

THE BODY'S DEFENSES

Ch. 43

There is not a day that you do not cross paths with some time of pathogen. Viruses, parasitic worms, bacteria, fungi, protozoa and other agents of disease would love to use your body as a breeding ground. Fortunately, we have an efficient system for protection. Physical barriers, proteins and nonspecific cellular components and the specific immune system offer defense against the onslaught of intruders. In order to cause and infection, a microbe must be able to adhere to the surface of the host, invade the host, evade the host's defenses, multiply within the host, leave the host and return to its reservoir (where it lives before/after infection; eg. Another human, an animal, soil, water)



1) VERTEBRATE NON SPECIFIC DEFENSE.

a) Barriers

i) Skin

- (1) Prevent entry of pathogens (intact epidermis, hairs to filter)
- (2) Secrete acids (inhibit growth of microorganisms, destroy bacteria in food), mucous (wash away and trap) and chemicals (lysozyme to destroy cell walls)

b) Phagocytes

- i) Lysosomes within cells fuse with pathogens and release hydrolytic enzymes.
- ii) **Neutrophils** (phagocytosis of pathogens). Most common w.b.c.
- iii) Monocytes (phagocytize pathogens) some are wandering (through out interstitial fluid and lymph) others are fixed (found in lymph nodes, alveoli of lungs)
- iv) Eosinophils
- v) Killer cells (kill infected cells)

c) Proteins

i) **Interferons.** "Interfere" with viral reproduction.

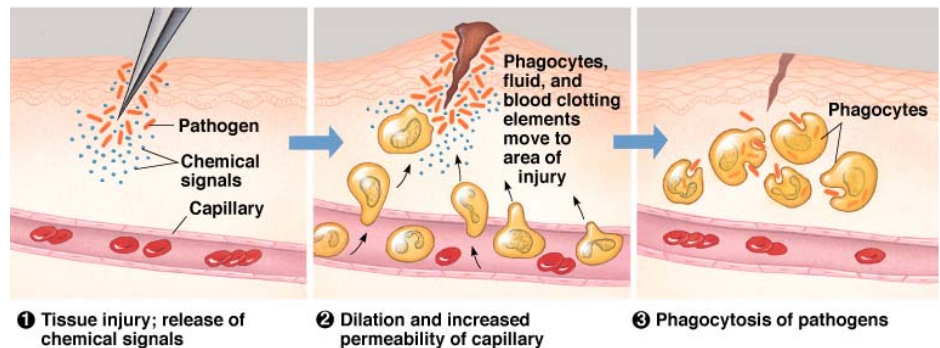
- (1) Secreted by infected cells, stimulate neighboring cells to produce antiviral proteins to inhibit growth of virus
- (2) Active only against viruses.
- (3) Recombinant DNA technology used to make synthetic forms in hope of slowing cancer growth.

ii) **Complement System**

- (1) Attract phagocytes; found in plasma (component of plasma protein)
- (2) Triggered by antibodies bound to antigen. Complement proteins form pore in bacteria.

d) Inflammation

- i) Cells release histamine causing dilation of vessels.
- ii) Increased blood supply due to dilation causes **redness and warmth**.
- iii) **Swelling** (edema) of affected area caused by fluid loss from vessels.



©1999 Addison Wesley Longman, Inc.

AP BIOLOGY. UNIT 14.

Vessels become more permeable/leaky (caused by histamines)

- iv) Increased blood flow brings larger numbers of phagocytes to infected area.
- v) **Fever**: widespread inflammatory response. **Pyrogens** (released from wbc's) reset thermostat in hypothalamus. Fever interferes with viral activity.

2) VERTEBRATE SPECIFIC DEFENSE

- When non-specific defense mechanisms are unable to prevent infection, the immune defense system is activated.
- Product of immune system. **Exhibits specificity, diversity, self/non-self recognition and memory.**
- May require several days to become fully activated. The immune system deploys cellular and chemical weapons. Extremely powerful.
- Two main types of immunity are cell-mediated immunity (lymphocytes attack the invading pathogen) and antibody-mediated immunity (lymphocytes produce antibodies to destroy pathogens)
 - a) **Specificity.**
 - i) Response is not random. Recognize and eliminate particular microorganisms and pathogens.
 - ii) Body responds to **antigen** (substance that initiates response [capsule, cell wall, toxin]; unique molecular shape conferred by surface proteins) by releasing **Antibody** (protein produced by B-cells that bind to antigens)
 - b) **Diversity.**
 - i) Antibody amino acid sequence on variable region constantly modified.
 - c) **Self/Non-self Recognition.**
 - i) Blood groups, tissue grafts and organ transplants, autoimmune disorders.
 - ii) Major histocompatibility complex (MHC). Proteins embedded in plasma membranes.
 - d) **Memory.**
 - i) Memory cells survive in system for long period of time. Activated during secondary immune response.

