

# SH Lecture - Lymphatic Structure and Organs

From Embryology



## 2013 Introduction

While the structure of the lymphatic system (*lymp* = clear water) is well described, there is much to still learn about the complex development and function of this "system".

1. Immune - “monitor” of body surfaces, internal fluids
2. Extracellular fluid - returns interstitial fluid to circulation
3. Gastrointestinal tract - carries fat and fat-soluble vitamins

## Aim

This lecture will provide an overview of the histology of key lymphoid organs, including the lymph nodes, spleen and thymus, as well as extranodal lymphoid tissues including mucosal associated lymphoid tissues (MALT)

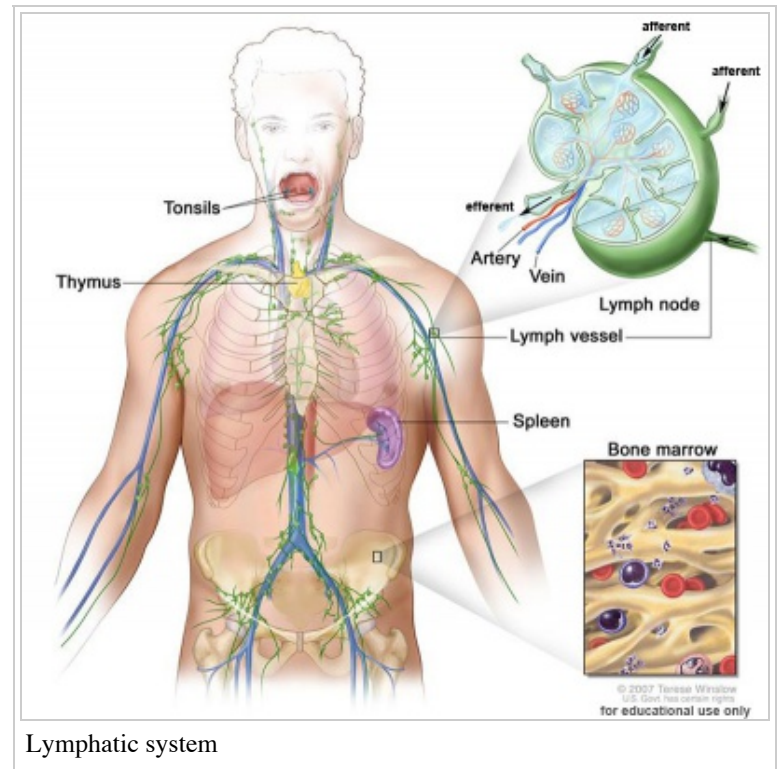
Note - Immunity is covered in detail elsewhere in the course, current lecture is limited to Lymphoid Organ structure/location.

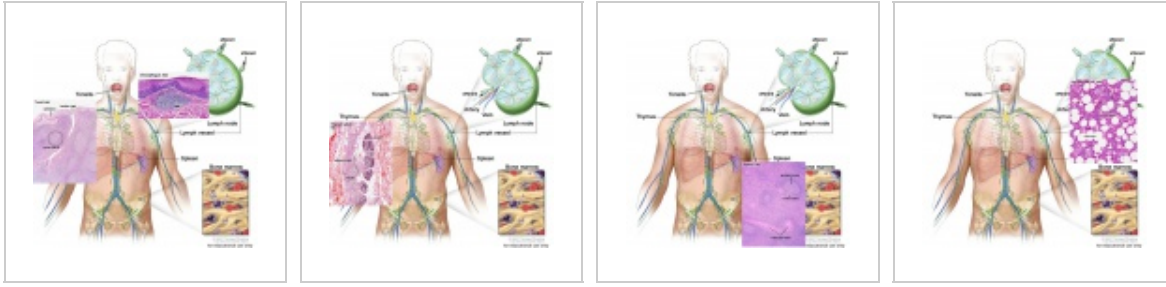
## Key Concepts

1. Lymphatic System
2. Organs - Thymus, Spleen
3. Lymph Nodes and Nodules
4. Bone Marrow
5. Extranodal Lymphoid Tissues
6. Mucosal Associated Lymphoid Tissues (MALT)

## Textbook References

- SH Laboratory Support
- **Janeway’s Immunobiology** (see in additional information) NCBI Bookshelf (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=imm.TOC&depth=2>)
- **Histology and Cell Biology** - A.L. Kiersenbaum (2001) Chapter 6: Blood, Chapter 10: Immune-Lymphatic
- Previous Lectures: 2012 ([http://php.med.unsw.edu.au/embryology/index.php?title=SH\\_Lecture\\_-\\_Lymphatic\\_Structure\\_and\\_Organs&oldid=115513](http://php.med.unsw.edu.au/embryology/index.php?title=SH_Lecture_-_Lymphatic_Structure_and_Organs&oldid=115513)) | 2010 ([http://php.med.unsw.edu.au/cellbiology/index.php?title=2010\\_Society\\_and\\_Health\\_-\\_Lymphatic\\_organ\\_histology](http://php.med.unsw.edu.au/cellbiology/index.php?title=2010_Society_and_Health_-_Lymphatic_organ_histology)) | 2008 (<http://cellbiology.med.unsw.edu.au/units/medicine/SHlymph.htm>)





Tonsil and MALT

Thymus

Spleen

Bone marrow

**Immune Links:** Introduction | Blood | Spleen | Thymus | Lymphatic | Lymph Node | Antibody | **Med Lecture - Lymphatic Structure** | Med Practical | Immune Movies | Category:Immune

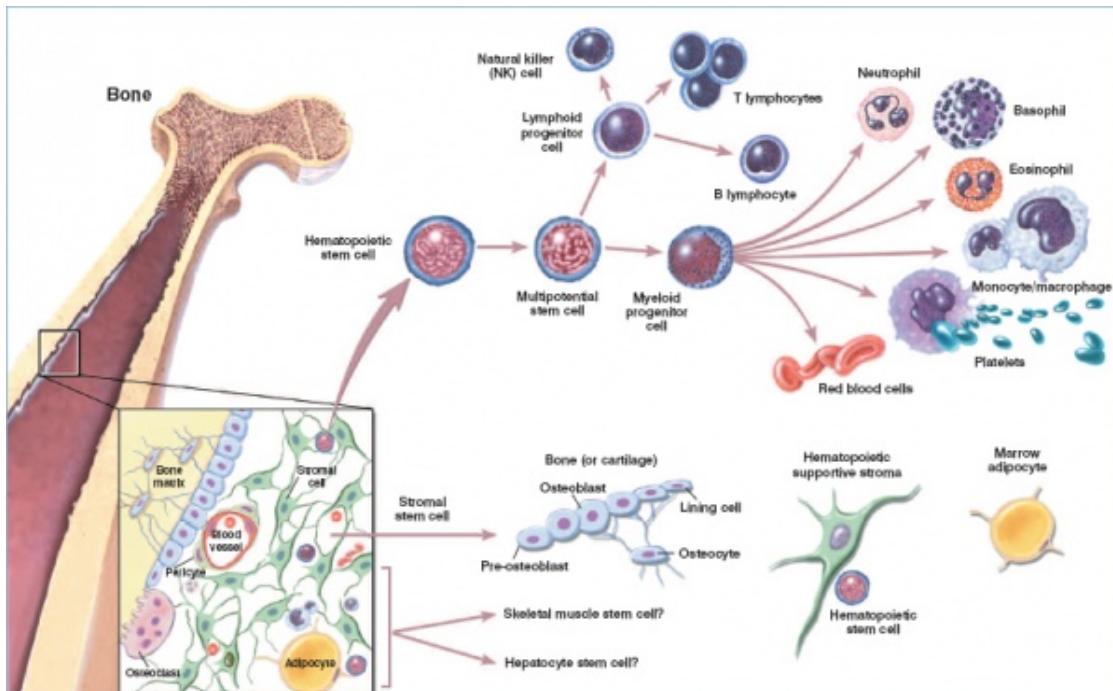
**Historic Embryology:** 1918 Gray's Lymphatic Images | 1916 Pig Lymphatics | 1919 Chicken Lymphatic | 1922 Pig Stomach Lymphatics | Historic Disclaimer

