Chapter 21: Innate and Adaptive Body Defenses

I. 2 main types of body defenses
   A. Innate (nonspecific) defense: not to a specific microorganism or substance
   B. Adaptive (specific) defense: immunity – to a specific substance

II. Innate defenses
   A pathogen is a disease-causing microorganism
   Innate (nonspecific) disease resistance is automatic

   A. Surface barriers: the body’s first line of defense
      1. Skin and mucous membranes
         a. Physical barriers: many layers of cells
         b. Chemical barriers
            1) Acid: prevents growth of some microorganisms
               a) Stomach: mucosa secretes concentrated HCl, enzymes
               2) Enzymes: destroy bacteria
a) **Lysozyme**: in saliva, lacrimal solution

3) **Mucin**: sticky mucous traps microorganisms

4) **Defensins**: mucosae secrete broad spectrum antimicrobial proteins

B. **Internal innate (non-specific): cells and chemicals**: second line of defense - when skin or mucous membranes are breached

1. **Phagocytes**: found just under the skin and mucous membranes

(a) A macrophage (purple) uses its cytoplasmic extensions to pull rod-shaped bacteria (green) toward it. Scanning electron micrograph (4800x).

(b) Events of phagocytosis.

a. **Macrophages**: the body’s main phagocyte

b. **Neutrophils**: white blood cells waiting for pathogens

2. **Natural killer cells**: kill cancer and virus infected cells before the immune system is activated
3. Inflammation: tissue response to injury

a. Inflammatory chemical release
   1) Mast cells: histamine is a potent vasodilator
   2) Prostaglandins, complement, lymphokines: vasodilation

b. 4 signs of inflammation
   1) Redness
   2) Heat
   3) Swelling: due to increased vascular permeability
   4) Pain chemicals, microbial toxins and swelling sets off pain sensors

c. Vasodilation and increased capillary permeability
   1) Hyperemia: congestion with blood

2) Phagocyte mobilization
   a) Leukocytosis:
   b) Margination: cells line up along edge of capillary
   c) Diapedesis: cells squeeze out into interstitial areas
   d) Chemotaxis: damaged tissue cells release chemicals that attract neutrophil and macrophage
   e) Amoeboid movement: cells move like amoeba
3) Antimicrobial proteins

a) Interferon: small proteins that help fight viruses
b) Complement: a group of 20+ proteins circulating in blood in an inactive state
   (1) This is the main microbial control mechanism
   (2) 2 ways to activate complement
      (a) Classical: antibody must be bound to pathogen
      (b) Alternate: complement proteins interact with polysaccharide on pathogen surface
      (c) Either method: results in the formation of the membrane attack complex (MAC)
      (d) MAC: complement proteins arrange themselves into a doughnut shape

4) Fever: abnormally high body temperature
   a) Pyrogen: a chemical released by macrophages and pathogens which resets the hypothalamus to a higher temperature setting

III. Adaptive defense - Immunity
A. Introduction
   1. 3rd (and last) line of defense
   2. Recognizes: a particular foreign substance to destroy
   3. Three characteristics of the immune system
      a. Antigen specific
      b. Systemic: whole body, not limited to initial infection site
      c. Memory: the system “remembers” prior infections of same type
4. Two main branches
   a. Humoral immunity
   b. Cell mediated immunity

B. Antigens (Ag): a substance that can turn on the immune system

1. Complete Ag has two properties:
   a. Immunogenicity: can be recognized by immune system
   b. Reactivity: the ability to react with products of turned on immune cells
2. Hapten (incomplete Ag): substances smaller than 10,000 molecular weight

3. Antigenic determinants: the precise location on the antigen where antibodies physically attach

4. Special antigen types
   a. Agglutinogen: found on red blood cells
   b. Allergen: the type of Ag that causes allergies
   c. Self-antigens: MHC proteins: major histocompatibility complex

C. Cells of the adaptive immune system

1. B cells (lymphocytes) the main cell of humoral immunity

2. T cells (lymphocytes) the main cell of cell-mediated immunity

3. APCs (antigen presenting cells)
D. Humoral immune response
   Antigen challenge: *usually occurs in spleen or lymph node*

1. Activation of B cells - clonal selection
   
   a. Antigen: *binds to several receptors on B cell*
b. B cell: endocytoses receptor/Ag complex
c. This stimulates B cell cloning
   1) Plasma cells: make antibodies for the current infection
   2) Memory cells: “remember” the infection for the future

2. Immunological memory
   a. Primary immune response: the first exposure to an antigen

b. Secondary immune response: any subsequent exposure

3. Active and passive humoral immunity
   a. Active immunity
      1) Naturally acquired: catch a cold, flu etc

      2) Artificially acquired: injection of dead or attenuated pathogen (or parts) etc.

