Definition: **Lymph Nodes** from *Black’s Medical Dictionary, 42nd Edition*

Swellings which occur at various points in the lymphatic system through which LYMPH drains. They have two main functions: (1) the interception and removal of abnormal or foreign material from the lymph; (2) the production of immune responses (see IMMUNITY). The lymph nodes become enlarged when the area of the body which they drain is the site of infection or as a manifestation of some systemic diseases. Occasionally they are the site of primary or metastatic malignant disease.

Summary Article: **Lymph Nodes** from *Encyclopedia of Life Sciences*

**Introductory article**

**abstract**

The lymph nodes are numerous encapsulated structures occurring in mammals along the lymphatics. They contain lymphoid cells with a precise microanatomy organized to react to a variety of antigens via humoral and cellular immune responses. Lymph nodes consist of a cortex (B-cell zone) with primary and secondary follicles, a paracortical region (T-cell zone), sinuses and medullary cords. High endothelial venules represent a specialized vasculature with specific receptors for immune cells, which facilitate the migration of lymphocytes and dendritic cells. The main function of the lymph node is to generate an efficient immune response to antigens that have penetrated the organism in the areas drained by that node. Dendritic cells present antigen to naïve B cells, with the formation of germinal centres, as well as naïve T cells in the cortex. Malignant lymphoma represents the overwhelming majority of primary lymph node neoplasms, including both Hodgkin lymphoma and non-Hodgkin lymphoma.

**Key concepts**

- Lymph nodes are encapsulated structures present in mammals and distributed at specific sites throughout the body, which represent an important component of the secondary immune system.

- Lymph nodes have a specific microarchitecture, comprising a cortex, paracortical region, medullary cords and sinuses.

- The cortex is the B-cell compartment and includes primary and secondary germinal centres, whereas the paracortical zone is the T-cell compartment.

- Mature lymphocytes constantly recirculate between the lymph nodes and the peripheral blood, entering the lymph nodes passively via afferent lymphatics and actively via the high-endothelial venules of the lymph node via specific surface receptors.

- The B-cell compartment contain a range of B-cell maturation, from naïve primary follicle and mantle zone B-cells, to the centrocytes and then centroblasts of the germinal centre.

- The paracortical zone represents the site of T-cell activation and induction of specific T-cell migration to the follicles of the cortical region.

- The germinal centre represents a factory for the ultimate production of B-lineage effector cells.

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Most reactive diseases of the lymph node represent a form of exaggeration of the normal response.

Lymphoma represents the overwhelming majority of primary lymph node neoplasms, and may be B-cell non-Hodgkin lymphoma, T-cell non-Hodgkin lymphoma or Hodgkin lymphoma, the latter representing a distinctive neoplasm of Reed-Sternberg cells, unique cells derived from B cells.

**keywords**

lymphocytes
high endothelial venules
lymphocyte trafficking
germinal centre
malignant lymphoma

**Introduction**

The lymphoid tissues of mammalian can be divided into primary, secondary and tertiary lymphoid organs. The primary organs, the bone marrow and thymus, are the sites of production of functional lymphocytes. The secondary organs, including lymph nodes, spleen, tonsils and Peyer patches, are the sites of organized collections of lymphoid tissue capable of antigen-dependent and antigen-independent reactions with exogenous antigens. These reactions include both humoral and cellular immune responses, and involve the proliferation and differentiation of 'bursa-derived' (B) and thymus-derived (T) lymphocytes. The tertiary organs include all other tissues of the body, which contain varying amounts of lymphoid tissue depending on the degree of antigenic stimulation.