## Two Cellular Systems

- **Mononuclear Phagocytic System** (MPS, also called Lymphoreticular System or Reticuloendothelial System, RES) - circulating monocytes of peripheral blood and non-circulating (fixed) tissue macrophages found throughout the body
- **Lymphoid System** - three major types of lymphocytes (T, B, and NK), tissues, organs and vessels

### Lymphoid Organs

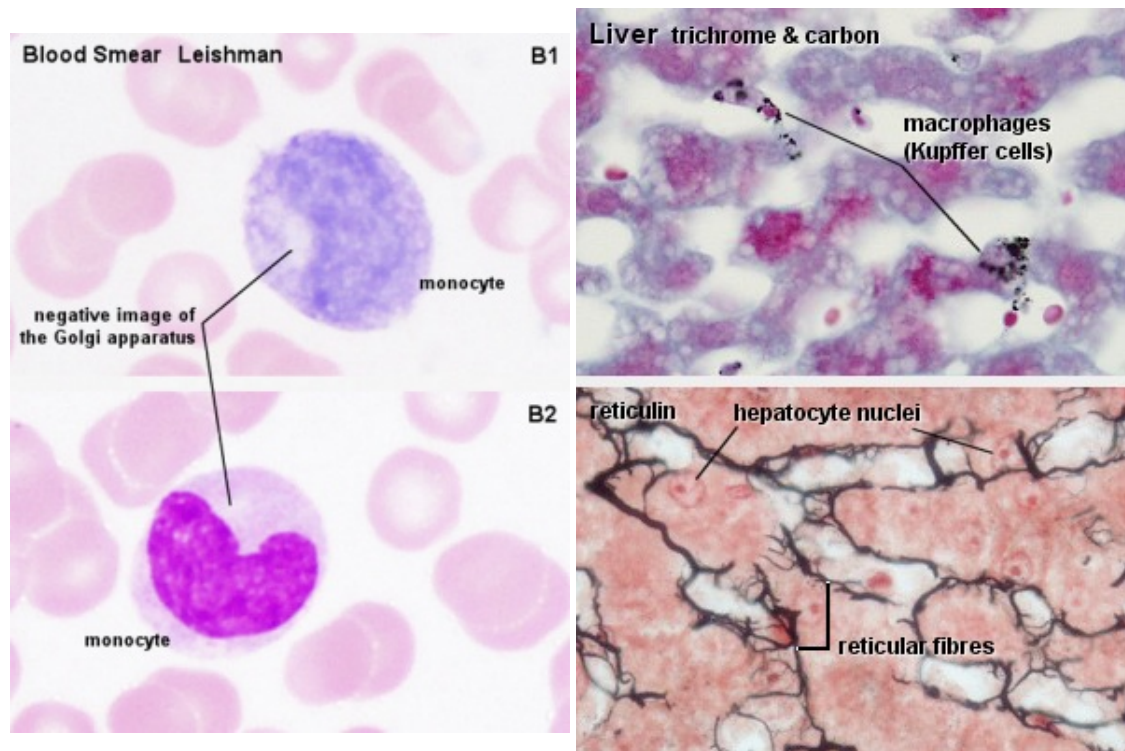
- Central - Lymphocytes develop from precursor cells in bone marrow. (see blood marrow image)
- Peripheral - Lymphocytes respond to antigen lymph nodes or spleen.



[show] Blood Cells

## Mononuclear Phagocytic System

(Mononuclear Phagocytic System MPS, also called Lymphoreticular System or Reticuloendothelial System, RES)

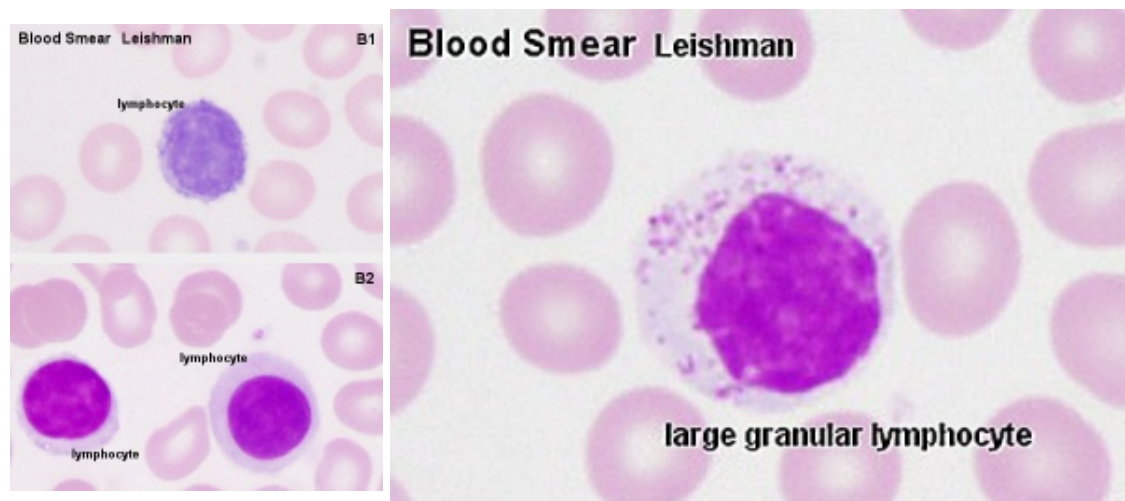


Mononuclear Phagocytes 2 types:

1. Circulating **monocytes** of peripheral blood (monocytes entering the connective tissue differentiate into **macrophages**)
2. Non-circulating (fixed) tissue **macrophages** (MΦ) found throughout the body (Liver (Kupffer cells), spleen and other tissues)

## Lymphoid System

Functional cells are the **lymphocytes** (B, T, NK) and **dendritic cells** (process antigen and present it on their surface).



### B Cell Development

### Germinal Centres

### Plasma cells

- Bone marrow
- blood
- Lymph node,

- Bone Marrow
- Medullary cords contain plasma cells

- secrete antibody directly into blood for distribution to all body
- in local extrafollicular sites are short lived 2–4 days

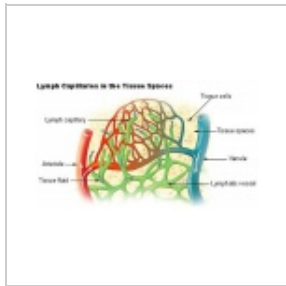
- nodule
- Lymphatic vessel
- Bone marrow

- longer-lived plasma cells in bone marrow 3 weeks to 3 months+

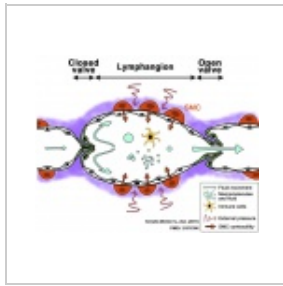
[show] Lymphocyte Electron Micrographs

## Lymph

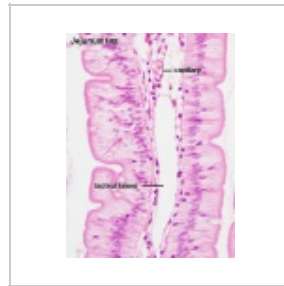
- Fluid portion of lymphatic circulation
- blood plasma will leave blood vessels into surrounding tissues
- adds to normal tissue interstitial fluid
- surplus of liquid needs to be returned to circulation
- Lymph vessels provide unidirectional flow of this liquid



