Cells and Organs of the Immune System

Jeffrey K. Actor, Ph.D.
Pathology and Laboratory Medicine
The University of Texas-Houston Medical School
Lecture Objectives:

- Identify cell types involved in the innate and adaptive immune response.
- Understand structure and function of primary and secondary lymphoid organs.
• Immune System cells are derived from **pluripotent hematopoietic stem cells** in the bone marrow.
Maturation of Granular Leukocytes

- Eosinophils
- Neutrophils
- Basophils

Myeloblast, Promyelocyte, Myelocyte, Metamyelocyte, Stab Cell
Nomenclature of Immune Cells

Location, Location, Location

Leukocytes

Granulocytes

“Polymorphs”

Phagocyte

Mononuclear Cells

Lymphocytes

Phagocyte

Blood

Neutrophil  Eosinophil  Basophil  Monocyte  T cell  B cell  NK cell  Platelets  RBC

Tissue

Tissue eosinophil  Mast cell  Macrophage (histiocyte)  T lymphocyte  Plasma cell  Natural killer cell  Dendritic cell
Leukocytes

White blood cells that provide either innate or specific adaptive immunity.

**Myeloid Cells**: First line of defense, non-specific innate immunity
- Neutrophils
- Eosinophils
- Basophils/Mast cells
- Monocytes/Macrophages/Dendritic Cells

**Lymphoid Cells**: non-specific immunity
- Natural Killer Cells

**Lymphoid Cells**: Humoral and Cell Mediated specific immunity
- B Lymphocytes
- T Lymphocytes (Helper and Cytolytic)
# Leukocytes: Myeloid

## Myeloid Leukocytes and Their Properties

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Morphology</th>
<th>Circulating Differential Count*</th>
<th>Effector Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil</td>
<td>PMN granulocyte</td>
<td>2-7.5x10⁹/L</td>
<td>Phagocytosis and digestion of microbes</td>
</tr>
<tr>
<td></td>
<td>PMN</td>
<td></td>
<td>Immediate hypersensitivity (allergic) reactions; defense against helminths</td>
</tr>
<tr>
<td>Eosinophil</td>
<td>PMN granulocyte</td>
<td>0.04-0.44x10⁹/L</td>
<td>Immediate hypersensitivity (allergic) reactions</td>
</tr>
<tr>
<td>Basophil</td>
<td>PMN granulocyte</td>
<td>0-0.1x10⁹/L</td>
<td>Immediate hypersensitivity (allergic) reactions</td>
</tr>
<tr>
<td>Mast Cell</td>
<td>PMN granulocyte</td>
<td>Tissue Specific</td>
<td>Circulating macrophage precursor</td>
</tr>
<tr>
<td>Monocytes</td>
<td>monocytic</td>
<td>0.2-0.8x10⁹/L</td>
<td>Phagocytosis and digestion of microbes; antigen presentation to T cells</td>
</tr>
<tr>
<td>Macrophage</td>
<td>monocytic</td>
<td>Tissue Specific</td>
<td>Antigen presentation to naïve T cells; initiation of adaptive responses</td>
</tr>
<tr>
<td>Dendritic Cell</td>
<td>monocytic</td>
<td>Tissue Specific</td>
<td></td>
</tr>
</tbody>
</table>

* Normal range for 95% of population, +/- 2 standard deviations
Neutrophils

Neutrophils are produced in the bone marrow from myeloblast-type stem cells, and are often called polymorphonuclear cells (PMN's). The neutrophil's main role is in inflammation. They are the first cells to arrive at the site of inflammation by leaving the blood, through the endothelium into the tissue (extravasation).

Neutrophils are attracted into the tissue by chemotactic factors that include complement proteins, clotting proteins (stimulated by tissue damage) and T cell derived cytokines.
Neutrophils

- In the tissues, **neutrophils are active phagocytes**. They are most effective at killing ingested microorganisms and can do this by oxygen dependent or independent pathways.
- Neutrophils produce **myeloperoxidases** to assist oxidated antimicrobial effects.
- They produce **lactoferrin and lysozyme** as direct antimicrobial agents.
- They produce **leukotrienes and prostaglandins**, products of the lipoxygenase and cyclo-oxygenase pathways, that mediate vascular functions.

