Chapter 43: The Immune System

1. Innate Immunity
2. Adaptive Immunity
3. Immune Disorders
1. Innate Immunity

Chapter Reading – pp. 946-952
Overview of the Immune System

Pathogens (such as bacteria, fungi, and viruses)

INNATE IMMUNITY (all animals)
- Recognition of traits shared by broad ranges of pathogens, using a small set of receptors
- Rapid response
- Recognition of traits specific to particular pathogens, using a vast array of receptors

Barrier defenses:
- Skin
- Mucous membranes
- Secretions

Internal defenses:
- Phagocytic cells
- Natural killer cells
- Antimicrobial proteins
- Inflammatory response

ADAPTIVE IMMUNITY (vertebrates only)
- Recognition of traits specific to particular pathogens, using a vast array of receptors
- Slower response

Humoral response:
- Antibodies defend against infection in body fluids.

Cell-mediated response:
- Cytotoxic cells defend against infection in body cells.
Cells of the Immune System...
These include all of the white blood cells (aka leukocytes), some of which appear “granular”...

**Granulocytes**
- Neutrophils: phagocytes with strangely shaped nuclei, poorly stained granular vesicles
- Basophils: release histamine, other mediators of inflammation, vesicles bind basic dyes
- Eosinophils: phagocytic, attack parasites with toxic proteins, vesicle bind acidic eosin dye

**Dendritic Cells**
- Phagocytes with very important roles in initiating adaptive immune response
...more Cells of the Immune System...

...& others which have an “agranular” appearance

**TABLE 16.1**  
**Formed Elements in Blood (continued)**

<table>
<thead>
<tr>
<th>Type of Cell</th>
<th>Numbers per Microliter (μL) in Cubic mm (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agranulocytes</td>
<td></td>
</tr>
<tr>
<td>1. Monocytes (3–8%)</td>
<td></td>
</tr>
<tr>
<td>2. Lymphocytes (20–25%)</td>
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<tr>
<td>• Natural killer (NK) cells</td>
<td></td>
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<tr>
<td>• T cells</td>
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<tr>
<td>• B cells</td>
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</tbody>
</table>

**Agranulocytes**

- monocytes become actively phagocytic macrophages when stimulated via infection, injury

**Monocytes/Macrophages**

- recognize and destroy cells with features of tumor cells, cells with intracellular pathogens

**Natural Killer (NK) cells**

- have central roles in adaptive immunity (covered in ch. 16)

*Discussed in Chapter 17.*
The Lymphoid Organs

Bone Marrow

- blood cell formation
  - “where all blood cells (red & white) are born”

Thymus

- where T cells are “educated”
  - weeds out T cells that would react to “self” molecules

Spleen

- immune response to pathogens, foreign material in blood
The Lymphatic System

Adenoid Tonsils

Lymphatic vessels

Thymus

Peyer's patches (small intestine)

Appendix (cecum)

Spleen

Lymph nodes

Blood capillary

Interstitial fluid

Tissue cells

Lymphatic vessel

Lymphatic vessel

Masses of defensive cells

Lymph node

Tissue cells

Lymphatic vessel

Lymphatic vessel

Masses of defensive cells

Lymphatic vessel

Blood capillary

Interstitial fluid

Tissue cells

Lymphatic vessel

Lymphatic vessel

Masses of defensive cells

Lymphatic vessel

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Interstitial fluid

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Lymphatic vessel

Masses of defensive cells

Lymphatic vessel

Blood capillary

Interstitial fluid

Tissue cells

Lymphatic vessel

Lymphatic vessel

Masses of defensive cells

Lymphatic vessel
Innate Immunity

The innate immune defenses are the body’s 1st line of defense and includes:

1) physical barriers between inside & outside
   • the skin and the mucous membranes of the digestive, respiratory and genito-urinary tracts
   • all substances secreted at these barriers and all of the normal microbiota that live on these surfaces

2) non-specific cellular & physiological responses
   • i.e., inborn (innate) general responses to the presence of pathogens that breach the body’s physical barriers
   • independent of prior exposure, response is immediate
   • eliminates the vast majority of pathogens that gain entry
Phagocytosis

This is the process by which a cell ingests a solid extracellular particle (such as a bacterium) by engulfing it within a membrane enclosed vesicle or vacuole.

