as has been pointed out by SCHÜPPEL (90) and others. Again, in the observations which were made by ZIEGLER (88) on the formation of pathological connective tissue (his method consisted in introducing small glass plates, carefully cemented at the edges, into the abdominal cavity or, by preference, into the subcutaneous connective tissue); he found at first a number of small cells, which in his view gave origin to epithelioid cells and to granular cells (Bildungszellen); these two new forms of cell in turn become, in some cases, giant cells. Without expressing any opinion as to the actual origin of the epithelioid and granular cells which he found, it is at least quite evident that they could not have arisen from the remains of epithelial cells, either in the peritoneal cavity or in the subcutaneous connective tissue. There is therefore no reason to believe because there are epithelioid cells in the thymus that they must have arisen from remains of epithelial cells which formed the original gland.

Again, there is a remarkable similarity in the formation of fibrous tissue, as described by ZIEGLER (88) and TILLMANNS (89)—the latter author introduced portions of hardened tissues into the abdominal cavities of Rabbits—to that which we have described in the thymus at pages 1086 and 1087, and represented in Plate 88, figs. 36 and 38; the granular cells, in many cases, are seen attached by long processes, to newly-forming fibrous-tissue, and are evidently taking part in its formation. And there is an equally great similarity in the way in which the giant cells are formed in these pathological new formations to that in which they are formed in the thymus, as described at page 1088, and represented in Plate 90, fig. 50.

ZIEGLER (88) and TILLMANNS (89) consider that the granular and epithelioid cells are formed from colourless blood corpuscles. We have already shown at page 1087 that we consider that in the thymus they arise from connective-tissue-corpuscles; but the after-steps of the formation of giant cells and fibrous-tissue from the epithelioid and granular cells appear to take place, in the thymus, in a very similar manner to that which has been described by those authors in pathological new formations.

We may further add, that the study of the involution of the thymus, with its gradual transition into fibrous-tissue, will be, no doubt, of considerable value to pathologists.

CILIATED EPITHELIUM IN THE THYMUS OF THE DOG.

REMAK (57) noticed (see History, p. 6) that in the Cat ciliated cysts are attached to the upper border of the thymus.

In the thymus of the lower forms of Vertebrates, cysts are not uncommon. The ciliated cells in the Dog occur only in connexion with cysts, which are found in the interior of the follicles.* These cysts are never met with during the earlier periods of growth; they are always formed either from concentric corpuscles, or from masses of epithelioid cells, which become cysts without passing through the stage of concentric

* I have examined the thymus of Cats of various ages, but have never found in them any ciliated cysts.

corpuscles. If sections are made of the thymus of a Dog from six to nine years old, some of the follicles will be found to contain large cysts (see Plate 94, fig. 84); these cysts are lined by ciliated epithelium. In the thymus of Dogs from eight to thirty months old we shall find (1) small concentric corpuscles, (2) small cysts lined by epithelioid cells, and (3) small cysts lined by ciliated epithelium. If the thymus of a young Dog from one to four months old be examined, the follicles will be found, both as regards the cortex and the medulla, to resemble those met with in the Calf or other animals, and to contain small concentric corpuscles; no cysts can be found.

We will first describe the cysts as met with in older animals (see Plate 94, fig. 84). The follicles are small; there is a considerable amount of fat and connective tissue between them, which has to some extent penetrated into them (see Plate 94, fig. 84, F). In the follicle, cysts are present of such size as to be visible to the naked eye. They contain, in most cases, a deep yellow mass, somewhat resembling extravasated blood (see Plate 94, fig. 84); although this mass never contains any coloured corpuscles, even in preparations where the corpuscles can be clearly seen in the neighbouring blood vessels. The borders of the cysts are lined, over the greater part, by ciliated epithelium; in other places, apparently by a thickening of the tissues of the thymus, although it is possible that the cysts are lined throughout by ciliated epithelium, but that the cells have been lost in making the specimen.

These epithelial cells are either columnar, as in Plate 94, fig. 91, or sub-columnar, as in Plate 94, fig. 90. The individual cells can be separated by teasing in saline solution, and are very similar to the epithelial cells of the trachea (see Plate 94, fig. 92). I have attempted, in five instances, to find out if any active movement of the cilia takes place in these cells during life, but without success, except in one case, in which the trachea had been accidentally opened, and where the result was of no great value.

The chief point is to trace the origin of the cysts and of the ciliated epithelium.

If we make sections of the thymus of a Dog from eight to sixteen months old, we shall find (*a*) quite small concentric corpuscles with small vacuoles (see Plate 94, fig. 85); or (*b*) small concentric corpuscles, containing cysts or vacuoles, partially filled with degenerated cells which often show traces of vacuolation (see Plate 94, fig. 86). Further, we find in Dogs between these ages (*c*) small cysts containing either (1) degenerated epithelioid cells (see Plate 94, figs. 88, *dg*, and 89)—the masses of degenerated cells show traces of vacuolation (see Plate 94, fig. 89, *va*), and they are at times attached to the sides of the cysts (see Plate 94, figs. 88 and 89);—or (2) masses of granules, showing only traces of cell origin (see Plate 94, fig. 87); or (3) masses of hæmoglobin. The cysts are lined wholly, or in part (1), by ciliated epithelial cells; or (2) by masses of protoplasm, not, apparently, completely differentiated into cells, although these masses bear cilia on their surface (see Plate 94, figs. 88 and 89); or (3) by epithelioid cells (see Plate 94, fig. 89, *ep*). (Compare the epithelioid cells, *ep*, in Plate 94, figs. 87 and 88.) The ciliated cells, when they are found in these smaller cysts, are sometimes sub-columnar, but frequently cubical or even flattened. It will further be noticed that

there are all transitional forms between flattened epithelioid cells and ciliated epithelium (see the smaller left-hand cyst in Plate 94, fig. 89).

It is quite easy to show gradual transitions, from small concentric corpuscles to the large cysts containing columnar ciliated epithelium. The various steps may be artificially classed as follows: First, concentric corpuscles, the peripheral cells of which are connected to, and continuous with, the network of the medulla (see Plate 94, fig. 85); secondly, concentric corpuscles, containing in their centre a mass of degenerated cells, which have been separated from the surrounding cells by a process of vacuolation (see Plate 94, fig. 86); thirdly, small cysts which are bordered by epithelioid cells, and which contain either a degenerated cell mass or a mass of hæmoglobin (see Plate 94, fig. 87); fourthly, cysts partly lined by epithelioid cells, and partly by ciliated epithelium (see Plate 94, figs. 88 and 89); and fifthly, large cysts, in some cases of nearly half the width of the follicle, lined by columnar ciliated cells, and generally containing masses of hæmoglobin in their interior (see Plate 94, fig. 84).

The ciliated cysts can therefore be shown to arise from concentric corpuscles; and these, as we have seen above, always primarily from connective-tissue-corpuscles. We therefore come to the conclusion *that the connective-tissue-corpuscles can undergo certain changes, which finally transform them into ciliated epithelium.* There is no doubt a considerable *à priori* improbability in this statement, as we should expect ciliated epithelium to be found in association with a higher organization, and not as one of the methods of involution or degeneration of the tissues; and further, the view stated above is incompatible with those which have been so long held concerning the respective functions of mesoblast and hypoblast. There seems, however, no other conclusion left to us, unless we grant that in the development of the thymus, certain traces of epiblastic tissue have been left: a view which we have discussed somewhat at pages 1091 and 1092, and which, as we shall afterwards see in studying the development, is not established.*

Changes in the Thymus during involution.

Some of the changes occurring in the thymus have been mentioned at pages 1079 and 1080; others, of which we have to treat, are: the formation of connective and fibrous-tissue in the follicle; the increase of the interfollicular connective-tissue, the invasion of this tissue into the follicle, the deposition of fat in this invading tissue and between the

* Ciliated cells have long been known to occur on the surface of the peritoneal cavity of Frogs. Waldeyer (91) considered them only a continuation of the genital mucous membrane. Klein (92) described ciliated endothelium in the peritoneal cavity of Frogs, and figured (see his fig. 18) a vacuolated cell, containing fine cilia projecting into the vacuole. Neumann (93) noticed a transition between the endothelium of the peritoneal cavity of the Frog and ciliated epithelium; and Nicolsky (94) found that in all Frogs ciliated epithelium exists on the serous cavities, and in young male Frogs on the pericardium. This ciliated epithelium is not to be classed as belonging to the female genital organs, but as transformed endothelial cells.

follicles; the changes in the blood vessels; and the final disappearance of the gland and its replacement by fat and connective-tissue.

The involution of the gland, though to the naked eye it appears to take place at a definite period of the gland's existence, does not really do so, but is a very gradual process; for we must consider the formation of epithelioid cells and of granular cells, as the primary indication of involution, and this first takes place during fœtal life. Again, the giant cells and the concentric corpuscles also aid in involution, and they are present during the middle and latter end of fœtal life, and during the period of the growth of the organ; while the formation of fibrous-tissue takes place during quite the latter end of growth, and during all the period of decrease in size. Further, various animals of the same species differ greatly, in accordance with the activity of their life, and the amount of food they have taken. And again, various parts of the same thymus differ considerably; thus in the Calf, the upper part of the thymus in the neck undergoes involution some time before the lower part.

The formation of fibrous-tissue within the follicle.

We have already stated that the granular cells become transformed directly into fibrous-tissue (see p. 1087). This transformation also takes place in the thymus of old animals. If we study a section of the medullary portion of the thymus of an Ox from six to eight years old, we find, among the lymphoid cells, and to a great extent replacing them, bundles of interlacing fibrous-tissue, with a considerable number of granular cells attached to their edges. If the thymus of a very old animal be examined, the whole of the medulla is seen to be transformed into fibrous-tissue and blood vessels, few granular cells remaining.

The giant cells also appear, to some extent, to take part in the formation of fibrous-tissue, their long processes being in some instances transformed into it.

In the medulla, the fibrous-tissue is formed also by connective-tissue-corpuscles. They increase in size, and become spindle-shaped (see Plate 93, fig. 79), and these spindle-shaped cells are then fibrillated, and become directly transformed into fibrous-tissue (see Plate 93, fig. 79, *f*, and 78, *f*).

The vessels of the medulla have often a very thick adventitia of newly-formed connective-tissue. This seems to be formed in two ways: partly by the action of the granular cells, and partly by the proliferation of the pre-existing adventitia of the vessel; such a vessel is shown in Plate 93, fig. 81. The vessel is seen to be surrounded by newly-formed connective-tissue. In the lower part of the figure, fibrous-tissue is attached to the vessel. The large veins surrounding the medulla have often a very thick covering of fibrous-tissue, and in shaking the specimens roughly, it sometimes happens that the whole of the medulla shakes out, and leaves a ring formed of trabeculæ of fibrous-tissue and vessels, the ring surrounding an apparent central cavity.

In the cortex, very few granular cells or giant cells are present; in the majority of specimens not one can be found; it is therefore clear that any formation of connective-

tissue cannot here arise from them, and in the cortex the network of connective-tissue-corpuscles is directly transformed into connective-tissue (see Plate 93, fig. 80). The network is thickened, until the breadth of the threads is as great as or greater than that of the meshes; at the same time the adventitia of the vessel enlarges. These changes are gradually continued, until we obtain, lastly, a few lymphoid corpuscles, shut in by bands of newly-formed tissue, in which later on fibrillæ often appear.

Growth of the interfollicular tissue, and invasion of this tissue into the follicle. Plasma cells and formation of fat.

An important factor in involution is the growth of the connective-tissue between the follicles (see Plate 83, fig. 2; and Plate 84, figs. 3 and 4). In this tissue there is a deposition of plasma cells (see Plate 86, fig. 13*). Each plasma cell has a considerable zone of protoplasm surrounding its nucleus; this protoplasm contains granules, somewhat resembling the granules of hæmoglobin; they, however, stain very differently, and are not composed of hæmoglobin or of fat. The cells stain in a very characteristic manner in indigo-carmine and carmine (see Plate 86, fig. 13), the nucleus staining deep pink and the granules of a blue colour; the hæmoglobin of the coloured blood corpuscles in the preparation is green. These cells exactly resemble, both in staining properties and general appearance, many of the cells met with in the medulla of bone. They are evidently here the forerunners of fat cells.† By this growth of interfollicular-connective-tissue and fat, involution is probably assisted, the follicle being compressed.

It has been stated (see p. 1079) that some of the blood vessels, surrounded to a slight extent by connective-tissue, pass from the outside of the follicle, between the portions of cortical tissue, to reach the medulla; and it is found that these vessels, with their surrounding connective-tissue, in their passage through the cortical-tissue, are separated from it by the capsule of the follicle, the vessels piercing the capsule to enter the medulla. These vessels, as they enter the medulla, have at this point a perivascular sheath, *i.e.*, where they are surrounded by the endothelium of the capsule. The connective-tissue seems to press the capsule further in on the vessel, so that we get finger-like projections of the interfollicular-tissue, with an extension of the perivascular space. It is the extension of this perivascular space along the vessels, with the invasion of the interfollicular-connective-tissue into the follicle, which is of such importance in involution.

These projections of connective-tissue gradually widen and invade the follicle,

* For an account of the views of various authors concerning plasma cells, see p. 1074.

† In the thymus stained by dahlia, after the manner of EHRLICH (79), cells staining deeply with the dahlia are met with in the centre of the follicle (see Plate 86, fig. 12). The nucleus becomes purple, and the granules of the same colour, but of a much deeper tint. The cells are often near the granular cells, which are themselves unacted upon by the blue solutions. They are of the same size as those met with in the interfollicular tissue. It is difficult to state the significance or function of these deeply staining cells, the method of EHRLICH not being very satisfactory except as a method of detection.

pressing further into it (see Plate 86, fig. 10), and sending out lateral processes which join on to the other invading processes, they isolate portions of the cortex, or even large parts of the follicle (see Plate 86, fig. 10). The processes have generally a narrow neck, and widen out considerably at the end. In these projections we find at first some retiform tissue, stretching from the vessel to the perivascular sheath. This soon gives place to cells of two kinds: plasma and granular cells. The plasma cells are the forerunners of fat cells. The granular cells are here often found on the walls of large veins (see Plate 88, figs. 33 and 34), they form fibrous-tissue and blood vessels. Thus we have penetrating into the follicle bands of fibrous-tissue containing fat cells; and by this means fat invades the follicle; but there is never any fatty metamorphosis of the lymphoid corpuscles.

Changes in the vessels.

In the invading processes of connective-tissue there is a considerable formation of new vessels: they are very peculiar. They are enclosed first of all between the membranes formed by the capsule of the follicle; they often have, in addition, a perivascular membrane, in some cases a membrane inside this again, like a double perivascular sheath; but the most remarkable feature is their adventitia, which often looks like a second layer of endothelium outside the vessel (see Plate 94, fig. 95). In some cases, there are two or even three layers of cells, forming such an adventitia (see Plate 94, fig. 96). These vessels are often seen to be filled with blood, and the lumen does not appear to differ from that of other vessels; they do not become concentric corpuscles, as AFANASSIEW (51) has stated; for they are not found in numbers until the thymus is undergoing involution, nor found to any extent except in the invading processes of connective-tissue.* These vessels are much enlarged during involution, and it is possible that this adventitia is the means by which the vessel increases in size.

To sum up the changes in involution: we find a large formation of connective-tissue and fat between the follicles; this tissue invades and divides the follicles. At the same time there is a change taking place in both the cortex and medulla—produced in the cortex by the connective-tissue-corpuscles, in the medulla by the granular cells, giant cells, and connective-tissue-corpuscles, the cortex disappearing much the more rapidly of the two.

The gland, diminished in size, though with enlarged blood vessels, is transformed into connective-tissue, and in Mammals is finally buried in fat. ("*In adipe circumfuso sepelitur,*" HALLER (35)).

THE THYMUS OF BIRDS, REPTILES, AMPHIBIA, AND FISH.

During the growth of the organ the microscopical characters of the thymus of all animals are very similar. When the point of full development has arrived, then, and

* Except in the Tortoise, where all the vessels in involution partake of this nature.

during involution, there are considerable differences in the thymus of different animals. Thus, in the Bird and the Tortoise the concentric corpuscles are often enlarged, and transformed into small cysts. In the Dog the cysts are lined in great part (as we have already seen) with ciliated epithelium. In Mammals, fat invades the follicle; while in the other classes of Vertebrates none is found.

Thymus of the Bird.

The thymus of the Fowl, the Turkey, and the Pelican have been examined.

In the Bird, the thymus is attached by connective-tissue to the vein and the nerve of the neck; so that in cutting longitudinal sections, the follicles are found to be attached to a central string, composed of fat, some small amount of connective-tissue, and sometimes including the large vein and the nerve. In the Chicken of five or six weeks old, the microscopical characters of the gland, as regards both cortex and medulla, are very similar to those of the fully-formed organ in Mammals. In involution, which takes place at an early period of life in the Bird, the distinction between cortex and medulla is lost, as the cortical portion soon disappears, and the great number of concentric corpuscles gives the appearance of numerous medullary portions in the follicle.

The concentric corpuscles differ somewhat in their origin, and in their arrangement, from those of Mammals. They are formed principally of large epithelioid cells (see Plate 95, fig. 99), only a few granular cells taking part in their formation. These epithelioid and granular cells form masses, which are not so much compressed, nor are they so definitely arranged in concentric layers as in the case of Mammals (see Plate 95, figs. 100 and 101). They contain vacuoles of various sizes, with thickened borders. The vacuoles are formed and increase by the coalescence of the vacuoles of the individual epithelioid and granular cells. (Compare Plate 95, figs. 99, 100, and 101.) Within them, we often meet with granular masses and masses of hæmoglobin. On teasing and examining the thymus, we find many vacuolated cells (see Plate 95, fig. 98). Sometimes the cells exist as only a small ring of nucleated protoplasm, surrounding the vacuole (see Plate 95, fig. 98, *b″*).

A few giant cells are present (see Plate 95, fig. 97), where one is shown enclosing a granular mass.

The fibrous-tissue is formed in two ways: either from the granular cells or from the concentric corpuscles, the edge of the vessels being thickened in involution. Fat does not invade the follicles, nor is the gland finally surrounded by fat. The essential process in involution is, however, similar to that in Mammals; the points of contrast are: the rapid diminution of the cortex, the large number of epithelioid cells, and the large number of concentric corpuscles, the rapid involution, and the absence of invading connective-tissue and of fat. The gland is finally replaced by a small amount of connective-tissue.

Thymus of the Reptile.

The thymus of the Tortoise will be described first, as specimens of that animal were procured of various ages. The thymus of one young American Alligator, three months old, and of a fully-grown Python, were also examined.

The thymus of the Tortoise, when the animal is quite small, resembles that of the Mammal; and then the follicle is composed of cortex and medulla; but as the animal grows older the follicle is composed of three parts: an outer cortical part, which is formed of flattened cells, with a delicate reticulum stretching between them (see Plate 95, fig. 105); a medullary portion, containing most of the concentric corpuscles; and between these two a zone of tissue, looking as if it were compressed, containing a ring or rings of vessels, and many lymphoid cells. This peculiarity of the thymus of the Tortoise depends on the fact that the cortex does not disappear more rapidly than the medulla, as in the Mammal or Bird; but the lymphoid cells disappear, and the network of connective-tissue-corpuscles increases, and takes their place. A change, something like this, is shown in the Mammal in Plate 93, fig. 80, but it does not there proceed to anything like the same extent, as in the Tortoise, where the cortex finally contains hardly any lymphoid cells. Many pigmented cells can be seen in the connective-tissue at the edge of the follicle, and surrounding the invading blood vessels; these appear to correspond to the plasma cells of the thymus of Mammals.

Further, there are follicles (as has been noticed by AFANASSIEW (33)) which are entirely formed of flattened, spindle-shaped cells. These follicles will be more completely noticed in the description of the thymus of the Alligator.

The concentric corpuscles of the thymus of the Tortoise present intermediate forms between the concentric corpuscles of the Bird and the ciliated cysts of the Dog. There are at times found in the thymus a few granular cells (see Plate 95, figs. 104 and 107). The protoplasm of the largest of these cells is marked by concentric rings (see Plate 95, fig. 104). The concentric corpuscles are formed in great measure by epithelioid cells; they contain vacuoles of various sizes, in which sometimes a granular cell is present (see Plate 95, fig. 106). In Plate 95, fig. 107, two granular cells are seen to be enclosed in a large vacuole.

