The Immune System

• The immune system is comprised of two systems working together where anything determined to be foreign is deemed harmful - both can work either independently or in concert with one another
  
  – Innate (nonspecific system)
    
    • Always on guard, responds within minutes
    
    • Two “branches” to this system
      
      – First Line of Defense – external barriers to invaders; skin and mucosal membranes
      
      – Second Line of Defense – if barrier is broken cells and chemicals are called in to “attack” invaders – key aspect to this line of defense is the inflammatory response
The Immune System

- Adaptive (specific) defense system

  - More like elite fighting core; highly specialized with special “weapons” specific to the invader
  
  - Makes up the body’s third line of defense
    
    - Takes considerably longer to respond
    
    - Works in conjunction with the innate response
The Immune System

- **Innate (Non-specific) Immunity**
  - **First Line of Defense – Skin and Mucous Membranes**
    - Intact epidermis of the skin and mucous membranes - Skin produces sebum (low pH), lactic acid
    - Lacrimal apparatus, tears mechanically flush the area and contain lysozyme
    - Saliva mechanical flushing also contains lysozyme
    - Sticky mucous
    - Cilia
    - Flow of urine
    - Defecation and vomiting
    - Gastric juice
    - Vaginal secretions – slightly acidic
The Immune System

- Second Line of Defense – Internal Defenses – internal antimicrobial proteins, phagocytes, natural killer cells, inflammation, and fever
  - Phagocytes – two major types neutrophils and macrophages
    - Five (5) phases of phagocytosis
The Immune System

– Natural Killer (NK) Cells and Phagocytosis—have the ability to kill a wide variety of infectious microbes plus certain spontaneous arising tumor cells

• Natural Killer Cells

  – 5-10% all lymphocytes in blood (also in spleen, lymph nodes, and red bone marrow

  – Kill cells in two ways

    » Perforins – cause cytolysis

    » Virus infected or tumor cells, kill by releasing chemicals that cause apoptosis, and phagocytosis of particles
The Immune System

- Inflammation – occurs when cells are damaged in any way
  
  • Typically characterized by four (4) cardinal signs:
    - Redness
    - Pain
    - Heat
    - Swelling
    - Sometimes loss of function depending upon the site and extent of injury

  • Serves as a protective and defensive mechanism
    - Eliminates microbes, toxins or foreign material from the site
    - Prevents their spread to other organs
    - Prepares the site for tissue repair
The Immune System

- Stages of the Inflammatory Response
  - Vasodilation and increased permeability of blood vessels
  - Phagocytic migration
  - Repair
The Immune System

- Mediators of Inflammation

  » Histamine – vasodilation and increased permeability

  » Kinins – polypeptides - produced from kininogens – vasodilation, increased permeability, and chemotaxis

  » Prostaglandins – lipids – released by damaged cells – enhance histamine and kinins, also aid in emigration

  » Leukotriens – from basophils and mast cells – increase permeability, aid adherence of phagocytes and pathogens, and chemotaxis

  » Complement – enhance histamine, neutrophilic chemotaxis, promote phagocytosis, and in some cases can kill bacteria directly

- After phagocytosis the phagocytes die and along with damaged tissue and fluid form pus – if the pus accumulates and abcess forms
The Immune System

- **Antimicrobial Proteins**
  - **Interferons**
    - produced by virus infected cells, diffuse to uninfected neighboring cells prevents viral replication in those cells by blocking protein synthesis
    - Enhance the activity of phagocytes and natural killer (NK) cells
    - Inhibit cell growth
    - Suppress tumor formation
The Immune System

- Complement System – a group of blood proteins that when activated enhance certain immune, allergic and inflammatory reactions

Figure 8-2
The Immune System

» Classical Pathway – requires an antibody and antigen to form a complex to initiate the path

» Alternate Pathway – requires certain polysacharrides on the surface of some microbes to initiate the path

» Both pathways lead to the formation of membrane attack complex (MAC) that opens a channel in the microbe and kills it

– Transferrins – proteins that bind with iron, inhibiting the amount of iron needed by some bacteria
The Immune System

Classical pathway:
- Antigen–antibody complex
- C1 + C4 + C2 Complex

Alternative pathway:
- Microorganisms’ cell wall polysaccharides
- Factor B, Factor D, and Factor P (properdin)

Opsonization:
- Coats bacterial surfaces, which enhances phagocytosis

MAC:
- C3b
- C5b
- C6
- C7
- C8
- C9

Causes inflammation:
- Stimulates histamine release, increased blood vessel permeability, chemotactic attraction of phagocytes, etc.

