

As worked out for the pig it was found that the lymphatic system is at first symmetrical and grows out from the veins at four points, that is at the junction of the veins of the limbs with the cardinal veins, viz., at the junction of the subclavian and precardinal veins in the base of the neck, and in the lumbar region at the junction of the sciatic and femoral veins with the post-cardinals. Slightly beyond its origin from the vein each of the four original lymph trunks or ducts dilates to form a lymph sac or lymph heart. In lower forms, as the frog, lymph hearts contain striated muscle and are rhythmically contractile; it has not yet been shown, however, whether these sacs in the developing mammal are contractile or not.

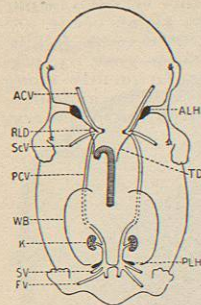


FIG. 3307.—Diagram of the Lymphatic System of an Embryo Pig 20 Mm. Long.  $\times 2$ . (Sabin.) ACV, Precardinal vein; RLD, right lymphatic duct; SCV, subclavian vein; PCV, post-cardinal vein; WB, Wolffian body; K, kidney; SV, sciatic vein; FV, femoral vein; ALH, anterior lymph sac or lymph heart; TD, thoracic duct; PLH, posterior lymph sac or lymph heart. It is to be noted that the lymphatic system is symmetrical, but that in the cephalic part of the body it is considerably more advanced than in the caudal half.

As demonstrated in the following figures the lymphatics develop first in the cephalic half of the body; the system is symmetrical, but soon the left side preponderates; the connection of the lymphatics with the veins in the caudal half of the body is soon lost; there are very early two chylocysts, and two thoracic ducts, but as both thoracic ducts grow down to join the lumbar ducts from the left side, the asymmetry of the lymph trunks in the cephalic half of mammals is original and not secondary. It is also seen that the lymphatics as they grow out to the periphery are in a close-meshed network, the ends of the tubes forming the network ending blindly, and extending farther and farther over the body by a continual sprouting of the tubes. The lymphatic glands are developed from a network of lymph vessels by an ingrowth of lymphoid tissue and by the formation of a connective-tissue capsule around the outside. Finally it should be stated that beginning with Kölliker in 1879 an increasing number of embryologists have come to believe that the real origin of the lymph corpuscles of the body is from the epithelial cells of the thymus (Beard<sup>11</sup>).

**Methods.**—The lymphatic vessels are so thin that unless they contain some liquid or solid they are not visible. One of the first ways of making the general lymphatics visible was to inject water or colored gelatin into the arteries of an organ. The mass exudes and fills the lymph vessels; this is especially successful if the vein is tied. The lacteals are made evident by feeding the animal some fatty food, like milk, an hour or two before death.

Vessels of sufficient size may be injected centrad with starch or plaster-of-Paris. It is not necessary to tie the cannula in place; simply pressing upon it with the fingers is sufficient. The insertion of the cannula is greatly

facilitated by first inserting a beaded bristle into the lymphatic, then by raising the bristle the cut in the vessel may be seen. Where the vessels are too small to be seen, very successful injections may be made by the puncture method. That is, a hypodermic cannula is connected with a syringe or a constant-pressure apparatus, and inserted where lymphatics are supposed to be. The cannula is forced in as in ordinary hypodermic injections, and the mass allowed to flow or it is forced in. If the attempt is successful, the fine network and collecting trunks of a limited area will be injected. The toes and the finger-tips of man are favorite places for injection. In animals the pads of the feet and the bare spot on the snout are good. A lymphatic gland is always easy to inject. For an injecting mass mercury was much used by the older anatomists. Colored gelatin was also used and is now much more employed than mercury as it flows readily through the lymph glands. An excellent gelatin mass is Hoyer's chrome yellow: dry gelatin, 15 gm.; water, 75 c.c. After the gelatin is softened it is melted over a water-bath and heated to 80° C., then 75 c.c. of a cold saturated solution heated to 80° C., is added to a cold saturated solution

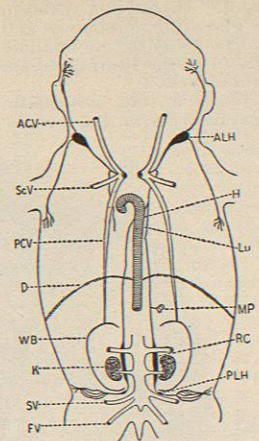


FIG. 3309.—Diagram of the Lymphatic System in the Embryo Pig 30 Mm. Long.  $\times 2$ . (Sabin.) MP, Mesenteric chylo (chylocyst); RE, receptaculum (chylocyst). The other letters as in Fig. 3307. It will be seen that in this figure the chylocyst is double, and that the thoracic duct is also double nearly to its termination. In this stage the caudal lymph sacs have lost their connection with the vein, and from now on the only connection with the vascular system is through the thoracic duct as in the adult.

of bichromate of potash, the gelatin; finally, 75 c.c. of acetate of lead is heated to 80° C. and added with constant stirring. Berlin blue in gelatin is preferable for microscopic specimens (Plate XLIV, and Figs. 3293, 3300). India ink in water is also of great service, especially in embryos.<sup>10</sup>

The puncture method was used by Hunter, Mascagni, and Cruikshank. Cruikshank, in his "Anatomy of the Absorbing Vessels" (1790), p. 44, says: "I have sometimes injected the lacteals from punctures made by the side of the veins where I knew they must be, though they were then invisible to the naked eye." He also injected the lymphatic glands by puncture.