The fully-formed concentric corpuscles contain either a mass of cells balled together in the interior of the vacuole, evidently undergoing degeneration, or masses and granules of hæmoglobin (see Plate 95, fig. 108).

The blood vessels of the medulla are very large; most of the vessels in the thymus of old animals have perivascular sheaths and thickened adventitia, and are very similar to those which we have described in the thymus of the Calf. A few giant cells are present. As involution proceeds the ring of vessels between the cortex and the medulla enlarges.

The thymus of the young Alligator is composed of cortex and medulla, the cortex

much resembles that of the Tortoise (see Plate 95, fig. 105). In the medulla there are a few concentric corpuscles formed of epithelioid cells.

In the thymus there is a follicle composed entirely of flattened, spindle-shaped cells; this exactly resembles those which are met with in the Tortoise, and which have been supposed by AFANASSIEW (33) to be individual follicles, undergoing involution before the rest of the gland; there is no evidence that this is the case; on the contrary, all the facts point to its being some other gland which is situated among the thymic follicles. As in the first place, it is found in quite young Reptiles, as in the small Tortoise and the young Alligator; and in Mammals and the other classes of Vertebrates we do not find individual follicles undergoing involution before the rest of the gland. Secondly, when a follicle undergoes involution the process is a very gradual one, and is never characterised by a change of the whole follicle, equally and everywhere, into one tissue. Thirdly, these follicles are composed everywhere of flattened, spindle-shaped cells, and no such tissue is met with in the undoubted thymic follicles of either old or young Reptiles. Fourthly, no such tissue is met with in the thymus of Fish, Amphibia, or Birds; exactly such follicles are, however, found in Mammals, where hibernating glands exist, as in the Hedgehog. We conclude that these follicles are those of some other gland, probably of the nature of the hibernating gland of Mammals.

In the large Snake the thymus is small and to a great extent transformed into fibrous-tissue. The follicles contain many concentric corpuscles of large size, and a large number of granular cells, and the steps of transition between granular cells and fibrous-tissue are well seen.

This gland also contains a follicle, composed entirely of flattened, spindle-shaped cells, such as we have just spoken of, and there is no resemblance between this follicle and the thymic follicles which are undergoing involution by the invasion and new formation of fibrous tissue.

Thymus of Amphibia.

In the Frog the medulla contains many granular cells, as many as forty to sixty can often be seen in a section of the small organ. The granular cells are clup-shaped, and are attached by their smaller ends to fibrous tissue.

The thymus of the Axolotl is situated in nearly the same position as in the Ray-fish. It often contains cysts of considerable size. Its cells are very large.

Thymus of Fish.

In the Ray-fish the thymus begins as one follicle (see Plate 84, fig. 5), which is afterwards divided into numerous follicles. These are, in the later stages of involution, widely separated from one another. The thymus is very soft, and requires hardening with great care, lest in making sections the greater part of the lymphoid tissue should be lost.

Many colourless blood corpuscles are found in the connective-tissue and in the follicles. They are easily distinguished from the lymphoid cells by their granular appearance and greater size. The Ray fishes used in this research (with the exception of the smaller ones) had all been dead about ten or twelve hours before they were procured. The presence of colourless corpuscles in the tissues may possibly be only due to wandering of colourless corpuscles from the vessels after the death of the animal.

The cortical tissue does not differ from that of Mammals, and is represented in Plate 95, fig. 103. During involution there are great changes in the vessels; they become surrounded by one or more perivascular sheaths.

The tissue found in the Cod-fish, by cutting through the lining membrane of the upper and back part of the gill cavity, is much harder than the thymus of the Ray-fish. The whole tissue is encapsulated with connective-tissue, from which proceed trabeculæ, dividing the lymphoid masses into definite follicles, of which the outer are larger than the inner.

The lymphoid tissue does not show any differentiation between cortex and medulla, nor any central ring of vessels; and the trabeculæ are covered on each side by endothelial cells.

This tissue is probably a lymphatic gland.

DEVELOPMENT.

In the History (p. 1073) an account of the various views which have been held concerning the development of the thymus has been given. On the one hand are the observations of FRIEDLEBEN (3) and AFANASSIEW (33), who describe the thymus as arising independently in connective-tissue; and on the other hand, the observations of the authors who believe that the thymus arises from the respiratory tract, or the pharynx, or from the branchial clefts.

The development has been traced in the thymus of the human embryo, and in that of the Rabbit and the Chick.

In the human embryo about two and a-half inches long, it is found in the thorax and the neck, as a double gland; the upper part of each half consists of a single follicle, not differentiated into cortex and medulla. The wall of the gland has projections on its exterior (see Plate 87, fig. 23), and the connective-tissue has slightly invaded the gland.

In the human embryo twelve weeks old, the thymus consists of several follicles, partially differentiated into cortex and medulla; it also contains a few concentric corpuscles (see Plate 86, fig. 11).

In the fœtal Rabbit sixteen days old, we find the thymus in the neck, lying in front and to the inner side of the carotid artery. It is seen, at its upper end, as a single tube, and below as a number of tubes, some of which are solid and others hollow; the hollows are of very different sizes. The cells in cross-sections of the tube vary from two or three to many in number; they are epithelioid in character, and differ in

appearance from the epithelial cells of the thyroid, which lie in approximation to the upper part of the tube. The lumen of the tube is in some cases closely packed with blood corpuscles; and appears to be continuous with vessels which pass out through the epithelioid cells.

In the fœtal Rabbit eighteen days old there are present in the neck three glands: first, the thyroid; secondly, a gland similar in appearance to the thyroid, and lying on its outer side, and in front and to the inner side of the carotid artery; this gland does not extend so high up in the neck as the upper part of the thyroid, but reaches down nearly to the upper end of the thymus; and in the embryo of twenty days, it extends still further, and lies behind and to the outer side of the upper end of the thymus. We also find in embryoes eighteen days old, thirdly, the thymus, which in the upper part is composed of a tube or tubes, and in the lower part is more branched. The upper part of the thymus retains its fœtal form much more than the lower part, as was noticed by KÖLLIKER (76). Vessels and some connective-tissue are seen to pass into the follicle, and the outer cells forming the border of the follicle are more epithelioid in character than the inner cells. The growth of the thymus can be easily traced in specimens of this age; and it will be seen that long processes of epithelioid cells are pushed out in the surrounding connective-tissue (see Plate 95, fig. 109, *a*).

In the fœtal Rabbit of twenty-one or twenty-two days old the cells are much smaller, and do not resemble epithelioid cells, except at quite the upper part of the gland. In the embryo of thirty days old the cells are still smaller, and the thymus nearly resembles that of newly-born animals.

In sections of the Chick, early in the seventh day of incubation, two small circular collections of cells are found, behind, and to the outer side of the nerve and vein of the neck (see Plate 87, fig. 29). The first growth is the enlargement of the gland, pushing out the wall in projections, similar to those in Plate 87, fig. 23. This can be well seen on the eleventh day. On the fourteenth day the connective-tissue has invaded the gland, and divided it into separate follicles; and on the eighteenth day these are differentiated into cortex and medulla. The large epithelioid cells are not seen until the cortex has been differentiated from the medulla.

It will be seen from the above that we do not accept the epithelial origin of the thymus.

If, however, we accepted the views of those authors who conclude that the thymus arises from epithelial cells, it appears to me that the view of KÖLLIKER (76) must be maintained, and that the opinion of STIEDA (53) is incorrect. The latter author considers that the epithelium forms the concentric corpuscles, and that the lymphoid tissue is formed from the middle layer which invades the gland; if, however, sections of the thymus are made, at various stages of growth, it will be seen that the epithelioid cells become smaller and smaller, and that they are pressed to the outside of the follicles, while the connective-tissue and blood vessels invade the interior of the follicle; and it is certain that the concentric corpuscles are found chiefly in the interior of the follicle,

and that the cortical part of the follicle is composed of lymphoid cells and retiform tissue.

The so-called Hibernating Glands.

The situation of these glands has been well-described by Barkow (21). He divides them into four: cervical, thoracic, axillary, and dorsal. Their structure is somewhat foreign to our present purpose of describing the thymus; as these glands only occur, to any extent, in a few animals, most of which hibernate. It was, however, necessary to examine them, as there has been so much confusion between hibernating glands and thymus.

They are well seen in the Hedgehog, and we have also examined them in the Alpine Marmot and in the Rat, and have found microscopical traces of them in the Cat. The hibernating gland in the last animal appears to have been seen by Remak (57), as he says that at the upper end of the thymus of newly-born Kittens there is a small yellow gland, which consists of granular yellow cells (like liver cells) lying close together.

As seen by the naked eye, or by low powers, the shape of the lobules, in the hibernating gland and in the thymus, is identical; but the situation and the colour of the glands are so different, that at once the eye can distinguish between them; the one being of a red-brown, and the other of a pale grey colour. Their microscopical appearances are very different. The glands are composed of granular polygonal cells, placed close to one another, often arranged in rows, and having narrow capillaries between the cells. In their minute anatomy these glands rather resemble the liver, than any lymphoid tissue.*

Hæmoglobin contained in Cysts and in Colourless Cells.

In the thymus of all animals, hæmoglobin is found, either contained within cysts (the cysts, as we have noticed before, arise from the concentric corpuscles), or in cells; these cells appear to be always situated near to the concentric corpuscles, and often form part of them.

The cysts in the Dog, Bird, and Tortoise are, when small, filled with degenerated cells, and when large with hæmoglobin masses and granules (see pages 1093, 1098, 1099).

* In the Rat, the thymus is contiguous to the hibernating gland, which in its turn runs up to the salivary glands.

In the Hedgehog, there are present in the thorax the thymus, a lymphatic gland, and the hibernating gland, in contiguity to one another. The hibernating gland has two kinds of alveoli, one composed of spindle-shaped cells, and the other of polygonal cells, which have been described above.

The thymus of the Rat and of the Hedgehog, therefore, present unusual difficulties; and conclusions drawn from them are not of great weight, unless shown to be in accordance with the structure of the gland in other animals.

In what way this hæmoglobin arises, seems uncertain; whether from a conversion of the protoplasm of the cells into hæmoglobin, or from an extravasation of the colouring matter of the blood into the cysts.

Hæmoglobin is also found in cells. These cells are of three kinds: (1) spherical or oval cells of various sizes, in which the hæmoglobin is met with (*a*) in the form of granules (see Plate 86, figs. 19 and 20, *c*, *d*); or (*b*) in the form of spherules or masses, some of which exactly resemble the coloured blood corpuscles (see Plate 86, fig. 21). These masses of hæmoglobin enclosed in cells are oval in the Bird, Reptile, and Fish; but circular in all Mammals, except in the Camel (see Plate 86, fig. 21; and Plate 92, fig. 77, *d*). These cells will be referred to afterwards. (2) The branched cells of the reticulum contain hæmoglobin, generally in fine granules, at times in large masses (see Plate 86, figs. 18, *h*, and 14). (3) Cells or masses of protoplasm attached to the concentric corpuscles also often contain hæmoglobin (see Plate 86, figs. 16, *h.h*, and 15, *h*), and the concentric corpuscles themselves often contain this substance (see Plate 86, fig. 17, *h*).

The Lymphoid Cells of the Thymus, when examined in the fresh state.

In teasing the thymus of any animal, either with or without the addition of saline solution, the first point which attracts attention is the great number of small cells, varying somewhat in size (see Plate 92, figs. 74 and 76, *Thc*). The smallest are nearly the same size as the coloured blood corpuscles if the animal be a Mammal, (compare Plate 92, fig. 76, *bc* and *Thc*). These thymic cells are nearly spherical, and have a very low refractive power. They are seen in many cases to be composed of a nucleus and of a delicate zone of protoplasm; in the very smallest, no zone of protoplasm can be found. If they are treated with saline solution, they appear to contain from three to six dark granules, which look like nucleoli; but on using a high power, and focussing carefully, and making the cells roll over under the microscope, the protoplasm is seen to be irregularly heaped up, and the corpuscles have somewhat of the horse-chesnut shape (see Plate 92, fig. 70).

Characters of the Lymph and Blood issuing from the Thymus.

The lymph and blood, as they issue from the thymus, were obtained from Calves and Oxen of various ages, from fourteen weeks to thirty months. The animals, seven in number, were killed in the ordinary manner by the pole-axe. The tissues of the neck were then divided, down to the lower part of the cervical portion of the thymus; the largest of the veins issuing from the thymus were tied, including in the ligature some slight amount of additional tissue; and the animal was left for ten or fifteen minutes. By that time, in every case but one, the lymphatic vessel issuing by the side of the veins was easily perceptible, and was seen to be filled with a very pale-

pink fluid. The lymph vessels, before being opened, were slightly washed with saline solution, which was carefully collected, to be afterwards tested; then the lymphatic was cut, and the issuing lymph collected in a pipette. This method was employed, as the lymph-vessels are so small that it is impossible to introduce any capillary tube into them with certainty of success. The lymph of the large lymphatic of the neck, the blood of the thymic veins and of the jugular vein, were also collected.

It was found that the lymph collected from the lymphatics of the thymus contained many colourless corpuscles of three varieties, of which the first is by far the most common. There are (1) small lymphoid cells, exactly resembling in every respect the small cells obtained by teasing the thymus (see Plate 92, fig. 71, *Thc*); they show very faint amœboid movements, have a grey homogeneous aspect, and contain fine granules; (2) spherical or oval cells of various sizes, containing granules, spherules, or masses of hæmoglobin; some of these hæmoglobin masses exactly resembling coloured blood corpuscles (see Plate 92, fig. 71 C, D, E); (3) large cells with many radiating processes (see Plate 92, fig. 71 B). Some of these last cells contain hæmoglobin granules, and others do not; they are more numerous than the second variety, but much fewer in number than the first.

The lymph issuing from the thymus contained a very small proportion of coloured blood corpuscles, less than 1 per cent.; whereas that of the lymphatic of the neck contained a larger proportion.

We therefore conclude that *there are present in the lymph issuing from the thymus cells containing coloured blood corpuscles, and hæmoglobin granules; and that in the lymphatics of the thymus there are more colourless cells than in the lymphatics of the neck.* Whether there are more colourless cells in the blood of the thymic veins, than in the blood of the jugular vein, could not be determined; in two cases out of six there seemed to be some increase in number, but in the other four, no increase could be detected. However, the blood of the thymic vein contained many masses of granular matter; the so-called *Zimmermann's* corpuscles.

Physiological Conclusions.

In considering the uses of the colourless cells which issue from the thymus by the lymphatics, the first thought that presents itself is that these cells form colourless blood corpuscles. Two circumstances must, however, be borne in mind: the first, that though in Mammals there is no great difference in size and appearance between some of the colourless blood corpuscles and the thymic cells (see Plate 92, figs. 71 and 76, *cbc* and *Thc*), there are considerable differences in Amphibia and Reptiles (see Plate 92, figs. 73 and 74, *cbc* and *Thc*), still greater differences in the Bird (see Plate 92, fig. 75), and greatest of all in the Ray-fish (see Plate 92, fig. 72). The second circumstance is, that the fluid which passes along the lymphatics from the thymus does not, in Mammals, pass directly to the blood, but first into lymphatic glands or

even into a succession of glands, where it is possible that these colourless cells may be changed. It is therefore difficult to form any very certain conclusions as to the functions of these colourless cells, although probably *they form one source of the colourless blood corpuscles.*

The difference in size between the thymic corpuscles and the coloured blood corpuscles is seen to be very great in some classes of Vertebrates, and we have no reason to believe that the one are ever immediately transformed into the other (see Plate 92, figs. 72, 73, 74, and 75, *bc* and *Thc*).

There is one fact which presents considerable difficulties—*i.e.*, that the blood of the fœtus and of the newly-born animal contains a considerably larger proportion of coloured to colourless blood corpuscles than is the case in the blood of adults. This was first noticed by DENIS (95), and then by PANUM (96), and yet the thymus is certainly more active during fœtal life and during the first years of growth than it can be during adult life, when it is composed in a great measure of connective-tissue.

In considering the uses of the cells containing hæmoglobin, it has been stated above that we find large colourless cells containing masses in shape exactly identical with, though in size generally smaller than, the coloured blood corpuscles; and this is true, not only in all Mammals with circular corpuscles (see Plate 86, fig. 21), but in the Camel (see Plate 92, fig. 77, *d*), and also in the Bird, Reptile, and Fish. It is considered by KÖLLIKER (97) and most authors that these cells, as found in the spleen where they have long been known, are large colourless cells which have absorbed coloured blood corpuscles; but there are very great difficulties in holding that view—first, because we have found these cells in the lymphatics, in the blood in two cases of leucocythemia, in the thymus, the lymphatic glands, and the medulla of young bone,* and in no one of these situations have we any knowledge of any destruction of coloured blood corpuscles taking place; and secondly, because if such a destruction were taking place, it would seem somewhat difficult to understand how these contained masses of hæmoglobin, in undergoing solution, retain their form. And it seems to me that the older view of GERLACH (106) and SCHAFFNER (107) as to the origin of coloured blood corpuscles, is quite as worthy of support as any other, in the present state of our knowledge; and more especially so when we consider that the coloured blood corpuscles in the embryo in early life are formed from large colourless cells, as seen by KLEIN (108), BALFOUR (109), and others, in the Chick, and from connective tissue cells or network, as seen by SCHÄFER (110), WISSOZKY (111), and RANVIER (112) in young Mammals.

* Further, in two cases of pernicious anæmia, which were examined, the medulla of the long bones was found to contain large cells enclosing spherules and masses of hæmoglobin, some of them enclosing masses exactly resembling coloured blood corpuscles. PONFICK (98), FEDE (99), COHNHEIM (100), OSLER and GARDNER (101), LITTEN and ORTH (102), and RIESS (103) have described the occurrence of cells containing blood corpuscles in the medulla of patients who had died from pernicious anæmia, and NEUMANN (104), BIZZOZERO (105), PONFICK (98), LITTEN and ORTH (102) have seen them in the medulla after typhoid fever or other diseases.

We therefore conclude that *the coloured blood corpuscles take origin, in part, at least, from large colourless cells.*

I wish to thank Mr. DENT, of St. George's Hospital, and Mr. COMPTON for their kind help.

EXPLANATION OF PLATES.

The drawings, except where the contrary is stated, were made from sections of tissue hardened in chromic acid, and then in alcohol, and stained in hæmatoxylin.

The outlines of many of the drawings were made by means of an OBERHÄUSER'S camera lucida, with a large HARTNACK'S stand; in such cases the lens (HARTNACK'S) used with the camera lucida, and the approximate magnification, are given. The ocular and objective used in completing the drawings are also given.

In other cases where the camera lucida was not used, the ocular and lens used in making the drawing are given with the magnification. These figures, however, are not drawn to scale.

PLATES 83–95.

Figs. 1, 2, 3, 4. Camera lucida, with a simple lens, magnified about $12\frac{1}{2}$ times.

The four drawings show the appearance of the follicles in various stages of growth and involution. In each case the tissue was hardened for the same length of time in bichromate of potash and then in alcohol.

The cortical portion of the follicles is distinguished in the drawings, as in the original, by its darker colour.

The follicles are united by cortical-tissue at (*a*), by medullary-tissue at (*b*). In some follicles there are two or more portions of medullary-tissue, as at (*c*).

ct. Interfollicular connective-tissue; in figs. 2, 3, and 4 this tissue contains fat.

c′t′. Processes of the interfollicular connective-tissue, penetrating the cortex.

Fig. 1. Section of the greater part of a lobule of the thymus of Calf three months old.

Fig. 2. Section showing about two-thirds of a lobule of the thymus of Heifer two years old.

Fig. 3. Section of thymus of Ox six years old.

Fig. 4. Section of thymus of Cow, probably twenty years old. The vessels in the connective-tissue are very large.

Fig. 5. Camera lucida, simple lens $\times$ $12\frac{1}{2}$.

From Ray-fish, $4\frac{1}{2}$ inches across. The section is vertical, parallel to the greatest breadth of the fish, and made a little behind the spout cavity.

ca. Central cartilage.

NG. Spinal ganglia.

M. Muscles cut transversely.

M′. Muscle cut obliquely.

N′G′. Nerves and ganglia.

Th. Thymus, showing slight difference between cortex and medulla.

G. The gills.

c′a′. Cartilage supporting gills.

Fig. 6. Camera lucida, obj. 2, × 75, oc. III., obj. 4.

From Calf four days old. Section of follicle. The thymus was injected with carmine and gelatine, and hardened in alcohol.