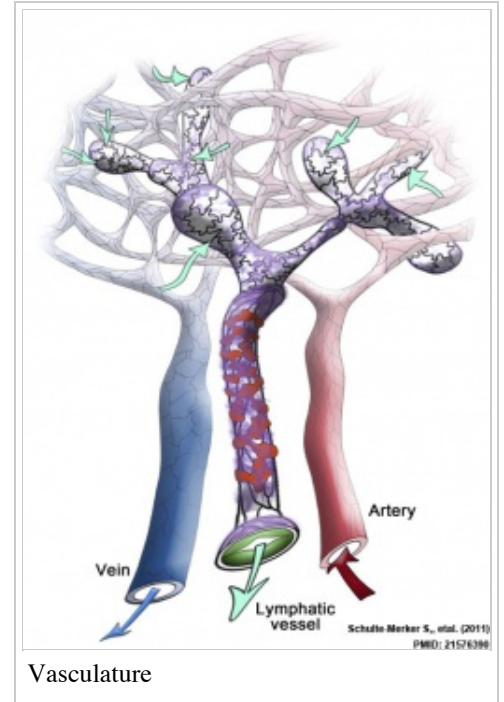
Lymph capillary



Lymphangion



Jejunum lacteal

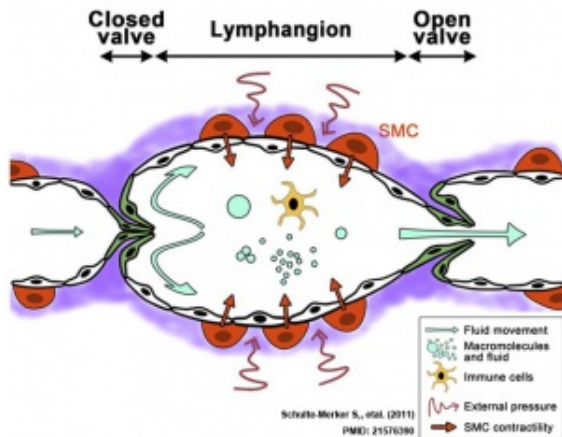


Vasculature

## Lymph Vessels

Three types based on size and morphology

- **Lymph capillaries** - begin as blind-ending tubes in connective tissue, larger than blood capillaries, very irregularly shaped
- **Lymph collecting vessels** - larger and form valves, morphology similar to lymph capillaries
- **Lymph ducts** - 1 or 2 layers of smooth muscle cells in wall



### Lymphangion

(Remember anatomy acronym - NAVL = Nerve, Artery, Vein and Lymph)

## Lymphocyte Circulation

- Microbial **antigens** are carried into the lymph node by **dendritic cells**, which enter via afferent lymphatic vessels draining an infected tissue.
- T and B cells** enter the lymph node via an artery and migrate out of the bloodstream through postcapillary venules.
  - Unless they encounter their antigen, the T and B cells leave the lymph node via efferent lymphatic vessels, which eventually join the thoracic duct.
- The thoracic duct empties into a large vein carrying blood to the heart.
- A typical circulation cycle takes about 12–24 hours.

**Links:** MBoC Chapter 24 - The Adaptive Immune System

(<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mboc4&part=A4419>) | MBoC Figure 24-14. The path followed by lymphocytes as they continuously circulate between the lymph and blood (<http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4442>) | Immunobiology (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=imm>)

## Diffuse Lymphatic Tissue

Alimentary canal, respiratory passage, urogenital tract

- Not enclosed by a connective tissue capsule**
- Located in subepithelial tissue - **lamina propria**
- Diffuse lymphatic tissue + nodules
- Reactive - enlarge when activated (by antigen)

### Lymphocytes

- travel to nodes and back again
- proliferation and differentiation

Adaptive immunity has 2 main classes

- Antibody-mediated** - B Lymphocyte secreting antibody = **Plasma Cell**
- Cell-mediated** - T Lymphocytes form **memory cell**, Cytotoxic T cells, T helper cell

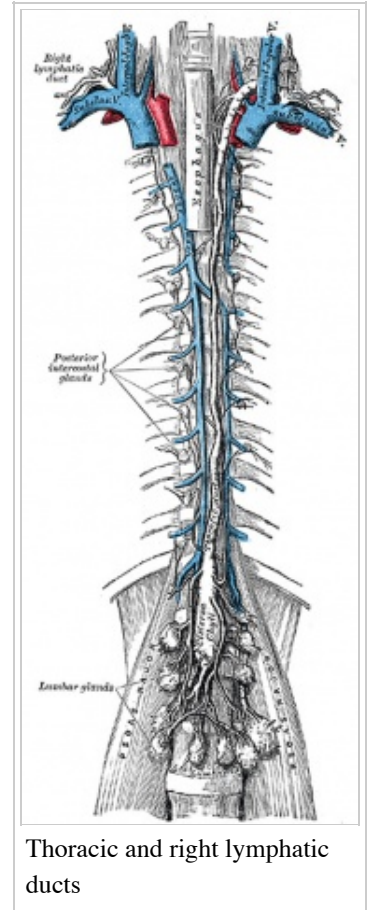
## Lymph Nodules

- Organized concentrations of lymphocytes
  - No capsule, covered by epithelia
- Nodules are also the unit structure seen in a node
- Oval concentrations in meshwork of reticular cells

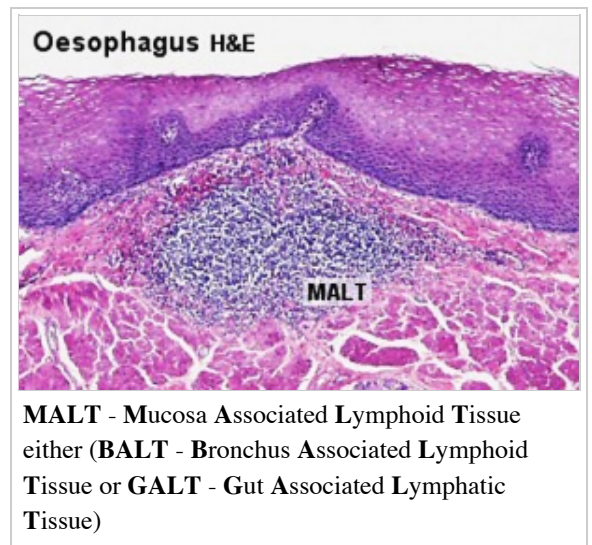
## Nodule States

- Primary Nodule** - Mainly small lymphocytes
- Secondary Nodule**
  - Central pale region (germinal centre) - Effector cells and macrophages
  - Dark outer ring (small lymphocytes)

## Gastrointestinal Tract



Thoracic and right lymphatic ducts



**MALT** - Mucosa Associated Lymphoid Tissue either (**BALT** - Bronchus Associated Lymphoid Tissue or **GALT** - Gut Associated Lymphatic Tissue)

- Oropharynx - Tonsils
- Distal small intestine (ileum) - Peyer's Patches
- Appendix, cecum

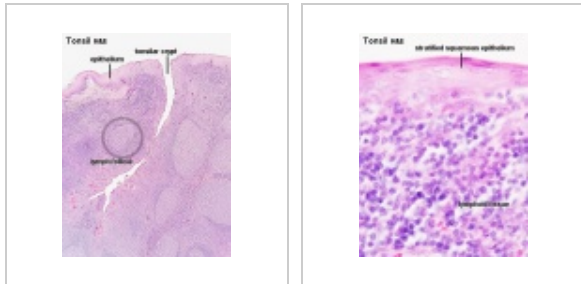
## Tonsils

Anatomical location - Palatine (**tonsils**), Lingual and Pharyngeal (**adenoids**)

Ring of oral adenoid tissue:

- anterior - **lingual tonsil** formed by the submucous adenoid collections.
- lateral - **palatine tonsils** and adenoid collections near the auditory tubes.
- posterior - **pharyngeal tonsil** on the posterior wall of the pharynx.
- between main masses are smaller collections of adenoid tissue.