Young animals are best for studying the lymphatics, and the leaner the animal the better. For investigating the embryology of the lymphatics, embryos in which the heart is still beating are best. After the embryos are cold they cannot be satisfactorily injected (Sabin<sup>10</sup>). In man lymphatics have been demonstrated in organs in

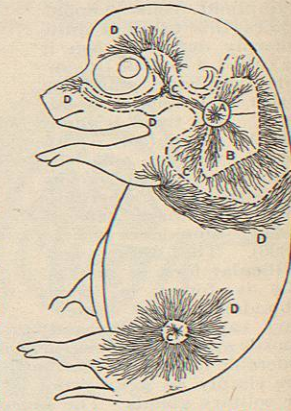


FIG. 3310.—Composite Picture of the Spreading of the Superficial Lymphatics in the Embryo Pig. (Sabin.) A, Area of lymphatics in a pig 18 mm. long; B, area in a pig 20 mm.; C, area in a pig 30 mm. long; D, area in a pig of 40 mm. long. In the stages shown there are no lymphatics beyond the outlines indicated.

the foetus when they could not be in the adult. Mature animals are better for the lymphatics of the reproductive

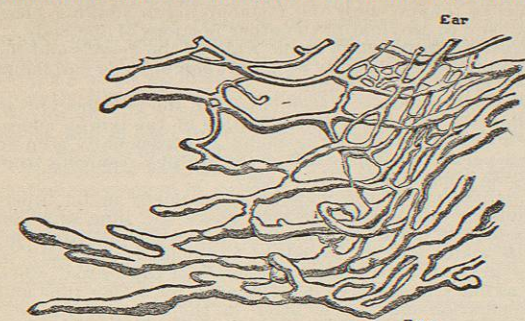


FIG. 3311.—Terminal Lymphatics of the Skin Between the Eye and Ear in a Pig 50 Mm. Long.  $\times 11$ . (Sabin.)

organs; and, for the pancreas, an old man or animal is to be chosen. Simon Henry Gage.

BIBLIOGRAPHY.

The writer wishes to express his great indebtedness to Professor Wilder for generous supplies of material for investigations in the comparative anatomy of the lymphatic system, for aid in purchasing costly works, and for hearty encouragement; to the library of the Surgeon-General's Office for the loan of rare and valuable works of reference, and, finally, to the editor for encouragement and suggestions.

In preparing the article free use has been made of the larger works on physiology: Flint's treatise, Landolt and Stirling; Milne-Edwards, Lecons, etc. In human anatomy, Allen, Gray, and Quain in English; Sappey in French; Henle, Krause, Gegenbauer, and Hoffmann in German. The clinical remarks are especially complete and satisfactory in Allen; many very suggestive remarks are also made in Sappey's Atlas. In comparative anatomy the works of Owen, Gegenbauer, and Parker's translation of Wiedersheim, in English, and Milne-Edwards' Lecons, in French, are the most satisfactory. For the bibliography of the subject Mascagni, Milne-Edwards, Hoffmann, and Robin (see below) are especially commendable, as is also the Index Catalogue of the Surgeon-General's library. Specific references have been made to the following:

- Sappey, Ph. C.: Description et Iconographie des Vaisseaux lymphatiques considérés chez l'Homme et les Vertébrés, folio, pp. 156, 48 plates, Paris, 1886. Also Traité d'Anatomie descriptive, third edition, Paris, 1876.
- Key and Retzius: Studien in der Anatomie des Nervensystems und des Bindegewebes, two folio vols., 75 plates, Stockholm, 1875 and 1876.
- Alexander, A.: Ueber die Lymphcapillaren der Choroida. Arch. f. Anat. und Phys., Anat. Abth., p. 117, 1889.
- Gifford, H.: The Directions of the Lymph Streams in the Eye. Archives of Ophthalmology, vol. xv, 1886.
- Robin, Ch.: On the Perivascular Lymphatics of the Central Nervous System, in Journal de la Physiologie de l'Homme et des Animaux, vol. II, pp. 537-548, 1859; Journal de l'Anatomie et de la Physiologie Normale et Path., vol. IV, pp. 1-34, 1867; Article, Système Lymphatique, in Dechambre's Dictionnaire des Sciences médicales, pp. 389-474, 1870. At the end of this article are over seven pages of bibliography.
- Krause: Handbuch der menschlichen Anatomie, third edition, 1879.
- Klein, E.: The Anatomy of the Lymphatic System, 2 vol., 16 plates.
- Recklinghausen, F.: The Lymphatic System, in Stricker's Histology.
- Warthin, A. S.: The Normal Histology of the Human Hemolymph Glands. Amer. Jour. Anat., vol. I, No. 1, p. 63-79. See also article on Hemolymph Glands in vol. IV of this HANDBOOK.
- Sabin, Florence R., M.D.: On the Origin of the Lymphatic System from the Veins, and the Development of the Lymph Hearts and Thoracic Duct in the Pig. American Journal of Anatomy, vol. I, pp. 367-389, 1902.
- Beard: The Source of Leucocytes and the True Function of the Thymus. Anatomischer Anzeiger, Bd. xviii., pp. 550-573, 1900.
- Hilton, W. A.: The Morphology and Development of Intestinal Folds and Villi in Vertebrates. Amer. Journ. Anat., vol. I, No. 4, 1902.
- Mascagni, Paulo: Vasorum lymphaticorum corporis humani Historia et ichnographia, folio, MDCLXXXVII. (1787).
- Mall, F. P.: Die Blut- und Lymphgefässe im Dünndarm des Hundes. Abhandlungen der math.-phys. Classe d. Königl. sächs. Gesellschaft der Wissenschaften, Bd. 14, 1887; and the Vessels and Walls of the Dog's Stomach. Johns Hopkins Hospital Reports, vol. I, 1893.