Insertion of MAC and cell lysis:
- Holes in target cell’s membrane

Complement proteins (C5b–C9)

Lesion

Target cell
The Immune System

• Fever – usually caused by an infection from bacteria and their toxins or viruses
  – Inhibits microbial growth by sequestering iron, and zinc needed by bacteria
  – Speeds up metabolism for repair

• Adaptive Defenses (Specific Resistance : Immunity) – involves the production of specific lymphocytes or antibodies against a specific antigen
  – Three important aspects
    • Specificity
    • Systemic
    • Possesses memory
The Immune System

- Types of Immune Responses

  • Cell-Mediated Immunity (CMI) – the destruction of antigens by T cells, always involves cells attacking cells – particularly effective against:
    - Fungi
    - Parasites
    - Viruses
    - Some cancer cells
    - Foreign tissue transplants

  • Antibody-Mediated (Humoral) Immunity (AMI) – refers to the destruction of antigens by antibodies - works against:
    - Antigens dissolved in body fluids
    - Extracellular pathogens

* Often a pathogen can provoke both types of immune response
The Immune System

- Antigens – chemical substances that are recognized as foreign (nonself) by antigen receptors when introduced into the body
  
  • Made up of large, complex molecules

  - Most often proteins

  - Nucleoproteins

  - Lipoproteins

  - Glycoproteins

  - Certain large polysaccharides

  - Partial antigens (haptens) are only reactive if attached to larger molecules
The Immune System

• Complete Antigens and Haptens
  – Complete antigens possess two important properties
    » Immunogenicity
    » Reactivity
  – Hapten (Incomplete Antigen)
    » Not immunogenic by themselves
    » Bind with larger molecules and can become immunogenic
    » Posses the property of reactivity but lack immunogenicity
The Immune System

- Antigenic Determinants
The Immune System

– Self-Antigens: MHC Proteins

  • Major Histocompatibility Complex (MHC) Antigens – are unique to each person’s cells
    – Are associated with self-antigens, aid in the detection of foreign invaders
    – All cells except RBC’s display MHC class I antigens
    – Some cells also display MHC class II antigens

• More in a bit
The Immune System

- Cells of the Adaptive Immune System
  - Lymphocytes – T and B Cells
    - Both are derived from the bone marrow
    - T cells complete their maturation in the thymus gland, where they become immunocompetent
    - B cell gain the immunocompetence in the red bone marrow
    - Before leaving either the bone marrow or thymus gland B and T cells acquire distinctive surface antigen receptors
The Immune System

① Lymphocytes destined to become T cells migrate to the thymus and develop immunocompetence there. B cells develop immunocompetence in red bone marrow.

② After leaving the thymus or bone marrow as naive immunocompetent cells, lymphocytes “seed” the lymph nodes, spleen, and other lymphoid tissues where the antigen challenge occurs.

③ Mature (antigen-activated) immunocompetent lymphocytes circulate continuously in the bloodstream and lymph and throughout the lymphoid organs of the body.
The Immune System

– Antigen-Presenting Cells (APCs)

• Present exogenous antigens together with MHC II molecules to T cells; antigen presenting cells include:
  – Dendritic Cells – connective tissues
  – Langerhan’s Cells - skin
  – Macrophages
  – B cells
The Immune System

- Antibody-Mediated (Humoral) Immunity (AMI) – involves B cells and the production of antibodies
The Immune System

- Immunological Memory

![Graph showing antibody titer over time for response to antigen x and y.](image)
The Immune System

– Active and Passive Immunity

**Acquired immunity**

- Naturally acquired
  - **Active**
    - Infection; contact with pathogen
  - **Passive**
    - Antibodies pass from mother to fetus via placenta; or to infant in her milk

- Artificially acquired
  - **Active**
    - Vaccine; dead or attenuated pathogens
  - **Passive**
    - Injection of immune serum (gamma globulin)
The Immune System

– Antibodies

• Proteins that can combine specifically with antigenic determinants on the antigen that caused their production

• Are composed of heavy (H) and light (L) chains, each of which has a variable and constant portion

Key:

- Disulfide bond
- CHO = Carbohydrate side chain
The Immune System

- Antibody Classes

IgD is virtually always attached to the external surface of a B cell, where it functions as the antigen receptor of the B cell; important in B cell activation.