### Palatine Tonsils



Tonsil overview

Tonsil detail

- the "tonsils", lateral wall of oropharynx
- covered by stratified squamous epithelium
- numerous crypts (10-20) infolds of surface epithelium
- Afferent lymph vessels absent
- Efferent lymph vessels are present

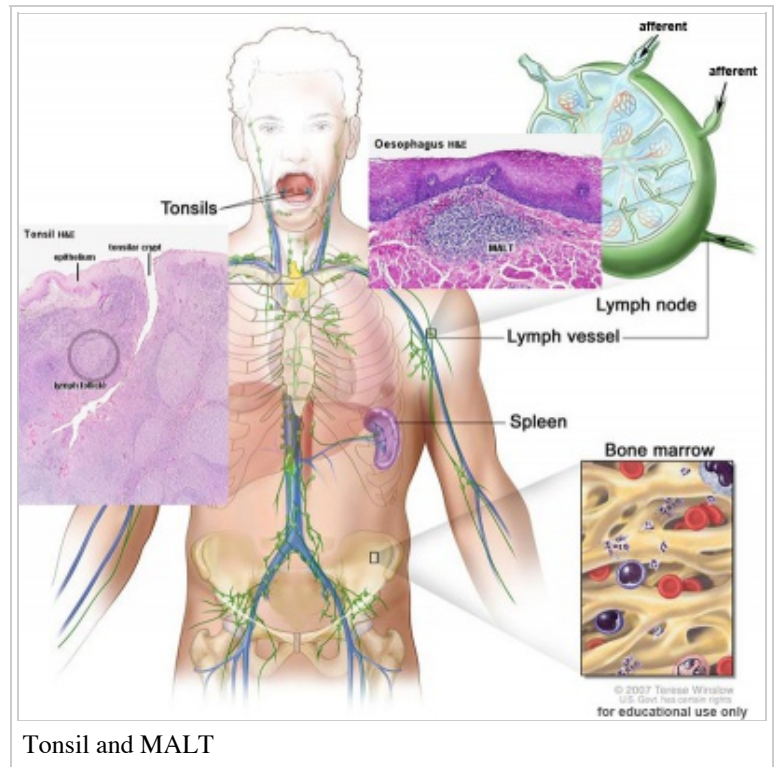
### Lingual Tonsils

- lamina propria root of tongue
- covered by stratified squamous epithelium
- salivary glands and skeletal muscle are directly adjacent

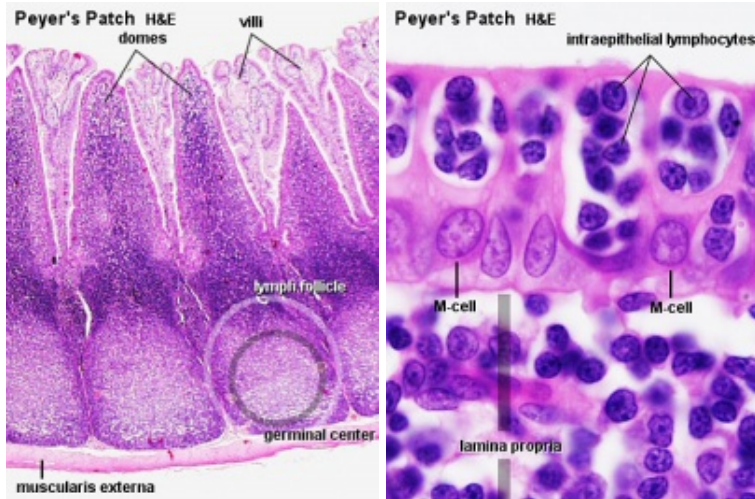
### Pharyngeal Tonsils

- **adenoids** or nasopharyngeal tonsils, upper posterior part of throat
- covered by a pseudostratified ciliated epithelium with goblet cells

### Gastrointestinal Tract - Peyer's Patch



Tonsil and MALT



Peyer's Patch, Ileum

microfold cells or M-cells

## Lymph Nodes

- Location throughout the entire body - Concentrated in axilla, groin, mesenteries
- Encapsulated organ (1 mm - 2 cm)
- Antigen transformed lymphocytes from the blood
- In lymph vessel pathways “filter”
- Afferent- towards node
- Efferent- away from node