**Definition**

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**Distribution**

The lymph nodes are found along the routes of the major lymphatic vessels (Figure 1). Thus, they are mostly numerous in the thorax, the pelvis and abdomen, and the head and neck, although they also occur in the upper and lower extremities. In the thorax, lymph nodes occur most commonly in the anterior, superior and posterior mediastinum; bronchial and hilar region of the lungs; intercostal region; internal mammary region and the diaphragm. In the pelvis and abdomen, they occur in the internal and external iliac, sacral, lumbar (retroperitoneal) and coeliac regions. Lymph nodes are also found draining the stomach, small intestine (mesenteric), colon, gallbladder and spleen. In the head and neck, they are particularly common in the occipital, posterior and preauricular (the latter associated with the salivary gland), buccal, internal maxillary, lingual and retropharyngeal regions. In the neck, lymph nodes are found in the submaxillary, suprahypoid and superficial and deep cervical regions. In the upper extremity, they are particularly found around the elbow (epitrochlear) and the axillary region, and in the lower extremity around the popliteal region.
extremity in the superficial and deep inguinal, anterior tibial, popliteal, gluteal and ischiatic regions. See also: Lymphatic System

**Structure**

Grossly, the lymph node is a spherical to ovoid encapsulated structure varying from several millimetres to over one centimetre in greatest dimension. Afferent lymphatics and a few afferent blood vessels enter through the capsule, while efferent lymphatics and most afferent and all efferent blood vessels enter and leave through a depressed central area called the hilum. On cut section, four main architectural zones can be discerned: the cortex, the paracortical region, the sinuses and the medullary cords (Figure 2 and Figure 3).

The cortex (B-cell zone), present in the peripheral portion of the lymph node, is the site of primary and secondary B-cell follicles. Primary follicles are nodules of small, darkly stained, lymphoid cells, whereas secondary follicles have palely stained centres composed mostly of larger lymphoid cells and
macrophages. Unstimulated lymph nodes generally have a greater number of primary than secondary follicles, whereas the reverse is seen in antigenically stimulated lymph nodes.

The paracortical zone (T-cell zone), present between and central to the cortical follicles, is also primarily lymphoid in nature with a predominance of small lymphoid cells mixed with scattered larger cells. The paracortex expands in size in antigenically challenged lymph nodes.

The sinuses include subcapsular sinuses, which receive lymph from the afferent lymphatics; medullary sinuses, which deliver lymph to the efferent lymphatics; and radial (trabecular) sinuses, which connect the two systems. The sinuses tend to be more extensive and dilated in mesenteric lymph nodes.

The medullary cords are thin cords of lymphoid cells located between the medullary sinuses.

**Cellular Composition**

The primary follicles of the cortex are composed of small lymphocytes which represent both naive and memory B lymphocytes expressing a high density of surface immunoglobulin composed of μ and δ heavy chains combined with either κ or λ light chains. These cells also express B-cell leukaemia/lymphoma (bcl) 2 protein and lack cluster designation (CD)10 and bcl-6 protein. Molecular studies have demonstrated that the cells are clonally diverse and largely express germline immunoglobulin heavy chain variable (V) regions. The same cells comprise the outer region, or mantle zone, of the secondary follicles. See also: B Lymphocytes

The centre of the secondary follicle, called the germinal centre, is composed of a mixture of cell types, including small and large B cells (centrocytes and centroblasts), macrophages containing abundant nuclear debris (tingible-body macrophages), antigen-processing cells called follicular dendritic (dendritic reticulum) cells and scattered small lymphocytes representing helper/inducer T lymphocytes. Centrocytes usually possess a condensed chromatin pattern, but often have an irregular nuclear outline, whereas centroblasts have a vesicular chromatin pattern and usually have rounded nuclear outlines. In highly reactive states, the centrocytes and T-helper/inducer cells tend to cluster towards one pole (the pale or light zone) facing the antigenic stimulus, whereas the centroblasts and tingible-body macrophages tend to cluster towards the other pole (the dark zone). Centrocytes and centroblasts are both bcl-2 protein negative (although they have a high level of bcl-2 messenger ribonucleic acid) and CD10 and bcl-6 protein positive. They may contain cytoplasmic immunoglobulin (μ, γ, α and occasionally δ heavy chain with either κ or λ light chain), but have low levels of surface immunoglobulin. Molecular studies by Kuppers and colleagues have demonstrated that germinal centres are dominated by a few large B-cell clones that exhibit intraclonal diversity by ongoing somatic hypermutation. Follicular dendritic cells are nonbone marrow-derived cells which are difficult to identify by light microscopy, but are multinucleate cells with long processes forming a complex concentric network. On ultrastructural study the processes show interconnection with one another through numerous desmosomes. Follicular dendritic cells express CD21 and CD35, the complement (C) 3d and C3b receptors, respectively, and the processes of the follicular dendritic cells contain immunoglobulin complexes (γ, α and μ heavy chains with κ and λ light chains). Tingible-body macrophages express lysosome markers such as CD68, while the helper/inducer T lymphocytes are CD4 positive and CD8 negative. See also: Complement Receptors; Follicular Dendritic Cells (B Lymphocyte Stimulating); Macrophages; T Lymphocytes: Helpers

