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Thesis by Thomas T. Bunting

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THE HISTOLOGY

OF

LYMPHATIC GLANDS

BY

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March 1904.
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INTRODUCTORY.

THIS Thesis deals with the general and comparative Histology of Lymphatic Glands. It consists of a summary of the most important literature on the subject; and of an account of my own observations, and of their bearing on the conclusions of previous writers.

At the outset the question arises as to what is included in the term lymphatic gland. It is not easy to draw a vital distinction between the bodies generally so named in English textbooks, and the various masses and nodules of lymphoid tissue found in many parts of the body. Brücke made a distinction by dividing the Lymphdrüsen into peripheral, or those which are included within some other organ, and true, which are independent bodies. Fleury (63) makes practically the same distinction by dividing lymphatic bodies into those which have both afferent and efferent lymphatic vessels - these are the true glands, and those which have only efferent vessels. But he states later that the true glands of birds bear a greater resemblance histologically to the lymphoid mass on the heart of the Sturgeon, than to any other true lymphatic glands. Retterer (51) points out another difference which if correct would make a more definite distinction. He considers that peripheral nodules are developed from the ectoderm,
and true lymphatic glands from the mesoderm. It does not appear, however, that this difference in source is followed by any essential differences in the adult organs. A distinction of more importance is that most of the peripheral lymphoid organs send the cells which are formed in them largely on to free surfaces, while all the cells formed in true lymphatic glands go directly or indirectly into the blood. There seems no good reason for the distinction, but it is one of considerable convenience, and I have adopted it. I shall speak therefore only of lymphatic glands usually so called, though naturally much that is true of them is true also of the peripheral lymphoid masses.

The Thymus and Spleen are more definitely distinct, - the Thymus both by the presence of Hassall's Corpuscles, and by the absence of afferent lymphatics; and the Spleen by the fact that it has not a closed blood vascular system, and that blood circulates in its sinuses instead of lymph. The case of Haemolymph glands is not so clear. They differ from lymphatic glands in having their sinuses generally wider, and filled with blood instead of with lymph, and also, according to Warthin (83) in having no afferent lymphatics. But Swale Vincent and Harrison (84) consider them to be developed from lymphatic glands, a supposition which is supported by the existence of intermediate forms. Retterer (54)
goes further and says that they are merely lymphatic glands in which the lymph current is weak, with a consequent collection in the sinuses, of the red corpuscles which he believes to be formed by all lymphatic glands. He says that by artificially raising or lowering the lymph pressure lymphatic glands can be converted into Haemolymph glands, or vice versa. Drummond (85) however has pointed out that the distribution of the two kinds of glands in the body is different, and that Haemolymph glands can be recognised as separate structures at as early a period in development as can the lymphatic glands. His belief that the two kinds of glands are distinct from each other is borne out by the fact that Haemolymph glands are constantly found in certain positions, e.g. in front of the spine, and along the renal artery. The point is still doubtful, but I shall, for the present, exclude Haemolymph glands from consideration as lymphatic glands, and regard them as more probably allied to the Spleen.

While this thesis treats of the whole Histology of the lymphatic glands, I should point out here that my own work has dealt more particularly with the arrangement of the trabeculae, the nature of the reticulum, including the so-called endothelium, the constitution of the germ-centres, and a small portion of the comparative histology.
MATERIAL.

The Material which I have examined for the purpose of this thesis is as follows:- I have not kept a record of the number of glands examined, nor of the animals from which they were taken, when it exceeded three, and as I frequently made more than one preparation from one gland I am not able to ascertain the exact number of glands from a count of my slides.

OX. Numerous mesenteric glands from many different animals killed by butcher.

SHEEP. Numerous mesenteric glands from several different animals killed by butcher.

PIG. Several mesenteric glands from two different animals killed by butcher.

RABBIT. Numerous cervical and mesenteric glands from several animals killed by chloroform. Also tonsils and peyers patches from the same animals.

GUINEA-PIG. Numerous mesenteric, inguinal, and axillary glands from three different animals, killed by chloroform.

CAT. Numerous inguinal, axillary, cervical, and mesenteric glands from many animals, some killed by chloroform, the remainder by carbon dioxide poisoning.

(1)
The animals were of every age, the youngest was only two hours; the oldest, of unknown age, was showing signs of senile decay. I also examined some intestinal nodules from some of these animals.