THE IMMUNE SYSTEM RESPONDS IN THREE ESSENTIAL STEPS:

- I. **Recognition of Invader** (*Caught on the Radar!*)
- II. **Activation of System** (*Man your Battle Stations!*)
- III. **Response to Invader** (*Fire all Weapons!*)

IMMUNE SYSTEM AND IMMUNITY

The immune system is more effective than the nonspecific methods, and has a memory component that improves response time when an invader of the same type (or species) is again encountered. Immunity that an individual obtains can be conferred actively or passively.

1) ACTIVE IMMUNITY:

- a) Individual is infected and forms a defense against pathogen by mounting either a *humoral response* (antibody formation) or a *cell-mediated response* (lymphocytes)
- b) **Vaccinations** {Jenner} (weakened forms of pathogen, toxin) stimulate antibody production and formation of memory cells without causing the disease. Vaccines are made from killed pathogens or weakened strains that cause antibody production but not the disease.

AP BIOLOGY. UNIT 14.

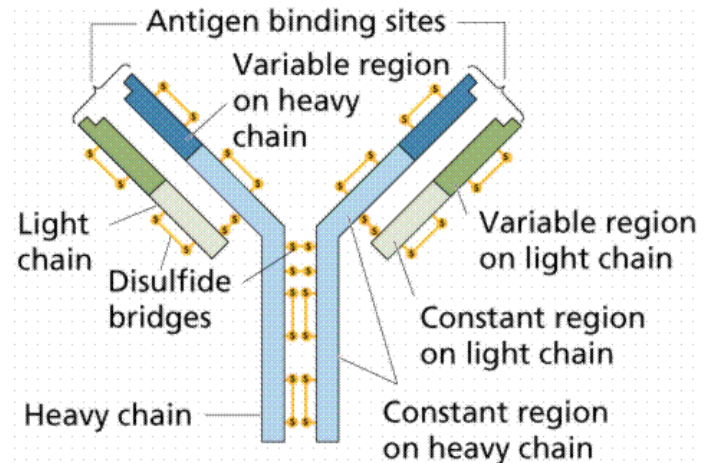
2) PASSIVE IMMUNITY:

- Transferred from one individual to another (mother to baby). Antibodies transferred in colostrum of nursing mothers.
- Antibodies can be given to adults as well.
- Temporary, jump-start to immunity. Work long enough to prevent infection.

Once the immune system has been activated (actively or passively) the response can be the formation of antibodies (humoral) or lymphocytes (cell-mediated).

1) Humoral Response

- Antibodies are Y-shaped protein molecules composed of two identical long polypeptide (Heavy or H chains) and two identical short polypeptides (Light or L chains).
 - Function of antibodies includes:
 - Recognition and binding to antigens
 - Inactivation of the antigen
- Regulated by **B-cells**. B cells form and develop from stem cells in marrow.
 - Concentrated in lymph nodes, spleen. [*Spleen* is the largest lymphatic structure. It is responsible for the production of B cells, phagocytizes bacteria and worn out/damaged r.b.c.'s, stores and releases blood in case of demand (i.e. hemorrhage)]
 - Have antigen receptors on membrane to recognize specific pathogen. Can only bind to one type of antigen.
- Other cells in immune system that have also met up with same pathogen secrete chemicals that stimulate B cells to form **Plasma Cells**.
 - Plasma cell secretes antibodies specific for antigen. (*about 2000 molecules/sec!*)
- B-memory cells** also formed that provide immunological memory (live for months or years). Become activated only during second infection by pathogen presenting proper antigens. Once activated produce a new batch of plasma cells to create new antibodies. Part of secondary immune response. Much more rapid and aggressive attack on pathogen.



Antibodies bind to antigen forming antigen-antibody complex that identifies it for destruction using:

- Neutralization:*** antibodies completely surround pathogen and bind up attachment sites. Renders the pathogen useless.
- Agglutination:*** common for bacteria pathogens. More than one bacteria and antibody form clumps due to cross-linking of antibodies. Easier for macrophages to seek and destroy.
- Activation:*** uses complement proteins (non-specific defense) forming membrane-attack complex (MAC) that embeds itself into the plasma membrane of the attacker. Salts enter the invader, facilitating water to cross the membrane, swelling and bursting the microbe.

AP BIOLOGY. UNIT 14.