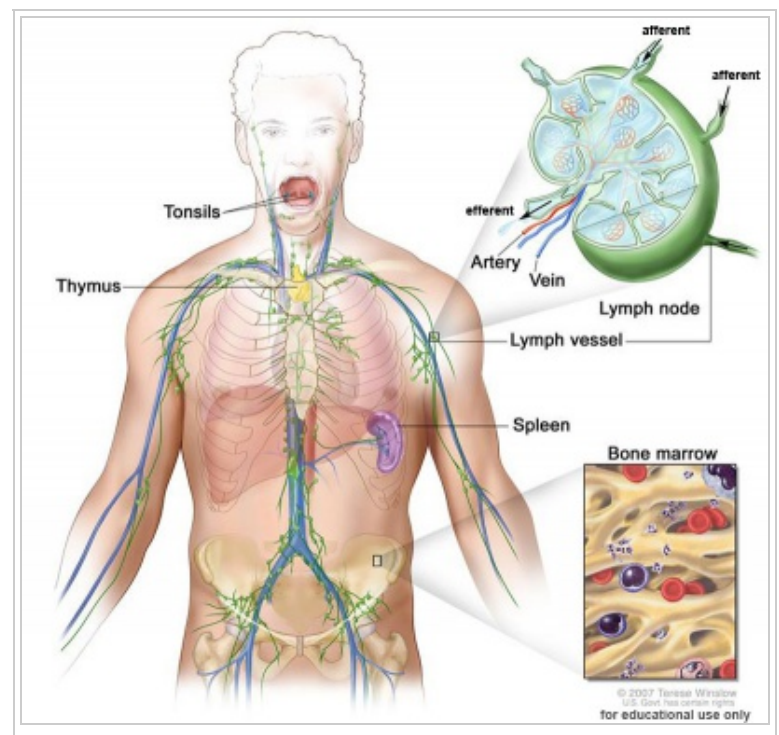
Lymph flow

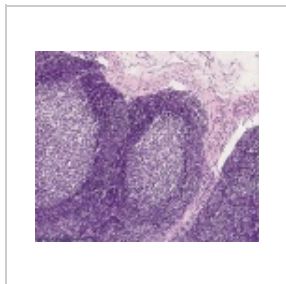
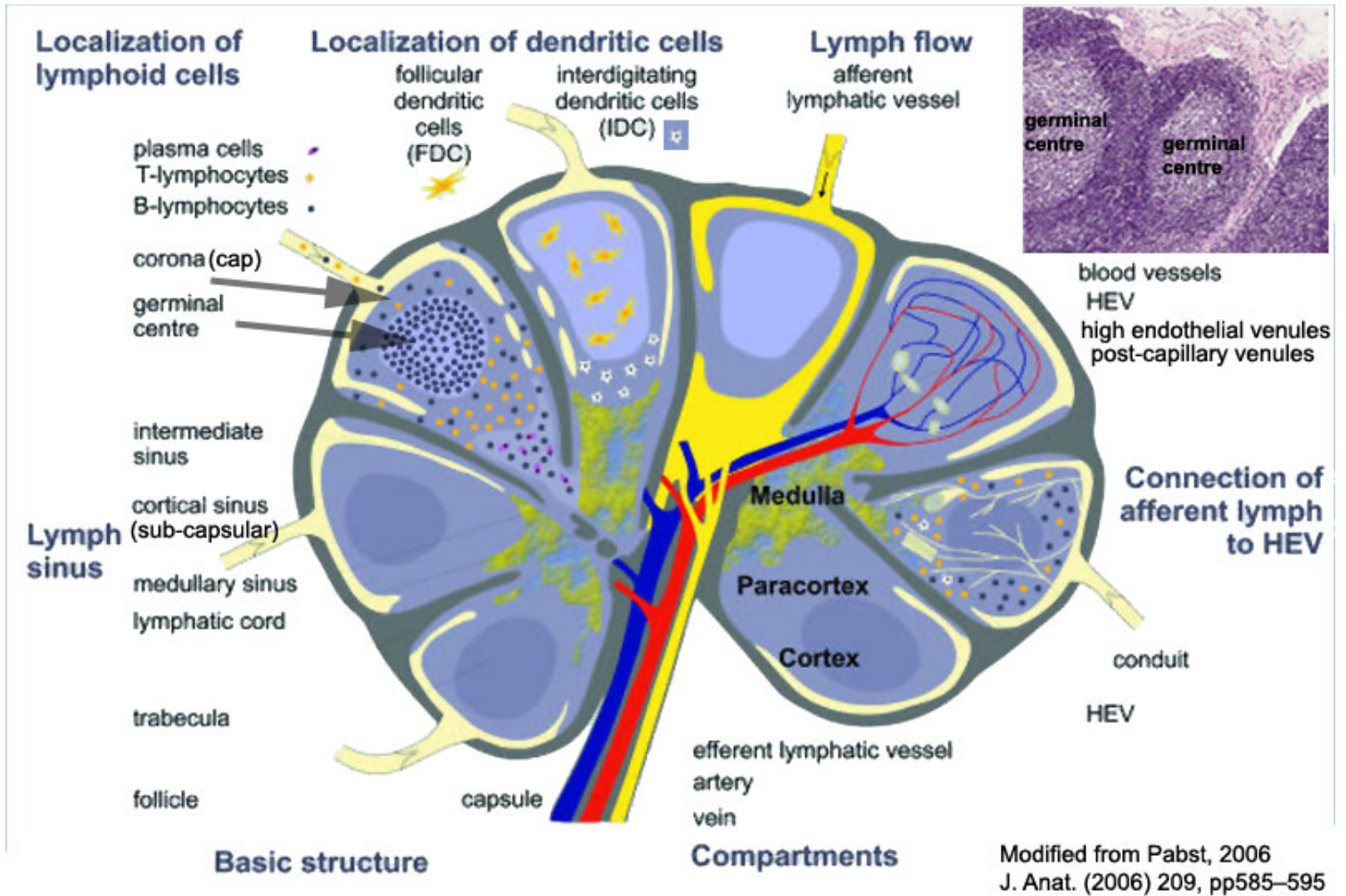
- enters the node through **afferent vessels**
- filters through the **sinuses**
- leaves through **efferent vessels**

## Lymph Node Structure

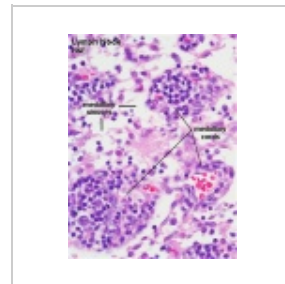
Connective Tissue

- **Capsule** - dense connective tissue (irregular CT, some adipocytes)
- **Trabeculae** - dense connective tissue
- **Reticular Tissue** - Reticular cells and fibers, supporting meshwork (collagen type III)
  - Reticular cell produces reticular fibers (**collagen type III**) and surrounds the fibers with its cytoplasm
  - reticular fibers can also be produced by fibroblasts





Lymph node histology



Lymph node cortex histology

Subcapsular sinus = marginal sinus

Continuation of trabecular sinus

Lymphocyte (T and B) Traffic

1. Enter from high endothelial venules (HEVs also called post-capillary venules)
2. Spend 8 to 24 h in the lymph node interstitium.
3. Enter a network of medullary sinuses.
4. Drain from sinuses into efferent lymphatic vessels.

**Links:** Immunobiology - Figure 1.8. Organization of a lymph node



(<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A47>)

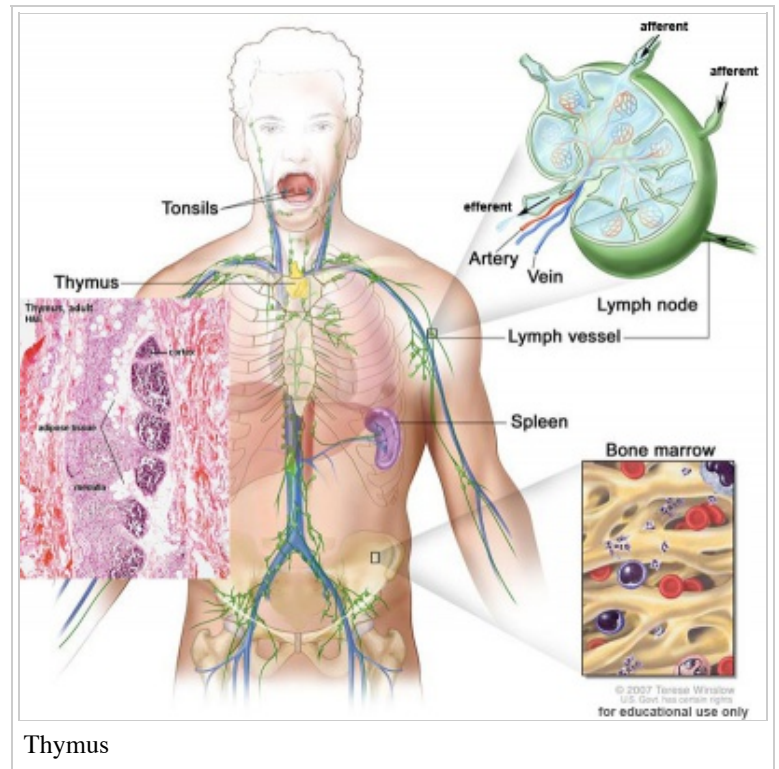
# Thymus

## Thymus Anatomy

- Superior mediastinum, anterior to heart
- Bilobed lymphoepithelial organ
  - Contains reticular cells but no fibers
- Stem lymphocytes
  - proliferate and differentiate
  - forms long-lived T- lymphocytes

## Thymus Cells

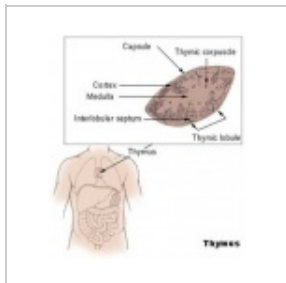
- **Reticular cells**
  - Abundant, eosinophilic, large, ovoid and light nucleus 1-2 nucleoli
  - sheathe cortical capillaries
  - form an epitheloid layer
  - maintain microenvironment for development of T-lymphocytes in cortex (thymic epitheliocytes)
- **Macrophages**
  - cortex and medulla
  - difficult to distinguish from reticular cells in H&E
- **Lymphocytes**
  - cortex and medulla - more numerous (denser) in cortex
  - majority of them developing T-lymphocytes (= thymic lymphocytes or thymocytes)