Deficiencies in pathways increase susceptibility to infections.
Eosinophil

- Eosinophils are granulocytes that stain intensely with 'eosin'. They have a bilobed nucleus and contain many basic crystal granules in their cytoplasm. The granules are mediators that are toxic to many organisms and also to tissues, as seen in asthma. **Eosinophils are motile, phagocytic under certain conditions, and are particularly active in parasitic infection (organisms too big to engulf).**
Basophil

- Basophils are found in low numbers in the blood. They are involved in Type I hypersensitivity responses. They have high affinity Fc receptors for IgE on their surface. **Cross-linking of the IgE causes the basophils to release pharmacologically active mediators** (histamine, prostaglandins, leukotrienes). Basophils, act like mast cells, except that they reside in blood instead of tissue.
Mast Cells

- Mast cells are formed in the tissue from undifferentiated bone marrow precursor cells released into the blood. They have a similar **importance in allergic reactions** to those of basophils, and are **only found in tissues**. They contain granules with preformed mediators to be released after stimulation (histamine, prostaglandins and leukotrienes).

- Stimulation of mast cells occurs by the **anaphylatoxins** (C3a and C5a) of the **complement system** or by **cross-linking of surface IgE**.
Cells of the Reticuloendothelial System

The “phagocytic system” of the body, including fixed macrophages of tissues. ...rather old fashioned term...

Cells of the RES provide natural immunity against microorganisms.

- **Phagocytosis** and intracellular killing
- **Cell Recruitment** via cytokine production (molecular mediators)
- **Presentation** of peptide antigens to lymphocytes

Cells of the RES include:

- circulating **monocytes**
- resident **macrophages** in the liver, spleen, lymph nodes, thymus, submucosal tissues of the respiratory and alimentary tracts, bone marrow, and connective tissues
- macrophage-like cells including **dendritic cells** in lymph nodes, **Langerhans cells** in skin, and **glial cells** in the central nervous system.
Monocytes/Macrophages

- Monocytes circulate in the blood after leaving the bone marrow. Monocytes usually circulate in the blood for only a day or so before they enter the tissue to mature into macrophages.

- Monocytes and Macrophages are involved in phagocytosis and intracellular killing of microorganisms.
  
  Generation of toxic metabolites through respiratory burst.
  Production of nitric oxide, hydrogen peroxide, superoxide anion.

- Monocytes/Macrophages are antigen processing and presenting cells. Macrophages present antigens (as APC's) to T cells.
  Degrative enzymes in lysosomal granules.
Macrophages

- When monocytes enter the tissues and become macrophages they enlarge and increase production of intracellular lysozyme allowing greater phagocytosis. In tissue, macrophages live for years and are motile.
- Activation of these cells occurs by phagocytosis of antigens, or in response to T cell derived cytokines.
- Activated macrophages recognize and remove unwanted particulate matter including products of inflammation and invading organisms, antigens and toxins.
Macrophages

- After activation, these cells secrete cytokines, chemokines, lysosomes and other factors to upregulate immune response. In chronic inflammation, macrophage scavengers can become “giant cells” or “foamy macrophages”.
Dendritic Cells

• Dendritic cells are specialized phagocytic cells.
• They are found in most tissues of the body. They are abundant at interfaces between the external and internal environments (skin, lining of the gastrointestinal tract), where they are ideally placed to encounter invading pathogens.
• They are actively motile and continuously sample their surroundings by endocytic processes.