V. Veins which lie just within the medullary portion.

V′. Veins passing out of the follicle in the interfollicular connective-tissue.

ar. Arteries.

gr. Granular cells.

cc. Concentric corpuscle.

Fig. 7. Camera lucida, obj. 4, × 150, oc. III., obj. 5.

From Kitten four months old. Section of thymus injected with carmine and gelatine, hardened in alcohol.

M. Margin of medulla.

d.d′. Two vessels are seen to penetrate the very large compound concentric corpuscle, the central portion of which has fallen out.

b.g. and *ce.* The central parts of the individual concentric corpuscles; they are not penetrated by the injection.

Fig. 8. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf twelve days old.

The drawing represents the method of double staining by hæmatoxylin granular cells of a brown colour, attached to blood vessel: the nuclei of the granular cells and vessels, purple; lymphoid cells, deep purple.

Fig. 9. Camera lucida, obj. 8, × 600. oc. III., obj. 9.

From young Calf; section of cortical portion of thymus, hardened in chromic acid and then in alcohol. The specimen was stained with indigo-carmine and carmine (method of MORRIS and SHAKESPEARE, see reference No. 87) in the proportion of one of the former to ten of the latter. The reticulum is blue-green. The lymphoid corpuscles are of a carmine colour.

Fig. 10. Camera lucida, with upper part of No. 2 lens, × about 36.

Section of a follicle of the thymus of Calf one year old. The thymus was hardened in chloride of gold and chromic acid.

ct. Connective-tissue surrounding the follicle, and penetrating into the interior, cutting off portions of the cortical-tissue.

c′t′. One of the invading processes of connective-tissue.

F. Fat in the invading connective-tissue.

Fig. 11. Camera lucida and a simple lens × $12\frac{1}{2}$.

Transverse section of the thymus of human fœtus of about the twelfth week.

cc. Concentric corpuscles.

ct. Connective-tissue which surrounds the gland, and has invaded it and divided up the follicle. The cortex is distinguished by its darker colour.

Fig. 12. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

Plasma cells, from medulla of thymus of Calf twenty-eight days old.

Tissue hardened in alcohol, stained in dahlia (method of EHRLICH, see reference No. 79).

Fig. 13. Camera lucida, obj. 7 × 450, oc. III., obj. 8.

Section of thymus of Calf. The tissue was hardened in bichromate of potash, and afterwards in alcohol, and stained in indigo-carmine and carmine, in the proportion of one of the former to seven of the latter (method of MORRIS and SHAKESPEARE, see reference No. 87).

v. Blood vessel showing perivascular sheath, and containing coloured blood corpuscles, which are stained green.

pl. Plasma cells.

Fig. 14. Oc. III., obj. 8, × 400.

Teased specimens.

(*a*). From thymus of human fœtus five months old.

(*b*). From Dog one year old. Connective-tissue network containing hæmoglobin.

Fig. 15. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Teased specimen of thymus of Calf seven months old.

In the lower part there is a concentric corpuscle ; above, a large mass of protoplasm containing (*h.*) hæmoglobin.

th. Coarse protoplasmic threads, with imbedded nuclei.

Fig. 16. Oc. III., obj. 8, × 400.

Teased specimen of thoracic portion of the thymus of Calf one year old.

Mass, probably part of a concentric corpuscle containing large masses of hæmoglobin (*h. h. h.*).

Fig. 17. Camera lucida, obj. 5, × 300, oc. III., obj. 7.

Teased specimen of thymus of Calf seven months old.

Concentric corpuscle containing (*h.h.*) hæmoglobin granules.

p. Vessel-like prolongation. The centre is filled with a mass of protoplasm, ending in a rounded extremity.

Fig. 18. Oc. III., obj. 8, × 400.

Teased specimen of thymus of Calf one year old.

Nucleated connective-tissue cells of medulla, a long process which contains hæmoglobin granules (*h.*).

Fig. 19. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Teased specimen of thymus of Calf one year old.

lc. Lymphoid corpuscles.

b. Coloured blood corpuscles.

c. and *d.* Cells containing hæmoglobin granules.

Fig. 20. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

Teased specimen of thymus of Calf seven months old.

c.d. Cells containing hæmoglobin granules.

Fig. 21. Oc. III., obj. 8, × 400.

Teased specimens.

a.b.c. From thymus of Dog one year old.

d. From thymus of Calf twenty days old.

The cells contain spherules, and masses of hæmoglobin, some of them as large as the coloured blood corpuscles.

Fig. 22. To illustrate the colours of the hæmatoxylin staining solutions.

They were all made with potash alum and extract of logwood, in the proportion of three to one.

(*a*). With old powdered alum.

(*b*). With old crystals of alum.

(*c*). With old alum. (This solution had been made four years, all the others only a few hours.)

(*d*). With old dried alum.

(*e*). With fresh crystals of alum.

(*f*). With freshly-made dried alum.

Fig. 23. Camera lucida, obj. 2, × 75, oc. III., obj. 4.

Transverse section of one-half of the thymus of human fœtus six to ten weeks old.

Only about one-third of the drawing is filled in.

There is no difference traceable between the medullary and cortical tissue.

ct. Connective-tissue surrounding the gland.

v. Blood vessels.

The lymphoid cells are drawn a little too small.

Fig. 24. Natural size, represents three lobules of the thymus of Calf seven months old. Separated after the tissue had lain for some hours in dilute bichromate of potash.

Figs. 25 and 26. From the cortex of follicle of the thymus of Calf twelve days old.

In fig. 25, the specimen was shaken very carefully; in fig. 26, roughly for a long time.

Fig. 25. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

c. Capsule with the blood vessels running obliquely through it.

th. Strong threads.

A network, formed of star-shaped cells and their processes, unites the blood vessels and the threads, and forms an adventitia to the blood vessels.

Fig. 26. Camera lucida, obj. 5, × 300, oc. III., obj. 8.

c. and *th.* As in fig. 25.

Figs. 27 and 28. Cortex of follicle, from the thymus of fœtus three months old.

Fig. 27. Camera lucida, obj. 9, × 750, oc. III., obj. 11, immersion.

The reticulum is seen as a fine network, with deeply-stained, irregularly-shaped nodes ; the lymphoid cells are nearly spherical, and are not so deeply stained.

Fig. 28. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

The section was somewhat shaken.

a.a. The nuclei of connective-tissue-corpuscles.

v. Blood vessel showing two nuclei.

r. The reticulum which is deeply stained.

l.c. Lymphoid corpuscles.

Fig. 29. Camera lucida, simple lens, × 12½.

Section through the neck of Chick on the seventh day of incubation.

c. Medullary canal.

ao. Aortæ.

Th. Thymus.

Jv. Jugular vein, behind it is seen the vagus nerve.

œ. Œsophagus.

Tr. Trachea.

Fig. 30. Camera lucida, obj. 8, × 600, oc. III., obj. 11, immersion.

From thymus of Calf twelve days old.

ct. Star-shaped connective-tissue-corpuscles.

c′t′. Epithelioid cells.

To the left of the figure the protoplasmic network has left spaces, which are partly filled with large granular spheroidal masses.

Fig. 31. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

Section from thymus of Calf twenty-eight days old. The tissue was hardened in osmic and chromic acids.

Spheroidal cells are seen, partly overlapping one another. The centres of the cells are composed of spheroidal granular masses. The nuclei lie at the borders of the cell. At (*g*) there are four nuclei.

v. Blood vessel.

r. Reticulum of which only traces are seen here and there.

lc. Lymphoid corpuscles.

Fig. 32. Oc. III., obj. 8, × 400.

Teased specimen from thymus of Calf one month old.

Spheroidal cells containing granular masses.

Figs. 33 and 34. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

From the upper end of cervical portion of thymus of Calf fully one year old.

The figures show granular cells.

In fig. 33 the central part only is granular.

gr. Granular cell with very coarse granules.

In fig. 34 all parts of the cells are granular.

V. Vein.

Figs. 35, 36, 37, and 38. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Drawings to demonstrate the attachment of the granular cells to the blood vessels, and to the connective-tissue trabeculæ.

Shaken sections of the thymus of Calf twelve days old.

Fig. 35. The granular cell is attached to a capillary blood vessel; the vessel has a perivascular sheath.

Figs. 36 and 38. Granular cells attached by processes to newly-formed connective tissue.

In fig. 36 the processes of some of the granular cells are fibrillated.

Fig. 37. The granular cells are attached, in the upper part of the figure, to newly-formed connective-tissue (*ct.*) and below to (*v.*) a capillary blood vessel.

Figs. 39 and 40. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

Fig. 39. From shaken section of thymus of Calf twelve days old.

a and *b.* Granular cells attached to network.

c and *d.* Granular cells of large size and various shapes.

Fig. 40. From thymus of Calf nearly one year old.

e and *f.* Granular cells with processes.

Fig. 41. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf twelve days old.

ctc. Connective-tissue-corpuscle, containing a nucleus and granular mass.

Fig. 42. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf twelve days old.

Granular mass, attached to part of network of connective-tissue-corpuscles.

Fig. 43. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf nearly one year old.

A granular cell attached to a blood vessel.

Figs. 44, 45, and 46. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Sections of thymus of fœtal Lamb six inches long. The tissue was hardened in osmic and chromic acids.

Fig. 44. Epithelioid connective-tissue-corpuscles, containing granular masses of various sizes. The granular masses are apparently nucleated in D. and E.

A. Epithelioid cell, containing a small granular mass, and a nucleus.

Fig. 45, A, B, C. Epithelioid cells, some showing nuclei, others containing smaller or larger granular masses.

va. Vacuolated cells, containing granular mass.

Fig. 45, A, *gr.* Granular cell containing two nuclei.

g. A cell containing a nucleus and a small granular mass.

Fig. 46, A, B, C. Granular cells, which are more or less vacuolated.

Fig. 46, D. Granular cell with two nuclei and containing a large vacuole.

Fig. 46, E. Multinucleated protoplasm, surrounding a vacuole which contains a vacuolated granular cell.

This is one of the earliest stages of formation of a concentric corpuscle.

Fig. 46, F. Epithelioid cell which is much enlarged, the protoplasm is very transparent; the outer edge of the cell is somewhat thickened.

Fig. 46, G. Multinucleated protoplasm surrounding an epithelioid cell. The whole forms a commencing concentric corpuscle.

Fig. 47. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Very large transparent epithelioid cell.

From section of thymus of fœtal Lamb eleven inches long. The tissue was hardened in osmic and chromic acids.

Fig. 48. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Granular cell with three nuclei.

From section of thymus of Calf nearly one year old, stained by solution of Brazil wood.

Fig. 49. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Section of thymus of fœtal Lamb six inches long. The tissue was hardened in osmic and chromic acids.

In the lower part of the figure two concentric corpuscles are seen; above them, lymphoid and epithelioid cells; and in the upper part of the figure, many granular cells.

cc. Commencing concentric corpuscle.

gr. Granular cell with three nuclei.

v. Blood vessel.

Fig. 50. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Section of thymus of fœtal Lamb eleven inches long. The tissue was hardened in osmic and chromic acids.

In the lower part of the figure a concentric corpuscle is seen. To the left of the figure, two giant cells; to the right, at (*cc.*) commencing concentric corpuscles.

gr. Granular cells, probably forming a giant cell.

th. Coarse threads attached to the concentric corpuscles.

Figs. 51, 52, and 53. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Multinuclear masses of protoplasm, enclosing granular masses.

Fig. 51. Section of thymus of Calf three days old.

The tissue was hardened in chloride of gold and chromic acid.

Figs. 52 and 53. From thymus of Calf one year old.

Fig. 54. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

From thymus of Calf nearly one year old.

Multinuclear masses of protoplasm, at right angles to newly-formed band of fibrous-tissue (*ct.*).

The protoplasmic masses are arranged so as to leave oval spaces or gaps.

Fig. 55. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Giant cell with central cavity, from thymus of Calf twelve days old.

Fig. 56. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

Giant cell with various processes, from teased specimen of thymus of Calf six months old.

Fig. 57. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

Teased specimen from thymus of Calf one year old.

Giant cell with processes in various planes.

Figs 58, 59 *a* and *b*, 60, 61, 62. Oc. III., obj. 8, × 400.

Teased specimens from thymus of a Child.

Fig. 58. *cc.* Concentric corpuscle, whose outline only is drawn; it ends in a vessel-like prolongation; the prolongation branches, and at this point there is a granular cell.

Fig. 59 *a.* Concentric corpuscle, containing a dark mass, which extends down the vessel-like prolongation of the concentric corpuscle.

Fig. 59 *b.* One of the cells of the periphery of the concentric corpuscle.

Fig. 60. A compound concentric corpuscle.

In the lower part of the figure, coarse connective-tissue threads.

Figs. 61 and 62. From the periphery of a concentric corpuscle to show the coarse threads with imbedded nuclei.

Fig. 63. Camera lucida, obj. 5, × 300, oc. III., obj. 8.

From thymus of Child, stillborn.

Three concentric corpuscles, connected to one another by fibrillated processes. Attached to one of the concentric corpuscles is a long thread.

v. Blood vessel.

Fig. 64. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Section of thymus of Calf three days old, hardened in chloride of gold and chromic acid.

Two commencing concentric corpuscles. The upper one consists of vacuolated protoplasm containing a granular cell. The two commencing concentric corpuscles are united by connective-tissue cells; so that the whole has somewhat the appearance of a vessel containing granular cells.

Fig. 65. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

From thymus of Calf one year old. In the upper part of the figure a network is seen, containing one granular cell.

Below, is a large granular mass in continuity with a vessel-like formation. The whole is attached to the cells forming the network.

Fig. 66. Camera lucida, obj. 7, × 450, oc., III., obj. 9.

Section of thymus of Calf one year old, hardened in chloride of gold and chromic acid.

Two granular cells, and a small cell surrounded by a thick border; the whole forming a commencing concentric corpuscle.

Fig. 67. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

From thymus of Calf one year old.

Multinuclear protoplasm surrounding a vacuole, which contains a granular cell. The whole forms an early stage in the formation of a concentric corpuscle.

Fig. 68. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

From thymus of Calf twelve days old. In the lower part of the figure a commencing concentric corpuscle is seen, composed of epithelioid and granular cells. The central granular cell (*gr*) is surrounded by a vacuole.

v. Blood vessel, to which is attached a network of connective-tissue-corpuscles and granular cells.

f. A bundle of newly formed fibrous-tissue.

Fig. 69. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

From thymus of Calf twelve days old. Shaken specimen. At the upper part of the figure a small concentric corpuscle is seen; the centre is formed by a granular cell.

v. Blood-vessel.

The neighbouring connective-tissue-corpuscles are very large.

f. Newly formed fibrous-tissue, attached to the wall of the vessel, in the lower part of the figure.

th. Coarse connective-tissue threads, with imbedded nuclei.

gr. Granular cells.

Fig. 70. Oc. III., obj. 11, immersion × 850.

A thymic corpuscle treated by $\frac{3}{4}$ per cent. saline solution.

Fig. 71. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

cbc. The outlines of the colourless blood corpuscles, from one of the thymic veins of an Ox twenty-two months old.

Thc. The outline of the thymic corpuscles, from one of the lymphatics of the thymus of the same animal.

B, C, D, E, not drawn to scale.

B. Large cell, with processes containing fine granules, but no hæmoglobin.

C, D, E. Various cells containing larger or smaller masses of hæmoglobin.

Figs. 72, 73, 74, 75, and 76. Camera lucida, obj. 8, × 600, oc. III., obj. 9. These figures show the exact comparative sizes of the outlines of the coloured and of the colourless blood corpuscles, and of the Thymic corpuscles in the various classes of Vertebrates.

cb. and *cbc.* Coloured and colourless blood corpuscles, examined without reagent.

Thc. Thymic cells, examined in $\frac{3}{4}$ per cent. saline solution.

Fig. 72. From Ray-fish two feet seven inches across.

Fig. 73. From Frog about one-fourth grown.

Fig. 74. From Tortoise half-grown.

Fig. 75. From Pigeon three months old.

Fig. 76. From Dog eighteen months old.

Fig. 77. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

bc. Coloured blood corpuscles of adult Camel.

cbc. Colourless blood corpuscle of the same.

d. Large cell, not drawn to scale, containing small oval coloured blood corpuscles from the lymphatic gland of the same.

Fig. 78. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of medulla of follicle, from thymus of Calf twelve days old.

f. Commencing fibrous-tissue; at this point, the connective-tissue-corpuscles are much closer together, and the nuclei are more abundant than in other parts of the figure. A little above the middle, three granular cells are seen; to the left, connective-tissue-corpuscles forming a network. They are drawn as if they branched only in one plane.

A few lymphoid cells are seen.

Fig. 79. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Section of medulla of follicle, from thymus of Calf one year old, hardened in chloride of gold and chromic acid.

To show the formation of fibrous-tissue from spindle-shaped cells.

Figs. 80 and 81. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf nearly one year old.

Fig. 80. From cortex of a follicle.

v. A blood vessel, with adventitia of newly-formed tissue.

The network is composed of broad, closely-meshed connective-tissue.

Fig. 81. From centre of medulla of a follicle.

A blood vessel, with adventitia of newly-formed connective-tissue. The vessel is unchanged.

f. Fibrous-tissue attached to the adventitia.

Fig. 82. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

From thymus of Calf twelve days old.

Three granular cells, attached to newly-formed fibrous-tissue; the largest has a distinctly fibrillated process.

Fig. 83. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of the thymus of Calf nearly one year old.

Granular cell, whose process is in connexion with a dark reticulum.

Epithelioid cells are also seen.

Fig. 84. Camera lucida and simple lens, × $12\frac{1}{2}$.

From thymus of Dog nine years old. One follicle is shown, divided into two parts by invading fat tissue (*F*).

ce. Five cysts lined by ciliated epithelium. The cysts contain hæmoglobin.

Figs. 85, 86, 87, 88, and 89, demonstrate the formation of ciliated epithelium in the thymus of the Dog.

Camera lucida, obj. 7, × 450, oc. III., obj. 8.

Fig. 85. From thymus of Dog thirty months old.

A small giant cell, whose edges are attached to connective-tissue-corpuscles.

Fig. 86. From thymus of Dog five months old.

Concentric corpuscle.

ce. Cyst containing degenerated cells.

Fig. 87. From thymus of Dog five months old.

Concentric corpuscle with large cavity. The interior is filled with degenerated cells. The border of the cavity is lined with epithelioid cells (*ep*).

Fig. 88. From thymus of Dog sixteen months old.

Two cysts, partially lined by sub-columnar ciliated cells.

dg. Mass of degenerated cells.

ep. Epithelioid cells, partially lining one cyst.

Fig. 89. From thymus of Dog sixteen months old.

Two small cysts. That on the right is lined in great measure by ciliated epithelium. The cyst on the left is lined by ciliated epithelium in its upper part, but below is bordered by large epithelioid cells (*ep*).

va. Vacuolated and degenerated cells.

Fig. 90. Camera lucida, obj. 5, × 300, oc. III., obj. 7.

From thymus of Dog nine years old, showing a row of ciliated cells, which line a large cyst. The cells are in more than one layer. Only part of the drawing is filled in.

v. Blood vessel.

Fig. 91. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

From thymus of Dog sixteen months old, showing columnar ciliated epithelium.

v. Blood vessel.

Fig. 92. Camera lucida, obj. 7, × 450, oc. III., obj. 8.
Teased specimen, from thymus of Dog about two years old.
Two ciliated epithelial cells.

Figs. 93 and 94. Camera lucida, obj. 7, × 450, oc. III., obj. 8.
To illustrate the formation of vessels.
Fig. 93. From thymus of Calf one year old.
The vessel is inter-epithelial.
Fig. 94. From thymus of human fœtus, probably three months old.
The new vessel is intra-epithelial and granular, and is formed from a granular cell.

Figs. 95 and 96. Camera lucida, obj. 7, × 450, oc. III., obj. 8.
Fig. 95. Section of thymus of Calf one year old.
The tissue was hardened in chloride of gold and chromic acid.
A vessel with thickened adventitia.
Fig. 96. From thymus of Calf one year old.
Vessel with adventitia composed of more than one layer of cells.
pe. Perivascular sheath.

