SLIDE 1 During this week’s presentation, we will introduce the cells of the immune system. These white blood cells are extremely important to the initial and adaptive defense against pathogens. Many of these cells assist the innate immune response, as they do not have specificity for antigens, but they function to protect the body in case an intruder is spotted. These innate cells (for example, macrophages and dendritic cells) are extremely important as they often serve to present antigens to their adaptive cell counterparts to trigger a response. Adaptive cells (B and T lymphocytes) then specifically recognize pathogens, and can mount a strong, long-lasting response against them that is both antibody and cell-mediated.

SLIDE 2 Objectives of Cells of the Immune System. These objectives will be tested in both the unit activities and quiz, so especially focus on the topics mentioned on this slide as you move through the presentation.

SLIDE 3 The total blood volume for an average person is ~5.5 liters! Blood tests are commonly used to diagnose disease, and cell markers can even be used to identify tumors. The complete blood count (CBC) is a routine test that is used to determine the counts of various blood cell types. Increased white blood cells often indicate an infection, but a low count may indicate that something (HIV) is interfering with the bone marrow’s ability to create WBCs.
SLIDE 4 The cells of the immune system include the variety listed on this slide. They are differentiated upon the basis of morphology (or cell shape) and the CD System. CD means cluster designation and refers to groups of monoclonal antibodies that bind specifically to a particular molecule. In the laboratory, these groups of monoclonal antibodies were used to distinguish different cell subsets.

SLIDE 5 There are four major cell lineages that compose the cells in the blood stream. The lymphoid cell lineage is responsible for acquired immunity. Only T and B lymphocytes can specifically recognize antigen.

SLIDE 6 This slide shows the development of the different cell lineages in the blood. This process starts with pluripotent stem cells. From these stem cells, the myeloid and lymphoid progenitors develop. The myeloid progenitor eventually develops into the erythrocytes (or red blood cells), the megakaryocytes (or platelets which are megakaryocyte fragments), and the granulocytes and mononuclear cells. The lymphoid progenitor develops into T cells, B cells, and natural killer (NK) cells.
Slide 7

**Lymphoid Cell Lineage**

- T lymphocytes
- B lymphocytes
- Natural Killer (NK)
- Dendritic

SLIDE 7 Four important cell types in the immune system include T lymphocytes, B lymphocytes, Natural Killer (NK) cells, and dendritic cells. Although B and T cells can specifically recognize antigen, NK cells can not do this activity. Dendritic cells present antigen to other immune cells and are found in the different lymphoid organs.

Slide 8

- B cells
  - Produce abs to neutralize or remove microbe
- T cells
  - Cell-mediated effects to kill (CTLs) or activate (helper) accessories to remove antigen
- Natural Killer
  - Non-adaptive killing of infected cells in body

SLIDE 8 This slide shows 3 of the lymphoid cell types, including B lymphocytes, T lymphocytes, and Natural Killer cells. Note that only B cells & T cells have specific antigen recognition! Natural killer cells are part of the innate immune response, and do not have specificity for antigen. All of these cells have important effector functions to remove or neutralize microbial antigens. B cells produce antibodies which bind to the microbe or antigen and stimulate phagocytosis & complement to neutralize & eat up the antigen. Helper T cells play an important role by linking antibody & cell-mediated immunity to provide a dual attack against a particular antigen. These cells can also release cytokines that stimulate inflammation, phagocytosis, and proliferation for a robust immune response. Cytolytic & natural killer cells can directly target & kill an infected cell.
Slide 9

T lymphocytes
- Found in thymus dependent areas of lymph nodes, spleen & in peripheral circulation
- Function to specifically recognize antigen via TCR
- Activated by Ag recognition

SLIDE 9 T-cells are usually 6-10 um in diameter. They have a high nucleus to cytoplasm ratio. And, they are normally found in thymus dependent areas of the lymph nodes, the spleen and the peripheral circulation where they represent largest number of circulating lymphocytes. T-cells specifically recognize antigen via the T-cell receptor (TcR) (95% BA & 5% dg). They are activated by antigen recognition in context with MHC I and MHC II on antigen-presenting cells (APCs). They can also be stimulated by mitogens such as ConA, PHA and PWM (both). Mitogens are substances that can nonspecifically activate T and B cells.

Slide 10

T lymphocytes
- Subsets of T lymphocytes
  - Three Types:
    - Cytotoxic = CD8
    - Helper = CD4 (Th1 & Th2)
    - Suppressor
  - Regulators of the immune response
  - Cell mediated immunity, cytotoxicity
  - Assist humoral immunity as well
  - Help B cells make Ab response
  - Mitogens: ConA, PHA & PWM (both)

SLIDE 10 T-cells are responsible for cell mediated immunity and cytotoxicity (or cell killing). In addition, they help regulate the immune response and stimulate B-cells to produce antibodies. There are three subsets of T-cells including helper-CD4 T-cells, cytotoxic-CD8 T cells, and suppressor T regulatory cells. T-helper lymphocytes are further divided into TH1 and TH2 cells.