• Dendritic cells are very efficient at activation of T cells to respond to a particular antigen, and can dictate T cell development to control future responses to that antigen.
Lymphoid Leukocytes

<table>
<thead>
<tr>
<th>Lymphoid Leukocytes and Their Properties</th>
<th>Total Lymphocytes</th>
<th>Effector Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>B Cell</td>
<td>monocytic</td>
<td>Adaptive</td>
</tr>
<tr>
<td></td>
<td>1.3-3.5x10^9/L</td>
<td>Humoral immunity</td>
</tr>
<tr>
<td>Plasma Cell</td>
<td>monocytic</td>
<td>Adaptive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Terminally differentiated, antibody secreting B cell</td>
</tr>
<tr>
<td>T Cell</td>
<td>monocytic</td>
<td>Adaptive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cell-mediated immunity</td>
</tr>
<tr>
<td>Natural Killer Cell</td>
<td>monocytic</td>
<td>Innate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Innate response to microbial or infection</td>
</tr>
</tbody>
</table>
Natural Killer Cells

• NK cells are functionally cytotoxic representing an innate population that kill viral infected or tumor target cells.

• The killing by NK cells is nonspecific in that they do not need to recognize foreign antigens presented on the target cell. NK cells do not have a specific cell receptor. The recognition of targets works through a Killer Inhibitory Receptor, KIR, which is lacking on infected and tumor targets.

• NK cell kill targets by releasing perforin which damages the target cell membrane leading to death. NK cells also cause death by inducing apoptosis in the target.

• Do not confuse NK cells with NK T cells.
Specificity and Antigenic Recognition

- B and T cells.

Splenic Germinal center indicating active B-lymphocytes. Helper T-cells mingle with the plasma cells at the rim of the nodule. Note the periarterial sheath immediately surrounding the central arteriole.
B Lymphocytes

• **B cells produce antibodies.** Antibodies have specificity for antigens. Activated B cells are called **Plasma cells.**

• **B cells develop from stem cells in the bone marrow.** At the youngest stages in the bone marrow, these cells develop antigen-specific surface antibody. The naive B cells enter the circulation and travel around the blood and lymphatics through tissue and lymphoid organs.

• **Upon activation, a B cell can switch to produce a different class of antibody, with the same antigen specificity.**
Activation of B Lymphocytes

- Activation of B cells into antibody secreting cells is antigen-dependent.
- Specific antigen binds to surface Ig molecules which triggers differentiation into plasma cells.
- B cells are the most efficient presenting cell in the body.
- Interaction with T cell secreted factors triggers isotype (class) switching.
Terminology: Cluster Of Differentiation (CD)

• Cell surface molecules are identifiable by monoclonal antibodies (unique binding antibodies). In humans, these molecules have been given number designations. **The acronym CD describes the cluster of antigens with which the antibody reacts**; the number describes the order in which it was discovered.

• **As of March, 2010, the list of determinants was to CD350, with another 13 listed as “provisional”**.

  • [http://hcdm.org/MoleculeInformation/tabid/54/Default.aspx](http://hcdm.org/MoleculeInformation/tabid/54/Default.aspx)

**CD-specific monoclonal antibodies have been useful for:**

• Determining the functions of CD proteins.

• Identifying the distribution of CD proteins in different cell populations in normal individuals.
Surface Molecules of B Lymphocytes

- Ig H+L, B cell receptor for antigen.
- Ig α/β, signal transduction molecules.
- HLA-D, class II restricted major histocompatibility marker.
- CR21 and CD35, complement receptors.
- CD19, B-cell co-receptor subunit.
- CD20, CD5, signal transduction molecules.
- CD40, co-stimulatory.
- CD5, co-stimulator-activator.
- CD32, FcγRII.
- CD45, leukocyte common antigen.

Receptors (specificity)
Signal Transducers
Co-stimulators/Activators
T Lymphocytes

- T lymphocytes regulate immune responses and are integral in cell mediated immunity.
- Critical in B cell-antibody production.
- Mature T cells display either CD4 or CD8.
More on T Lymphocytes

• T lymphocytes develop in the thymus.
• The cells with a CD4 marker are called helper T cells (Th cells). The CD8 positive cells that develop are cytotoxic T cells (Tc cells).
• Each T cell has a TCR: a transmembrane heterodimer composed of two polypeptide chains. The TCR specifically recognizes antigen.
Surface Molecules of T Lymphocytes

- TCR, T cell receptor.
- CD3, TCR signaling complex.
- Thy-1, mouse T cell marker.
- CD45RO, Leukocyte common antigen for memory T cells.
- CD45RA, Leukocyte common antigen for naive T cells.
- CD2, LFA-3 adhesion molecule.
- CD28, co-stimulatory molecule that binds B7.
- CD5, co-stimulatory molecule.
- CD7, signal transduction.

