The Body's Defenses

[Note: This is the text version of this lecture file. To make the lecture notes downloadable over a slow connection (e.g. modem) the figures have been replaced with figure numbers as found in the textbook. See the full version with complete graphics if you have a faster connection.]

Three lines of defense

First line:

- **Nonspecific defenses include sebaceous (“oil”) and sweat glands secreting antimicrobial proteins and decreasing the pH to 3-5.**
- **Mucus traps microbes and cilia sweep them out of the system.**

[See Fig. 43.1]

Second line (part one): Antimicrobial proteins

Proteins of the complement system (discussed later) and interferons (antiviral proteins secreted by infected cells) reduce infection.

Three lines of defense

Second line (part two): Cells of the body's defenses

- **Neutrophils (60-70%) of all leukocytes. Self-destruct during action**
- **Monocytes (5%) become macrophages. Some migrate in interstitial fluid, others stay in lung, liver, kidney, brain, connective tissue, lymph nodes, spleen.**
- **Eosinophils (1.5%) attack larger invaders like blood flukes.**
- **natural killer (NK) cells kill infected body cells**

[See Figs. 42.13, 42.14]

Phagocytosis

- **Foreign invaders are engulfed, digested, and parts are presented by macrophages.**

[See Fig. 8.18a]

The lymphatic system traps and destroys invaders

[See Fig. 43.4]

Second line (part three): Inflammation

- **Signals for inflammation include histamine released by basophils & mast cells and release of prostaglandins**
- **chemotaxis of phagocytes is caused by chemokines released by injured tissue**
- ***Inflammo* = to set on fire.**
- **Increased blood supply and fluid entry leads to edema (swelling)**
- **Fever is caused by an increase in the body's thermostat by toxins or by pyrogens secreted by leukocytes.**
- **Pus in injured area consists primarily of dead phagocytes, released proteins, and fluid.**

[See Fig. 43.5]

Third line of defense: specific defenses (the immune system)

[See Fig. 43.10]

Primary components of the immune system are lymphocytes (B and T cells) and antibodies.

Development of the immune system

• B lymphocytes (a.k.a. B cells) develop primarily in bone marrow (were discovered in bursa of birds)

They secrete antibodies and have membrane-bound antibodies (membrane immunoglobulins)

[See Fig. 43.8]

• T lymphocytes (a.k.a. T cells) develop primarily in the thymus (organ in the chest)

They have only membrane-bound receptors (similar to antibodies) called T cell receptors

• Both cell types circulate through the body and concentrate in the spleen and lymphatic system.

- **Antibodies are proteins that bind to specific molecules or regions of macromolecules**

- **Molecules or regions of macromolecules that bind to an antibody are called epitopes**

- **The molecule, macromolecule, or cell containing the epitope is called an antigen (for antibody generator).**

[See Fig. 43.14]

• **Antibodies consist of two identical heavy chains and two light chains that are all held together by disulfide bridges.**

C = constant region that is the same for each class of antibody
V = variable region that is different for every epitope

[See Fig. 43.15]

- **Different antibodies (Immunoglobulins) are generated by genetic recombination during differentiation of lymphocytes.**

- **The five different classes are determined by heavy chain C region:**

IgG = *secreted monomer, most common in blood*
IgD = *surface of B cells, monomer*
IgE = *surface of mast cells and basophils, monomer*
IgA = *secreted dimer, found near epithelia*
IgM = *secreted pentamer, first response*

[See Fig. 19.6]

Clonal selection of lymphocytes

- **B Cells become plasma or memory cells after binding to foreign antigen**
- **T Cells become effector or memory T cells**
- **Cells that recognize “self” antigens are inactivated or killed**
- **Plasma cells can produce 2000 antibody molecules/sec for 4-5 days**

[See Fig. 43.6]

Primary and secondary immune responses

[See Fig. 43.7]