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The paracortical zone contains a mixture of cell types, but in the unstimulated state contains a marked predominance of small, mature T lymphocytes with only small numbers of B lymphocytes. The ratio of CD4-positive, CD8-negative helper/inducer to CD4-negative, CD8-positive cytotoxic/suppressor cells may vary markedly, but CD4-positive cells generally predominate. In various reactive states, scattered larger lymphoid cells can also be identified; these represent a mixture of B and T lineage cells. The B cells, termed B immunoblasts, generally have a pale chromatin pattern with a prominent nucleolus and abundant basophilic cytoplasm, whereas the T cells may have a wide variety of appearances. In addition to lymphoid cells, the paracortical regions contain interdigitating dendritic (interdigitating reticulum) cells. Most interdigitating dendritic cells are cells closely related to, and probably derived from, Langerhans cells, and have a medium-sized pale (vesicular) nucleus with a ‘coffee-bean’ nuclear outline and abundant cytoplasm with long processes (which lack desmosomes). Similar to Langerhans cells, interdigitating dendritic cells are S100 protein positive, but lack Birbeck granules or CD1 expression. Some interdigitating dendritic cells are derived from plasmacytoid dendritic cells, lymphoid-derived cells best recognized by their expression of CD123, which reach full maturation upon stimulation by interleukin-3. Other cells that may be present in the paracortex, depending on the degree of antigenic stimulation, include histiocytes, plasma cells and eosinophils. The structural elements of the paracortical regions have been collectively termed fibroblastic reticulum cells, but probably represent a heterogeneous population of spindle cells which may express vimentin, desmin, myosin, the isoform of α actin specific for smooth muscle, desmoplakin I, desmoglein or keratin. See also: Eosinophils; T Lymphocytes: Cytotoxic

The sinuses are lined by endothelial cells expressing the vascular marker CD31. The sinuses contain lymph as well as numerous macrophages (particularly the medullary sinuses) and variable numbers of red blood cells, neutrophils, lymphocytes and plasma cells. Occasionally, in some reactive states, the sinuses contain large numbers of monocytoid B cells or B immunoblasts. The medullary sinuses contain a mixture of small lymphocytes of both B and T lineage (the latter mostly of helper/inducer phenotype), mature plasma cells, cells intermediate between B lymphocytes and plasma cells, lymphoplasmacytoid
High Endothelial Venules and Interaction with Lymphocytes

High endothelial (epithelioid, postcapillary) venules (HEVs) of lymph nodes are located in the paracortical region and have morphological and physiological features distinct from venules found at most other sites. Histologically, HEVs are lined by cuboidal rather than the typical flattened endothelial cells, and have fairly large nuclei and an unusually abundant amount of cytoplasm which appears to obliterate the vessel lumen almost completely. It has been known for many years that HEVs must possess specific properties that attract lymphocytes, as mature lymphocytes bind selectively to HEVs when incubated on frozen sections of HEV-bearing lymphoid organs.

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The molecular basis for the specific interaction between HEVs and lymphocytes has been elucidated. There are at least four steps involved: primary adhesion, lymphocyte activation, activation-dependent arrest and diapedesis.