Figs. 97, 98, 99, 100, and 101. Camera lucida, obj. 7, × 450, oc. III., obj. 8.
From thymus of Turkey seven and a-half months old.
Fig. 97. Giant cell, whose central part is formed by a granular mass.
lc. Lymphoid cell.
Fig. 98. Teased specimen.
a. Granular cell.
b, b′, b″, b‴. Various forms of vacuolated cells.
c. Cell with hæmoglobin granules.
Fig. 99. Shows part of the medullary portion of follicle.
Epithelioid cells, showing traces of reticulum between the cells.
gr. Two granular cells, one of which has four nuclei.
lc. Lymphoid corpuscles.
Figs. 100 and 101. Concentric corpuscles with large central cavity formed by vacuolation.
In fig. 101 individual vacuolated cells are seen.

Fig. 102. Camera lucida, obj. 8, × 600, oc. III., obj. 9.
From thymus of Turkey seven months old.
Shows small epithelioid cells, the lymphoid corpuscles, and the reticulum.

Fig. 103. Camera lucida, obj. 8, × 600, oc. III., obj. 9.
From thymus of Ray-fish $4\frac{1}{2}$ inches across.
The lymphoid corpuscles and traces of the reticulum are seen.
ea. Large endothelial cell of the capsule of the follicle.

Figs. 104, 105, 106, 107, and 108. Camera lucida, obj. 7, × 450, oc. III., obj. 8.
From thymus of Tortoise.

Fig. 104. From medulla of follicle of Tortoise, probably twenty-one months old.

Granular cells, the largest shows concentric rings.

Fig. 105. From Tortoise, probably eighteen months old.

From cortex of the follicle, showing epithelioid cells and the reticulum.

Figs. 106 and 107. From thymus of medium-sized Tortoise.

Two concentric corpuscles which contain granular cells.

r. Traces of reticulum.

lc. Lymphoid corpuscles.

Fig. 108. From thymus of medium-sized Tortoise.

A large cyst, lined by columnar and sub-columnar epithelium.

h. Masses of hæmoglobin.

Fig. 109. Camera lucida, obj. 2, × 75, oc. III., obj. 4.

Transverse section of one-half of the thymus of fœtal Rabbit eighteen days old.

a. Process formed of epithelioid cells, continuous with the thymus.

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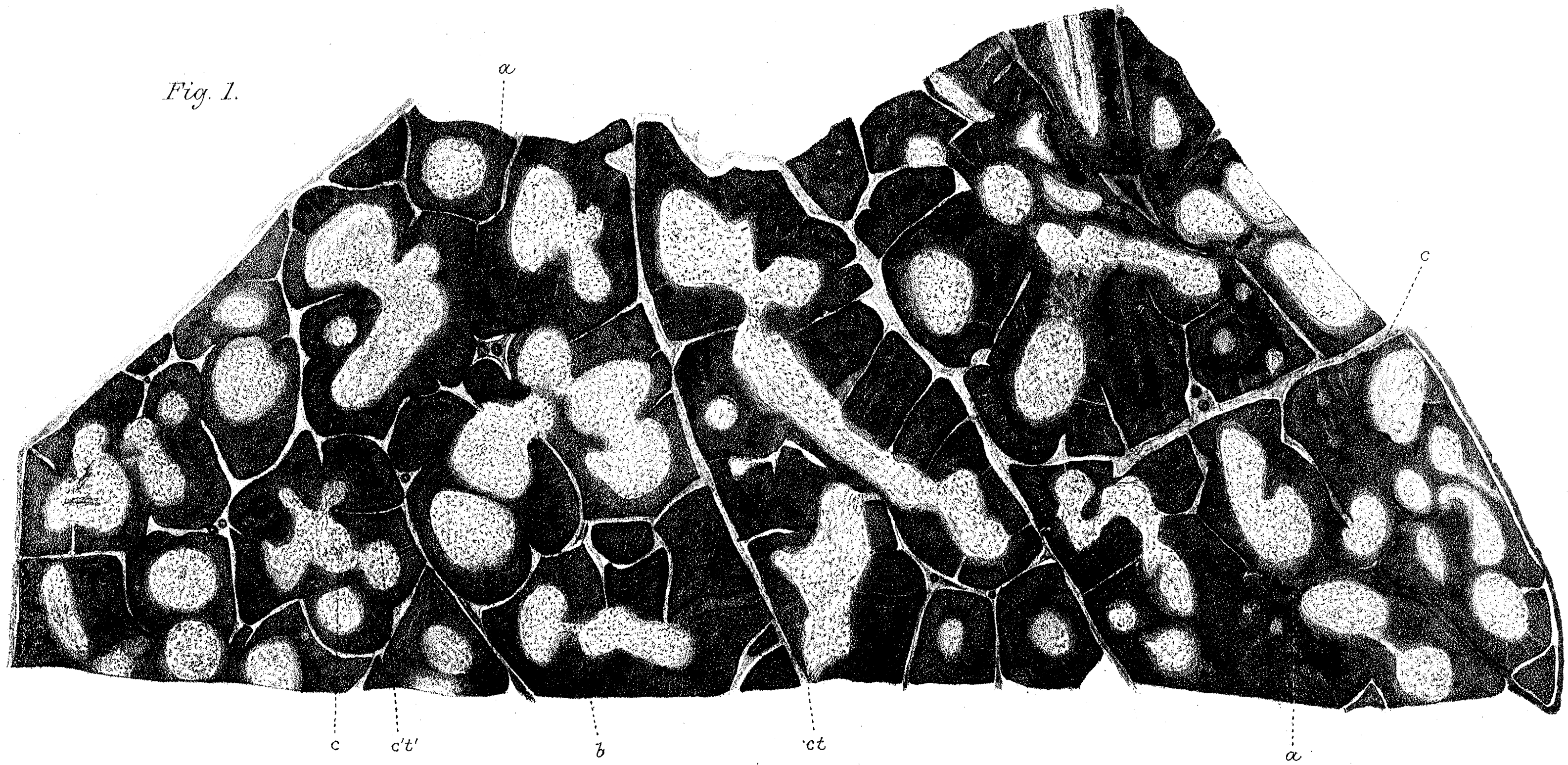
Fig. 1.



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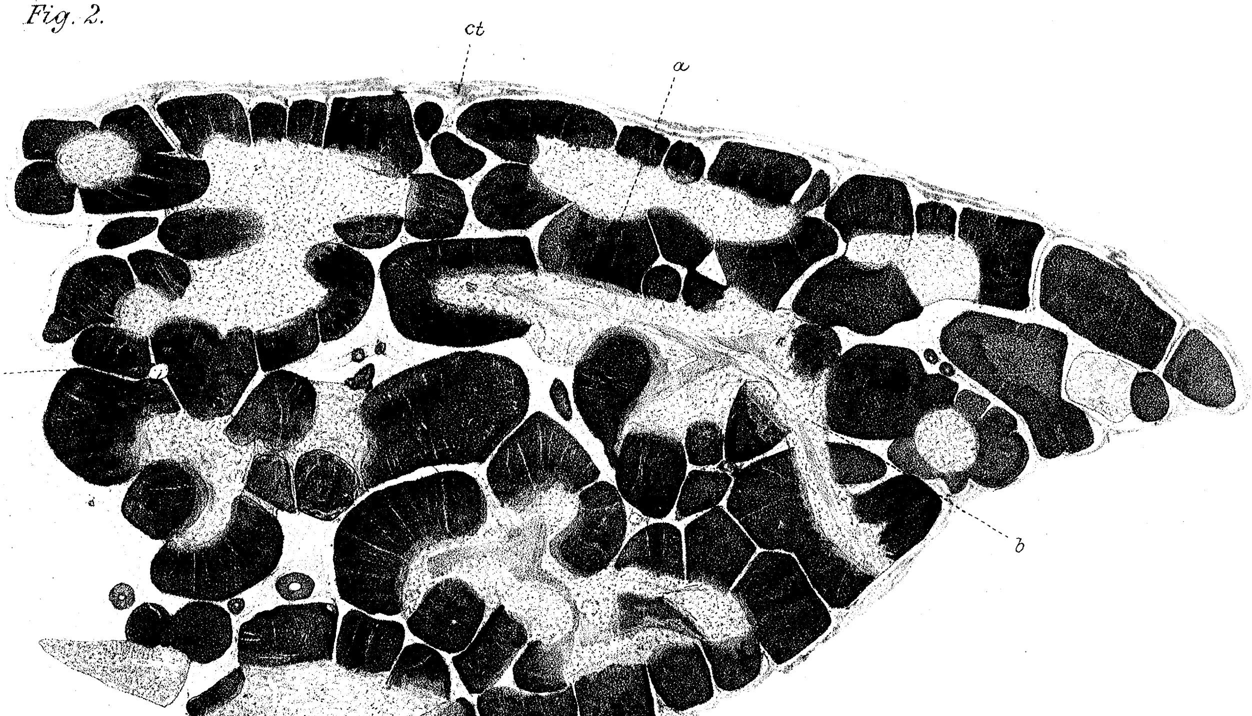

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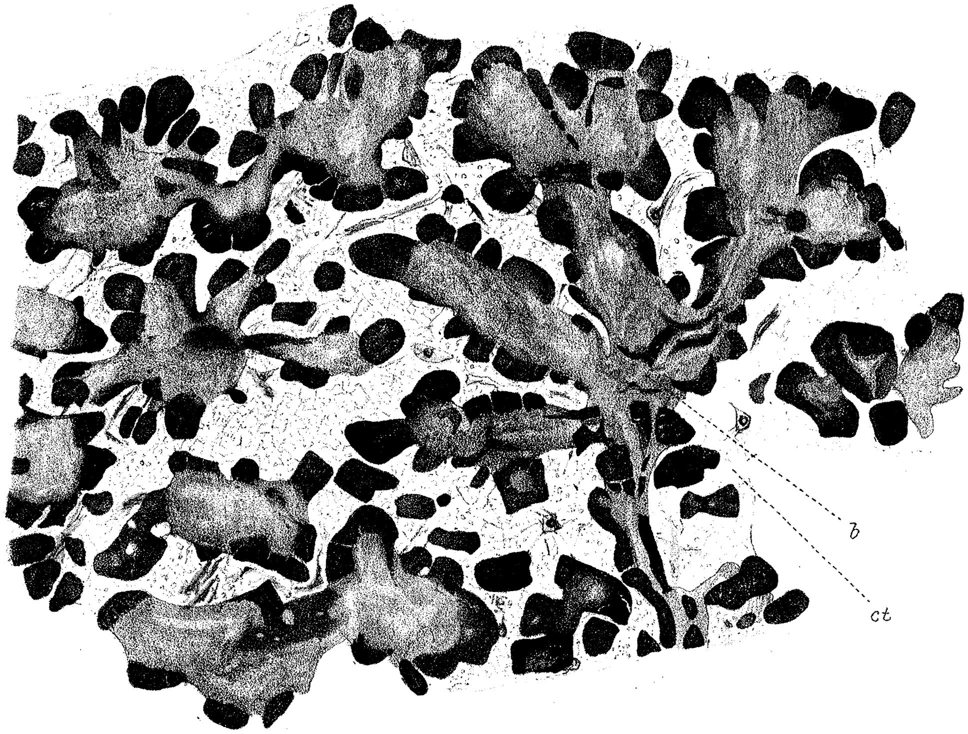

Fig. 4.

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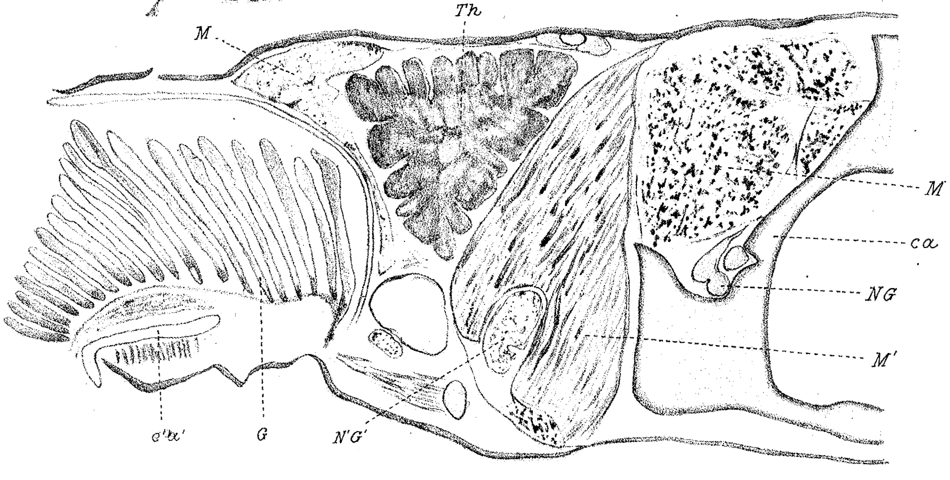

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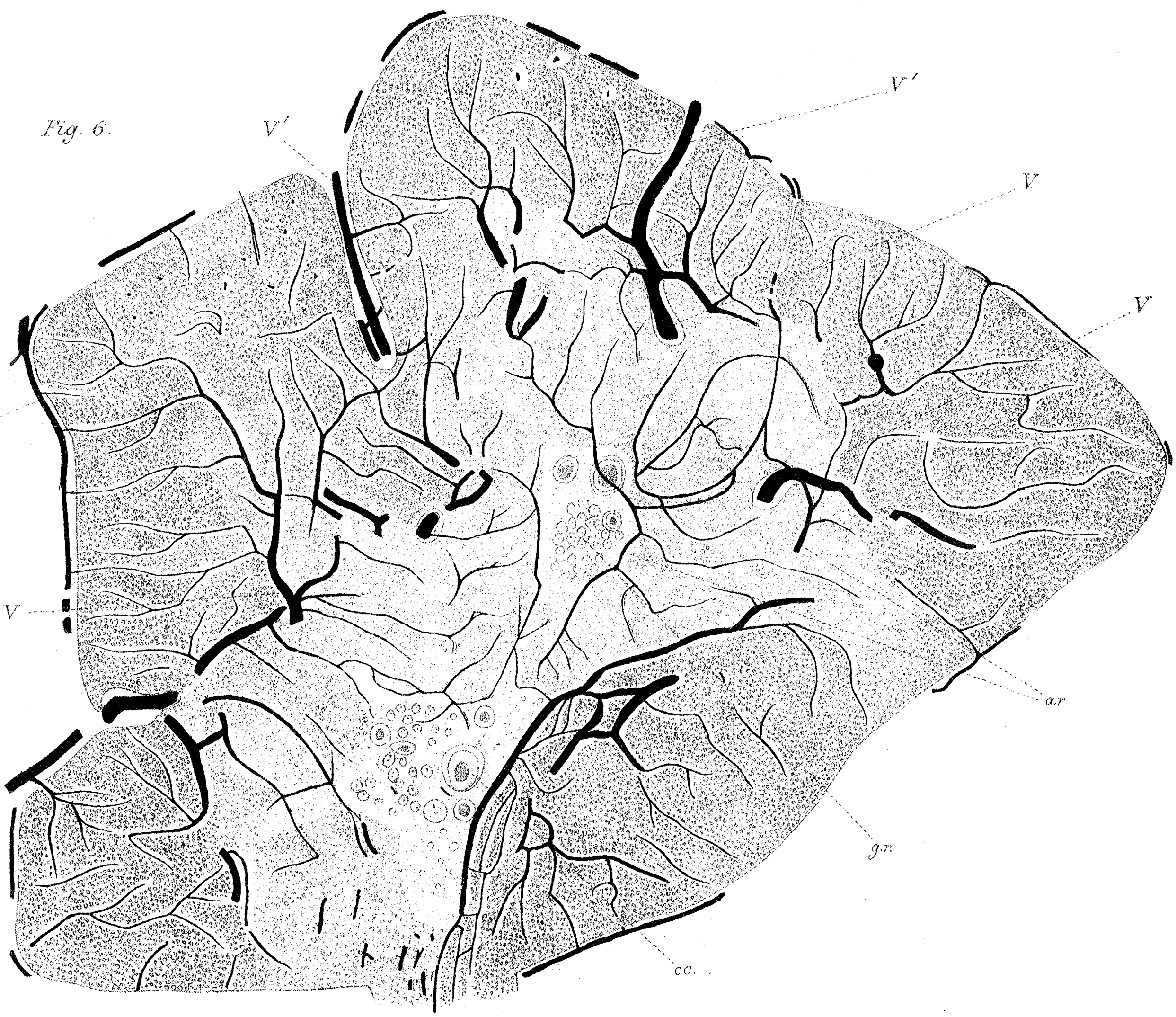

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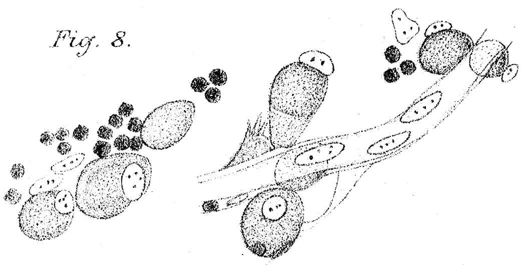

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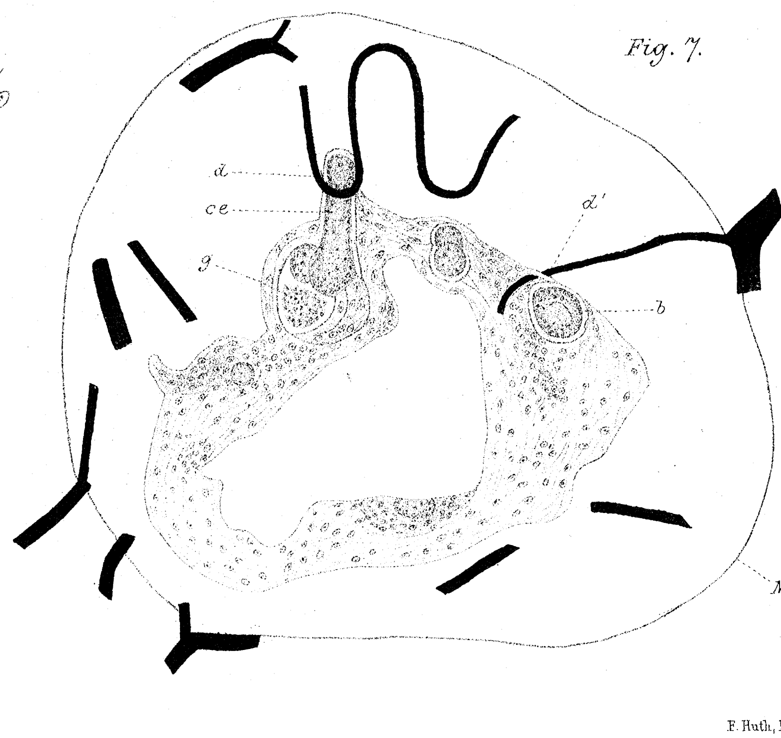

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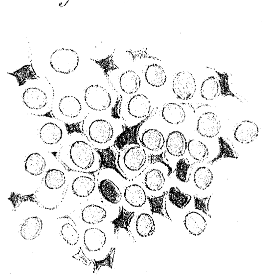