IgM exists in monomer and pentamer (five united monomers) forms. The monomer, which is attached to the B cell surface, serves as an antigen receptor. The pentamer (illustrated) circulates in blood plasma and is the first Ig class released by plasma cells during the primary response. (This fact is diagnostically useful because presence of IgM in plasma usually indicates current infection by the pathogen eliciting IgM’s formation.) Because of its numerous antigen binding sites, IgM is a potent agglutinating agent and readily fixes and activates complement.

IgG is the most abundant and diverse antibody in plasma, accounting for 75–85% of circulating antibodies. It protects against bacteria, viruses, and toxins circulating in blood and lymph, readily fixes complement, and is the main antibody of both primary and secondary responses. It crosses the placenta and confers passive immunity from the mother to the fetus.

IgA monomer exists in limited amounts in plasma. The dimer (illustrated), referred to as secretory IgA, is found in body secretions such as saliva, sweat, intestinal juice, and milk, and helps prevent attachment of pathogens to epithelial cell surfaces (including mucous membranes and the epidermis).

IgE is slightly larger than the IgG antibody. It is secreted by plasma cells in skin, mucosae of the gastrointestinal and respiratory tracts, and tonsils. Its stem region becomes bound to mast cells and basophils, and when its receptor ends are triggered by an antigen, it causes the cells to release histamine and other chemicals that mediate inflammation and an allergic reaction. Typically only traces of IgE are found in plasma, but levels rise during severe allergic attacks or chronic parasitic infections of the gastrointestinal tract.
The Immune System

- **Antibody Targets and Functions**

  - **Neutralization** (masks dangerous parts of bacterial exotoxins; viruses)
  - **Agglutination** (cell-bound antigens)
  - **Precipitation** (soluble antigens)
  - **Complement**

  Inactivates by
  Fixes and activates

  Enhances
  Enhances
  Leads to

  - **Phagocytosis**
  - **Inflammation** (Chemotaxis, Histamine release)
  - **Cell lysis**

Antigen → Antigen-antibody complex → Antibody
The Immune System

- Cell-Mediated Immunity – involves T cells, which can be of varying types:
  - Helper T (T4) cells
    - Display CD4 protein
    - Recognize foreign fragments associated with MHC II molecules
    - Secrete several cytokines, especially interleukin-2 that is a costimulator of helper T cells, cytotoxic T cells and B Cells
  - Cytotoxic T ([Killer], [Tc], [T8]) cells
    - Display CD8 protein
    - Recognize antigen fragments associated with MHC I molecules
  - Suppressor T cells (T_s)
  - Gamma delta T cells (T_{gd}) – bind with MHC I type antigens found typically on tumor cells
The Immune System
The Immune System
The Immune System

1. Bacterium (pathogen phagocytosed)
2. After synthesis at the ER, the class II MHC protein, with the invariant chain still attached, migrates to the phagolysosome
3. In phagolysosome, antigen degraded and invariant chain removed for peptide loading
4. Loaded MHC protein migrates to the plasma membrane

Extracellular fluid

In ER cisterna, invariant chain prevents class II MHC binding to peptides in the ER

Cytoplasm

Lysosome merges with phagosome, forming a phagolysosome

Antigenic peptide

Class II MHC

Class II MHC

Plasma membrane of an APC
The Immune System

- **Viral antigen**
- **Body cell**
- **Processed viral antigen (peptide) presented in combination with class I MHC protein**
- **Class I MHC protein**
- **CD8 protein**
- **Immunocompetent cytotoxic T cell**
- **Infected tissue cell presenting antigenic peptide recognized by cytotoxic T cell**
- **T cell receptor (TCR)**
- **Clone formation**
- **Cytotoxic T memory cell**
- **Mature cytotoxic T cells**
The Immune System
"From Goldberg, S., 'Clinical Physiology Made Ridiculously Simple'; MedMaster, 2004"
The Immune System

• Elimination of Invaders – two methods
  – Production of perforin, results in destruction of cell via cytolysis
  – Production of lymphotoxin – cell’s DNA is disrupted resulting in cell’s death
The Immune System

• Organ Transplants and Prevention of Rejection
  – Autographs
  – Isographs
  – Allographs
  – Xenographs
  – Immunosuppressive Therapy
    • Corticosteroids
    • Antiproliferative Drugs
    • Immunosuppressant drugs
The Immune System

• Be sure to look over Homeostatic Imbalances of Immunity pages 818 – 822 and A Closer Look pages 822 - 823

• There will not be many questions on the exam

• If you understand the material presented in chapter 21 you should be able to understand the explanations of these disorders

• I suggest that you review them on your own and if you have any questions be sure to ask me to help explain the conditions presented