First, there is initiation of contact through microvillous receptors on the lymphocyte with separable contact formation ('tethering') with rolling of the lymphocyte along the vessel wall until the lymphocyte slows to a stop. The ligands on the HEV of the lymph node are a number of glycoproteins, including CD34 and other protein cores, which comprise peripheral lymph node addressin (PNAd). PNAd is found in high concentration on the luminal surface of HEVs, and in particular on ridge-like structures. The receptor present on lymphocytes is L-selectin (CD62L), a protein concentrated on the tips of lymphocyte microvilli. L-selectin is a C-type lectin with an affinity for sulfated, fucosylated, carbohydrate ligands such as the glycoproteins comprising PNAd. See also: Lectins; Lymphocytes

This is followed by activation of the lymphocyte, a process that may take 1-20s, mediated through the chemokine CCL21 present on the luminal surface of HEVs binding to the chemokine receptor CCR7 of lymphocytes. This leads to increased affinity of integrins expressed on lymphocytes for the immunoglobulin superfamily ligands ICAM-1 and ICAM-2, which mediates firm adhesion, a process that is reversible over minutes.

Finally, once arrest has occurred, diapedesis of the lymphocyte through the HEV occurs, gaining entrance to the paracortical region, a process that takes approximately 10 min.

**Lymphocyte and Dendritic Cell Trafficking**

Most mature lymphocytes constantly recirculate, averaging about one to two circuits between tissue and peripheral blood per day, with T cells migrating somewhat faster than B cells. Lymphocytes enter lymph nodes by two ways: passively from the lymph system via afferent lymphatics and actively from the blood via high endothelial venules. Both naive T and, to a lesser extent, B lymphocytes express L-selectin, and are therefore able to migrate through the HEVs and into the paracortical region of the lymph node. Although memory lymphocytes recirculate faster than naive lymphocytes, they recirculate to tertiary as well as to secondary lymphoid organs. In addition, they exhibit a pronounced selectivity in their homing behaviour. One example of this behaviour is their preferential return to the secondary tissue of origin. For example, it is known that adhesion of lymphocytes to lymph nodes in the gastrointestinal tract specifically requires interactions of LFA-1 and α4β7 integrins with their ligands ICAM-1 and ICAM-2 and MAdCAM-1, respectively. The regulation of lymphoid trafficking must include a mechanism for the homeostasis of mature lymphocyte populations. The patterns of lymphocyte circulation may vary depending on the degree of antigenic stimulation of the lymph node. The presence of antigen induces an increase in blood flow, thus increasing the overall numbers of lymphocytes entering the lymph node; furthermore, some antigens may cause a transient shutdown in lymphocyte exit. The febrile response also augments lymphocyte homing to lymph nodes, by increased L-selectin- and α4β7-dependent adhesive interactions, as well as by upregulating HEV expression of ICAM-1 and CCL21 via cytokine-dependent and cytokine-independent pathways. See also: Lymphocytes: Recirculation; Mucosal Lymphoid Tissues

Once T and B lymphocytes have been recruited into the paracortical region of the lymph node, it is not clear how the specific microenvironmental domains are formed. However, it is thought that each specific environment is determined by the interplay between adhesive receptors (such as integrins and CD44) and their ligands; regulatory factors, such as sequential chemotactic (perhaps chemokines) or contact guidance mechanisms; and particularly exposure to antigen. Under whatever influence, many of the B
lymphocytes migrate to primary follicles and the mantle zones of secondary follicles.

Dendritic cells also undergo a process of migration. Although a simplification, immature dendritic cells residing in the periphery, after antigen-uptake, downregulate the expression of receptors involved in antigen-uptake and acquire the function of antigen-presenting cells. In this process, these cells upregulate surface MHC molecules necessary for the presentation of pathogen-derived peptides, upregulate the expression of receptors for chemokines such as CCR7 that bind to HEVs, and express co-stimulatory molecules important for the interaction with antigen-specific T cells within lymph nodes, either directly or indirectly via dendritic cells resident in the lymph nodes.

