Internal Defense Notes
AP Biology Mrs. Laux

- **Internal environment of animals provides attractive area for growth of bacteria, viruses, fungi**
- **Harm via:**
  1. destruction of cells
  2. production of toxic chemicals
- **To protect against foreign invaders, humans possess 3 levels of defense**

I. Nonspecific First Line of Defense

A. Basics:

1. physical barriers that prevent entrance of pathogens (skin, mucous membranes)

2. not specialized

a. humans→oil and sweat glands acidify skin (pH~3-5) which discourages microbial growth

b. saliva, tears, mucous secretions

i. wash away invading microbes

ii. contain antimicrobial proteins (ex: lysozyme) that break down cell walls of many gram (+) bacteria

c. mucous membrane-cilia sweep invaders out of trachea, bronchi

d. gastric juice of stomach (pH 1.5 to 2.5) kills most bacteria

e. symbiotic bacteria in digestive tract and vagina outcompete other organisms that could cause damage (ex: yeast infection)

II. Second Line of Defense

→nonspecific mechanism

A. Amoeboid WBCs→phagocytosis of microbes that pass 1st line

1. Neutrophils (kamikaze cells)

a. become phagocytic in infected tissue

b. attracted by chemical signals

c. only live a few days and destroy self while destroying pathogens

2. Monocytes→Macrophages

a. large phagocytic cells

b. found in interstitial fluid or permanently in organs and connective tissue

c. phagocytize pathogens, other foreign cells, neutrophils with pathogens

3. Eosinophils

a. limited phagocytic activity

b. contain destructive enzymes; discharged against outer covering of invading pathogens

c. used mainly against parasitic worms (tapeworms)

4. Natural killer cells (NK cells)

a. destroy body's own cells when:

i. cells are infected by viruses

ii. abnormal body cells, such as tumors

b. do not phagocytize cells, attack cell membranes, which cause cells to lyse

c. part of both specific and nonspecific lines of defense

B. Antimicrobial Proteins

1. either directly attack pathogens or interrupt their reproduction

2. most important: complement

a. 20 proteins in plasma, ICF

b. inactive until body is exposed to an antigen

c. non specific because will react against any foreign antigen

d. functions:

i. cause lysis of pathogens by poking holes in cell membrane

ii. coat pathogens so that phagocytes will engulf

iii. attract WBCs to area of infection by releasing attracting chemicals

iv. increase inflammation by stimulating release of histamine (dilates and makes capillaries more permeable)

C. Cytokines

1. type of cytokines

a. regulatory proteins

b. important in signaling immune response

c. how immune cells communicate with one another

2. Interferons

a. chemicals produced by virus-infected cells (like macrophage or some tissue cells)

b. activate immune response to come and kill cell with virus inside

3. Interleukins

a. cytokines secreted mainly by macrophages and lymphocytes

b. activate different cells of immune system

c. ex: lymphocytes are "tagging" destroying pathogens-will attract macrophages to come and clean up the "mess"

d. IL-1, IL-2-numbered in order of discovery

D. Inflammatory Response

1. occurs when there is damage to tissue or entry of pathogens

2. cut in skin, bacteria enters-series of events occur:

a. Basophils and mast cells (connective tissue cells with granules) secrete histamine→causes:

i. vasodilation of blood vessels surrounding damaged area

a. increases blood supply for increased # WBCs, increased pressure pushes WBCs to tissue

b. increases % nutrients to supply cells and WBCs

c. causes redness, increased temperature, and swelling (edema)
d. increased temperature favorable for WBCs, unfavorable for pathogens

ii. capillaries become more permeable
a. Antibodies pass from blood to infected area
b. causes edema and pain

b. phagocytes migrate because attracted by complement

i. neutrophils arrive first, then macrophages
a. neutrophils kill pathogens and then die
b. macrophages→destroy pathogen and clean up remains of damaged tissue cells and dead neutrophils
c. dead cells and fluid from capillaries may accumulate as pus

ii. phagocytes release interleukin-1: cause fever

3. Widespread (systemic)-inflammatory response

a. may occur as a result of severe infections (ex: meningitis, appendicitis)
b. may be a large increase in # of WBCs within hours (white count)
c. system wide inflammatory response→fevers develop
→too high, dangerous
→moderate: facilitate phagocytosis, increase tissue repair