**Receptors (specificity)**

**Adhesion**

**Signal Transducers**

**Co-stimulators/Activators**
T Helper Cells

- Different phenotypic populations exist.
  - $T_{H1}$, $T_{H2}$, $T_{H3}$, $T_{H17}$, Treg
- All express the CD4 molecule.
- Aid effector T lymphocytes in cell-mediated immunity.
- Aid antigen-stimulated subsets of B cells to proliferate and differentiate toward antibody-producing cells.
- Regulatory role for tolerization events.
T Helper Cells: Functional Subclasses

Cell-Mediated Immunity
- IFNγ
- LT
- Th1
  - T-bet
  - IL-4
  - IL-12
  - Thp
  - GATA-3
  - Th2
    - IL-4
    - IL-5
    - IL-13
    - IL-25/IL-17E
  - TGFβ
  - IL-10
  - Treg

Inflammation & Autoimmunity
- IL-17A
- IL-17F
- IL-6
- TNFα
- IL-22
- Th17
  - RORγt
  - IL-4
  - IFNγ
  - Thp
  - TGFβ
  - IL-6

Humoral Immunity
- Suppression
T Cytotoxic Cells

- T cytotoxic cells (CTLs) are cytotoxic against tumor cells and host cells infected with intracellular pathogens.
- These cells express CD8.
T Suppressors/Regulatory Cells

- T suppressor cells suppress the T and B cell responses.
- Commonly thought that these cells were a subpopulation that express CD8 molecules.

- Treg:
  - More recent data suggests that a population of T helper cells (CD4+CD25+), characterized by TGF-β secretion, also serve as regulators of response. These cells express the regulatory molecule Foxp3.
Natural Killer T Cells

- Natural killer T cells (NKT) are a heterogeneous group of T cells that share properties of both T cells and natural killer (NK) cells.
- These cells recognize an antigen presenting molecule (CD1d) that binds self- and foreign lipids and glycolipids.
- They constitute only 0.2% of all peripheral blood T cells that coexpressing a heavily biased, semi-invariant T cell receptor.
- Natural killer T (NKT) cells should not be confused with natural killer (NK) cells.
Antigen Presenting Cells

- APCs are found primarily in the skin, lymph nodes, spleen and thymus.

- Their main role is present antigens to antigen sensitive lymphocytes.

- APCs are classified according to their ability to phagocytose antigens, location in the body, and expression of MHC related molecules.
# Antigen Presenting Cells

<table>
<thead>
<tr>
<th>Phagocytes (monocyte/macrophage)</th>
<th>Phagocytosis</th>
<th>type</th>
<th>location</th>
<th>Class II expression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>monocytes</td>
<td>blood</td>
<td>(-) -&gt; +++ inducible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>macrophages</td>
<td>tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>marginal zone macrophages</td>
<td>Spleen/lymph node</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kupffer cells</td>
<td>liver</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>microglia</td>
<td>brain</td>
<td></td>
</tr>
<tr>
<td>non-phagocytic constitutive antigen presenting cells</td>
<td>-</td>
<td>Langerhans' cells</td>
<td>skin</td>
<td>++ constitutive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interdigitating dendritic cells</td>
<td>lymphoid tissue</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Follicular dendritic cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lymphocytes</td>
<td>-</td>
<td>B cells and T cells</td>
<td>Lymphoid tissue, site of immune reaction</td>
<td>(-) -&gt; +++ inducible</td>
</tr>
<tr>
<td>facultative antigen presenting cells</td>
<td>+</td>
<td>astrocytes</td>
<td>brain</td>
<td>inducible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>follicular cells</td>
<td>thyroid</td>
<td>inducible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>endothelium</td>
<td>vascular and lymphoid tissue</td>
<td>(-) -&gt; +++ inducible</td>
</tr>
<tr>
<td></td>
<td></td>
<td>fibroblasts</td>
<td>connective tissue</td>
<td>(-) -&gt; +++ inducible</td>
</tr>
</tbody>
</table>
Critical Molecules in Antigen Presentation