**LYMPH NODES, DISEASES OF.**—ANATOMICAL CONSIDERATIONS.—The proper appreciation of the pathological changes met with in the lymph nodes presumes a slight knowledge of the normal anatomy of these organs. They are small, bean-shaped or oval nodules

which lie in the course of the lymphatic vessels and on the more protected portions of the body, as, for example, in the lateral regions of the neck, the axilla, the inguinal regions, about the peritoneal and pleural cavities, and in the folds of the mesentery. A small depression, known as the hilus, is usually present at one portion of the node, marking the point of exit of the efferent lymphatics and the blood-vessels. The nodes lie in a soft connective tissue and are quite freely movable in the fat which often surrounds them. They are normally of a reddish-gray color, and a cross-section of a freshly removed node is usually somewhat translucent.

The nodes are surrounded by a thin, fibrous capsule containing some fat tissue and blood-vessels, and occasionally a few smooth muscle fibres. The capsule sends processes into the node which are known as trabeculae. The capsule and the trabeculae send off fine connective-tissue fibres into the substance of the node, forming a delicate network in the meshes of which lie the leucocytes forming the parenchyma of the organ. These cells are chiefly of the variety known as lymphocytes, which possess a single large spherical nucleus and a relatively small amount of cell body.

The masses of lymphocytes near the periphery of the node are collected into nodules known as the follicles or secondary lymph nodules. They are surrounded by a lymph sinus, derived from the division of the afferent lymphatics into an anastomosing network of spaces lined with flattened endothelium. In the centre of the follicles a lighter area can often be seen in stained sections, where the cells are slightly larger than in the periphery of the nodule and often show karyokinetic figures. The lymphocytes are formed in these germinal centres, as they are called, and pass from them to the periphery of the nodule, from which they are set free in the lymph stream of the sinus.

In the centre of the lymph nodes the arrangement of the lymphocytes is somewhat different. They do not lie in masses as in the cortical nodules, but are suspended in strands in the connective-tissue network lying between the trabeculae, and are called medullary cords. Each cord is surrounded by a lymph sinus which separates it from the trabeculae.

The lymph sinuses are formed from the afferent lymphatics, some of which enter the node at the sinus, others through the capsule. They pass to the periphery of the node and break up there into an anastomosing series of vessels which pass inward and surround the follicles and the medullary cords, and finally reunite to form the efferent lymphatics and pass out at the hilus. The lymph sinuses so formed are lined with flattened endothelium.

The blood-vessels enter chiefly at the hilus and are distributed first to the medullary cords and then to the secondary nodules.

Reticular tissue containing lymphocytes is not confined to the lymph nodes, but is found in the organs and especially in the mucous membrane of the digestive tract. The tonsils and crypts in the tongue, the solitary and agminate follicles of the intestine are examples of such collections. The structure of these deposits of lymphoid tissue varies from that of the lymph nodes. The development of lymph sinuses and germinal centres is much less complete than in the nodes. The lymphocytes are also not wholly carried off in the lymph circulation, but many of them wander out through the epithelial layer covering these collections of lymphoid tissue and enter the digestive tract.

The agents which incite pathological changes in lymph nodes are as a rule carried in the lymphatics to the node and first enter the lymph sinuses at the periphery of the node. Coarser particles of foreign matter, such as dust or soot, are often deposited in this portion of the node, and are taken up by the phagocytic endothelial cells of the sinus. The same is true of the cells of tumors which are found first in the periphery of the node where they occupy the sinuses. The effects of bacterial poisons are often most marked in the peripheral portions, though the bacteria are usually caught in the filters of the nodules or

medullary cords. Thus, tuberculous foci generally begin near the centre of the node and may leave the peripheral portions in a more or less normal state.

**THE PATHOLOGICAL CHANGES IN LYMPH NODES.—Pigmentation.** The pigment which is most frequently found in lymph nodes is derived from soot or coal dust. Siltaceous material inhaled by stone-cutters or grinders may also be transported to the bronchial lymph nodes. Deposits of iron oxide are found in the nodes of iron workers. The pigment may also be derived from the substances used in tattooing, which are chiefly India ink and vermilion. Finally, the pigment may arise in the body from the destruction of the red blood corpuscles, either following hemorrhage or produced by parasites, such as the plasmodium malarie. The brown pigment which colors the skin and mucous membranes of those suffering from Addison's disease, may also be carried to the lymph nodes.

The pigment collects first in the lymph sinuses at the periphery of the node, being carried thither either by the lymph stream or by phagocytes. It may remain in this position either in the meshes of the fibrous reticulum or in the endothelial cells lying in the sinus. If the amount of pigment be very large, it is finally carried to all portions of the node and fills the nodules and the lymph cords.