**Role in Generation of Immune Responses**

The main function of the lymph node is to generate an efficient immune response to antigens that have penetrated the organism in the areas drained by that node. This involves recognition of the antigen; activation, proliferation and differentiation of effector cells and dispersal of the cells to appropriate sites of antigen. Antigen enters the lymph node via the afferent lymphatics. Much of the antigen is ingested by macrophages residing in the subcapsular sinuses within hours, and there is also an accumulation of neutrophils and a markedly increased blood flow to the lymph node. Within 24 h antigen is localized to the processes of follicular dendritic cells, and within 48 h antigen is found in the paracortical regions, probably in association with interdigitating dendritic cells. Follicular and interdigitating dendritic cells are able to retain antigens on their surface for weeks to months, and present antigens to B and T lymphocytes, respectively, in association with class II histocompatibility antigens. 6Ckine/CCL21 is a potent chemokine for mature dendritic cells and naive T cells, and may help in their co-localization. Numerous cell surface receptors are involved in the interactions between dendritic cells and T cells, including ICAM-3 on dendritic cells and DC-SIGN, the corresponding ligand on naïve T cells. **See also:** Antigen Presentation to Lymphocytes; Antigenpresenting Cells; Follicular Dendritic Cells (B Lymphocyte Stimulating)

Liu and colleagues have shown that 24-48 h after exposure to antigen, T- and B-lymphocyte activation and proliferation occur in the paracortical region. The T-cell response peaks after about 3 days and persists for up to 7 days after exposure to antigen, whereas the B-cell response peaks at about 4 days and persists for a longer period of time. The B-cell response results in the activation of a population of B cells that migrates to the follicles of the cortical region and the generation of short-lived plasma cells producing predominantly immunoglobulin (Ig) M heavy chain antibodies. In addition, antigen-specific lymphocyte clones are retained and concomitantly become depleted from the recirculating pool of lymphocytes. The T-cell response results in T-cell activation and the induction of specific T-cell migration to the follicles of the cortical region. **See also:** T-lymphocyte Activation

Although the B-cell response begins in the paracortical regions, the main sites of proliferation of B cells are the follicles of the cortical region. Events in the follicles are probably stimulated by the interaction of antigen present on the processes of follicular dendritic cells, the migration of antigen-binding B cells, probably attracted by the presence of antigen, and the migration of T-helper/inducer cells from the paracortical region. B cells proliferate in the follicles starting at about 36 h, within 3-4 days forming a central area called a germinal centre. The germinal centre is an oligoclonal structure with, on average, three founder B cells, derived from a small polyclonal population of activated B cells expressing unmutated antibodies present in the dark zone. These latter cells probably derive from B cells that have been activated in the paracortical region and have migrated to the germinal centre.

With the formation of a germinal centre, the follicle is now called a secondary, rather than a primary,
Germinal centre formation peaks at about 7 days. The B lymphocytes, now termed centroblasts, are highly proliferative, with a generation time of about 6 h. Centroblasts are nonmigratory cells (lacking homing receptors), and express very low levels of surface immunoglobulin, which shifts from class IgM to IgG (and, in mesenteric lymph nodes, IgA). Morphologically, they have large nuclei, a high mitotic rate and congregate in the dark zone adjacent to the paracortical area. It is at this place and time that the somatic hypermutation phenomenon at the immunoglobulin gene V region occurs, resulting in the selection of B-cell clones with high affinity for the specific stimulating antigen. There is a high rate of apoptosis in this bcl-2 protein-negative population, reflecting a high degree of selection, and resulting in the presence of abundant tingible-body macrophages phagocytosing the resulting cellular debris. See also: Antibody Classes; Immunoglobulin Gene Rearrangements