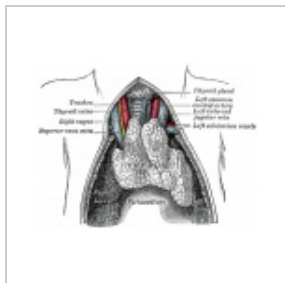
## Development Changes

{Changes with age Overall Size

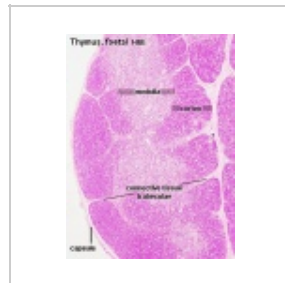
- birth 10-15 g
- puberty 30-40 g, after puberty - involution
- middle-aged 10 g, replaced by adipose tissue



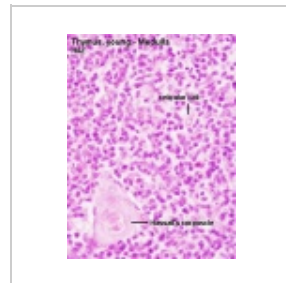
Fetal thymus anatomy



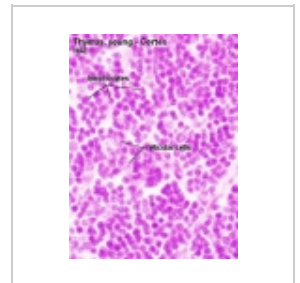
Fetal thymus



Young medulla

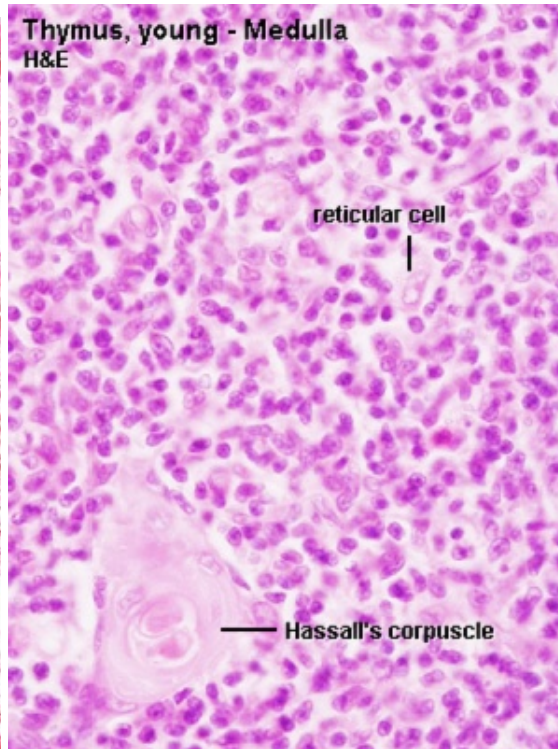
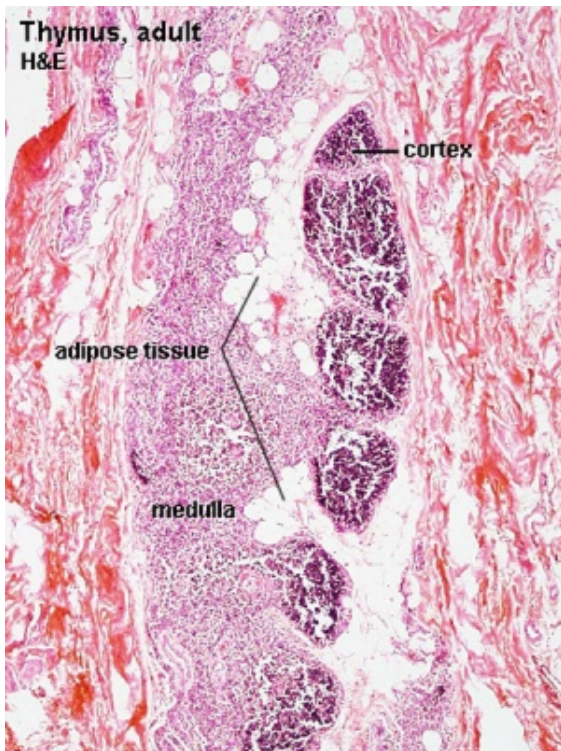


Young cortex



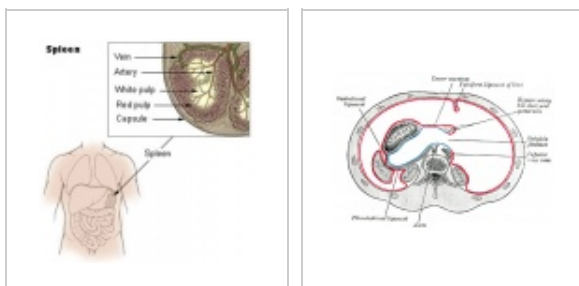
## Adult Thymus

- Cortical lymphoid tissue is replaced by adipose tissue
- Increase in size of thymic corpuscles
- **Thymic corpuscle** - (Hassall's corpuscle) mass of concentric epithelioreticular cells.



**Thymus Histology:** Fetal Thymus overview | Fetal Thymus Medulla | Fetal Thymus Cortex | Adult Thymus | unlabeled fetal overview | unlabeled fetal medulla unlabeled fetal thymic corpuscle unlabeled fetal cortex | unlabeled adult overview | Category:Thymus | Immune System Development

## Spleen



## Spleen Function

### 1. Immune

- filters blood in much the way that the lymph nodes filter lymph.
- **Lymphocytes** in the spleen react to pathogens in the blood and attempt to destroy them.
- **Macrophages** then engulf the resulting debris, the damaged cells, and the other large particles.

### 2. Red Blood Cell Removal

- The spleen (and liver) removes old and damaged erythrocytes from the circulating blood.
- Like other lymphatic tissue, it produces lymphocytes, especially in response to invading pathogens.

**3. Blood Reservoir**

- The sinuses in the spleen also act as a reservoir for blood.
  - In emergencies, such as hemorrhage, smooth muscle in the vessel walls and in the capsule of the spleen contracts.
  - This squeezes the blood out of the spleen into the general circulation.

**Structure**

- Capsule, trabeculae (dense connective tissue)
- Splenic pulp white pulp, red pulp - based on appearance and cell content.