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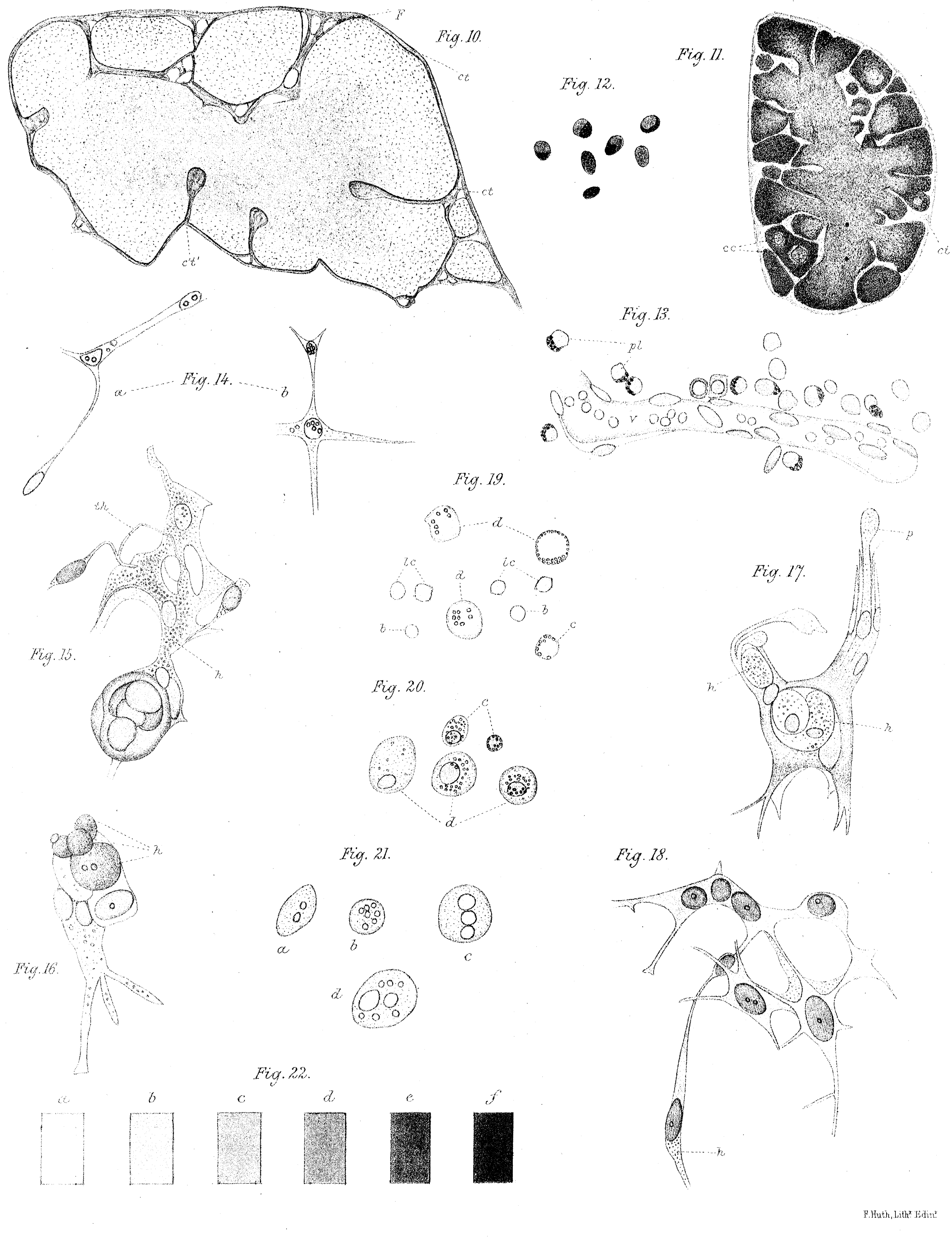

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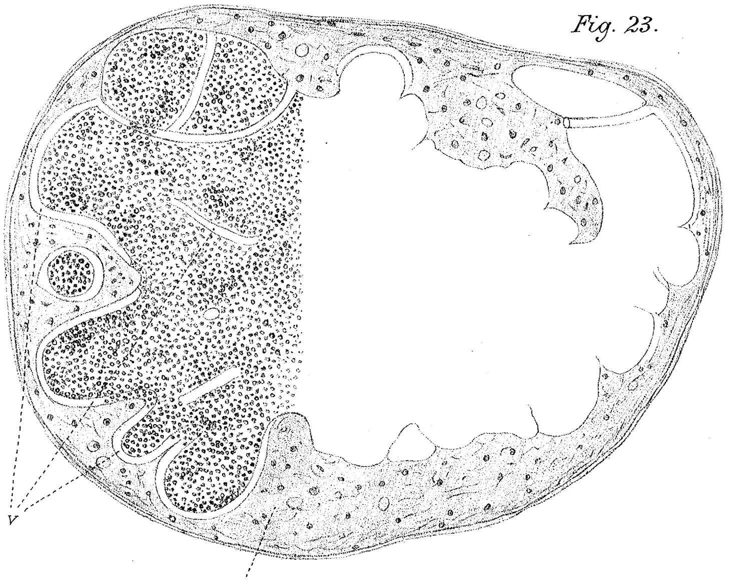
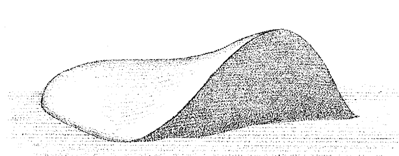
Fig. 23.





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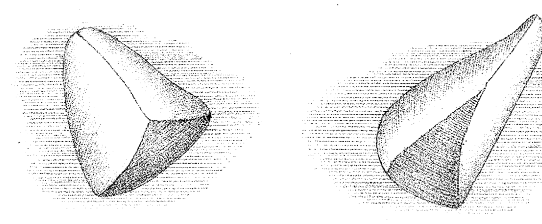

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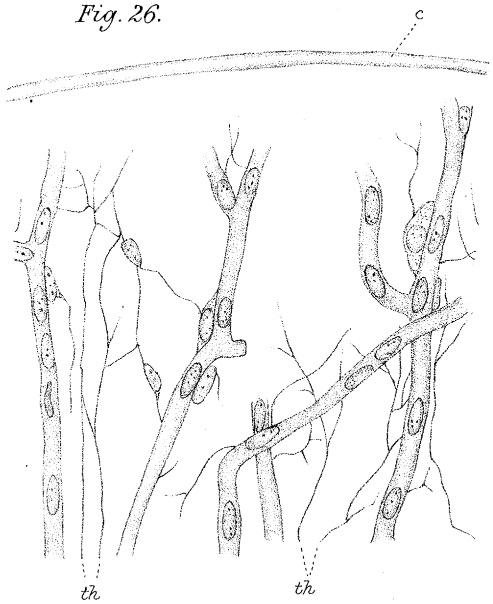

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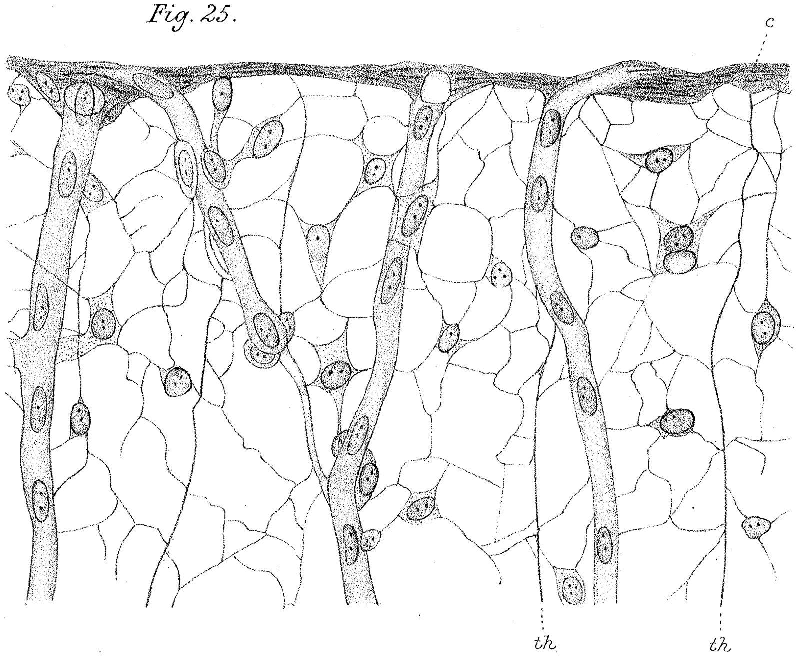

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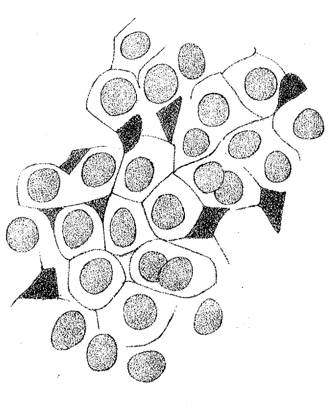

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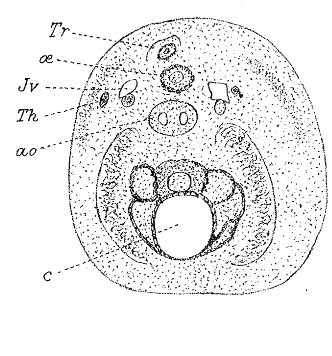

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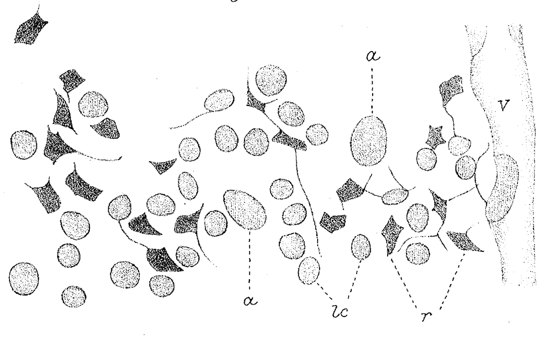

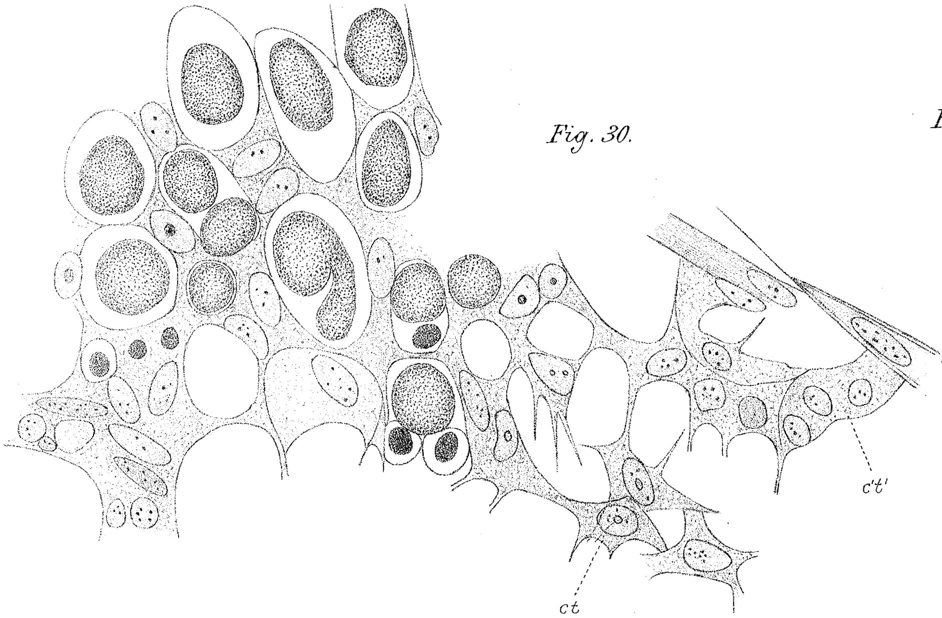

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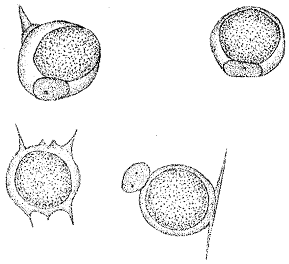

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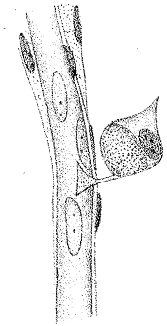

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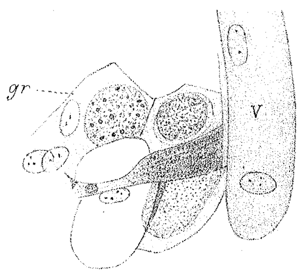

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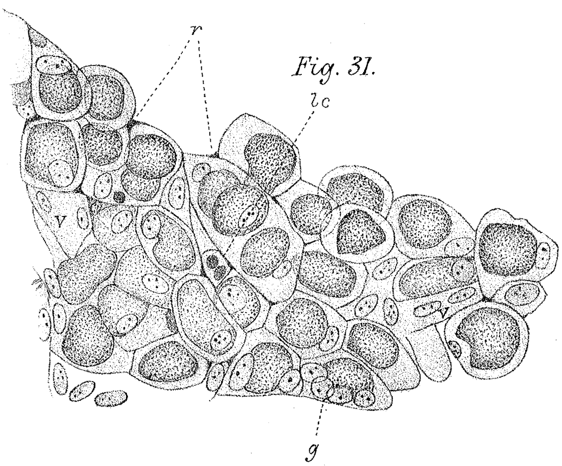

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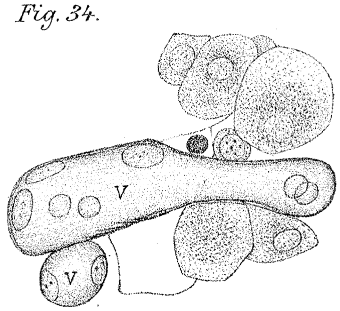

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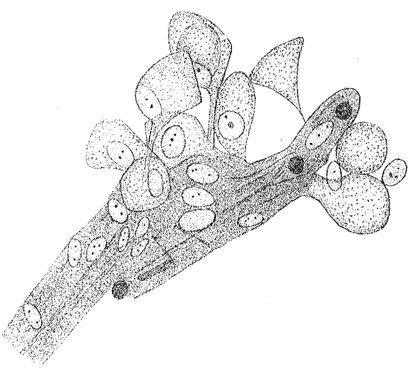

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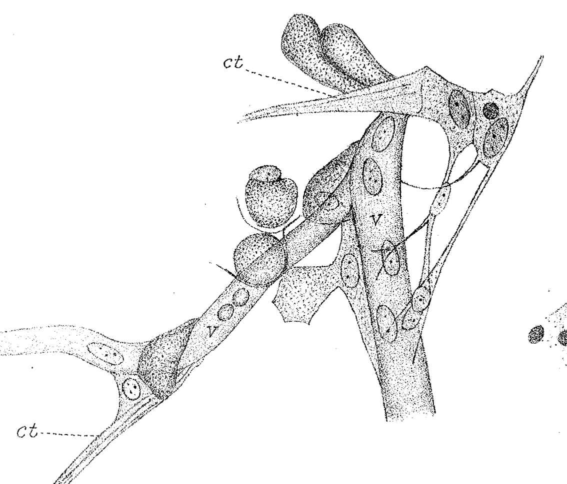

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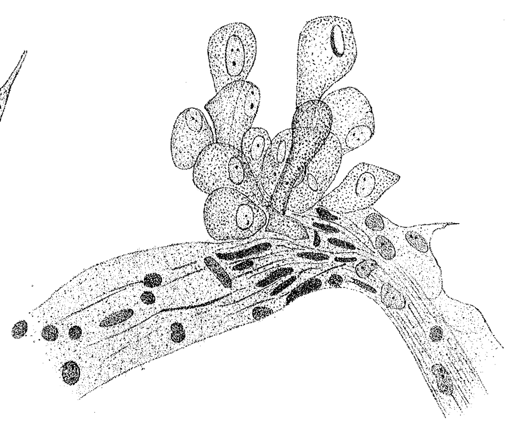

Fig. 38.

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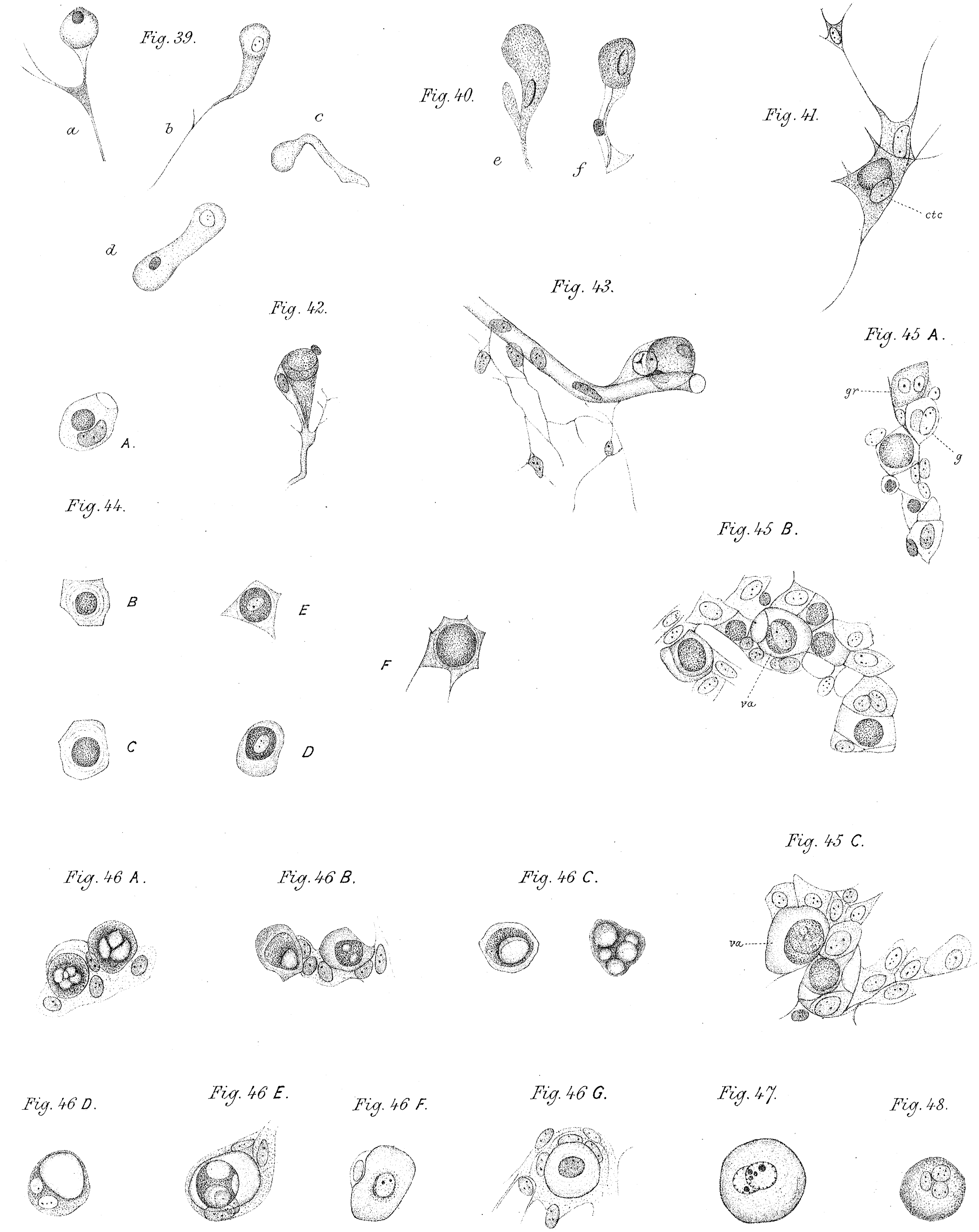

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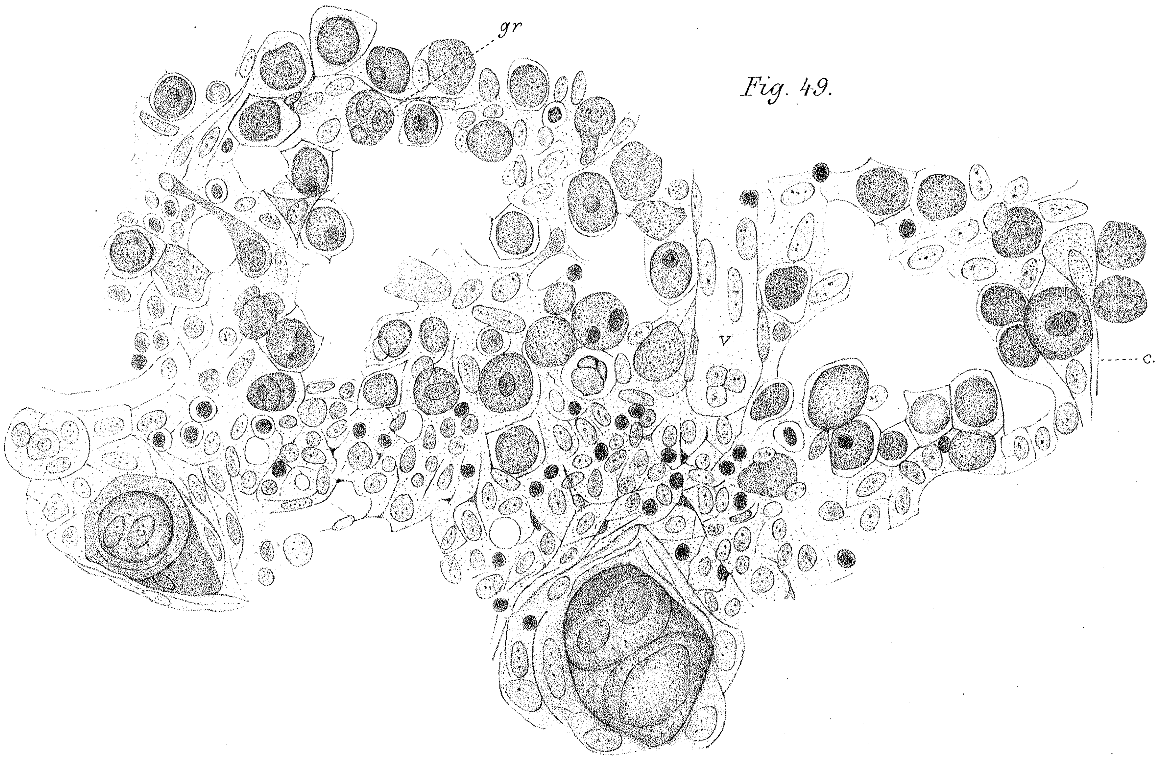