Centroblasts progress to centrocytes, which are smaller, less blastic-appearing, B cells with smaller nuclei containing a more condensed chromatin pattern. Centrocytes are not in cell cycle but still maintain a high degree of apoptosis. They appear to be selected by their ability to interact with the antigen present on the processes of follicular dendritic cells. Centrocytes take up the antigen via surface immunoglobulin, process it and present it to the T-helper/inducer cells in conjunction with class II antigens. Through this cognate interaction, the T cells are induced to express CD40 ligand, which is recognized by CD40 present on the centrocytes and induces differentiation into small, resting, memory B cells, increasing their amount of surface immunoglobulin and dramatically increasing their amount of bcl-2 protein, and losing their bcl-6 protein and CD10 expression. Through additional signals, possibly CD23 and interleukin 1α, a subset of centrocytes differentiates into immunoglobulin-secreting plasma cells. The plasma cell pathway is regulated by expression of the transcription factor IRF4 (MUM-1) and the transcriptional repressor Blimp-1. Plasma cells lose CD20 expression, gain expression of CD138 and generate large amounts of immunoglobulin. See also: Antigen Processing; CD Antigens; Interleukins

Once a germinal centre has been formed, there is little cellular traffic into it, and it gradually subsides about 3 weeks after exposure to antigen. However, with continuing exposure to antigen, germinal centres may persist for much longer periods of time. Although a subpopulation of germinal centre cells may show plasmacytoid features, particularly in the outer layers of cells in the pale zone, mature plasma cells generally are not evident until the cells enter the paracortical region. Plasma cells, plasmablasts and lymphoplasmacytoid cells tend to collect in the medullary cords before their exit from lymph nodes via medullary sinuses and efferent lymphatics.

Disease: Reactive and Neoplastic

Lymph node biopsies are most often performed because of unexplained enlargement of one or more nodes. Lymph node dissections, or removal of multiple lymph nodes from an anatomical site, are often performed as a part of a diagnostic or therapeutic procedure for a malignancy arising at a site drained by the lymph node group. Most biopsies performed for unexplained enlargement show reactive (nonmalignant) changes of the lymph node (Table 1). Usually, this takes the form of exaggeration of the normal immune response. Thus, expansion of one or more of the normal compartments of the lymph node is seen. Reactive follicular hyperplasia, an increase in the number of secondary follicles; paracortical hyperplasia, in which the paracortical region is expanded and has more than the usual range of cell types; sinus hyperplasia, in which the sinuses are expanded; or various combinations may be found. Common diseases causing reactive follicular hyperplasia include rheumatoid arthritis and other collagen vascular diseases, human immunodeficiency virus (HIV) infection and toxoplasmosis. In HIV infection, the follicular dendritic cells, helper T lymphocytes and macrophages of germinal centres represent reservoirs for the virus. Other viral infections are a common cause of paracortical

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hyperplasia. In addition, patients with skin disorders often show migration of Langerhans cells to the paracortical regions of lymph nodes causing a paracortical expansion termed dermatopathic lymphadenitis. Infections may lead to lymph node enlargement, including granulomatous disorders such as tuberculosis or fungal infections, and suppurative disorders such as cat-scratch disease and *Yersinia* infection. Noninfectious granulomatous disorders such as sarcoidosis may also lead to lymph node enlargement. See also: Human Immunodeficiency Viruses (HIV); Rheumatoid Arthritis; Toxoplasmosis; Tuberculosis

### Common lymph node disease

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Malignant lymphoma represents the overwhelming majority of lymph node neoplasms; only rare primary histiocytic, dendritic cell or stromal neoplasms occur. Malignant lymphomas are usually divided into Hodgkin lymphoma and the non-Hodgkin lymphomas. Hodgkin lymphoma is a distinctive lymphoma in which the neoplastic elements, termed Reed-Sternberg cells, comprise only a small proportion of the cells of the lymph node, the others being nonneoplastic small lymphocytes, eosinophils, plasma cells and histiocytes. Reed-Sternberg cells are probably derived from activated germinal centre B cells that have crippling mutations of the rearranged immunoglobulin genes which prevent them from expressing surface immunoglobulin yet do not undergo apoptosis as a result of an as yet unidentified mechanism. Hodgkin lymphoma has been subclassified into lymphocyte predominance, nodular sclerosis, mixed cellularity and lymphocyte depletion subtypes. Many cases of the lymphocyte predominance subtype is a distinct clinicopathological entity, characterized by the presence of a variant of Reed-Sternberg cells called lymphocytic and histiocytic cells, which are a variant of B cells that retain the coding capacity of the rearranged immunoglobulin genes. See also: Hodgkin Disease; Leukaemias and Lymphomas; Non-Hodgkin Lymphomas