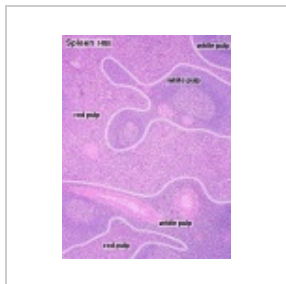
**White Pulp**

- lymphocytes surround central arteries
- as periarterial lymphoid sheath (PALS)

**Red Pulp**

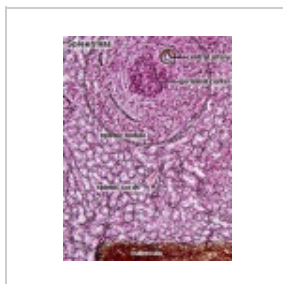
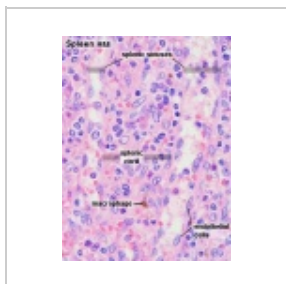
- Red blood cells
- Splenic cords and sinuses

**Reticular Fibers** (type III collagen) act as supporting meshwork.



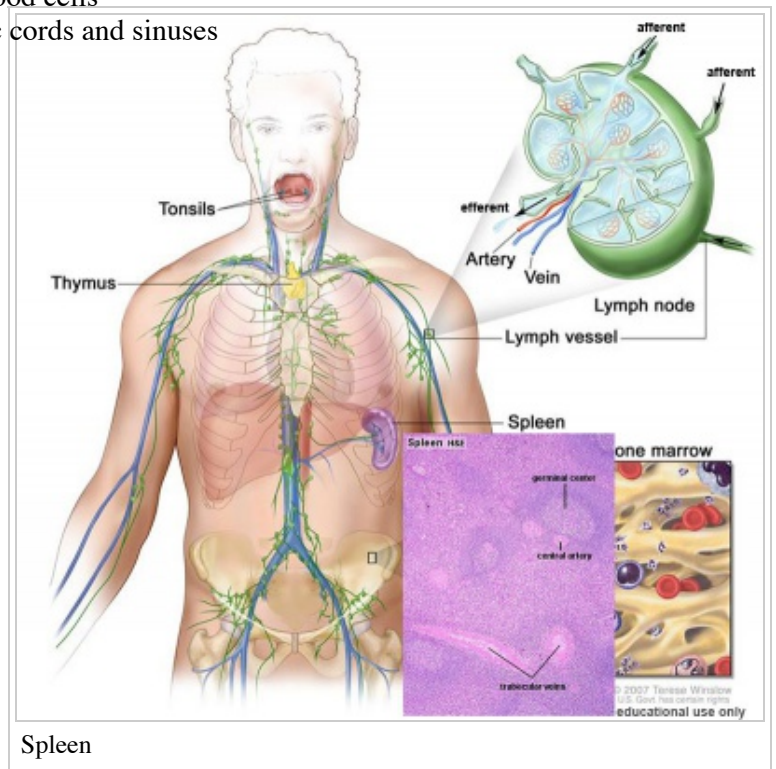
Overview Red and White Pulp

Overview Red and White Pulp

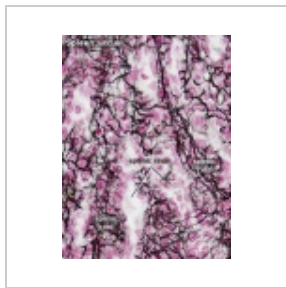


Cords and Sinuses

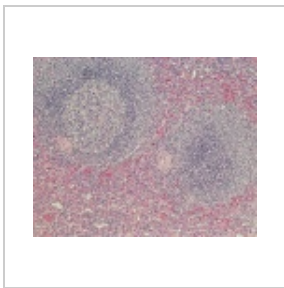
Reticular Fibre overview



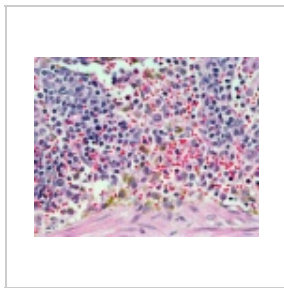
Spleen



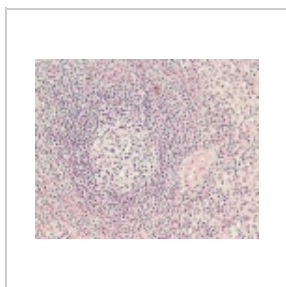
Reticular Fibre detail



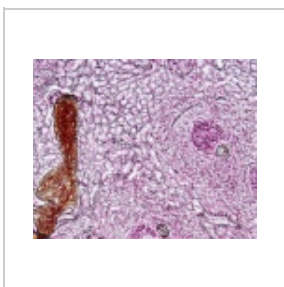
unlabeled red and white pulp



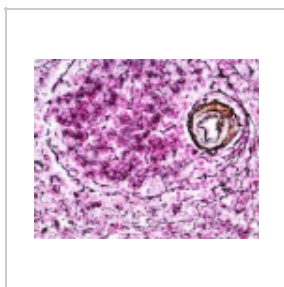
unlabeled red pulp and macrophages



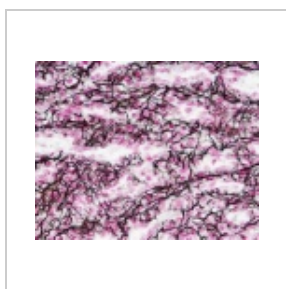
unlabeled white pulp germinal centre



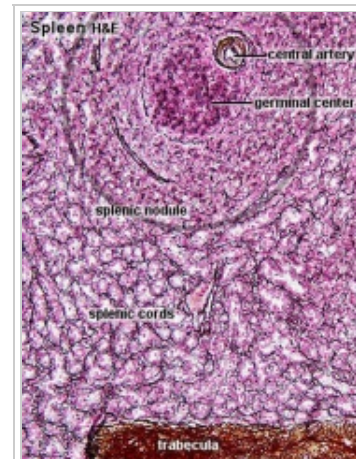
unlabeled reticular fibre



unlabeled white pulp reticular



unlabeled red pulp reticular



White pulp -periarterial lymphoid sheath (PALS)

**Spleen Development:** Overview Red and White Pulp | Overview Red and White Pulp | Cords and Sinuses | Reticular Fibre overview | Reticular Fibre detail | unlabeled red and white pulp | unlabeled red pulp and macrophages | unlabeled white pulp germinal centre | unlabeled reticular fibre | unlabeled white pulp reticular | unlabeled red pulp reticular | Structure cartoon | Cartoon and stain | Category:Spleen | Histology Stains | Immune System Development

## Additional Information

*The following is not part of the lecture and is for reference purposes only.*



**SH Practical - Lymphatic Structure and Organs** associated practical support page. Note that virtual slides will be used in the associated practical class and this linked page is provided for student self-directed learning of concepts from the virtual slides.

[show] **Additional Images**

[show] **Janeway's Immunobiology**

[show] **Blood Cells**

[show] **Anatomy of the Human Body (1918) - Lymphatics**

Textbook Links: MBoC Figure 24-6. The development and activation of T and B cells |

[<http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4430/> Figure 24-7. Electron micrographs of nonactivated and activated lymphocytes (<http://www.ncbi.nlm.nih.gov/books/NBK26921/figure/A4429/>) | Immunobiology - Figure 1.9. Organization of the lymphoid tissues of the spleen (<http://www.ncbi.nlm.nih.gov/books/NBK27092/figure/A48/>)

## Terms

A few key terms associated with the Lymphoid system.