III. Third Line of Defense→Immune Response

A. Definition-Immune system characteristics

1. Specificity→system's ability to recognize and eliminate particular microorganisms and foreign molecules

a. antigen

i. any molecule, usually a protein or polysaccharide, that may be identified as foreign and will elicit an immune response
ii. ex: toxin (insect bite, bacteria) protein coat of a virus-molecule unique to a cell membrane of bacteria, worms, pollen, protozoa, …
iii. each antigen has a unique molecular shape and stimulates production of a particular antibody that defends against that antigen

b. antibody (Ab) or immunoglobulin (Ig)

i. antigen-binding protein that acts as an effector for immune response
ii. secreted by B-lymphocytes

iii. structure: 4 polypeptide chains-(2 light, 2 heavy); C-region-amino acid chain is constant within class; V-region-unique to antibody for a particular antigen

2. Diversity

a. immune system has ability to respond to numerous kinds of invaders

b. each invader is recognized by a particular antibody(ies)

3. Memory

a. ability to recognize previously encountered infections

b. body reacts quickly and efficiently to repeat infections

c. acquired immunity

d. ex: chicken pox

4. Self-nonself recognition

a. body can distinguish between itself and foreign antigens

b. body uses major histocompatability complex (MHC) to distinguish between self and nonself cells

i. collection of glycoproteins (proteins and carbohydrates) that exist on cell membrane

ii. biochemical fingerprint-no 2 people, except identical twins, have identical MHCs

iii. immune systems react when they come in contact with MHC of another organism

iv. more related-more MHC proteins in common

v. 2 important classes:

a. MHC class I antigens are found on most nucleated cells

b. MHC class II antigens are found on B-cells, macrophages; allow these cells to become antigen presenting cells (APC)-macrophages-once engulf pathogen will degrade within itself, then bring protein part to its MHC; has become an APC-will travel to lymph nodes to meet up with lymphites and initiate specific response

B. Active vs. Passive Immunity

1. Active Immunity

a. immunity acquired after recovery from infectious disease

b. depends on response of own immune system→responds, fights, and remembers

c. may be acquired:

i. naturally→from infection

ii. artificially→from vaccine

a. may be: bacterial toxin, dead pathogen, weakened pathogen

b. can no longer cause disease, but do stimulate immune response

d. long-term response

2. Passive Immunity
a. when immunity is transferred from one person to another via transfer of antibodies
b. temporary-few weeks or months
c. natural: pregnant mother→smaller antibodies to fetus, nursing
d. artificial→injecting person with antibodies from another person or animal when initial infection would kill the person
i. ex: rabies, tetanus, snake venom

C. Cells of the Immune System
→primarily: lymphocytes:
1. B cells→antibody-mediated immunity
a. originate and mature in bone marrow
b. cell membrane is characterized by antibodies (specialized antigen receptors)
c. differentiate into plasma, memory cells
2. T-cells→cell mediated immunity:
a. produced in bone marrow, mature in thymus
b. no antibodies
c. differentiate: T_H, T_C, memory cells (different from B cell memory cells)
3. mature B and T cells are concentrated in lymph nodes, spleen, and other lymphatic organs→most likely to make contact with antigens
4. both have antigen receptors:
a. B cells→antibodies
b. T cells→receptors embedded in membrane