b. Passive immunity
4. Antibodies: *a class of proteins called immunoglobulins*

   a. Basic structure of the antibody monomer
   1) 4 polypeptide chains linked by covalent bond
      a) 2 light chains plus 2 heavy chains
      b) Each monomer: *possesses variable and constant regions*
         (1) Variable: Ag binding sites
         (2) Constant: *the same for all members of an Ab class*
         (3) Bivalent: due to 2 Ag binding sites

   b. Antibody classes
   1) IgD: *monomer, important in activating B cells*

   2) IgM: *pentamer, the first class released during primary response*

   3) IgG: *monomer, the main Ab of primary and secondary response*

   4) IgA: *dimer, protects mucosal surfaces*

   5) IgE: *monomer - binds to mast cells to release histamine*
c. Antibody targets and functions

1) **Neutralization:** is the simplest mechanism - blocks active sites on viruses, toxins etc

2) **Agglutination:** possible because of the bivalent nature of antibodies

3) **Precipitation:** soluble molecules settle out

4) **Complement fixation:** the main defense against bacteria and incompatible blood

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**E. Cellular immune response:** (cell mediated immunity)

1. Several classes of T cells
   a. **Cytotoxic T cells (T\text{C}):** CD8, T8 cells, killer cells = effector cells
   b. **Helper T cells (T\text{H}):** CD4, T4 cells
   c. **Regulatory T cells (T\text{Reg}):** suppress the immune response

2. **MHC (major histocompatibility complex):** like a cellular fingerprint
   1) **Class I MHC:** found on all body cells (except red blood cells) – recognized by CD8 cytotoxic cells
      a) **Groove holds and displays Ag:** self or “foreign”
   2) **Class II MHC:** only on APCs and B cells that present Ag to CD4 cells
      a) **Displays “foreign” Ag**

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<table>
<thead>
<tr>
<th>CLASS I</th>
<th>CLASS II</th>
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<tbody>
<tr>
<td>Displayed by</td>
<td>All nucleated cells</td>
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<tr>
<td></td>
<td>Class I MHC</td>
</tr>
<tr>
<td></td>
<td>APCs (dendritic cells, macrophages, B cells)</td>
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<tr>
<td></td>
<td>Class II MHC</td>
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<tr>
<td>Recognized by</td>
<td>Naive CD8 cells and cytotoxic T cells</td>
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<tr>
<td></td>
<td>C8 protein</td>
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<td></td>
<td>Naive CD4 cells and helper T cells</td>
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<td></td>
<td>CD4 protein</td>
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<tr>
<td>Foreign antigens on MHC are</td>
<td>Endogenous (intracellular pathogens or proteins made by cancerous cells)*</td>
</tr>
<tr>
<td>Foreign antigens on MHC send this message</td>
<td>If displayed by an APC: “I belong to self, but have captured a foreign invader. This is what it looks like. Kill any cell that displays it.”</td>
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<td></td>
<td>If displayed by any other body cell: “I belong to self, but have been invaded or become cancerous. Kill me!”</td>
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<td>Exogenous (phagocytized extracellular pathogens)</td>
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<td>“I belong to self, but have captured a foreign invader. This is what it looks like. Help me mount a defense against it.”</td>
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3. Clonal selection and differentiation of T cells
   a. Co-stimulation: 2 step process
      1) T cell binds to Ag-MHC complex: on APC
      2) Co-stimulatory molecule: must also bind to this on the APC

   b. Role of T cells
      1) T helper cells: recognize foreign Ag bound to MHC II presented by APCs to stimulate B and T cell cloning

2) T cytotoxic: recognizes foreign Ag presented by MHC I on virtually any body cell
   a) Mechanism of killing
      (1) Tc cell: binds tightly to target cell
      (2) It releases perforin: a protein it inserts into target cell membrane
      (3) The T cell then leaves: in search of other targets
      (4) A short time after T cell leaves: perforin polymerizes and forms transmembrane pore
      (5) Granzymes enter the pore: to activate enzymes that cause death in 2 hours
      (6) Can secrete tumor necrosis factor (TNF): kills tumor cells by unknown mechanism
Regulatory T cells: release lymphokines to suppress the immune system

F. Summary chart - immune response
G. Homeostatic imbalance

1. Immunodeficiencies: can be congenital or acquired
   
   1) Severe combined immunodeficiency disease (SCID)
   
   2) Acquired immune deficiency syndrome (AIDS)

2. Hypersensitivities (allergies): abnormally strong immune response to something that is not actually a threat

   a. Immediate hypersensitivities: begin almost immediately after contact with allergen

   1) Anaphylaxis is “against protection”

3. Autoimmune diseases
   
   a. Virus may change cells
b. Antigen similar to “self”

H. Blood typing

1. ABO Blood groups

2. Rh

a. Hemolytic disease of newborn