A small amount of pigment may not cause any change in the structure of the node, but large quantities induce a chronic hyperplasia of the fibrous tissue which may result in a more or less complete destruction of the cells and the reticulum of the node, and their replacement by dense pigmented connective tissue. This chronic inflammation may involve the periglandular structures and give rise to dense connective-tissue masses about the node. Such nodes are of course functionless.

**Atrophy.** The lymph nodes of children are larger than those of adults, so that a slight atrophy of these structures takes place during life. In old age a more complete atrophy, with a diminution in the number of lymphocytes and thickening of the fibrous tissue of the node, is a regular occurrence. The node may be reduced to a mere shell, the centre of which is filled with fat tissue; or it may be small and hard and the fat tissue lie about it. Such nodes are paler than normal owing to the increase in the amount of connective tissue and to a diminution in the blood supply.

**Amyloid degeneration** of the reticulum and of the walls of the blood-vessels may appear in the lymph nodes as a part of a general amyloid degeneration of the organs of the body following prolonged suppuration, tuberculosis, or syphilis, or it may be limited to the nodes. In the

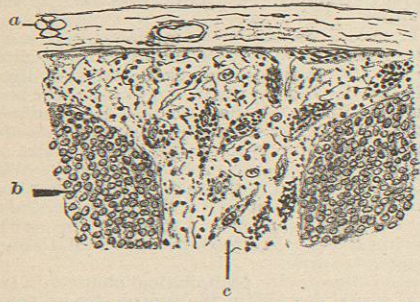


FIG. 3312.—Pigmentation of Lymph Node, with Chronic Inflammation. a, Capsule; b, follicle; c, dilated sinus with phagocytes carrying pigment. (Dr. F. C. Wood.)

latter case, amyloid degeneration is most frequently seen in the hyperplastic nodes of pseudoleukemia, and in chronic or tuberculous inflammation. In advanced cases the fibres of the reticulum may become greatly swollen so as to cause the parenchyma of the node to undergo atrophy. Under such circumstances the node is hard and

transparent and gives a mahogany brown when treated with tincture of iodine. Sections stained with methyl violet or thionin show the metachromatic staining characteristic of amyloid in the other portions of the body.

**Hyaline degeneration** of the walls of the vessels and the reticulum is occasionally seen in tuberculous or carcinomatous nodes or in old age.

**Fatty degeneration** is seen chiefly in the lymphocytes in connection with acute inflammation of the lymph nodes.

**Fatty infiltration** of the nodes is occasionally seen in obese persons, and may follow the atrophy resulting from chronic inflammation or old age.

**Calcification** of the nodes is seen chiefly in old tuberculous or suppurative lesions where the lime salts are deposited in the necrotic areas, but occasionally carcinomatous nodes will be found to be calcified, especially in slow-growing scirrhous carcinomata of the breast, when the axillary nodes have been invaded for a long time and degeneration has taken place in the tissue of the new growth.

**Animal parasites** have been found in the lymph nodes in rare cases. The embryos and adult worms of the filaria sanguinis hominis have been seen, and also the embryos of the trichina spiralis. Cysticercus and the echinococcus embryos have also been seen.

**Acute Lymphadenitis.** Acute inflammation of the lymph nodes is due to the presence either of micro-organisms or of their toxins. In these conditions the lymph nodes are enlarged and contain a considerable amount of serum. The capsule is distended and the blood-vessels are strongly injected. The color of the node under these conditions is a much darker red than normal. When the condition is advanced, the node softens and the softened tissue can easily be scraped from the cut surface. According to the microscopical changes which take place lymphadenitis may be divided into the hyperplastic and the exudative forms. In the hyperplastic form the changes are largely due to a proliferation of the cellular elements of the follicles, of the endothelial cells of the sinuses, and of the connective-tissue cells of the node.

The endothelial cells, especially in typhoid fever, can often be found lying free in the sinuses or attached to the trabeculae and very much swollen. The germ centres may be large and may show numerous mitoses in the early stages of the disease. Later, necrosis of the hyperplastic tissue is frequently seen and the cells cease to take any stain. In other cases the inflammation is distinctly suppurative, and in addition to the hyperplastic changes there are present lymphocytes and leucocytes from the circulation, together with hemorrhages from the blood-vessels. The tissues in the centre of the node soften, break down, and form, in this way, larger or smaller abscesses.

In very severe infections the inflammation takes on a hemorrhagic character, and the sinus may be filled with blood and a fibrin network which may finally extend between the necrosed cells of the follicles. The diphtheria bacillus is usually the inciting agent in the production of the hemorrhagic type of acute lymphadenitis, though the typhoid and anthrax bacilli may act in a similar manner. The bacillus of plague has a like action on the lymph nodes, and the nodes invaded by this organism are quite constantly the site of extensive hemorrhages, due to the necrosis of the walls of the blood-vessels produced by the toxin of this bacillus.

Very frequently the process does not remain confined to the node, but extends to the perinodular tissues, forming a periadenitis. When the process is confined to the nodes, healing may take place by resorption of the contents of the necrotic areas, and repair by the production of fibrous tissue; or, if these areas are of considerable extent, it may take place by absorption of the fluid and encapsulation of the dry mass by fibrous tissue. The debris remaining often undergoes a final process of calcification.