**DOG.** Several mesenteric and inguinal glands, from several different animals, killed by carbon dioxide poisoning.

**BADGER.** Several mesenteric and cervical glands from two animals, one adult, the other scarcely half grown. They died from unknown causes.

**JACKAL.** One gland from the meso-rectum of an animal, which died from an unknown cause.

**CIVET CAT.** Two mesenteric glands from one animal, which died from an unknown cause.

**OPOSSUM (American)** Two inguinal glands from one animal, which died from an unknown cause.

**OPOSSUM (Australian)** One inguinal gland from one animal, which died from an unknown cause.

**MAN.** Several glands from the mesentery and axilla of three different subjects, who died from disease.

**LIZARD.** The root of the mesentery, and the groin from two green lizards, killed by chloroform.
METHODS.

All the glands which I examined, except when taken from animals which had died, were removed from the animals within a few minutes of their being killed. For the preparation of ordinary sections they were immediately plunged into a fixature, the very large ones having been first incised, or cut up. About half were fixed in Zenker's solution, the remainder in Flemming's weak solution.

After fixing they were washed in water, then passed through alcohols of increasing strength, cleared in Xylool, and saturated with paraffin. The sections were fixed to the slides by being floated on distilled water, and kept at a temperature of about 45 deg. C. until all the water had evaporated.

They were stained on the slide by Carmalum alone, carmalum followed by picric acid, Safranin, Safranin and Kernschwarz, Haematoxylin with and without eosin, thionin, Hansen's picro-fuchsin, the Mallory-Stöhr stain, the Israél-Pappenheim stain, followed by haematoxylin, or Weigert's resorcin-fuchsin stain. The last four were used according to the directions of Thomé (61) and Retterer (51).

Sections for washing were some of them cut fresh and unfixed, by the freezing method; others were washed after being prepared as above described and cut in paraffin. To wash sections several were
placed in a long testube, about half full of water, which was violently agitated for fifteen minutes. Some were taken out during this time, and thus showed the washing in progress. The washed sections were usually stained by haematoxylin, though occasionally other stains were used.

In investigating the nature of germ centres I placed stained sections under the microscope (objective Zeiss A. eyepiece Zeiss No. 2) separated the germ-centres from the surrounding parenchyma by means of fine needles, and then tore them to pieces with the needles. I also pencilled sections with a small brush, under the same magnification.

For studying the endothelium I injected into the glands, by means of a small hypodermic syringe, a solution of silver nitrate, of strength varying from 1-100 to 1-500. The gland was allowed to lie for half an hour and was then plunged into absolute alcohol, and was afterwards cut by freezing or in paraffin.

I also exposed a few sections to the same silver solution after they had been cut. For the endothelium on the inner surface of the capsule I stripped off pieces of capsule from the cortical portions of glands, removed all adherent parenchyma, as well as possible, by needles, and then exposed to the silver solution.

For small animals, where the glands are dif-
-ficult to find on account of their size, I find Retterer's procedure very useful. He cuts out the whole tissue in which the glands lie, fixes it, passes it through alcohol, and clears it. The whole tissue is then transparent except certain small nodules. These are the lymphatic glands, they are now easily seen, and readily removed.
The early literature on lymphatic glands is more curious than important. Retterer gives a very full summary of it in the Journal de l'Anatomie et de la Physiologie 1901. I shall here mention only one or two writers whose work seems to have made real advances in knowledge. I am indebted to Retterer's article for my knowledge of them.

HIPPOCRATES thought that they absorbed the superfluous moisture of the intestine.

GALEN on the contrary thought that they moistened the intestine.

SYLVIUS DE LE BÖE was the first to separate them from glands with ducts. To these, together with the other ductless glands, he gave the name conglobate.

A. NUCK (1) described two capsules, the external thin, and formed of circular fibres, the internal thick, with fibres in all directions. The fibres of the internal capsule traverse and partition the gland. He noticed a pink colouration of the lymph in the efferent lymphatics, and explained this by supposing a communication inside the gland, between arteries and lymphatics. He demonstrated this communication by inflating the arteries with
gas, and noticing that it passed into the lymphatics.

MALPHIGI (2) Demonstrated by injection, that the afferent and efferent lymphatics were continuous with each other. He was also the first to point out nodules in the glands, which he called Folliculi Glandulosi.

MASCAGNI (3) denied any communication between the blood and lymph vessels. He thought the gland consisted only of a plexus of the two kinds of vessels.

BICHAT (4) treated the glands by boiling, and by acids and alkalies. He was the first to describe a proper gland substance between the blood and the lymph vessels. He compared the vesicles of this substance to those of the thyroid.