Importance of memory cells in the <u>humoral</u> (blood) and <u>cell-mediated</u> immune responses

[See Fig. 43.10]

- **MHC molecules (*major histocompatibility complex*) are important for separating "self" from foreign or "non-self" cells (MHC a.k.a. HLA for *human leukocyte antigen*). Important for organ transplants.**
- **All nucleated cells display Class I MHC**
- **Macrophages, B cells, and cells of the thymus all display Class II MHC**

[See Fig. 43.9]

Central role of the helper T cell (T_H) and cytokines (IL-1 and IL-2) in regulating the immune response

- **The interleukins stimulate cell proliferation (division) of T_H, T_C and B cells (example of positive feedback)**

[See Fig. 43.11]

[See Fig. 43.12]

How a cytotoxic T cell kills infected cells

T-dependent antigens stimulate helper T cells to secrete cytokines

T-independent antigens cause a weaker B cell stimulation directly

[See Fig. 43.13]

[See Fig. 43.16]

The classical pathway of cell lysis

[See Fig. 43.17]

- **The alternate pathway may also lead to cell lysis but doesn't involve antibodies, so it's part of the body's nonspecific defenses.**

- **Complement proteins also aid in a) inflammation, b) attraction of phagocytes, c) opsonization, and d) immune adherence (making invaders "sticky").**

Two forms of Immunity

1) <u>active immunity</u> is the natural response of the immune system to invaders.

<u>Immunization</u> (vaccination) is used to stimulate <u>memory cells</u> using parts of microbes or inactivated whole microbes.

2) <u>passive immunity</u> occurs when antibodies from another source fight invaders.

Mothers pass IgG through placenta to fetus and IgA is passed on to infant through early breast milk.

Where is immunity important?

***Blood transfusions*: ABO blood groups and Rh factor (positive or negative for D antigen)**

***Organ transplants*: MHC proteins need to be matched, suppress T_H cells; bone marrow transplant generates "foreign" immune system**

[See Fig. 14.10]

Where is immunity important?

***Allergies*: things that stimulate a reaction are called <u>allergens</u>. Some common severe ones are found in bee venom, penicillin, peanuts, fish.**

Severe ⇓ BP = <u>anaphylactic shock</u>. Injection of hormone <u>epinephrine</u> can prevent.

***Autoimmune disorders*: = self intolerance.**

<u>lupus</u> = general attack of DNA, histones, etc.

<u>rheumatoid arthritis</u> = attack of cartilage and bone of joints

<u>insulin dependent diabetes mellitus</u> = can result from attack of pancreatic β cells

<u>multiple sclerosis</u> = attack of myelin in CNS

Allergies

[See Fig. 43.18]

AIDS (Acquired Immunodeficiency Syndrome) results from infection by HIV (Human Immunodeficiency Virus)

- Death is nearly 100% certain, and caused by opportunistic diseases. Normally harmless protozoan can cause pneumonia (infection of lung), and rare cancers that are usually killed by the body (e.g. Kaposi's sarcoma) appear.

- HIV kills CD4 positive cells having chemokine receptors, especially T_H cells, also some macrophages and B cells.

- Spread only by bodily fluids containing infected cells, especially blood, semen, vaginal secretions, not spread by casual contact.

- Deadly behavior includes multiple sex partners and IV drug abuse with shared needles (syringes).

[See Fig. 18.7]

HIV is a retrovirus that integrates its genome into the host.

Treatments to slow infection include:

- **DNA synthesis inhibitors**
- **Reverse transcriptase inhibitors**
- **Protease inhibitors**

[See Fig. 18.7]

[See Fig. 43.20]

AIDS incidence is growing fastest for <u>all women</u>, but especially:

- **African-American women**
- **Hispanic women**

<u>infection due to heterosexual sex is the fastest growing risk group</u>

[See figs from the CDC
http://www.cdc.gov/nchstp/hiv_aids/stats/trends98.pdf]