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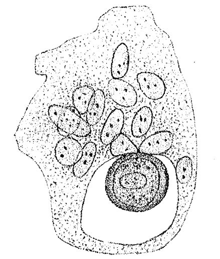

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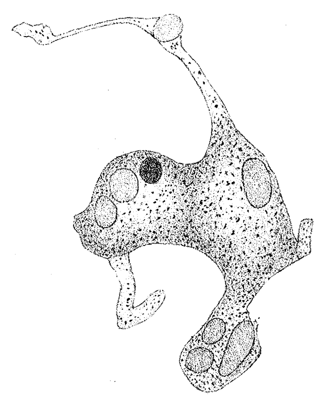

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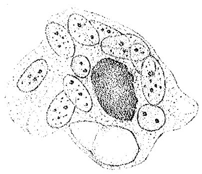

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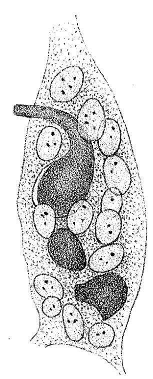

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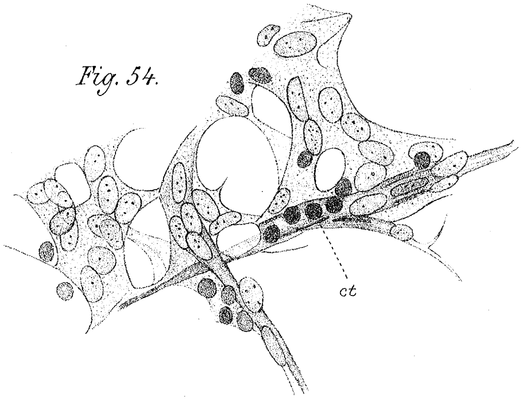

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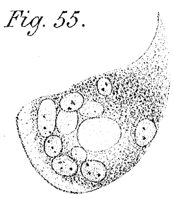

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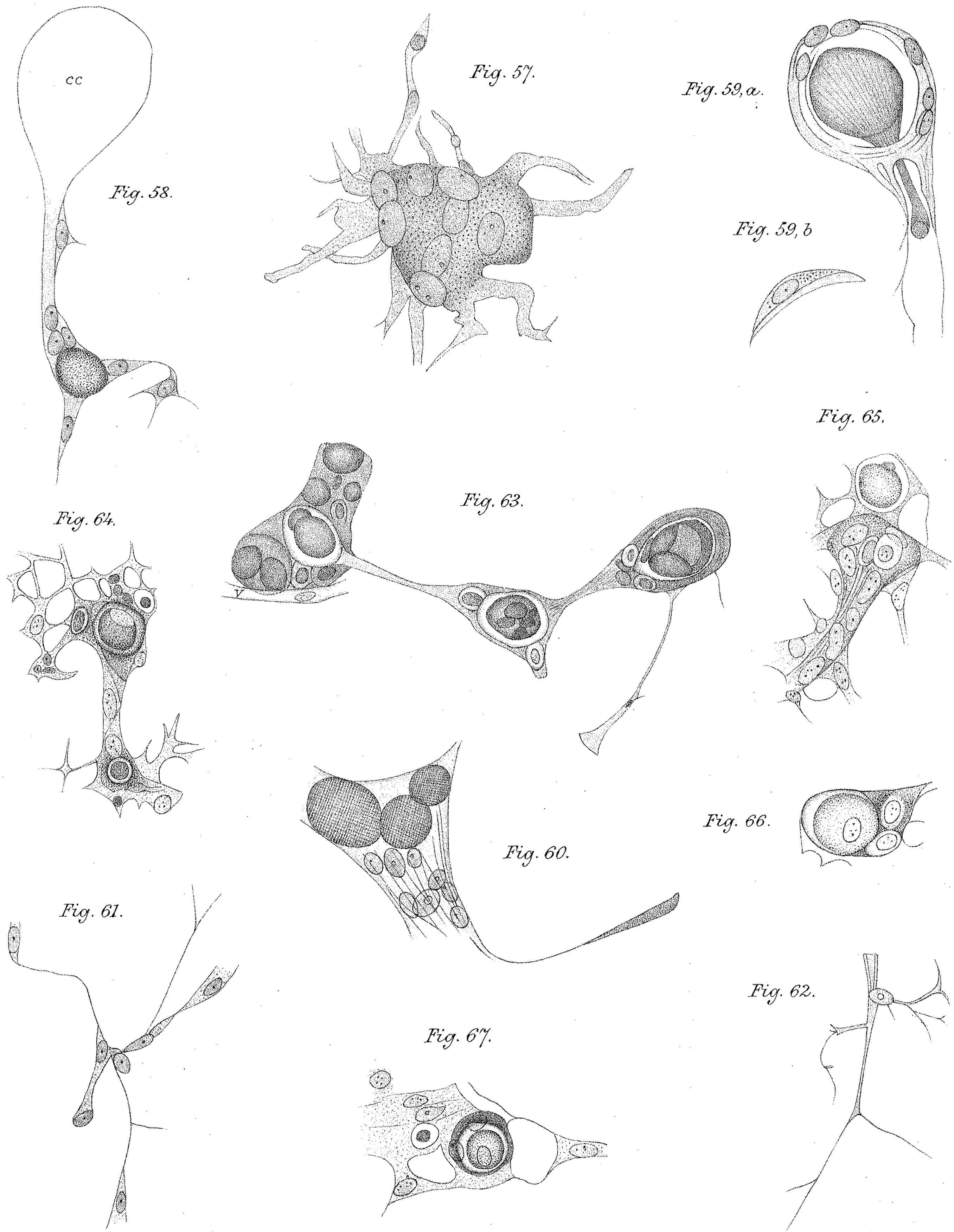

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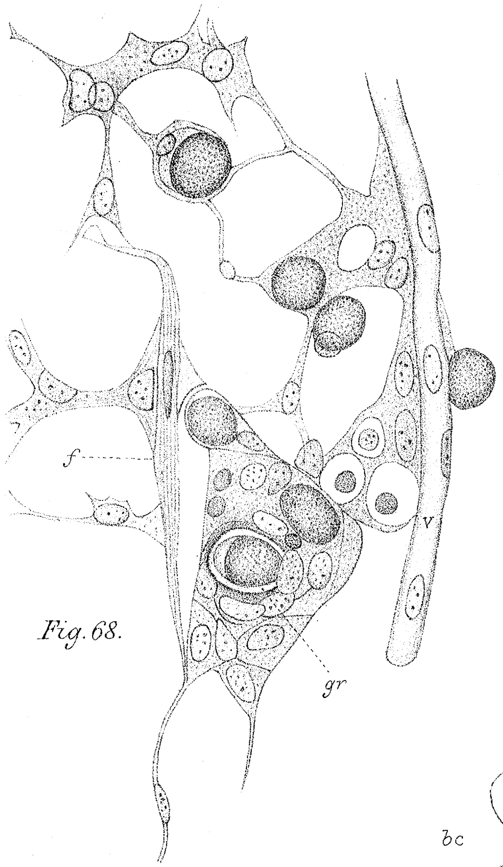

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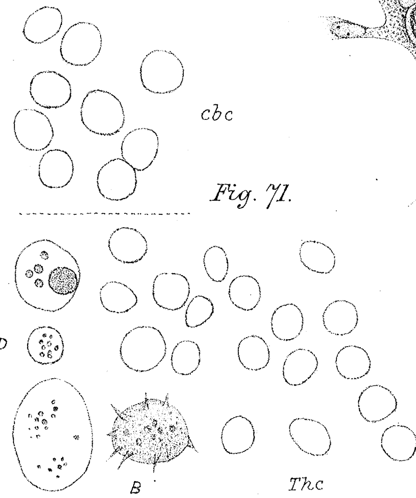

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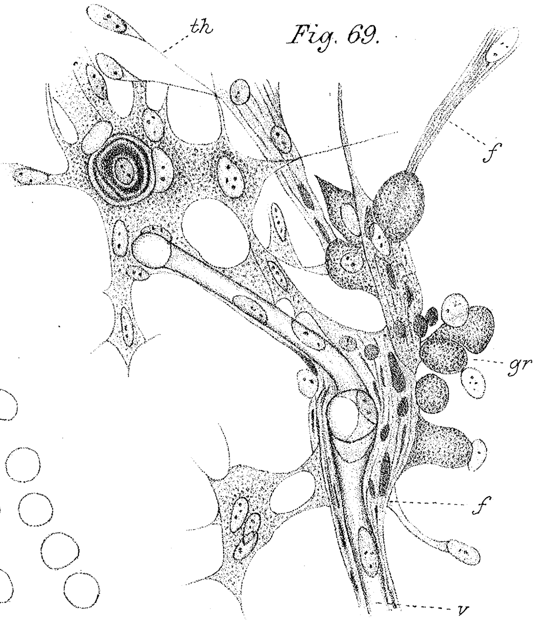

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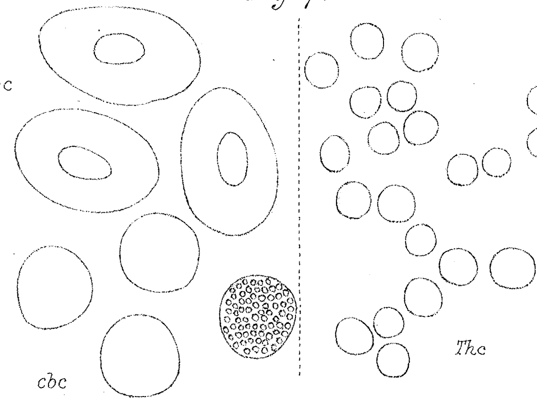


Fig. 72.

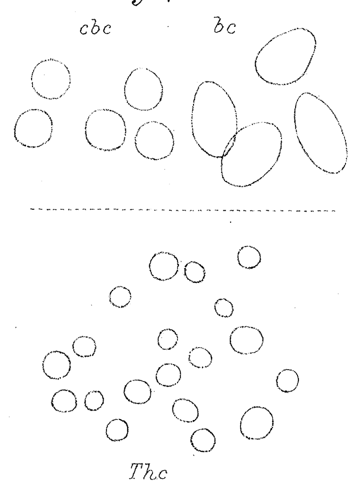
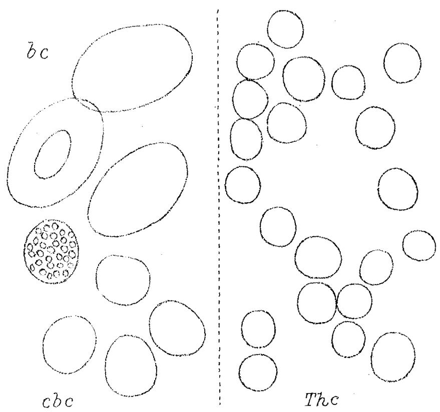


Fig. 75.



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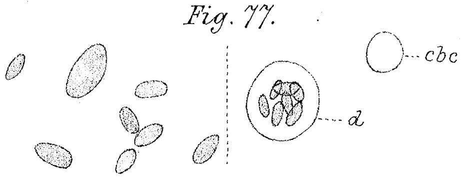

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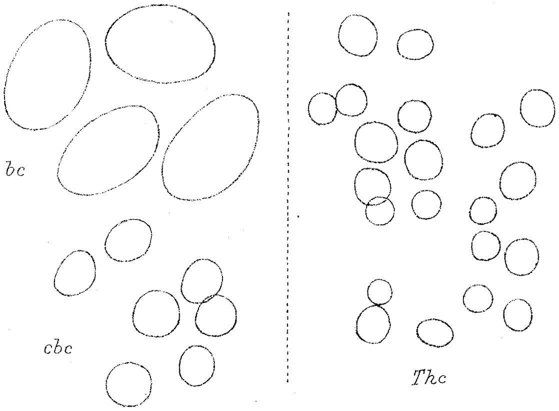

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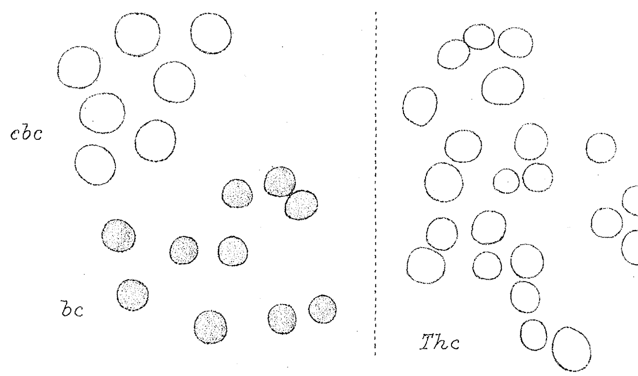
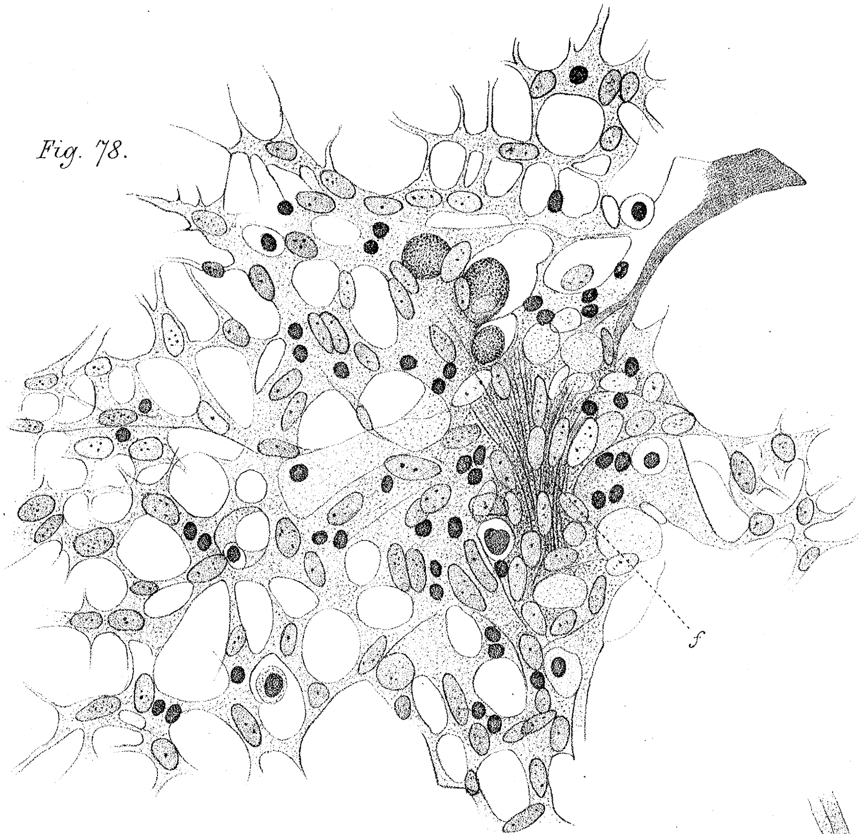


Fig. 76.

F. Huth, Lithr Edinr

Fig. 78.



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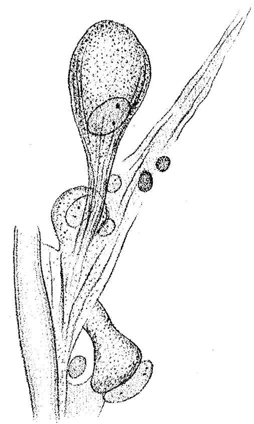

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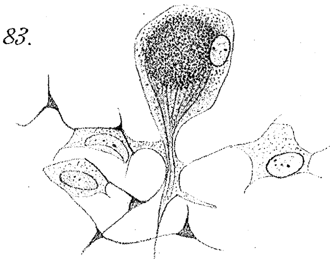

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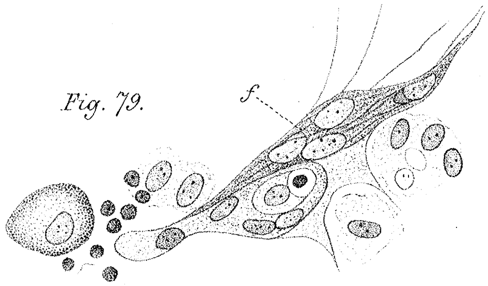

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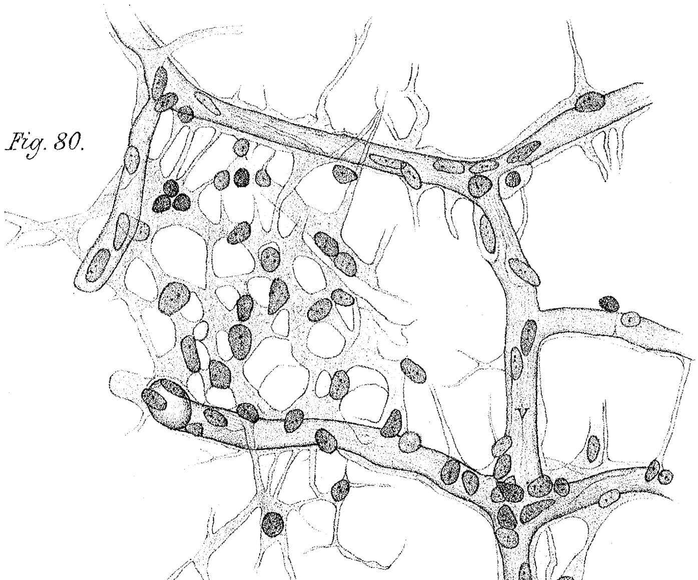

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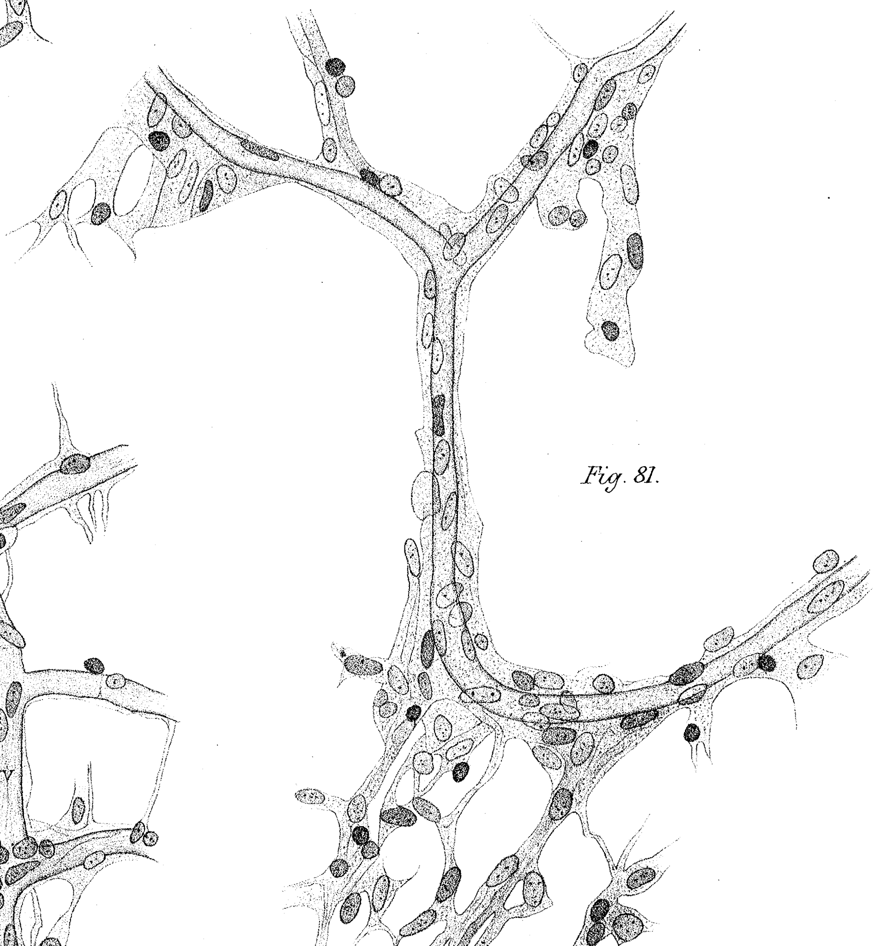
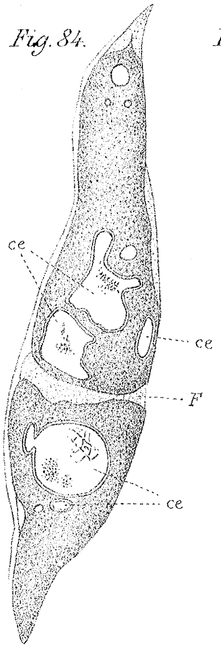


F. Huth, Lith^r Edin^r

Fig. 84.