The really important period in the literature dates from the middle of last century when Brücke, Kölliker, Frey, His and others carried out investigations which, collected together, gave us the classical description of the glands as given by Von Recklinghausen in Stricker's Handbook, and by Ranvier in the Traité Technique.

J. GOODSIR (5) in 1845 published what seems to be the earliest account of the parenchyma of the glands as it is now known. He however clung to the old idea of the gland being merely a plexus, and considered the parenchyma to be the modified inner coat of the lymphatics, of which the epithelium is "highly
developed for the performance of particular functions," while the outer coats have disappeared. He described this inner coat as consisting of nucleated particles, and his figures show a mass of nucleated cells; but he neither describes nor figures any reticulum.

KÖLLIKER A. (6) Described the reticulum. He said it was composed of anastomosing star shaped cells, which later in life became fine fibrils. These fibrils were not identical with those of connective tissue. He called it Cytogenic tissue. In the vacuoles (germ-centres) he said the reticulum had wider meshes, or might even be absent altogether.

NOLL (7) pointed out that lymph in passing from afferent to efferent vessels must filter through the reticulum.

O. HEYFELDER (8) pointed out the muscular fibres in the capsule and trabeculae.

E. BRÜCKE (9) described the relation of solitary follicles, and of the nodules of lymphatic glands, to the lymphatic vessels. He said that the sinuses of the glands have no definite walls. He showed that white corpuscles were formed in the glands.

TH. BILLROTH (10 & 11) was the first to demonstrate the reticulum in the solitary follicles. In young animals, he said, the reticulum consists always of stellate cells. In old animals he found
the nuclei of the reticulum comparatively rare. For him the gland was divided into alveoli by septa, and in the middle of each alveolus the reticulum became so tender that it was often impossible to show it.

H. FREY (12) compared the structure of lymph glands to that of Peyer's patches. He considered the reticulum to be cellular. The meshwork was narrower he said at the surface of the follicles, while at their centre it was very wide.

J. HENLE (13) in describing reticular tissue said that when developed to a greater extent it passes into a network of non-nucleated trabeculae, which are of far more rigid nature and often appear considerably expanded. In studying the glands he used washing. He said the reticulum was composed of connective tissue fibres, and that the cells were merely planted on the fibres of which they formed no integral part. He also found a second network which resisted alkalies more than the first and which he said was elastic tissue.

W. HIS (14) gave the first really clear description of the glands. He used the method of pencilling and thus, for the first time, revealed the lymph paths clearly. He used chiefly ox glands, a fact which explains the usual classical description of the trabeculae, as occurring in every sinus and as forming a complete system joining capsule to hilus all
over the gland. He described cortical "ampullae" and medullary "glandular tubes." By using silver he demonstrated endothelium on the surface of the parenchyma. He gave the name adenoid to the tissue which consists of a reticulum enclosing leucocytes. The reticulum he differentiated from the connective tissue trabeculae. It extends all over the gland. It consists, he thought, in the young, of anastomosing cells; later in life these cell processes surround themselves by a substance which has the characters of connective tissue fibres, the cells then usually atrophy and become indistinct. The result is that in the parenchyma of the adult gland the reticulum is mainly fibrous; but that in the sinuses it remains chiefly cellular. His also made a complete study of the circulation in the glands, which I shall notice separately.

F. TH. SCHMIDT (15) described a granular skin which was a modification of the reticulum, and which separated the sinuses from the parenchyma.

A. ROLLETT (16) describes retiform tissue as being a network composed of nucleated cells, enclosing areolae. The trabeculae of the network proceed from a substance surrounding, and somewhat thicker than the nucleus, they branch and anastomose.

E. VERNON (17) says that in the intestinal solitary follicles the nature of the reticulum varies.
It may be a tissue of anastomosing cells, with nuclei at the thickened nodal points (child, rabbit) or a plexus of rigid hyaline trabeculae (adult man, cat) or a fibrous network (young dog.)