- **LFA-3/LFA-1**, adhesion molecules.
- **CD28**, co-stimulatory molecule that bind **B7-1** or **B7-2**.
- **ICAM**, intracellular adhesion molecule 1 (needed for migration).
- **MHC**, Major Histocompatibility Complex

**Receptors** (specificity)

**Adhesion**

**Signal Transducers**

**Co-stimulators/Activators**
Primary/Secondary Lymphoid Tissues

- The immune system involves multiple organs, tissues, cell types, and proteins.

- Primary and Secondary Lymphoid Tissues.
Primary/Secondary Lymphoid Tissues

Primary:
- Foetal Liver
- Adult Bone Marrow
- Thymus Gland

Secondary:
- Spleen
- Lymph Nodes
- Tonsils
- Appendix
- Peyer’s patches
- Aggregates of cells in lamina propria (GALT, BALT, MALT)
- Bone Marrow

- Bursa of Fabricius (near cloaca)
Primary: Thymus
Primary: Thymus

- Thymocytes are educated to become T lymphocytes.
- Expression of specific receptors.
- T cells learn to recognize self as self.
Secondary: The Spleen

- The spleen is a filter for blood.

- **Red pulp = splenic cord and sinuses (RBCs).**
  - Cord of Billroth

- **White pulp = lymphoid tissue.**
Splenic Circulation

- Splenic artery enters at hilum and branch into trabecular arteries.
- Trabecular arteries branch repeatedly and eventually enter splenic pulp as central arteries.
- Central arteries are sheathed by T lymphocytes.
  - Periarterial Lymphatic Sheath (PALS)
  - PALS and follicles form the white pulp
- Central arteries form peniciller aterioles that empty into capillaries.
- Capillaries empty into sinusoid, which are drained into trabecular veins.
- Emptying of blood completed by exiting through splenic vein.
Splenic Circulation

- Splenic circulation diagram
- Central artery
- Marginal zone sinuses
- Periarterial lymphatic sheath (T cells)
- Closed circulation
- Trabecula
- Sinusoid
- Penicillar arteriole
- Red pulp
- Trabecular vein
- Pulp vein
- Peripheral white pulp (B cells)
- Trabecular artery
- Open circulation
• Red pulp contains RBCs, splenic cords and splenic sinuses.
• Splenic cords (cords of Billroth) are a network of reticular fibers.
• Splenic sinuses are lined by endothelial cells
  • Not tightly bound together
  • Allows macrophage movement to filter damaged cells and foreign particulates
The white pulp contains the lymphoid tissue, arranged around a central arteriole as a periarteriolar lymphoid sheath (PALS).

- PALS composed of a Germinal Center surrounded by a Mantle and Marginal Zones.

- Central Artery
- Periarterial Lymphatic Sheath
- Follicle/Germinal Center
- Mantle Zone (B cells)
- Marginal Zone (B and T cells)
• Follicle/Germinal Center
• Periarterial Lymphatic Sheath
• Central Artery
• Mantle Zone (B cells)
• Marginal Zone (B and T cells)
• A network of reticular fibers also supports the parenchyma of the white pulp.
Lymphatics – On the Road to the Lymph Node

• Lymph nodes receive lymph via terminal lymphatics
  – blind-ended, endothelium-lined tubes
  – present in most tissues in similar numbers to capillaries.

• In acute inflammation, the lymphatic channels become dilated and drain away fluid (inflammatory exudate)
  – Limits the extent of tissue edema.