The majority of non-Hodgkin lymphomas represent neoplasms of B cells at different stages of B-cell differentiation. These neoplasms generally show monotypic immunoglobulin, usually recognized by the demonstration of light chain restriction (demonstration of one and not the other light chain class), and at the molecular level show monoclonal rearrangements of the immunoglobulin heavy and/or light chain genes, indicating their origin from a single B-cell progenitor. The most common types are follicular lymphoma, a neoplasm of the germinal centre B cells; small lymphocytic lymphoma, a lymphoma of small mature lymphocytes; mantle cell lymphoma, a lymphoma of mantle cell lymphocytes; marginal zone lymphoma, a lymphoma usually derived from extranodal lymphocytes (and more commonly observed in extranodal sites); lymphoplasmacytoid lymphoma, a neoplasm of immunoglobulin-producing lymphoid cells; Burkitt lymphoma, a neoplasm probably derived from the most immature germinal centre cells and diffuse large-cell lymphoma, a heterogeneous group.

T-cell lymphomas comprise less than 10% of non-Hodgkin lymphomas. These neoplasms generally show monoclonal rearrangements of the T-cell receptor genes. T-lymphoblastic lymphomas represent lymphomas of immature thymocytes, whereas the many variants of peripheral T-cell lymphoma
represent lymphomas of mature T-cell origin. A higher proportion of T- than B-cell lymphomas arise outside the lymph nodes. A minority of non-Hodgkin lymphomas may show a derivation from natural killer cells, particularly those arising in the nasal cavities.

Metastatic tumours are the most frequent and most important non-haematopoietic lesions encountered in lymph nodes. They occur most commonly in carcinoma and malignant melanoma, but also occur, albeit infrequently, in some sarcomas. Carcinomas and malignant melanomas usually spread from the primary site of neoplasm to the lymph nodes in a stepwise, predictable fashion. On occasion, the lymph node is the first sign of disease; the histological appearance, the site of the affected lymph node and the immunohistochemical characteristics of the neoplasm may suggest where the unknown primary tumour is located. When metastases occur in lymph nodes, they usually involve the subcapsular sinuses first.

See also: Cancer

Further Reading


Glossary

**Carcinoma**
Malignancy of epithelial cells; the most common type of cancer.

**Diapedesis**
Passage of leukocytes through the intact walls of blood vessels.

**Granulomatous disorders**
Diseases characterized by the appearance of granulomas - clusters of activated histiocytes.

**Histiocyte**
Tissue-based cell derived from the monocyte which is capable of activation into a phagocyte that is specialized in ingesting a variety of substances and cellular material.

**Langerhans cells**
The dendritic cells of epithelium, particularly skin.

**Lymphocyte homing**
Specific trafficking of lymphocytes that directs lymphocyte subsets to specialized microenvironments.

**Malignant melanoma**
Malignancy of melanocytes, almost always arising in skin.

**Memory lymphocyte**
Lymphocyte that has previously been stimulated by specific antigen.

**Metastases**
Secondary implants of tumours away from the primary site of origin.

**Metastatic tumour**
Secondary deposit of cancer to a site at a distance from the primary neoplasm.

**Monocytoid B cells**
B cells with the cytological appearance of histiocytes which may collect in the lymph node sinuses in some reactive states.

**Naive lymphocyte**
Lymphocyte that has not previously been stimulated by specific antigen.

**Reed-Sternberg cell**
The neoplastic element of Hodgkin disease: a large cell, either binucleate or with a bilobate nucleus, and possessing prominent nucleoli.

**Toxoplasmosis**
Disease caused by infection with the parasite *Toxoplasma gondii*.

**Vascular addressins**
Tissue- or organ-specific endothelial cell molecules involved in lymphocyte homing.

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