**Chronic Lymphadenitis.** This condition is characterized by chronic hyperplasia of the various elements of the node. It may be seen in conditions in which the

node is subjected to long-continued irritation, either by bacteria, or by toxic substances—the product of the bacteria or of the metabolism of malignant tumors,—or, finally, by the mechanical irritation of particles of soot or dust which have been transported to the lymph nodes. The general structure of the lymph node is retained. The lymph sinuses are filled by the formed elements resulting from the hyperplasia of the endothelial cells. The germ centres are often better marked than in normal lymph nodes, and in case the process continues for some time a great increase of the fibrous tissue takes place.

**Tuberculous Inflammation.** The tuberculous inflammation may occur in single, isolated lymph nodes, or in small groups, or may be diffused through all the lymph nodes of the body. The macroscopical appearance of a node which is only slightly involved may not furnish any clew to the changes which have taken place. When the disease is advanced to a certain extent, the node will show on cut section small, opaque, white areas, a little paler than the surrounding lymphoid tissue. In advanced forms, when a large amount of degeneration is present, the disease is easily recognizable by gross examination.

This type of inflammation is caused by the presence of tubercle bacilli in the lymph nodes, brought in a vast majority of instances by the lymph stream and only rarely through the blood-vessels.

Several types of tuberculous inflammation can be distinguished. In the first, one finds many small tuberculous nodules which are situated in the lymph nodules at the periphery of the node and in the lymph cords. The tuberculous changes begin by a proliferation of the flat endothelial and connective-tissue cells of the reticulum. In the centres of these nodules cheesy degeneration often makes its appearance, and on the borders of the cheesy areas are often to be found large and small giant cells.

Another type of alteration in the lymph nodes produced by the tubercle bacillus is a diffuse hyperplasia of the flat cells of the tissues with the production of more or less necrosis. In early cases there may be no necrosis and no giant cells. In later cases the necrosis may extend to the capsule and the node may contain no giant cells and no remnants of the original structure. Such nodes may soften and break down, and then discharge their contents into the tissues or into an organ near by, such as the lung or the bronchi; or lime salts may be deposited in the cheesy matter and the whole node become calcified. The bacilli in these cases disappear from the node. In the acute cases the bacilli are found in the cheesy masses and in the giant cells, which often contain large numbers.

In those nodes in which the amount of infection is small the lesions of simple inflammation will be found in the periphery of the nodes and around the tubercles. The cells of the follicles and the sinuses will be increased in size, and there are often more or less swelling of the endothelial cells and a proliferation of the cells of the reticulum.

The lymph nodes, which are most frequently attacked by tuberculous inflammation, are those of the lateral aspects of the neck, especially the submaxillary nodes. The portal of entry for the infection may be tuberculous changes in the tonsillar tissues, tuberculous otitis, or a tuberculosis of the nose, or the bacilli may enter through carious teeth. It is possible also that tubercle bacilli may pass through the intact mucous membranes of the mouth and the pharynx.

The bronchial nodes come next in order in frequency of infection, and in tuberculous children the occurrence of tubercles in these nodes has been noted in seventy-five per cent. of the cases dying in hospitals. The infection is carried through the lungs to the bronchial nodes, or in rarer cases from tuberculous lesions of the bones of the thorax. The mesenteric nodes are frequently found to be tuberculous in children in whom the bronchial nodes have also become involved. Direct infection from the intestine, without other tuberculous lesions in the body, is probably a rare occurrence.

**Scrofulous Enlargement.** The chronic enlargement of

the lymph nodes in poorly nourished children, designated clinically as "scrofulous," is still of undetermined nature. While it is true that tubercle bacilli can be demonstrated in a considerable proportion of such nodes, yet it is also true that they are not constantly present. Some observers assume that

we have two separate conditions, one a mild tuberculous infection, the other a chronic simple inflammation of the nodes, due to other bacteria than the tubercle bacillus. It has also been suggested that the chronic nature of the process is due to the low virulence of the tubercle bacillus. Our present knowledge of the variability in virulence of the tubercle bacillus, however, is so incomplete that definite conclusions cannot be deduced and the question must be regarded as still open for investigation.

**Syphilitic Lymphadenitis.** The changes produced in the lymph nodes by the poison of syphilis vary according to the stage of the disease. During the existence of the initial lesion the neighboring lymph nodes often show a simple acute inflammation which may go on to suppuration and the formation of a bubo, especially if the primary sore is not kept clean.

During the secondary period the nodes swell and become hard, but remain perfectly movable. The increase in size is due chiefly to an increase in the number of lymphocytes; but there may also be an increase in the endothelial and connective-tissue cells, and an infiltration of the walls of the vessels with leucocytes. If the patient is treated with mercury, the cells undergo fatty degeneration and absorption and the node returns to a normal condition. If, however, the inflammation has persisted for any length of time, the fibrous changes are likely to be permanent.

Gummata may develop in the lymph nodes in tertiary syphilis, but this is rare and as a rule involves only single nodes. The changes which take place resemble morphologically those produced by the tubercle bacillus. No bacilli can be found, however; giant cells are not usually so abundant, and the necrotic areas tend to dry up rather than to soften and break down.

**Tumor Formation in Lymph Nodes.** The classification of the tumors found in lymph nodes is still incomplete. The source of the difficulty lies in the fact that certain chronic hyperplasias of the nodes seem to depend on infectious processes, and others, of a closely similar morphology, seem to be independent of such an inciting agent. Five types of progressive, tumor-like enlargement of the lymph nodes can be distinguished in our present state of knowledge.