- **adenoid** - (Greek " +*-oeides* = in form of) in the form of a gland, glandular; the pharyngeal tonsil.
- **Afferent lymph** - vessel carrying lymph towards a node.
- **Antibody mediated immunity** - the immune function of plasma cells (active B lymphocytes) secreting antibody which binds antigen.
- **antibodies** - mammals have five classes (IgA, IgD, IgE, IgG, and IgM)
- **antigen** - any substance that is recognised by the immune system and stimulates antibody production.
- **appendix** - is a gut-associated lymphoid tissue located at the beginning of the colon. The anatomy is as a finger-like structure that arises from the cecum. The length (2.5-13 cm) is longer in both infants and children and also has more abundant lymphatic tissue in early life. The wall structure is similar to the small intestine (though with no villi), nor plicae circularis. Lymph nodules surround the lumen of the gastrointestinal tract and extend from the mucosa into the submucosa.
- **B lymphocyte (cell)** - historically named after a structure called the **bursa** of Fabricius in birds, a source of antibody-producing lymphocytes. These cells develop in the bone marrow. (More? Electron micrographs of nonactivate and activated lymphocytes)
- **BALT** - Bronchus Associated Lymphoid Tissue
- **band cell** - (band neutrophil or stab cell) seen in bone marrow smear, a cell undergoing granulopoiesis, derived from a metamyelocyte, and leading to a mature granulocyte. Also occasionally seen in circulating blood.
- **cecum** - (caecum, Latin, *caecus* = "blind") within the gastrointestinal tract a pouch that connects the ileum with the ascending colon of the large intestine.
- **cell** - has a specific cell biology definition, but is often used instead of "lymphocyte" when describing B and T cells.
- **Cell-mediated immunity** - the immune function of T lymphocytes.
- **CD** - (cluster of differentiation) identifies immunological surface markers on cells.
- **CD4+** - (T helper cells) refers to T lymphocytes that express CD4 (glycoprotein of the immunoglobulin superfamily) on their surface.
- **CD8+** - (cytotoxic T cells) refers to T lymphocytes that express CD8 (glycoprotein of the immunoglobulin superfamily) on their surface.
- **"clockface"** - a term used to describe the appearance of plasma cell nuclei due to the clumping of the chromatin at the nucleus periphery. More clearly seen in tissue plasma cells that the bone marrow smear, where they are sometimes confused with the basophilic erythroblasts.
- **cords of Billroth** - spleen cellular columns located in red pulp. surrounded by splenic sinusoids. Cords contain reticular cells, macrophages, lymphocytes, plasma cells and erythrocytes.
- **cortex** - outer layer, used in association with medulla (inner layer or core) a general description that can be applied to describing an organ with a layered structure.
- **dendritic cells** - (DCs) immune cells that function to process antigen and present it on their surface to other immune cells.
- **Effector cells** - the immune functioning (active) B and T lymphocytes.
- **Efferent lymph** - vessel carrying lymph away from a node.
- **GALT** - Gut Associated Lymphatic Tissue
- **haemopoiesis** (hemopoiesis) formation of blood cells.

- **Hassall's corpuscle** - thymic corpuscle.
- **IgA** - the main class of antibody in secretions (saliva, tears, milk, and respiratory and intestinal secretions).
- **IgD** - the immunoglobulin B cell starts to produce as a cell-surface molecule after leaving the bone marrow.
- **IgE** - bind Fc receptors (surface of mast cells in tissues and basophils in the blood).
- **IgG** - the major class of immunoglobulin in the blood.
- **IgM** - the first class of antibody made by a developing B cell, which may switch to making other classes of antibody.
- **immunodeficiency** - when one or more components of the immune system is defective. (More? Immunobiology - immunodeficiency (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&db=books&rid=imm.section.1494>) )
- **involution** - in the Thymus refers to the replacement, mainly in the cortex, of cells by adipose tissue. (More? PubMed- thymus involution (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed&cmd=Search&term=thymus+involution&doptcmdl=Books>) ) | Cancer Medicine - Thymomas and Thymic Tumors (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Search&db=books&rid=cmed6.section.23856#23857>) )
- **lamina propria** - a layer of loose connective tissue found underneath the epithelium of mucosa.
- **Leukocyte**- (Greek, leuko= clear, white) white blood cell.
- **lingual**- related to the tongue.
- **lymph node** - connective tissue encapsulated lymphoid organ (1mm - 2cm in size), positioned in the pathway of lymph vessels.
- **M cell** - (microfold cell) found in the follicle-associated epithelium of the Peyer's patch. Function to transport gut lumen organisms and particles to immune cells across the epithelial barrier.
- **macrophage** - a large highly motile white blood cell which engulfs foreign material (bacteria etc) and both degenerating cells and cell fragments. Found in many different tissues and locations. (More? Immunobiology - Defects in phagocytic cells are associated with persistence of bacterial infection (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=imm.figgrp.1508>) )
- **MALT** - Mucosa Associated Lymphoid Tissue
- **medulla** - inner layer or core, used in association with cortex (outer layer) a general description that can be applied to describing an organ with a layered structure.
- **Memory Cell** - effector T cell (lymphocyte)
- **NK cell** - (Natural killer cell, large granular lymphocytes) are a type of cytotoxic lymphocyte, responding rapidly to virally infected and tumor cells.
- **normoblast** - seen in bone marrow smear, a developing erythroblast (red blood cell) that still retains a nucleus.
- **parenchyma** - (Greek = *enkeim* "to pour in") cells forming the functional cells of an organ or tissue. These cells carry out the function of the organ at a cellular level, and are not the structural cells, connective tissue, extracellular matrix (stromal).
- **periarterial lymphoid sheath** - (PALS) in the spleen the white pulp that surrounds the central arteries. (T-lymphocytes, macrophages and plasma cells)
- **Plasma Cell** - active B cell (lymphocyte) which is secreting antibody. Located in either bone marrow or peripheral lymphoid tissues, these cells have an increased cytoplasmic volume (due to increased rough endoplasmic reticulum) in comparison to the inactive (non-secreting) lymphocyte.
- **sentinel lymph node** - the hypothetical first lymph node or group of nodes reached by metastasizing cancer cells from a primary tumour.
- **splenic sinusoids** - enlarged spleen capillary spaces located in red pulp and surrounding cords of Billroth.
- **stroma** - (Greek = "a cover, table-cloth, bedding") tissue forming the framework/support of an organ or tissue. That is the structural cells which form connective tissue and secrete extracellular matrix, rather than the functional cells (parenchymal). All organs can therefore be functionally divided into these 2 components, stromal/parenchymal.
- **Subcapsular sinus** (=marginal sinus) space lying under the connective tissue capsule which receives lymph from afferent lymphatic vessels.
- **Thymic corpuscle** (=Hassall's corpuscle) a mass of concentric epithelioreticular cells found in the thymus. The number present and size tend to increase with thymus age. (see classical description of Hammar, J. A. 1903 Zur Histogenese und Involution der Thymusdrüse. Anat. Anz., 27: 1909 Fünfzig Jahre Thymusforschung. Ergebn. Anat. Entwickl.-gesch. 19: 1-274.)
- **thymic epitheliocytes** - reticular cells located in the thymus cortex that ensheath the cortical capillaries, creating and maintain the microenvironment necessary for the development of T-lymphocytes in the cortex.
- **T lymphocyte (cell)** - named after thymus, where they develop, the active cell is responsible for cell-mediated immunity. (More? Electron micrographs of nonactivated and activated lymphocytes (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.4430>) )
- **thymus** - thymus has a key role in the development of an effective immune system as well as an endocrine function. Immune system T cells are essential for responses against infections and research relates to the postnatal development

of T cells within the thymus. Thymus Development

- **tonsils** - mucosal-associated lymphoid tissues consists of: 2 palatine tonsils (tonsilla palatina), adenoids (tonsilla pharyngealis) and 1 lingual tonsil (tonsilla lingualis)
- **tonsillar ring** - ring of lymphoid tissue (tonsils) around where the mouth and nasal cavity meet the throat.
- **vermiform appendix** - see appendix, anatomical region containing gut-associated lymphoid tissue located within the gastrointestinal tract at the beginning of the colon. The anatomy is as a finger-like structure that arises from the cecum. The length (2.5-13 cm) is longer in both infants and children and also has more abundant lymphatic tissue in early life. The wall structure is similar to the small intestine (though with no villi), nor plicae circularis. Lymph nodules surround the lumen of the gastrointestinal tract and extend from the mucosa into the submucosa.

## Glossary Links

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