IV. Antibody-Mediated (Humoral) Response
A. B-cells→antibodies (Ig)
→structure associated with function
1. y-shaped molecule with 4 polypeptide chains:
2 light chains
2 heavy chains
a. all 4 chains have constant regions that vary little in amino acid sequence from one Ig to next
b. V-region→tips
i. extreme variation
ii. antigen-binding sites
iii. amino acid sequences enable antibody to recognize and "fit" into antigen
2. 5 classes of antibodies based on composition of constant regions:
a. IgM→pentamer (5 Ys)
i. circulating antibodies which appear in response to initial exposure to an antigen (primary response)
ii. too large to leave blood and lymph vessels
b. IgG→monomer
i. most abundant in blood

ii. small→diffuses through placenta
iii. also→bacteria, virus, fungi, toxins
iv. chief→secondary immune response (after initial)

c. IgA→dimer
i. prevents attachment of pathogens to epithelial surfaces
ii. found in saliva, tears, sweat

d. IgD→monomer
i. rare
ii. found on surface of B-cells

e. IgE→monomer
i. stem regions attach to basophils
ii. stimulate histamine response when triggered by allergen

3. How antibodies work:
a. do not directly destroy pathogen
b. binds to antigen-forming an antigen-antibody complex, which tags invaders for destruction by one mechanism:
i. antibody-antigen complex may inactivate pathogen or its toxin
ii. clumping of cells for easier destruction by the phagocytes
iii. activation of complement→lyses cells

B. Humoral Reaction (medieval times: humor = body fluids)
1. B-cells are circulating in blood and lymph
a. each carries specific antibodies
b. antibodies were created during embryonic development, just waiting for exposure to antigen
c. B cells are primary mode of bacterial infection
2. response begins when antigen binds to antibody on cell membrane of a B-cell
a. be presented by APC to T_H
b. usually activated by T_H cell
3. once B-cell is activated, B cells begin to proliferate (divide and differentiate) into two types of cells:
a. plasma cells
i. release and secrete antibodies
ii. antibodies will circulate in blood and lymph binding to antigens
iii. large areas fo rough ER synthesize antibodies
b. memory cells
i. long-lived B cells that do not release their antibodies at initial infecton
ii. circulate the body and respond to any subsequent infection by same antigen
iii. provides immunity after first occurrence of disease

c. theory of clonal selection
i. antigen "selects" which lymphocytes will divide to form clones
ii. permits body to make large quantities of antibodies only when needed

B cells: Humoral Response

B-cell in blood/lymph is activated

B cell
↓

plasma cells (millions)
↓
activate phagocytes
complement; inactivate toxins

memory cells
↓
ready for secondary infection

V. Cell-Mediated Response
A. T cells
1. antigen receptors are not antibodies, but are recognition sites for molecules displayed by nonself cells
2. self and non-self recognition:
a. MHC markers are used to distinguish nonself
b. APC cells display foreign antigens to initiate cell-mediated response
c. cancer cells, tissue cells, and others are recognized as nonself by T cells
3. Types (produced by clonal selection)
a. cytotoxic T cells (T_C cells)
i. killer T cells
ii. recognize and destroy nonself cells by puncturing them and causing them to lyse (perforin)
b. Helper T cells (T_H cells)
i. stimulate proliferation of B and T_C cells upon recognition of nonself cells
ii. important in both humoral and cell-mediated immunity
4. Activation of T cells:
a. respond to antigens on body's own cells

b. cannot detect free antigens in body fluids (humoral response)

c. process:

Macrophage (engulfed pathogen) → **Infected cell**

→ **Becomes APC by displaying MHC nonself markers (pieces of pathogen)**

→ **recognition of nonself cells stimulates differentiation of T cells**

T_H cells

→ **bind to nonself marker**

→ **release interleukins**

→ **proliferation of T_H cells**

→ **release more interleukins**

→ **more T_H (positive feedback)**

→ **activates B cells**

→ **humoral response**

→ **antibodies kill other free pathogens in blood and lymph**

→ **activates T_C cells**

→ **cell-mediated response**

→ **binds to antigen displaying nonself markers**

→ **secretes perforin**

→ **cell lyses**

5. T_C cells destroy:

a. macrophages with pathogen

b. cells infected with virus

c. foreign tissue cells
ex: organ transplants
d. cancer cells
i. periodically develop in body
ii. possess markers not found in normal cells
iii. TC recognizes as nonself
iv. cancer cells develop in individuals with defective or declining immune systems