1. **Lymphadenoma**—a progressive increase in the lymph nodes of the body accompanied by anemia. This condition is known clinically as Hodgkin's disease or pseudoleukemia. A group of nodes such as those in the cervical region may first be attacked, and the process may extend later to other groups; or the enlargement may begin simultaneously in all parts of the body. The enlargement is a simple hyperplasia, the structure of the nodes being in general retained, and the morphological distinctions between the germ centres, the follicles, and the sinuses are not entirely obliterated until the disease is far advanced. Nodes so affected do not, as a rule, break through their capsules, but remain discrete. When examined in a fresh condition, these nodes are found to be harder than



FIG. 3313.—A Portion of a Tubercle in a Lymph Node. In the centre is a giant cell surrounded by necrotic material; beyond this a layer of endothelial cells; and at the periphery the remnants of one of the follicles of the node. (Dr. F. C. Wood.)

normal and the cut surface is pale as compared to the gray color of a normal node. There is no tendency to necrosis.

There may be hyperplasia of the lymph nodules in the organs, such as the liver, spleen, and kidney, and in the walls of the intestine; but diffuse infiltration of the viscera with lymphocytes is not seen. The changes in the blood are those of a severe anemia of a chlorotic type, without increase in the number of leucocytes. Pinkus has recently claimed that all cases of Hodgkin's disease show a relative lymphocytosis, but this has not been proven and the cases which the writer has been able to observe have shown no such change. Death is usually due to some intercurrent condition or to the mechanical action of the tumors—as, for example, compression of the trachea.

2. Tuberculous hyperplasia of a smaller or larger number of nodes. A number of cases have been described which ran a clinical course exactly similar to that of Hodgkin's disease, but showed on autopsy either nodes with a large amount of necrosis and tubercle tissue, or a simple hyperplasia of the nodes without any morphological tubercles in these nodes. Tubercle bacilli can be demonstrated by staining or by animal inoculations. The blood of such cases shows the anemia characteristic of Hodgkin's disease. Pinkus claims, however, that a relative lymphocytosis is not present in the tuberculous cases.

3. Hyperplasia of the lymph nodes in connection with either lymphatic or myelogenous leukæmia. Such hyperplasia is of more or less constant occurrence, especially in the lymphatic types, but the enlargement rarely reaches the extent seen in Hodgkin's disease. The examination of the blood reveals the nature of the disease. The nodes may be simply hyperplastic, with a great increase in the number of lymphocytes and a loss of the characteristic morphology, as is seen in lymphatic leukæmia, or the nodes may show alterations known as myeloid degeneration in cases of myelogenous leukæmia. This change consists in the appearance, in the lymph node, of structures found under normal conditions in the bone marrow only. These are the myelocytes or characteristic cells of the marrow, with the granulations proper to the three types which are found in that situation. These myelocytes are deposited in the node and there proliferate, forming small masses of a structure strikingly different from that of normal lymphoid tissue with its small non-granular cells. The nodes in the acute forms of lymphatic leukæmia often show hemorrhagic areas; these are less common in the chronic leukæmias.

4. Lymphosarcoma. This form of primary new growth arising in lymph nodes is distinguished from the tumors formed in Hodgkin's disease by the fact that it does not retain the normal morphology of the node but rapidly proliferates and breaks through the capsule to infiltrate the surrounding tissues and to form metastases in other portions of the body. The tumors show a marked tendency to degenerate and soften at their centres. Another point of differentiation between lymphosarcoma and the hyperplasias of the lymph nodes is in the large amount of connective-tissue reticulum between the cells of the former. This also aids in differentiating these tumors from the small round-celled sarcomata in which the connective-tissue reticulum is small in amount, or entirely absent in portions of the growth.

5. Sarcoma. Primary sarcomata of the lymph nodes are rare. They must not be confused with the lymphosarcomata which usually involve a number of nodes simultaneously and diffusely infiltrate the organs of the body. The true sarcomata are confined as a rule to a single node, soon break through the capsule, and form nodular metastases by the transfer of tumor particles through the medium of the blood current, but they do not as a rule involve other lymph nodes.

The types of sarcomata which have been described as arising from lymph nodes are: spindle-celled sarcoma, with more or less fibrous tissue; melanosarcoma; angiosarcoma; and round-celled sarcoma; the last being often indistinguishable from the true lymphosarcoma. Ziegler figures an alveolar sarcoma of a lymph node.

Endothelial tumors have been described as arising in lymph nodes, but, inasmuch as the morphology is always suggestive of carcinoma, it is probable that the cases reported have been due to the invasion of a node from some internal carcinoma whose existence was not observed. The writer has in his possession two tumors from the region of the neck, one of which is morphologically an endothelioma of the cyindromatous type, the other an alveolar sarcoma derived apparently from the large endothelial cells of the trabeculae. It is possible, however, that both of these growths are congenital remains from some of the glandular structures in the neck, and that the lymphoid tissue which they contain is merely the lymphoid tissue so often seen about the congenital cysts and ducts of the cervical region.

Secondary invasion of the lymph nodes by sarcomata is rare. The tumor particles reach the nodes through the blood-vessels as a rule, and spread diffusely throughout the lymphoid tissue. Such metastases occur most frequently in certain types of sarcoma, notably the small round-celled and the melanotic forms. In central sarcomata of the bone the regional lymph nodes are frequently invaded.