• Antigens are also carried to the regional lymph nodes
  – Processing by APCs
  – Recognition by lymphocytes (immunologic surveillance).
Lymphatics and Circulation

- Vessels capture extracellular fluid in spaces between tissues.
- Terminal Lymphatics are blind-ended, endothelium-lined tubes
  - Present in similar numbers to capillaries.
  - Pass through collecting lymph nodes or lymphoid organs
  - Contents are sampled by immune system cells
  - Vessels empty into thoracic duct to rejoin venous system
Lymphatics to Lymph Nodes

- Lymph drains into collecting lymph nodes via afferent lymphatic vessels.
- Lymphatics drain in one direction, using specialized valves. Fluid leaves lymph nodes via efferent lymphatics.
- Lymphatic vessels empty into the thoracic duct which joins the venous system at the junction of the internal jugular and subclavian veins.
Lymph Nodes

- Ovoid- to kidney- shaped organs that filter lymph.
- Has a dense irregular collagenous connective tissue capsule.
- Made up of a network of reticular tissue that acts as a framework for housing lymphocytes and APCs.
- Has medula and cortex, separated by a paracortex.
Secondary: They Lymph Node
Figure 13.18. Structure (a) and photomicrograph (b) of a lymph node. X18.
Lymph Node – Cortex and Paracortex

- **Subcapsular sinus** located beneath the capsule. Lymph empties into the medullary sinuses via the cortical or paratrabecular sinuses.

- **Outer cortex** comprised of diffuse lymphoid tissue
  - macrophages, T-lymphocytes, plasma cells, and reticular cells
  - lymphoid nodules (primary follicles) composed of B-lymphocytes
  - germinal centers (2° follicles) composed of activated B, T, and macs

- **The inner (or deep) cortex (paracortex)** is a continuation of the outer cortex.
  - contains diffusely arranged T-lymphocytes
  - lymphoid nodules are not normally present.
Lymph Node Follicles

- Connective tissue sends trabeculae throughout the node.
- Primary follicles contain quiet B cells.
- Secondary follicles have active centers.
- Sinusoids can be seen in the medulla region.
Lymph Node Follicles

• Secondary follicles have active germinal centers, surrounded by a mantle zone.
  – Tingible body macrophages may be present with large cytoplasm
High Endothelial Venule (HEV) in Paracortex

Specialized vessels which serve as the point of entry for lymphocytes from peripheral blood into the lymph node parenchyma.
Secondary Lymphoid Tissue

Tonsils  Peyer’s Patches  Appendix

Remember: MALT, GALT, BALT (aggregates of cells in the lamina propria of musoca-, gut- bronchus).
Tonsils

• Palantine Tonsils
  – Stratified squamous nonkeratinized epithelium
  – Tonsilar crypts, germinal centers
  – Dense irregular capsule, septa present

• Lingual Tonsils
  – Stratified squamous nonkeratinized epithelium
  – Lymphatic nodules with germinal centers
  – Thin, ill-defined capsule
  – Seromucous glands open into crypt base

• Pharyngeal Tonsils (adenoids)
  – Pseudostratified ciliated columnar epithelium
  – Thin capsule, germinal centers, lack true crypts
  – Seromucous glands, ducts present
Secondary Lymphoid Tissue

MALT, GALT, BALT (aggregates of cells in the lamina propria of musoca-, gut- bronchus).

• Unencapsulated lymphoid aggregates.
• Structure of the lymphoid follicles is same as in lymph nodes.
• Mucosal B cell response usually produces IgA.
• Protects against exposure to foreign antigens that enter the respiratory or GI tract.

• Peyer’s Patch is a prime example.
  • Located in ileum
  • Each “patch has up to 200 nodules
  • Contains Microfold ("M") cells to transfer antigen across gut

We will look at some examples under the microscope.
Appendix

- A blind-ended tube connected to the cecum; a pouch-like structure of the colon.
- Located near the junction of the small intestine and the large intestine.
- May harbor and protect bacteria that are beneficial in the function of the human colon.
Accumulation of lymphoid cells can be evident during inflammatory responses.

- Infection
- Tissue Damage
- Stress
- Autoimmunity
Dermatitis
We’re almost finished.....
Q: How does the lack of spleen effect B cell function, and what are the implications towards immune responses to infective agents?
That's All Folks!
Which cell type is not an antigen presenting cell?