• cells that normally carry out this function are referred to as *phagocytic*, or simply as *phagocytes*
Types of Phagocytes

All of the phagocytes in the human body are types of white blood cells (leukocytes):

Neutrophils

• highly phagocytic cells that rapidly exit the blood into damaged or infected tissue, “gobble up” bacteria, etc…

Macrophages

• monocytes migrate to damaged, infected tissue from blood & differentiate into highly phagocytic macrophages
• some are fixed (non-mobile) in various tissues & organs

Dendritic Cells

• found in skin, mucous membranes, thymus, lymph nodes

Eosinophils (occasionally)
Some Antimicrobial Substances

There are many different kinds of antimicrobial substances, with some key ones shown below:

Complement system
  • a set of proteins present in the blood capable for destroying foreign cells among other things

Interferons
  • a class of cytokines that are especially important in controlling viral infections

Transferrins (bind & keep iron away from pathogens)

Antimicrobial peptides (cause lysis of microbes)
  • e.g. defensins
The Complement System

The complement system (aka “complement”) is a set of >30 proteins produced by the liver that circulate in the blood in an inactive state.

The presence of microbial pathogens activates the “complement cascade” in 1 of 3 ways to eliminate the pathogens by:

- **cytolysis** (cell lysis)
  - eukaryotic pathogens, Gram⁻ bacteria (not Gram⁺)
- triggering inflammation
- enhancing phagocytosis (opsonization)
Toll-like Receptors (TLRs)

TLRs are an important class of receptor proteins that bind to “Pathogen-Associated Molecular Patterns” or PAMPs

- when bound to ligand TLRs trigger the release of signaling molecules that stimulate innate and adaptive IRs
Local Inflammatory Responses

1) vasodilation & increased vascular permeability
2) migration of phagocytes & phagocytosis
3) tissue repair
2. Adaptive Immunity

Chapter Reading – pp. 952-964
The Nature of Adaptive Immunity

Unlike innate immunity, adaptive (acquired) immunity is highly specific and depends on exposure to foreign (non-self) material.

- depends on the actions of T and B lymphocytes (i.e., T cells & B cells) activated by exposure to specific antigens (Ag):

\[
\text{Antigen} = \text{any substance that is recognized by an antibody or the antigen receptor of a T or B cell}
\]

**Only antigenic material that is “foreign” should trigger an immune response, although “self antigens” can trigger autoimmune responses.**
Each T or B cell that survives development in the bone marrow or thymus has its own unique antigen receptor.

The “B cell receptor” is membrane bound antibody.

T cells have an antigen receptor called a “T cell receptor”.

Mature B cell

Mature T cell
Antibody Structure

Variable regions bind Ag & are unique for ea B cell

B cell antigen receptor

B cell

Cytoplasm of B cell

Transmembrane region

Plasma membrane

Heavy chains

Light chain

Disulfide bridge

Variable regions

Antigen-binding site

Antigen-binding site

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Antibodies

Proteins made by B cells that bind to a unique antigen:

• the variable (V) region recognizes specific antigen

• the constant (C) region is the same for all Ab’s in a given class:

   IgM   IgD   IgG
   IgA   IgE

(Ig = “immunoglobulin”)
variable regions bind Ag & are unique for ea T cell
DNA of undifferentiated B cell

DNA of differentiated B cell

1. Recombination deletes DNA between randomly selected V segment and J segment

2. Transcription

3. RNA processing

4. Translation

Antigen Receptor Gene Recombination

Light-chain polypeptide

Variable region

Constant region

Antigen receptor

B cell
Antigen: Antibody Specificity

- antibodies bind antigen in its unprocessed or native form (i.e., native Ag)

- each antibody binds to very specific molecular features or epitopes on the antigen