6. Carcinoma. Carcinoma of the lymph nodes is always secondary to a tumor of such portions of the body as contain epithelium. Such secondary invasion of lymph nodes by the cells of epithelial new growths takes place through the afferent lymphatics; and the cells, therefore, are first deposited in the lymph vessels and the sinuses at the periphery of the node. In very early cases the cells

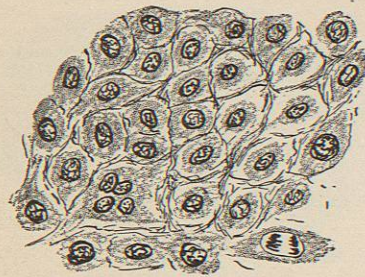


FIG. 3314.—Lympho-Sarcoma. The intercellular connective tissue is well developed in distinction from that in small round-cell sarcoma. (Dr. F. C. Wood.)

The lymphosarcomata may involve only a group of nodes, or a number of nodes in different portions of the body may enlarge simultaneously and by their metastases give rise to a general sarcomatosis with a diffuse infiltration of the tissues of the body, especially those of the liver and kidney.

5. Sarcoma. Primary sarcomata of the lymph nodes are rare. They must not be confused with the lymphosarcomata which usually involve a number of nodes simultaneously and diffusely infiltrate the organs of the body. The true sarcomata are confined as a rule to a single node, soon break through the capsule, and form nodular metastases by the transfer of tumor particles through the medium of the blood current, but they do not as a rule involve other lymph nodes.

The types of sarcomata which have been described as arising from lymph nodes are: spindle-celled sarcoma, with more or less fibrous tissue; melanosarcoma; angiosarcoma; and round-celled sarcoma; the last being often indistinguishable from the true lymphosarcoma. Ziegler figures an alveolar sarcoma of a lymph node.

Endothelial tumors have been described as arising in lymph nodes, but, inasmuch as the morphology is always suggestive of carcinoma, it is probable that the cases reported have been due to the invasion of a node from some internal carcinoma whose existence was not observed.

The writer has in his possession two tumors from the region of the neck, one of which is morphologically an endothelioma of the cyindromatous type, the other an alveolar sarcoma derived apparently from the large endothelial cells of the trabeculae. It is possible, however, that both of these growths are congenital remains from some of the glandular structures in the neck, and that the lymphoid tissue which they contain is merely the lymphoid tissue so often seen about the congenital cysts and ducts of the cervical region.

Secondary invasion of the lymph nodes by sarcomata is rare. The tumor particles reach the nodes through the blood-vessels as a rule, and spread diffusely throughout the lymphoid tissue. Such metastases occur most frequently in certain types of sarcoma, notably the small round-celled and the melanotic forms. In central sarcomata of the bone the regional lymph nodes are frequently invaded.

6. Carcinoma. Carcinoma of the lymph nodes is always secondary to a tumor of such portions of the body as contain epithelium. Such secondary invasion of lymph nodes by the cells of epithelial new growths takes place through the afferent lymphatics; and the cells, therefore, are first deposited in the lymph vessels and the sinuses at the periphery of the node. In very early cases the cells

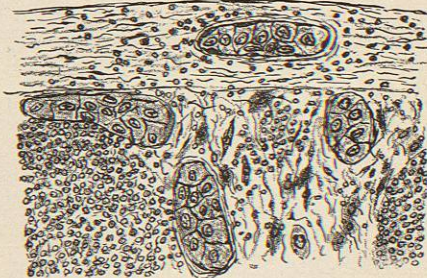


FIG. 3315.—Invasion of a Lymph Node with the Cells of a Carcinoma. The peripheral lymphatics and a portion only of the sinus are involved. (Dr. F. C. Wood.)

of the tumor may be confined to these points and not invade the follicles or cords. The tumor cells may attach themselves to the walls of the lymphatics and grow over the surface of the endothelial cells lining these vessels, giving rise to an appearance which has been erroneously interpreted as a new formation of carcinoma cells from

the endothelial cells of the vessel walls. The sinuses may be partially or wholly filled with the large cells of the new growth, which can be distinguished from the sinus endothelium by the more regular outline of the cell and the abundant chromatin of the nucleus. As the growth of the tumor cells continues the entire node may be replaced by them, but usually, before this takes place, there is a considerable increase in the amount of connective tissue present. Degenerative changes may take place in the tumor cells with necrosis of the tissue and softening of the centre of the node. Occasionally these softened nodes become infected and give rise to a suppurative peradenitis.

The presence of a malignant epithelial growth usually causes a slight hyperplasia of the neighboring lymph nodes, even though the tumor is not infected with microorganisms or ulcerated. These changes are confined chiefly to the peripheral sinuses and produce an hyperplasia of the sinus endothelium which may be mistaken by a careless observer for an invasion of the tumor cells. The germ centres of the follicles are also more prominent in these nodes than in those under normal conditions. Apparently the metabolic products of the tumor have the power of slightly irritating the lymph nodes through which they are filtered.

Lymph nodes invaded by the cells of a carcinoma can usually be diagnosed by gross inspection. The node is hard, and on section the areas involved are much paler than the normal node and more opaque; but occasionally nodes will be seen which, though invaded by the new growth, do not differ sufficiently from the normal to allow of a diagnosis by inspection, and recourse must then be had to microscopic examination. Nodes invaded by a sarcomatous new growth cannot usually be distinguished from the normal except by their size. An exception is seen when the sarcoma is of a melanotic type; such nodes may be almost black from the pigment of the tumor.

