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
Cells of the Immune System...
These include all of the white blood cells (aka leukocytes), some of which appear “granular”...

**Neutrophils**
- phagocytes w/strangely shaped nuclei, poorly stained granular vesicles

**Basophils**
- release histamine, other mediators of inflammation, vesicles bind basic dyes

**Eosinophils**
- phagocytic, attack parasites w/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

**Monocytes/Macrophages**
- monocytes become actively phagocytic macrophages when stimulated via infection, injury

**Natural Killer (NK) cells**
- recognize and destroy cells with features of tumor cells, cells with intracellular pathogens

**T & B cells (lymphocytes)**
- have central roles in adaptive immunity (covered in ch. 16)

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

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):

**Only antigenic material that is “foreign” should trigger an immune response, although “self antigens” can trigger autoimmune responses.**

Antigen Receptors

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”.

Antibody Structure

variable regions bind Ag & are unique for ea B cell
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:
  \[
  \text{IgM} \quad \text{IgD} \quad \text{IgG} \\
  \text{IgA} \quad \text{IgE}
  \]
  (Ig = “immunoglobulin”)

T Cell Receptors
Variable regions bind Ag & are unique for ea T cell

DNA of undifferentiated B cell
DNA of differentiated B cell

Antigen Receptor Gene Recombination
Recombination deletes DNA between randomly selected V segment and J segment

Functional gene
Transcription
Pre-mRNA
mRNA
Cleavage
Poly-A tail
Translation
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

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
Initiation of Adaptive IRs

T<sub>H</sub> cells become activated upon binding processed Ag • presented in MHC molecules by an APC

T<sub>H</sub> cells then activate B cells, T<sub>C</sub> cells & other cell types

Clonal Selection

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

Cell-Mediated Immunity

Cell-mediated immune response
• involves special cytotoxic T cells (T<sub>C</sub>) 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<sub>C</sub>
**Humoral Immunity**

Humoral immune response

- 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

**1º vs 2º Humoral Responses**

1º immunity 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.
3. Immune Disorders

Chapter Reading – pp. 964-968

Allergic Responses

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

<table>
<thead>
<tr>
<th>Latency</th>
<th>AIDS</th>
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<tbody>
<tr>
<td>Helper T cell concentration (in blood (cells/mm³))</td>
<td>Relative anti-HIV antibody concentration</td>
</tr>
<tr>
<td>Relative HIV concentration</td>
<td>Helper T cell concentration</td>
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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