F. von RECKLINGHAUSEN (18) in Stricker's Handbook combines his own views with a general account of the knowledge at that time. He says they exhibit a varying structure not only in different animals but in the same individual. The medullary substance is often at the surface at other places than the hilum. The trabeculae are direct processes of the capsule, and like it are of connective tissue, with smooth muscular fibres in many animals. The reticulum (of solitary follicles) consists of fine fibrils, which vary in thickness and pursue a straight course. Their nodal points are usually small and exhibit nuclei. It remains to be ascertained whether these are adherent to the fibrils or are contained within peculiar cells which occupy their interior. The fibrils at the periphery of the follicles are in direct connection with the intercellular substance of the surrounding connective tissue. The fibrils unite to form the trabeculae, and in sinuses which have no true trabeculae there are sometimes closer plexuses of fibrils which present nodal points analagous to trabeculae. In the medullary cords the fibrils are individually finer, and the meshes of the network, particularly at the
periphery, are smaller than in the sinuses. The lymph channels often contain pigment of which the granules cleave around nuclei or cells. He has so often satisfied himself of the presence of endothelium on trabeculae and septa that "I may venture to say" they are invested by an epithelium throughout the gland. This is continued upon the thicker fibrils but "it still remains to be ascertained whether this relation is generally present or is only partial, and whether the follicular cords (as has hitherto appeared to me) are destitute of epithelial cells, and thus lie naked in the lymph path." The chyle granules in the mesenteric glands can easily be demonstrated to have penetrated into the peripheral portions of the follicles, whence it follows that these are not completely excluded from the lymph path.

L. RANVIER (19) in the Traité Technique also combines his own observations with those of others. He is convinced of the fibrous nature of the reticulum, and compares the glands to the great omentum, which from the morphological point of view is a lymph gland spread out. The shape varies but all have a hilum. The colour is red or grey according to the amount of blood they contain, but there is no suggestion that this blood is elsewhere than in the bloodvessels. The proportion of cortex to medulla varies, and even in the same gland the thickness of the cortex changes. The afferent lymphatics reach
the capsule at different points and spread out on it like fingers grasping a ball. The capsule is of connective tissue, with connective tissue cells, yellow elastic fibrils, and, in some animals, muscle. The reticulum in the sinuses, although it branches, maintains a general direction from trabeculae to follicle. The fibrils, of the reticulum, do not combine when anastomosing, but are simply brought together. Some fibrils go directly through from sinus into parenchyma. More often the fibres of sinus and parenchyma unite indirectly by both joining the perifollicular network. With complete pencilling all the nuclei are removed from the fibres. We thus see that they are merely applied to the fibres. They have the characters of endothelial cells, and really belong to an endothelium which clothes all the fibres both of sinuses and of parenchyma. The lymph channels of the medulla are limited on all sides by endothelium; the parenchyma is therefore covered by it, and its boundary from the sinuses is always very clearly marked. The free cells, when squeezed out, show movement. All the forms of cell show this, but not all the individuals of each form. The small ones, with a slight amount of protoplasm are young cells.

The period following this has been marked chiefly by a continuation of the difference of opinion upon the nature of the reticulum, though with a
general tendency to adopt the views of Ranvier; and by a very great advance in our knowledge of the free cells. This advance was however made chiefly by studies of the cells elsewhere than in the glands. It will be followed in this Summary only so far as it is directly connected with the literature of lymph glands. Quite recently certain new methods of staining have thrown fresh light on the nature of the reticulum, and it is possible that they, together with a fuller consideration of the effect of age, may bring about a more general agreement upon the subject.

_G. BIZZOZERO_ (20) agrees with Ranvier as to the reticulum. It is only a special arrangement of connective tissue, in which the bundles are separated by leucocytes and are clothed by endothelial cells. The protoplasm of the clothing cells is greater in quantity in the sinuses than in the parenchyma. Some cells instead of clothing one fibre are framed in a mesh of the reticulum.

_E. KLEIN_ (21) studied the lymphoid patches in the serous membranes, by means of silver preparations. His chief results were as to development, these I shall consider later. The reticulum of these patches consists, in all stages, of branching flattened cells, which in some cases are continuous with the endothelium of a neighbouring lymph capillary, and in others are contained within a lymph capillary,
and spring from its walls. In the first of these varieties the cells of the reticulum are really ordinary connective tissue cells which have multiplied while the intercellular substance has more or less disappeared. In the second variety the cells develop from the endothelium of the vessel and therefore indirectly from connective tissue cells. He saw germinating cells in various places - on the surface of the omentum, in the branched cells of the connective tissue, in the endothelium and the reticulum of the lymphoid patches, in the endothelium of the lymph capillaries, around the stomata, and protruding in buds from the pseudo-stomata, all of these, whether connective tissue cells or endothelial cells, gave rise, he believed, to lymphoid cells. In one case he actually saw such cells in a lymphatic of a toad's mesentery, detach themselves and become carried away, and he says "I presume these form lymph corpuscles."