Francis Carter Wood.

**LYMPHOMA.**—This term has been used indiscriminately to indicate any enlargement of the lymphadenoid structures of the body, without regard for the true nature of the enlargement or its etiology. Most commonly it is applied in general medical literature to the generalized lymphadenoid hyperplasia associated with leukæmia and pseudoleukæmia (often distinguished as "malignant lymphoma"), or to the more localized glandular enlargements of lymphosarcoma, benign lymphatic hyperplasia, and primitive splenomegaly; yet it is by no means infrequently that "syphilitic lymphoma," "scrofulous lymphoma," or "acute lymphoma," is referred to under this title. In the proper use of the word, it should be limited to apply only to true neoplasms that reproduce the structure of lymphadenoid tissue. These tumors would be benign, since malignant tumors of similar nature would come, in the usual classification, under sarcoma, specified as "lymphosarcoma." A new growth of lymphadenoid tissue of infectious origin, whether the etiology is known or not, should not be called lymphoma. The confused condition of the classification of the various lymphatic enlargements is attributable to the ambiguous structure of the growth and the difficulty of distinguishing even those of known etiology from one another. That the term lymphoma continues to be used in this irregular way is probably because benign tumors reproducing lymph-gland structures, that are distinctly neoplasms, are so rare. Such a case has been described by Le Count,<sup>1</sup> but there seem to be few other instances in the literature, probably because they have not been recognized, rather than that they do not occur. Le Count's case is described as follows:

In section the fresh specimen is light reddish, its surface studded with areas resembling closely the Malpighian bodies of the spleen. The growth is encapsulated, has no coarse trabeculae, is not very vascular. Histologically it is characterized by reproducing quite closely, but with some differences, the structure of a normal gland. There are many nodes with an area of large pale cells,

of endothelial type, which are usually central and located at or near the point where an arteriole breaks into capillaries. Surrounding this are quite regular rows of small lymphoid cells. The tissue between the nodes is loose, consisting of a fine, non-nucleated reticulum, supporting small lymphoid cells.

Because of its rarity, and its eminently benign course, such a true lymphoma is merely of scientific interest. Of much more importance are the lymph-gland enlargements associated with leukæmia and pseudoleukæmia, which are what is commonly designated by the term lymphoma. While leukæmia is a fairly distinct condition, as well pathologically as clinically, the reverse is true of pseudoleukæmia, and to obtain any clear picture of its anatomical basis is almost hopeless. If we admit, however, that by pseudoleukæmia or Hodgkin's disease is understood a fairly definite symptom complex, characterized by general lymphadenoid hyperplasia, anemia without leucocytic increase, and a course always downward, and accept the view that these conditions may be produced by a variety of etiological factors, the situation is somewhat simplified. Then we can place on one hand those cases which are manifestly infectious, generally

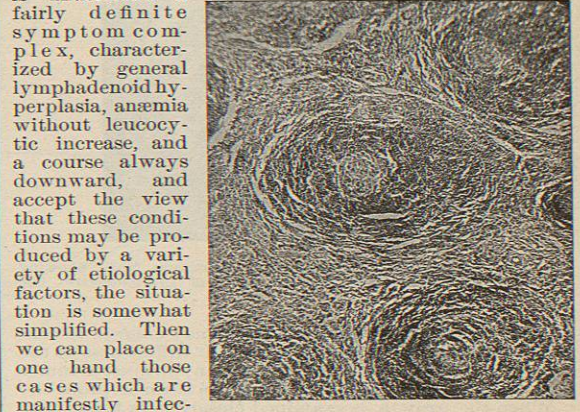


FIG. 3316.—True Lymphoma. Photograph of section showing lymph nodes and inter-nodal tissue. Slightly magnified. (Le Count.)

This leaves a group in which the glandular enlargement is much more like a tumor growth, both in structure and in absence of apparent cause. Two types of enlargement may be distinguished. In one the process resembles that of a malignant tumor, both macroscopically and microscopically. In the other, the change retains the essential features of benign growth, although multiple, and this benign enlargement corresponds anatomically to the localized enlargement of one or a small group of glands that is observed occasionally remaining for long periods without the accompanying manifestations of Hodgkin's disease, which local glandular enlargement is quite generally known among surgeons as lymphadenoma. This process then simulates a true benign tumor growth, and it is to this that the term lymphadenoma\* is best applied, to distinguish it from the malignant type of lymphadenoid growth, to which the term *lymphosarcoma* should be restricted.

The use of the termination *oma*, placing this condition among the tumors, is tentative, for there is much reason to believe that eventually such enlargements will all be found to be infectious; but as this is equally true in the case of many other tumors, such terminology is justifiable. It must be admitted, however, that the most substantial reason for using such a term as lymphadenoma at all lies in the fact that such usage is general, even by acknowledged authorities, and the function of such an article as this is rather to record what is than to suggest what should be.

\*Other names found in use to indicate the general glandular enlargement of Hodgkin's disease are: lymphadenosis, lymphosarcoma, lymphoma, malignant lymphoma, pseudoleukæmia, anaemia lymphatica, adénie, lymphadénie. Since these terms are in many instances contradictory, it is evident how loose the ideas and nomenclature on this subject really are.