Slide 11

B lymphocytes
- Specifically recognize antigen (with Ab molecule)
- "Bursal or bone marrow" dependent
- Transform into plasma cells which produce antibodies
- Humoral immunity

SLIDE 11 B-cells are responsible for humoral immunity. B-cells specifically recognize antigen via the surface immunoglobulins, IgM and IgD, that function as antigen receptors. Upon stimulation, B-cells transform into plasma cells which produce antibodies.
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| 12    | B Lymphocytes  
- Few in peripheral circulation  
- Mature B cells mostly reside in B cell dependent areas of spleen, LN & BM  
- Specifically recognize Ag via surface Ig (IgM & IgD)  
- Activated by Ag together with T cell "help"  
- Change into plasma cells to produce Ab (humoral response) |
| 13    | SLIDE 12 B-cells are normally found in the “Bursal or Bone marrow” dependent areas of the spleen, lymph nodes and bone marrow. Normally, there are only a few B-cells in the peripheral circulation. B-cells possess surface markers and receptors (such as MHC II, C’, Fc) which aid in their recognition of antigens and other cells. |
| 14    | SLIDE 13 Note the 3 stages of lymphocytes- naive, effector, and memory. Especially review the different characteristics and life spans of each cell stage. Also note that effector T cells migrate to peripheral tissues to fight the organism at the site of infection, whereas effector B cells produce & secrete antibodies into the lymph (the humoral response). |
|       | SLIDE 14 Natural Killer cells are lymphocyte-like and have a large granular lymphocyte (LGL) morphology. NK cells are approximately 15% circulating blood lymphocytes. They do not have TcR or Ab receptors for antigens and do not specifically recognize antigens. |
SLIDE 15 NK cells kill tumor and virally-infected cells, perform antibody-dependent cell mediated cytotoxicity (ADCC), and release interferon gamma (IFN). They recognize MHC proteins and may attack and kill abnormal cells lacking MHC proteins; and, cells that express normal MHC are protected against lysis by NK cells. In addition, NK cells help regulate hemopoiesis and immune responses by cytokine secretion. Cytokines provide communications between cells and can stimulate or inhibit cell function.

SLIDE 16 Dendritic cells are extremely important in capturing and presenting antigen to T cells and inducing the adaptive immune response. Watch the animation on this slide that shows how dendritic cells can crawl, use their long-fingerlike projections to trap antigens, and then present these antigens to other cells.

SLIDE 17 The next focus is on the myeloid cell lineage. This cell lineage produces granulocytes and mononuclear phagocytes.
**Myeloid: Granulocytes**
- PMNs
- Eosinophils
- Mast cells & Basophils
- Mononuclear Phagocytes:
  - Monocytes & Macrophages

**SLIDE 18** Polymorphonuclear cells (PMNs) are also known as granulocytes. These granulocytes are further subdivided into neutrophils, basophils, and eosinophils. Neutrophils are the “first responders” during acute inflammation. Deficiencies of neutrophils can lead to severe infections. Neutrophils are the most common leukocyte. They compose approximately 60 - 70 % of the peripheral leukocytes. They are normally short-lived. Each neutrophil has a multilobed nucleus and contains numerous granules. These granules contain antibacterial enzymes and proteins that can be used to destroy internalized antigens.

**Neutrophils**
- Also known as Polymorphonuclear (PMN) Cells
- “First responders”, acute inflammation
- Most common leukocyte in circulation
- Phagocytes that exhibit chemotaxis
- No antigen specificity
- Killing of intracellular pathogens
- Contain defensins – broad-spectrum antimicrobials & the most abundant protein type in neutrophils

**SLIDE 19** Continuing from the previous slide, polymorphonuclear cells are phagocytes and form phagolysosomes between their granules and their engulfed pathogen. Cells containing intracellular pathogens are also destroyed by this method. Polymorphonuclear cells also exhibit chemotaxis, which is defined by your book as the “directional migration of cells up a concentration gradient of a chemotatic molecule”.

**Neutrophils**
- Short-lived, 60-70% of peripheral leukocytes
- Have a multilobed nucleus
- Phagocyte deficiencies lead to severe infections
- Granules contain antibacterial enzymes & proteins; phagolysosomes

**SLIDE 20** A subtype of neutrophils is band neutrophils. Elevated levels of band neutrophils can signal an infection such as appendicitis. This slide also shows a diagram of a neutrophil. Notice the multilobed nucleus and the enzyme-containing granules.
Eosinophils

- 2-5% of WBCs in the peripheral circulation, degranulation to outside (MBP & ECP)
- Important defense against parasitic infections, degranulation onto surfaces (see pic)
- Dampen allergic & inflammatory responses (histaminase & aryl sulphatase)
- No antigen specificity

Mast Cells & Basophils

- Mast cells protect mucosal surfaces & tissues
- Basophils circulate
- Involved in allergic reactions (IgE), degranulation, no antigen specificity
- High affinity IgE receptors
- Granules contain heparin, leukotrienes, histamine & ECF-A

SLIDE 21 Eosinophils are 2 to 5% of the lymphocytes in the peripheral circulation. They are important in the defense against parasitic infections and do this by degranulating onto the surface of the parasite. They are not antigen specific. Eosinophil counts are usually elevated in many allergic states or parasitic infections.