A. Astrocytes
B. Dendritic cells
C. Langerhans cells
D. T lymphocytes
E. B lymphocytes

Option D (T lymphocytes) is correct. Antigen Presenting Cells (APCs) are found primarily in the skin, lymph nodes, spleen and thymus. They may also be present throughout the diffuse lymphoid system. Their main role is to present antigens to antigen-sensitive lymphoid cells. Facultative antigen presenting cells are those that may be induced to present antigens, and include multiple cell types such as astrocytes in the brain, follicular cells of thyroid and fibroblasts in connective tissue. B lymphocytes are extremely good at presenting antigen, especially after recognition by its specific surface expressed immunoglobulin.
A 7-year old child involved in a car accident developed complications leading to removal of her spleen. Which statement accurately describes the physical characteristics of the spleen?

A. The spleen is a filter for lymph
B. The red pulp contains the lymphoid tissue, arranged around a central arteriole as a periarteriolar lymphoid sheath.
C. Eosinophils cells are found in marginal centers where they present antigen to lymphocytes
D. The periarteriolar lymphoid sheath is composed of a germinal center surrounded by a mantle and marginal zones
E. Hassels corpuscles are located in the medulla

Option D (The periarteriolar lymphoid sheath is composed of a germinal center surrounded by a mantle and marginal zones) is correct. The spleen is a filter for blood that is histologically comprised of red and while pulp. The red pulp is composed of vascular sinusoids containing large numbers of macrophages, and is actively involved in the removal of dying and dead erythrocytes, as well as in the removal of infectious agents. The white pulp contains the lymphoid tissue, arranged around a central arteriole as a periarteriolar lymphoid sheath (PALS). The PALS is composed of T and B cell areas, and follicles containing germinal centers. The germinal centers are where B cells are stimulated to become plasma cells which produce and secrete antibodies.
The appropriate medical care and clinical course of action associated with loss of the spleen in this child includes all except which?

A. Updating immunizations
B. Aggressive antibiotic therapy
C. Vigilant monitoring for bacterial agents
D. Parental education

All answers are correct. Loss of a spleen would be more detrimental to a child than an adult, primarily due to a pre-established immune response (B cells and their ability to produce specific antibodies) to bacterial antigens in the adult. In the adult, pre-existing memory B cells surviving in other tissues (e.g. lymph nodes, GALT, MALT, BALT) may be activated, although the overall response in these adults is typically diminished. In the child, there is less likely to be a preexisting memory population. The lack of splenic lymphoid tissue to process antigen greatly decreases the opportunity for B cell activation and further production of plasma cells and memory B cells. Appropriate medical care involves antibiotic prophylaxis and updating immunizations. Antibiotic prophylaxis is initiated immediately upon the diagnosis because patients are considered immuno-compromised. Patients should receive standard immunizations, with emphasis given to receive conjugated *H. influenzae* type b and pneumococcal vaccines. Asplenic patients are at an increased risk of sepsis, especially from gram-positive organisms.
T Helper Cells
Functional Subclasses

- **T helper1 (Th1):**
  - Aid in cellular immunity.
  - Characterized by secretion of IL-2 and IFN-γ.

- **T helper2 (Th2):**
  - Aid B cells to produce certain classes of antibody.
  - Characterized by secretion of IL-4, IL-6, and IL-10.
T Helper Cells
Other T Functional Subclasses

• T helper3 (Th3):
  - Involved in oral tolerance.
  - Provide help for IgA production.
  - Suppressive/regulatory properties for Th1 and Th2
  - Characterized by secretion of IL-4 and TGF-β.

• T helper17 (Th17):
  - Newly identified population.
  - Effector cells for autoimmune disease progression.
  - Characterized by secretion of IL-17.
Cytotoxic T Lymphocytes

CTLs are able to kill target cells directly by inducing apoptosis.

- Preformed **perforins** are released at the target cell surface which generate transmembrane pores in the target cell, through which **granzymes** gain entry to the cytosol and induce the apoptotic series of events.

- Apoptotic signaling via membrane-bound molecules can occur via **Fas** on the target cell surface and **Fas ligand** on the CTL surface.