(a) B cell antigen receptors and antibodies

(b) Antigen receptor specificity
Roles of Antibodies

1) neutralization
   • prevents antigen (e.g., virus, toxin) from functioning

2) opsonization
   • enhancing the process of phagocytosis

3) activation of complement...
Antigen Presentation

- special phagocytes such as dendritic cells function as Antigen Presenting Cells (APCs)

- present pieces of processed antigen on MHC molecules for T cells to bind via their T cell receptors

(a) Antigen recognition by a T cell

(b) A closer look at antigen presentation

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TH cells become activated upon binding processed Ag
• presented in MHC molecules by an APC
TH cells then activate B cells, TC cells & other cell types
Clonal Selection

B cells that differ in antigen specificity

both B cells & T cells undergo clonal selection after binding antigen

Memory cells

Plasma cells
Cell-Mediated Immunity

Cell-mediated immune response

- involves special cytotoxic T cells ($T_c$) that kill cells containing intracellular pathogens (e.g., viruses)
- target cells are induced to undergo apoptosis by the release of perforin and granzymes from the $T_c$
Humoral immunity

- Involves antibodies made by B cells & released into the extracellular fluids (blood, lymph, saliva, etc…) to deal with extracellular pathogens.
Memory Cells

Both T and B cells will produce memory cells after initial activation which have the following characteristics:

- they are extremely long-lived (years!)
- activated directly upon subsequent exposure
  - generate more effector & memory cells
  - No need for T cell help!
- such secondary responses are much more rapid and much more intense than primary responses
  - this is the basis of prolonged immunity such as produced by immunizations
Primary immune response to antigen A produces antibodies to A. Secondary immune response to antigen A produces antibodies to A; primary immune response to antigen B produces antibodies to B.

Exposure to antigen A

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Antibody concentration (arbitrary units)</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>10^0</td>
</tr>
<tr>
<td>7</td>
<td>10^1</td>
</tr>
<tr>
<td>14</td>
<td>10^2</td>
</tr>
<tr>
<td>21</td>
<td>10^3</td>
</tr>
<tr>
<td>28</td>
<td>10^4</td>
</tr>
</tbody>
</table>

Exposure to antigens A and B

Antibodies to A

Antibodies to B
Summary of $1^{st}$ & $2^{nd}$ IRs

- **B cell**
  - Plasma cells
    - Secreted antibodies
      - Defend against extracellular pathogens
  - Memory B cells

- **Helper T cell**
  - Memory helper T cells
  - Antigen (2nd exposure)

- **Cytotoxic T cell**
  - Memory cytotoxic T cells
  - Active cytotoxic T cells
    - Defend against intracellular pathogens and cancer
3. Immune Disorders

Chapter Reading – pp. 964-968
Allergic reactions involve the activation of mast cells, eosinophils or basophils through binding of antigen to IgE on cell surface.

- requires prior exposure to generate IgE antibodies
Autoimmunity

Autoimmunity refers to the generation of an immune response to self antigens:

- normally the body prevents such reactions
  - T cells with receptors that bind self antigens are eliminated (or rendered anergic*) in the thymus
  - B cells with antibodies that bind self antigens are eliminated or rendered anergic in the bone marrow
- in rare cases T and/or B cells that recognize self antigens are activated

*anergic = non-reactive or non-responsive
HIV & the Development of AIDS

- Latency
- AIDS

Helper T cell concentration (in blood (cells/mm³))

Relative anti-HIV antibody concentration

Relative HIV concentration

Helper T cell concentration

Years after untreated infection
Key Terms for Chapter 43

- T cell receptor, B cell receptor
- native vs processed antigen, epitope
- humoral vs cellular immunity, 1° vs 2° IR
- antibody: heavy & light chains, variable, constant
- clonal selection, clonal deletion, memory cells
- PAMPs, TLRs, autoimmunity, allergy
- neutrophils, basophils, eosinophils, dendritic cells
- monocytes, macrophages, NK cells, T & B cells
- perforin, granzymes, antigen presentation, APCs
- complement, interferons, transferrin, defensins

Relevant Chapter Questions 2-8