SLIDE 22 This slide shows a diagram of an eosinophil. Notice the multilobed nucleus and the crystalloid granules which contain inflammatory mediators. Eosinophils also dampen allergic responses and the inflammatory response via histaminase and aryl sulphatase.

SLIDE 23 Mast cells and basophils are involved in allergic reactions including reactions to parasites. They are not antigen specific; however, they have high affinity IgE receptors. Alter IgE binds and crosslinks with an antigen on the cell receptor, the cell can degranulate and release heparin, leukotrienes, histamine, and ECF-A. These compounds cause the signs and symptoms of what we call allergy or atopy. Elevated levels of basophils may indicate different types of blood disease and poisonings. Usually basophils constitute 0.3 to 2% of WBCs. Mast cells protect mucosal surfaces and are found in the tissues; in contrast, basophils circulate in the blood.
SLIDE 24 This slide shows a diagram of a basophil. Notice the multilobed nucleus and the different granules.

SLIDE 25 The myeloid cells include the mononuclear phagocytes and granulocytes. All these cell types are phagocytes. As mentioned previously the granulocytes include the neutrophils, eosinophils, mast cells, and basophils. Next, the focus will be on the mononuclear phagocytes which include the monocytes and the macrophages. The mononuclear phagocytes include macrophages and monocytes. They are named according to their locations. Examples include Kupfer cells which are found in the liver and alveolar macrophages which reside in the lungs. Macrophages are fixed phagocytic cells that remove particulate antigens and kill intracellular pathogens. They are not antigen specific; however, they are antigen presenting cells and exhibit chemotaxis. Monocytes are circulating phagocytic cells that are not antigen specific. This slide shows a diagram of a macrophage. Notice its phagosomes, lysosomes, and phagolysosomes.
### Slide 26

**Macrophage**
- Extends thin pseudopodia to engulf foreign objects

SLIDE 26 Macrophages link innate and adaptive immunity through Antibody Dependent Cell-mediated Cytotoxicity. Pathogens can become coated with antibodies, which enhance opsonization by macrophages to digest & kill the invader.

### Slide 27

SLIDE 27 This slide shows a diagram of a monocyte. Notice its phagosomes and lysosomes. Monocytes normally make up 0.5 to 10% of WBCs. Elevated levels may indicate leukemias or infections.

### Slide 28

**Mononuclear Phagocytes**
- Reticuloendothelial System (with tissue endothelial cells)
- Functions: removal & killing of particular Ag (phagocytosis) & Antigen presentation to Th lymphocytes (LN, spleen, mucosa, skin)
- No Ag specificity (no specific Ag receptors)
- MHC II (APC) present on immune cells
- Receptors: Fc, sugars, C', cytokines (IFN, IL2 & TNF)
- Chemotaxis, Opsonization, Adherence

SLIDE 28 The reticuloendothelial system (or RES) is composed of all the phagocytic cells in the body that nonspecifically remove and kill particular antigens by phagocytosis. This system can be found in many areas including the lymph nodes, spleen, mucosa, and skin. Using the MHC II and other receptors (Fc, sugars, C’, cytokines (IFN, IL2, TNF), this system opsonizes pathogens and presents antigen to T helper (Th) lymphocytes.
SLIDE 29 This slide shows the numerous functions of macrophages in inflammation and immunity. Notice the variety of functions that macrophages perform in the immune system.

SLIDE 30 Platelets originate in the bone marrow, and are the smallest corpuscular components of human blood (diameter 2-4 μm). Resting platelets have a discoid shape, but upon activation they undergo a shape change to a globular form with pseudopodia (up to 5μm long). Platelets are involved in blood clotting and aggregate at sites of vascular endothelial cell damage. Approximately 30% of all the platelets in the body normally remain sequestered in the spleen. Platelets contain receptors and adhesion molecules. In addition, platelets contain granules that have serotonin and fibrinogen. Platelets and their compounds help increase capillary permeability at sites of injury and also function in complement activation and leukocyte chemoattraction.
This slide shows the normal blood cell counts. These figures may vary slightly according to gender and age; however, significant variations normally indicate a disease state.

In Summary
- Be able to differentiate between cell types
- Understand the function of each cell type
- Which cell types help the adaptive immune response vs. innate immunity?

What you need to know . . .

Self-Test Questions: Cells
- What cells are part of the innate system? (hint: not specific for antigen)
- What cells are part of the adaptive system?
- What cells are “first-responders”?
- What cells are professional antigen presenting cells?
- What is the function of each lymphoid cell type?

Self-study questions for Cells of the Immune System.