J. ORTH (22) also considered the reticulum to be cellular. The strands do not swell with acetic acid as do connective fibres, and like other cellular tissues they cannot resist dilute alkalies. In older individuals, he says, the cell body and nucleus disappear, leaving the cell processes to form the reticulum alone.

J. RENAUT (23) says the reticulum consists of connective fibres, which are clearly fibrillar.
He founds this chiefly on the results of silver methods. The lymphatic cells in the meshes are not in contact; for they leave no impression on each other, and they are movable.

J. H. CHIEVITZ (24) after pencilling sections, concluded that in the adult the reticulum always consists of fibres. In the embryo it is chiefly branching cells, and even in the newborn it is still partly cellular, and the cells are in direct continuity with the fibres. He dissented from the classical view of the build of the glands. Only a few septa, he said, go to the hilus, and they go straight, giving no branches. In medulla there are many sinuses without trabeculae. He studied glands of man and swine. In the latter he found a complete trabecular system.

W. FLEMMING (25) made a complete study of the structures which His had called vacuoles, and which were by some considered to be cavities, by others solid bodies. He fixed the glands by his chromo-osmium solution. He renamed these structures secondary nodules, or germ-centres. They are not confined to the cortex. They vary in size, they are sometimes absent, and are unequally distributed. For these reasons they are probably transitory structures which come and go as required. They show a central portion lightly stained, with comparatively few nuclei, and encircling this a zone staining dark, and showing many smaller nuclei. In the light cen-
-tral portion an unusually large number of cells show mitotic figures. In the dark zone there are practically no mitoses, although there are always a fair number in the surrounding parenchyma, and even in the sinuses. These secondary nodules then are places for the germination of leucocytes. Flemming asks, without definitely answering the question — what is the origin of the cells which divide in the germ-centres? They might be free cells in the meshes of the reticulum, fixed cells of the reticulum, or the cells of the capillaries. Flemming believed them to be the former for the reasons that (1) it is improbable that fixed cells in growing animals would show so highly organised in structure; (2) that he has separated out some of the dividing cells and found them to be round or oval and without processes, and (3) that in sections where the reticulum was well seen he could not find any branched cells amongst those dividing. He says however that it is practically impossible to give an absolute decision, and that it is quite allowable to believe that they may be reticulum cells which become round before dividing, the daughter cells going free after division. This may be supported by the fact that one certainly finds mitoses in the reticulum cells of the sinuses, and that those dividing cells are round. In either case the daughter cells go out gradually into the parenchyma and the sinuses.
C. TOLDT (26) said that the reticulum began as cells, but that nuclei were rare in the adult. To show the protoplasmic nature of the reticulum he injected anilin blue and found that the reticulum took it up as well as the lymphoid cells. The beams of the reticulum are homogeneous.

RIBBERT thought that the reticulum was covered by applied cells with clear, large, round or oval nuclei; but that the reticulum itself consisted of cellular processes, with angular or spindle shaped nuclei, which stained very deeply with safranin, and were found chiefly at the nodal points.

HANSEMANN (28) also described these two kinds of cells. Those with the large clear nuclei he called lymphoblasts. They are very like endothelium but differ from it in their method of mitosis. They lie in close connection with the fibres of the reticulum.

H. HOYER (29) Digested glands in pancreatic glycerin extract, and then washed them. He got a connective tissue reticulum quite free from cells, and therefore considered the reticulum to consist of fibres clasped by endothelial cells. He described large leucocytes (Macrophages) in the parenchyma, containing, among other things, red blood corpuscles, which were in much larger proportion than usual after phosphorus poisoning. They also contain a pigment free from iron, especially in the cervical glands.
J. L. Gibson (30) experimented on dogs. On different animals he (a) excised the spleen (b) tied the thoracic duct (c) withdrew a large amount of blood. He afterwards killed the dogs. In all he found the glands enlarged, and in all, scrapings from them showed many nucleated red corpuscles. The glands from (b) also contained more than usual of ordinary red corpuscles. In the blood of the animal with the ligatured thoracic duct the number of red corpuscles was reduced for thirty days and then returned to normal; the number of white was greatly increased at first, but after six days there were fewer than normal. In the same dog the spleen contained more nucleated red corpuscles than normal, and the marrow was red for practically the whole length of the femur and humerus. The glands contained no red corpuscle holding cells. He concludes that red corpuscles are formed in lymph glands, even in the normal animal. They are formed from white cells of which the protoplasm becomes haemoglobin while the nucleus disappears, and the cell shrinks.