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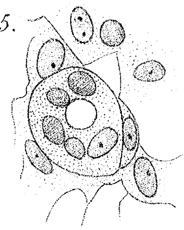

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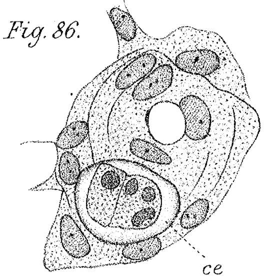

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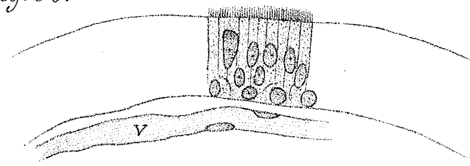

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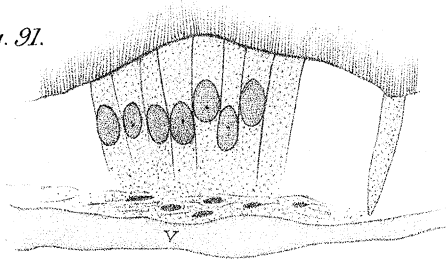

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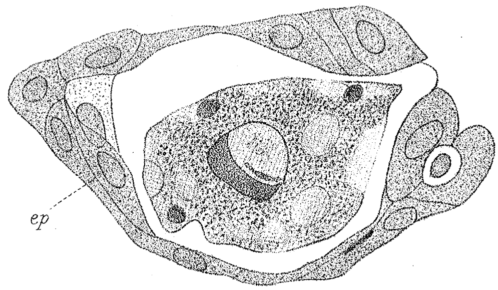

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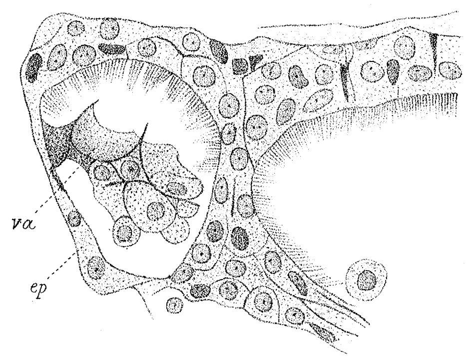

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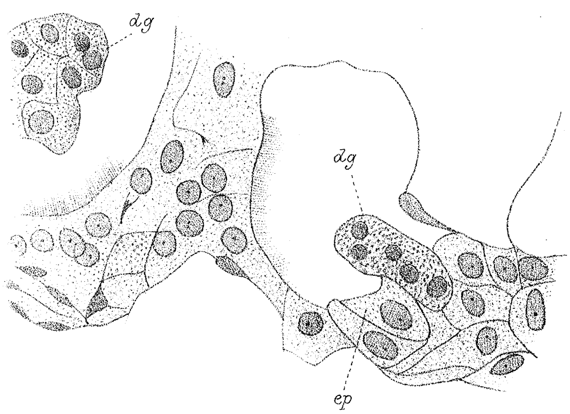
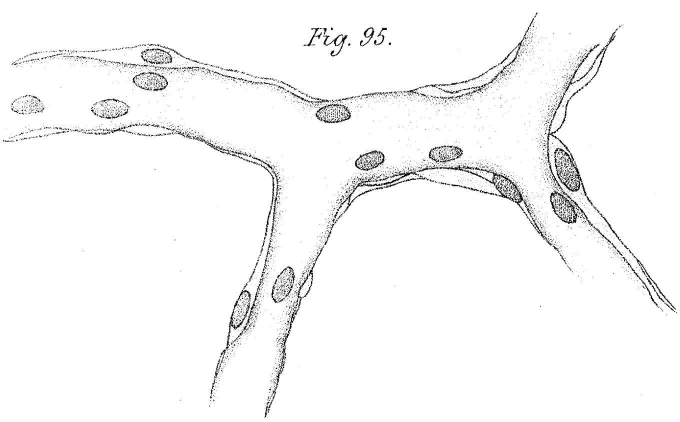


Fig. 92.

Fig. 95.



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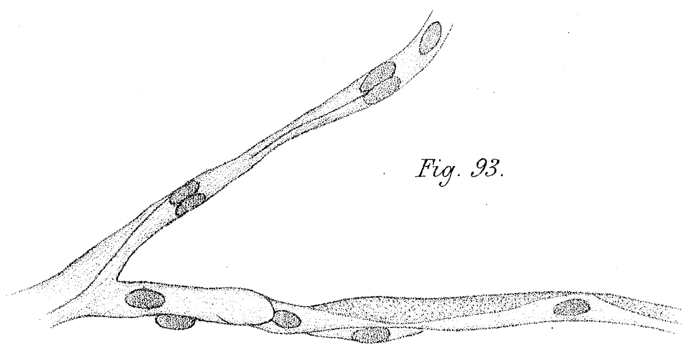

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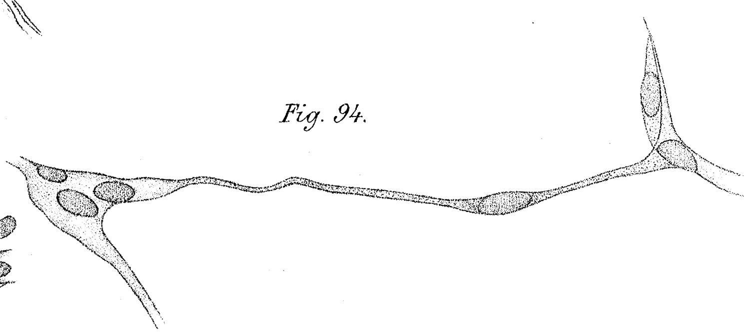

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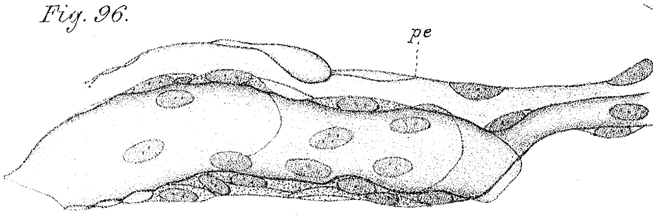


F. Huth, Lith^{r} Edin^{r}

Fig. 99.

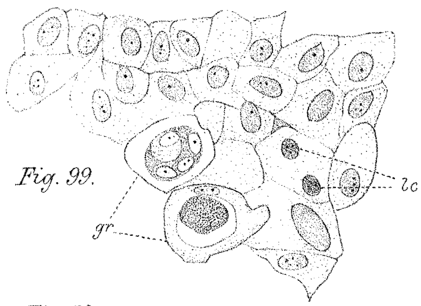
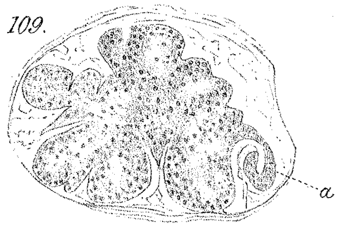


Fig. 109.



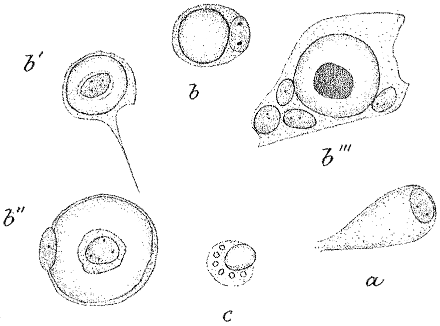
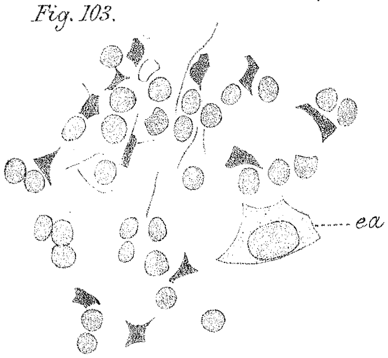


Fig. 98.

Fig. 103.



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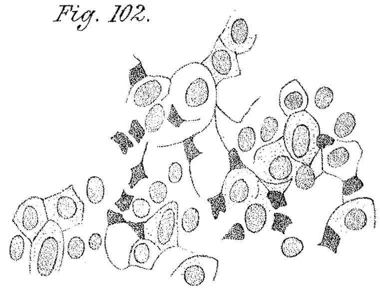

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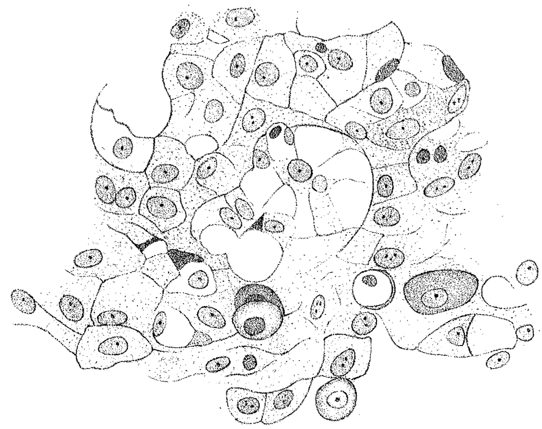

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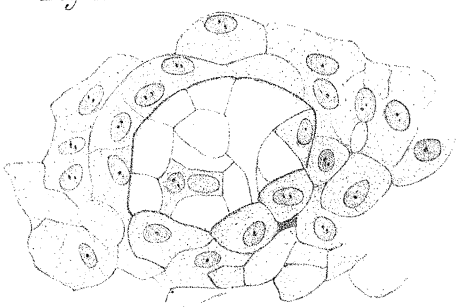

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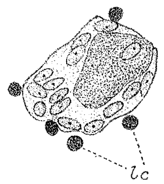

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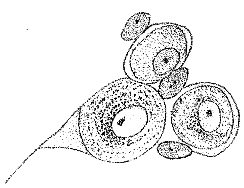

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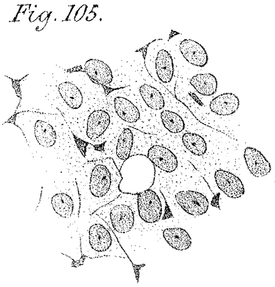

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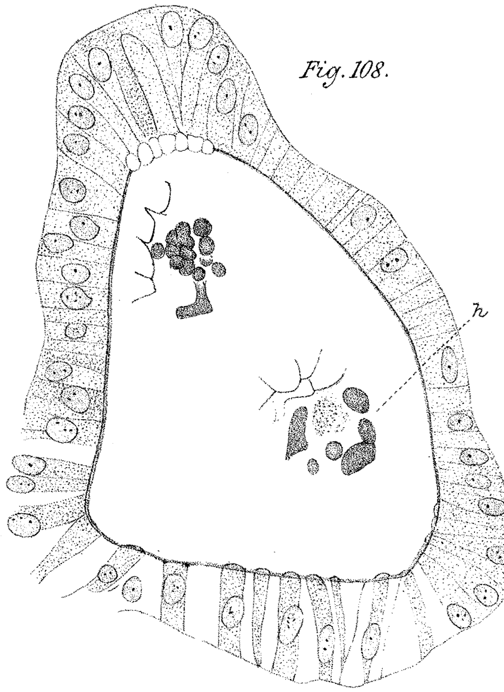


Fig. 107.

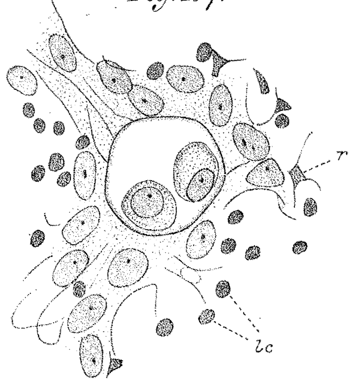


Fig. 106.

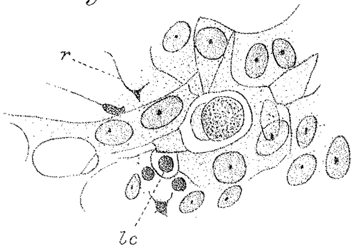


Fig. 1.

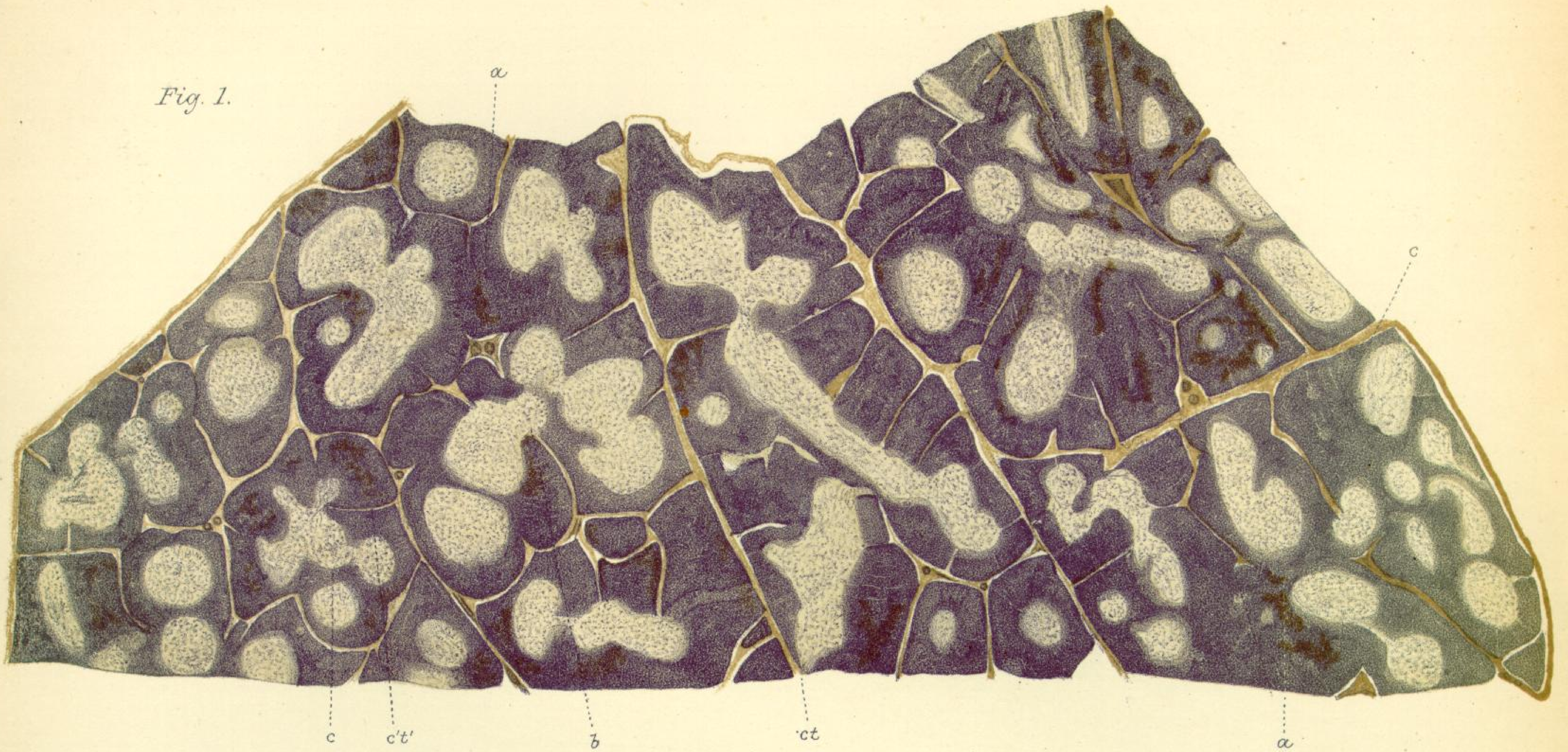


Fig. 2.