F. Mall (31) considered the nature of the reticulum from the chemical standpoint. He concluded that the reticulum consists of fibres which are not identical with ordinary connective tissue fibres. The chief differences are:
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<th>White Fibres</th>
<th>Reticulum Fibres</th>
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<tbody>
<tr>
<td><strong>Weak Potassic Hydrate</strong></td>
<td>Swell or dissolve.</td>
<td>No change</td>
</tr>
<tr>
<td><strong>Hydrochloric acid 3 - 6%</strong></td>
<td>Swell</td>
<td>No change</td>
</tr>
<tr>
<td><strong>Boiling</strong></td>
<td>Shorten and do not relax. Give gelatin readily recognisable</td>
<td>Shorten, the relax; give some gelatin not readily recognisable</td>
</tr>
<tr>
<td><strong>In Pepsin</strong></td>
<td>Digest quickly</td>
<td>Digest slowly</td>
</tr>
<tr>
<td>In Pancreatin 18 hours</td>
<td>Swell, but do not dissolve</td>
<td>Dissolve</td>
</tr>
<tr>
<td>then in 1/2%</td>
<td></td>
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<tr>
<td>Osmic acid one minute,</td>
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<tr>
<td>then heated to 95-100 deg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C, then in Pancreatin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dissolve in Hydrochloric acid, then add Alcohol</strong></td>
<td>There is a precipitate.</td>
<td>No precipitate</td>
</tr>
<tr>
<td><strong>Dissolve in Hydrochloric acid, then add Acetate of lead</strong></td>
<td>No precipitate</td>
<td>There is a precipitate.</td>
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With hydrochloric acid tendons from different parts of the body vary somewhat in reaction.

With the pancreatin, osmic acid, and heat there is no difference at any temperature except 95-100 deg. C. Mall tried many other reagents which gave the same result with both tissues.

**G. L. GULLAND** (32-3-4-5) discussed lymphatic glands and other adenoid tissue in a series of four articles. He wrote first on the life history of leucocytes, as seen in the glands (32). A leucocyte is, for him, a unicellular organism which, in
the midst of vertebrate tissues, retains the characters and habits of a protozoon; it therefore takes the same form in all animals, and has an existence quite independent of that of the animal in which it lives. In tracing their history he begins with the small daughter cells in the germ-centres. These are small, spherical cells almost wholly taken up by their nuclei, and with little power of amoeboid movement. A few lie within the germ centre, but most are heaped up at its periphery. These gradually acquire more protoplasm, and a larger nucleus. They are then microphages and are never found in the germ-centres, but are frequent in the ordinary parenchyma. These microphages develop in one of two different directions. Some, which are in a favourable condition as to food supply, remain comparatively stationary. They grow considerably larger. They never have more than one nucleus and their cell body is coarsely granular. They are phagocytes or macrophages. They may contain red blood corpuscles or pigment, and micro-organisms or other foreign particles. They are confined exclusively to the lymphatic organs, mainly in the sinuses, and medullary parts of glands, less frequently in the germ-centres. The remaining microphages wander into blood, lymph, or surrounding tissues, and become wandering leucocytes. These have become elongated, the chromatin filaments have thickened, and become more
crowded, and the nuclei have become polymorphous or have even broken up, in adapting themselves to the changes in shape of the cell. Of all these forms the smaller stationary cells, and the wandering cells are the only ones which at any time show signs of degeneration. This is shown chiefly by increase in the granular nature of the cell body, and by the chromatin running together into one or two homogeneous masses. The cells from which the daughter cells are developed are the wandering leucocytes. A few of these may have previously existed in the germ-centre as Flemming supposed, but most have certainly come in from the blood. In fact it is the peculiar arrangement and rich supply of capillaries, rendering emigration of the leucocytes unusually frequent, which determines the position of germ-centres. When these emigrated leucocytes find themselves comparatively stationary in the germ centres, and in a position to get good nourishment they grow, the nucleus expands, and mother cells are produced. Their nuclei are four or five times as large as a young leucocyte, they are round or oval, with much chromatin, and with several masses which look like nucleoli. The nuclei occupy nearly the whole cell, and the cell nearly fills the mesh in which it lies. These cells are now ready to divide and recommence the process. Gulland carefully distinguishes these cells from those of the reticular