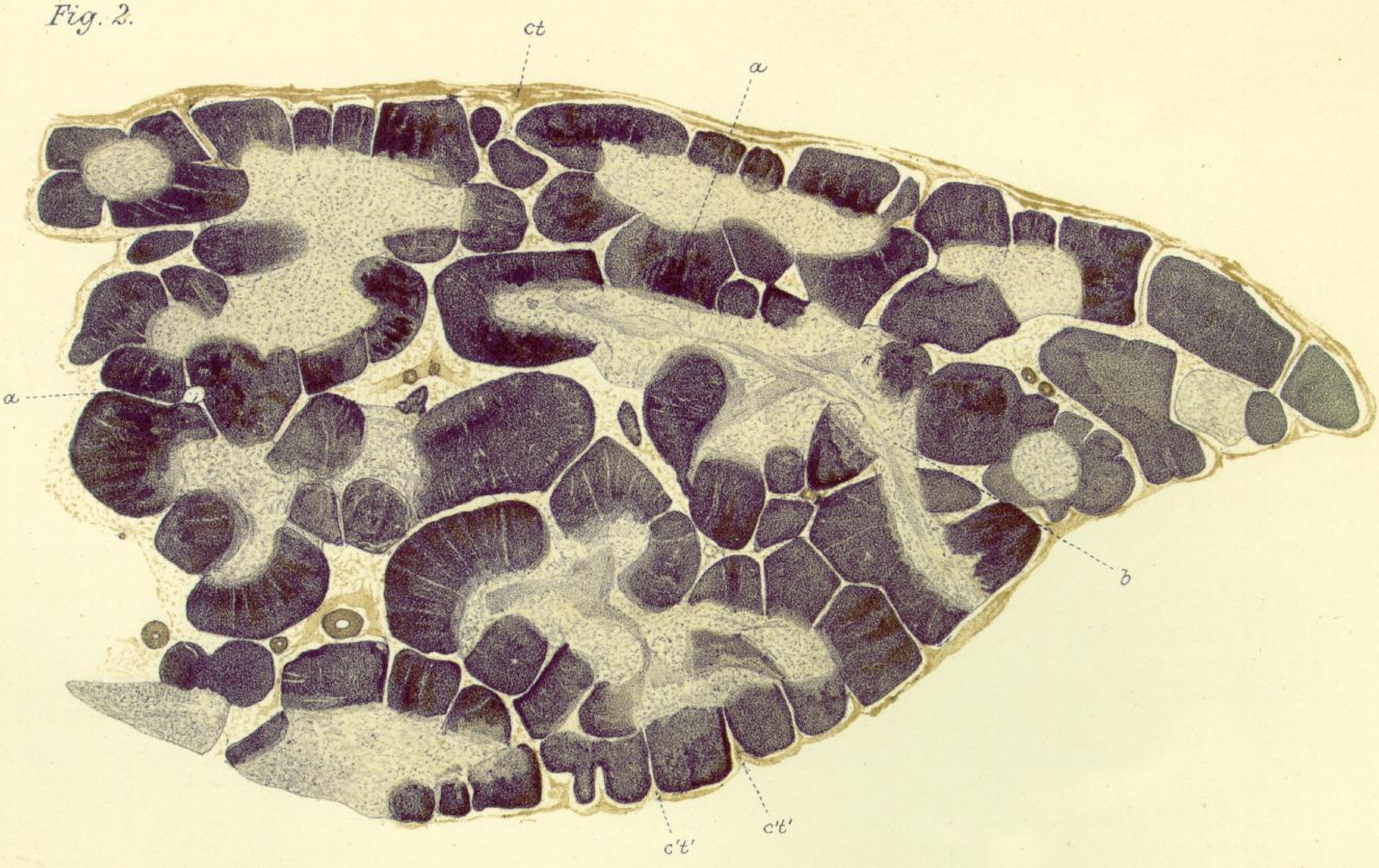
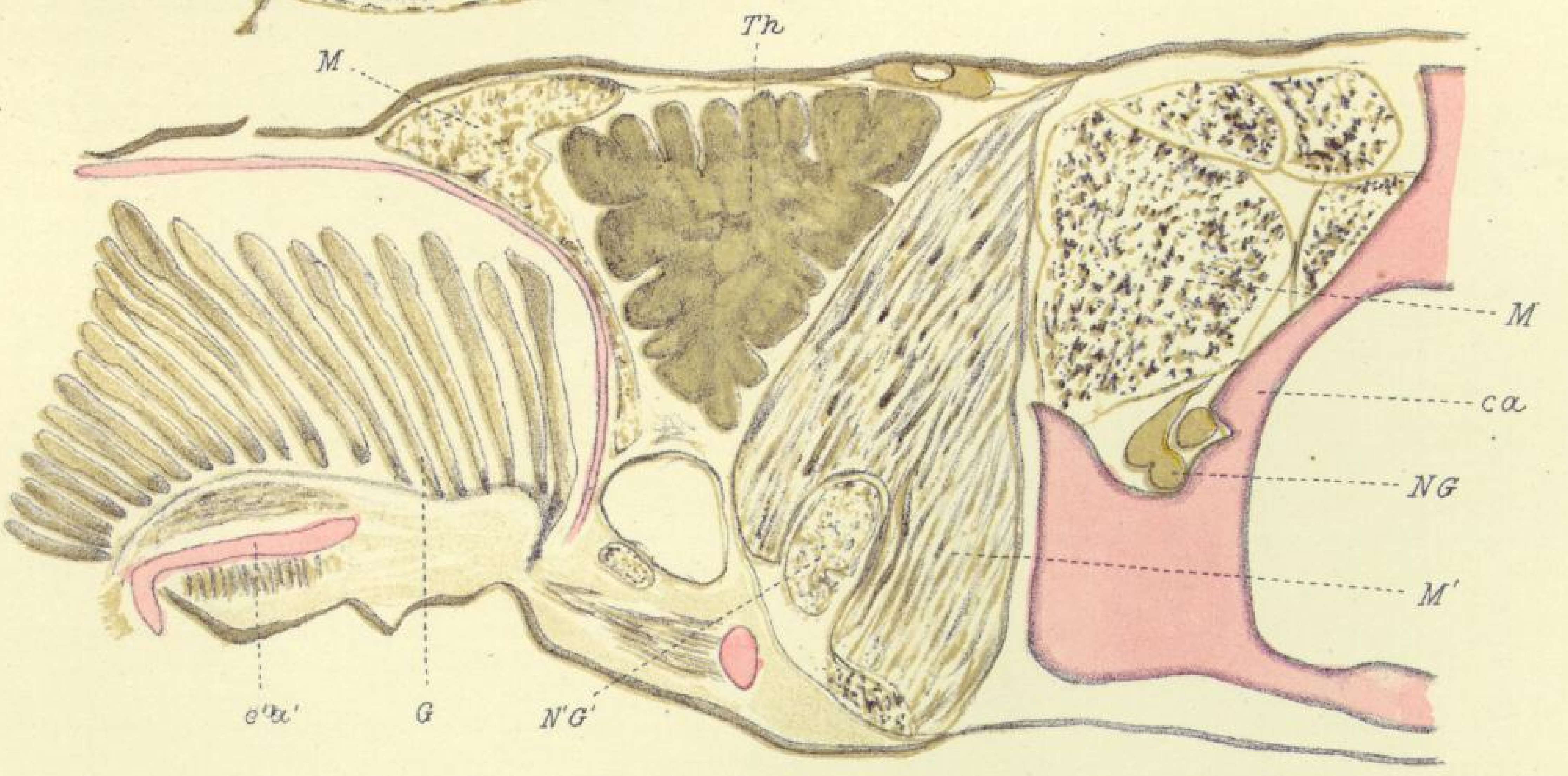


Fig. 3.

Fig. 4.

Fig. 5.



Figs. 1, 2, 3, 4. Camera lucida, with a simple lens, magnified about $12\frac{1}{2}$ times.

The four drawings show the appearance of the follicles in various stages of growth and involution. In each case the tissue was hardened for the same length of time in bichromate of potash and then in alcohol.

The cortical portion of the follicles is distinguished in the drawings, as in the original, by its darker colour.

The follicles are united by cortical-tissue at (*a*), by medullary-tissue at (*b*). In some follicles there are two or more portions of medullary-tissue, as at (*c*).

ct. Interfollicular connective-tissue; in figs. 2, 3, and 4 this tissue contains fat.

c't'. Processes of the interfollicular connective-tissue, penetrating the cortex.

Fig. 1. Section of the greater part of a lobule of the thymus of Calf three months old.

Fig. 2. Section showing about two-thirds of a lobule of the thymus of Heifer two years old.

Fig. 3. Section of thymus of Ox six years old.

Fig. 4. Section of thymus of Cow, probably twenty years old. The vessels in the connective-tissue are very large.

Fig. 5. Camera lucida, simple lens $\times$ $12\frac{1}{2}$.

From Ray-fish, $4\frac{1}{2}$ inches across. The section is vertical, parallel to the greatest breadth of the fish, and made a little behind the spout cavity.

ca. Central cartilage.

NG. Spinal ganglia.

M. Muscles cut transversely.

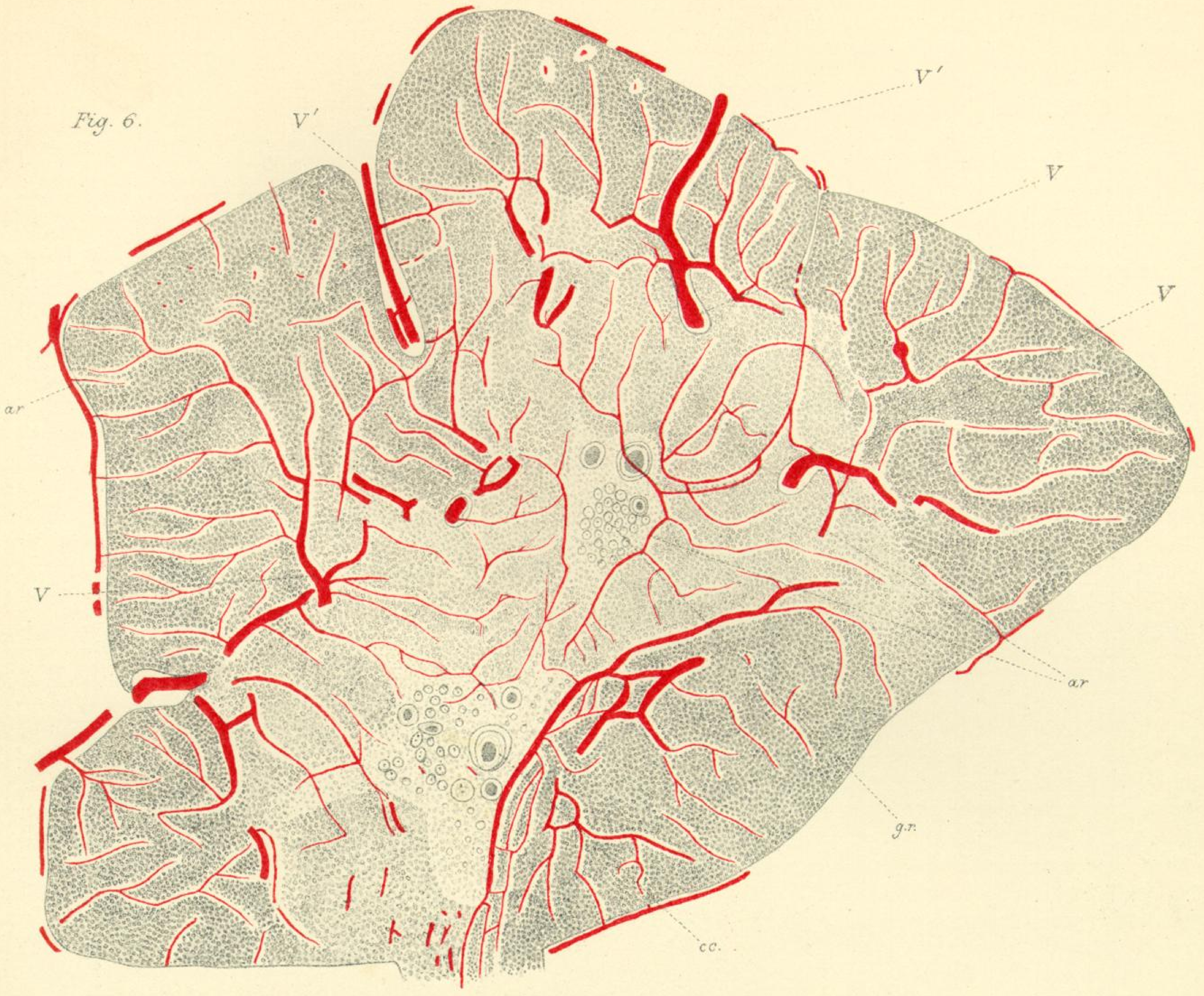
M'. Muscle cut obliquely.

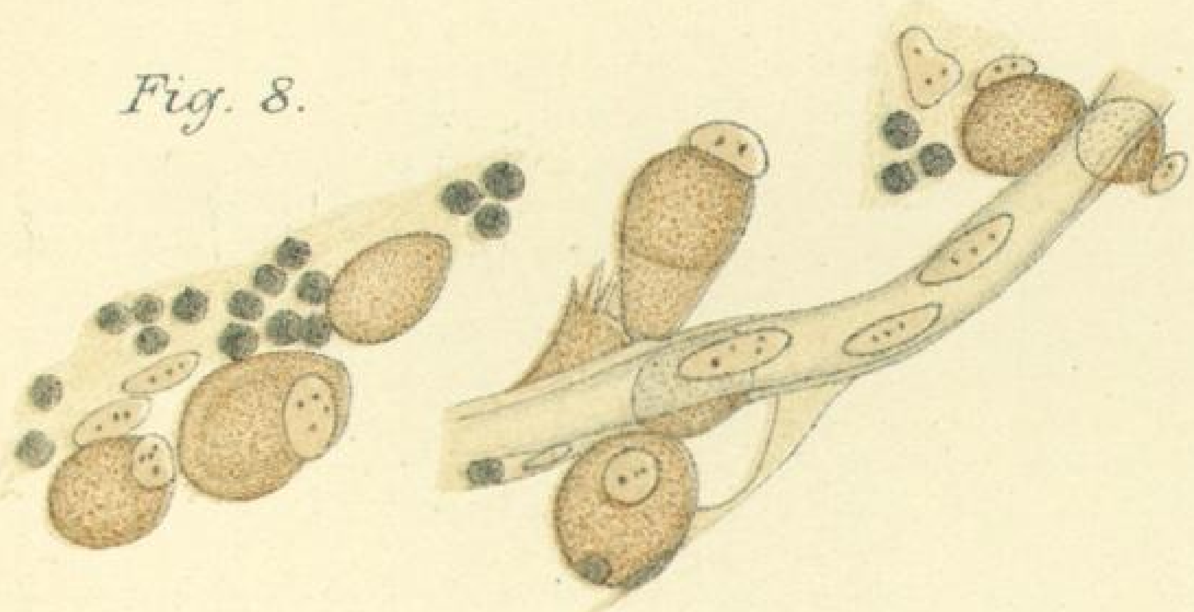
N'G'. Nerves and ganglia.

Th. Thymus, showing slight difference between cortex and medulla.

G. The gills.

c'a'. Cartilage supporting gills.





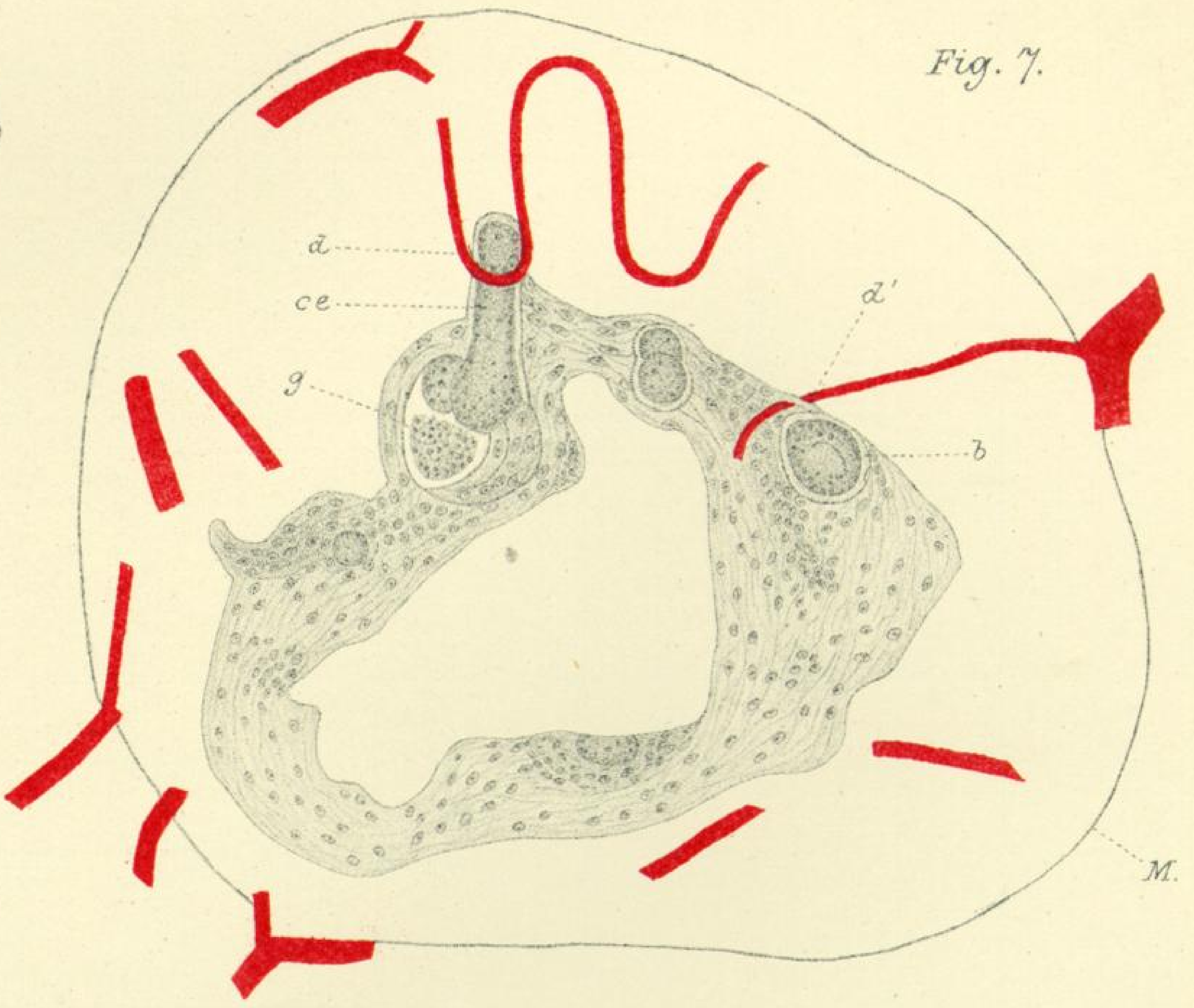


Fig. 6. Camera lucida, obj. 2, × 75, oc. III., obj. 4.

From Calf four days old. Section of follicle. The thymus was injected with carmine and gelatine, and hardened in alcohol.

V. Veins which lie just within the medullary portion.

V′. Veins passing out of the follicle in the interfollicular connective-tissue.

ar. Arteries.

gr. Granular cells.

cc. Concentric corpuscle.

Fig. 7. Camera lucida, obj. 4, × 150, oc. III., obj. 5.

From Kitten four months old. Section of thymus injected with carmine and gelatine, hardened in alcohol.

M. Margin of medulla.

d.d′. Two vessels are seen to penetrate the very large compound concentric corpuscle, the central portion of which has fallen out.

b.g. and *ce.* The central parts of the individual concentric corpuscles; they are not penetrated by the injection.

Fig. 8. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Shaken section of thymus of Calf twelve days old.

The drawing represents the method of double staining by hæmatoxylin granular cells of a brown colour, attached to blood vessel: the nuclei of the granular cells and vessels, purple; lymphoid cells, deep purple.

Fig. 9. Camera lucida, obj. 8, × 600. oc. III., obj. 9.

From young Calf; section of cortical portion of thymus, hardened in chromic acid and then in alcohol. The specimen was stained with indigo-carmine and carmine (method of MORRIS and SHAKESPEARE, see reference No. 87) in the proportion of one of the former to ten of the latter. The reticulum is blue-green. The lymphoid corpuscles are of a carmine colour.

Fig. 10. Camera lucida, with upper part of No. 2 lens, × about 36.

Section of a follicle of the thymus of Calf one year old. The thymus was hardened in chloride of gold and chromic acid.

ct. Connective-tissue surrounding the follicle, and penetrating into the interior, cutting off portions of the cortical-tissue.

c't'. One of the invading processes of connective-tissue.

F. Fat in the invading connective-tissue.

Fig. 11. Camera lucida and a simple lens × 12½.

Transverse section of the thymus of human fœtus of about the twelfth week.

cc. Concentric corpuscles.

ct. Connective-tissue which surrounds the gland, and has invaded it and divided up the follicle. The cortex is distinguished by its darker colour.

Fig. 12. Camera lucida, obj. 8, × 600, oc. III., obj. 9.

Plasma cells, from medulla of thymus of Calf twenty-eight days old.

Tissue hardened in alcohol, stained in dahlia (method of Ehrlich, see reference No. 79).

Fig. 13. Camera lucida, obj. 7 × 450, oc. III., obj. 8.

Section of thymus of Calf. The tissue was hardened in bichromate of potash, and afterwards in alcohol, and stained in indigo-carmine and carmine, in the proportion of one of the former to seven of the latter (method of Morris and Shakespeare, see reference No. 87).

v. Blood vessel showing perivascular sheath, and containing coloured blood corpuscles, which are stained green.

pl. Plasma cells.

Fig. 14. Oc. III., obj. 8, × 400.

Teased specimens.

(*a*). From thymus of human fœtus five months old.

(*b*). From Dog one year old. Connective-tissue network containing hæmoglobin.

Fig. 15. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Teased specimen of thymus of Calf seven months old.

In the lower part there is a concentric corpuscle; above, a large mass of protoplasm containing (*h.*) hæmoglobin.

th. Coarse protoplasmic threads, with imbedded nuclei.

Fig. 16. Oc. III., obj. 8, × 400.

Teased specimen of thoracic portion of the thymus of Calf one year old.

Mass, probably part of a concentric corpuscle containing large masses of hæmoglobin (*h. h. h.*).

Fig. 17. Camera lucida, obj. 5, × 300, oc. III., obj. 7.

Teased specimen of thymus of Calf seven months old.

Concentric corpuscle containing (*h.h.*) hæmoglobin granules.

p. Vessel-like prolongation. The centre is filled with a mass of protoplasm, ending in a rounded extremity.

Fig. 18. Oc. III., obj. 8, × 400.

Teased specimen of thymus of Calf one year old.

Nucleated connective-tissue cells of medulla, a long process which contains hæmoglobin granules (*h.*).

Fig. 19. Camera lucida, obj. 7, × 450, oc. III., obj. 9.

Teased specimen of thymus of Calf one year old.

lc. Lymphoid corpuscles.

b. Coloured blood corpuscles.

c. and *d.* Cells containing hæmoglobin granules.

Fig. 20. Camera lucida, obj. 7, × 450, oc. III., obj. 8.

Teased specimen of thymus of Calf seven months old.

c.d. Cells containing hæmoglobin granules.

Fig. 21. Oc. III., obj. 8, × 400.

Teased specimens.

a.b.c. From thymus of Dog one year old.

d. From thymus of Calf twenty days old.

The cells contain spherules, and masses of hæmoglobin, some of them as large as the coloured blood corpuscles.

Fig. 22. To illustrate the colours of the hæmatoxylin staining solutions.

They were all made with potash alum and extract of logwood, in the proportion of three to one.

(*a*). With old powdered alum.

(*b*). With old crystals of alum.

(*c*). With old alum. (This solution had been made four years, all the others only a few hours.)

(*d*). With old dried alum.

(*e*). With fresh crystals of alum.

(*f*). With freshly-made dried alum.