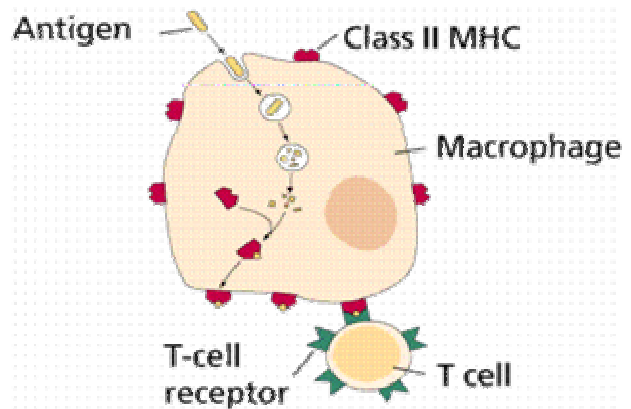
2) Cell mediated response

- ☒ **Lymphocytes** respond to an antigen.
- ☒ Work in concert with macrophages that have engulfed pathogen. Surface of macrophage bears signals (self vs. non-self) that are recognized by lymphocytes.
- ☒ T lymphocytes (T-cells) form from pluripotent stem cells, develop in thymus.
- ☒ Cells only activated by cells previously infected with an antigen [**Cell-to-Cell Combat**]. Cannot recognize free-floating antigens in body fluids (unlike antibodies). Once activated T-cells become specialized forms called helper T (T_H) or killer/cytotoxic T (T_C).
- ☒ Helper T cells activate B cells that produce antibodies. Cytotoxic (or killer) T cells destroy body cells infected with a virus or bacteria. Memory T cells remain in the body awaiting the reintroduction of the antigen.

1) How are T cells activated?

a) Helper T Cell Activation.

- i) Virus particles that have been engulfed by macrophages (non-specific) have their antigenic determinates present on the surface of the macrophage. The macrophage is called an antigen-presenting cell (APC).
- ii) This combination of *self and non-self* is detected by the inactive helper cell at the Class II MHC. T_H cells also have CD-4 molecule to enhance binding. This is the molecule that HIV seeks out. HIV has a glycoprotein on its surface to recognize the CD4 glycoprotein.
- iii) Once APC=Helper T Cell binding has occurred, changes in the T_H cell occur.
- iv) Interleukins (I-2) are released that stimulate growth and division, forming more T_H cells.



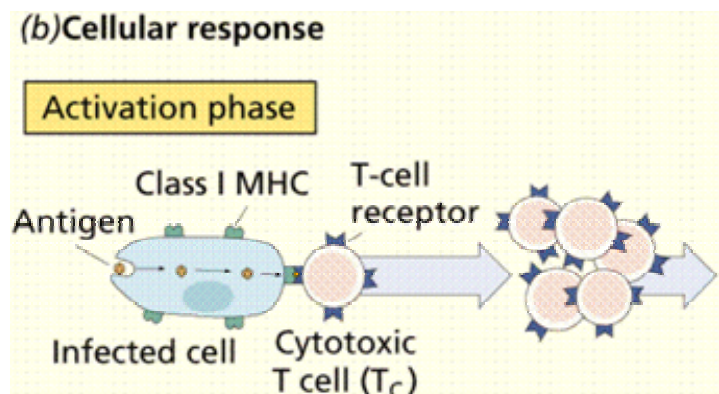
Macrophages can have many antigenic determinants on their surface (Allows for nonspecificity)

- b) T_H cells are also involved in the activation of B cells and the formation of plasma cells and memory B cells. Inactive B cells with the same antigen on its surface (at MHC II) bind to T_H cells. Clones of helper T's are formed. Chemicals secreted by the Helper T stimulate B cells to do their thing!

B Cells may have only one antigenic determinant on their surface

b) Cytotoxic T Cell Activation.

- i) A cell infected with a virus will display viral antigens on its plasma membrane (part of class I MHC). Since Killer T's bind to class I MHC, they can bind to any cell in body bearing appropriate antigen complex.



AP BIOLOGY. UNIT 14.

- ii) Killer T cells recognize the viral antigen and attach to that cell's plasma membrane.
- iii) The T cells secrete proteins (**perforin**) that punch holes in the infected cell's plasma membrane. The infected cell's cytoplasm leaks out, the cell dies, and is removed by phagocytes. Also, secrete chemicals to inhibit replication of virus, destroy DNA
- iv) Killer T cells may also bind to cells of transplanted organs causing transplant rejection or cells that are cancerous.

Flow of Defense:

Pathogen invades body → macrophage phagocytizes pathogen → foreign antigen-MHC complex (class I) displayed on macrophage cell surface → cytotoxic T cell activated by specific foreign antigen-MHC complex (self/non-self) → clone of cytotoxic T cells, memory cells, lymphokines produced → activated cytotoxic T cells migrate to area of infection (leave lymph node) → T cells release chemicals (perforin) to destroy target cell → cytotoxic T seeks out more infected cells

Secondary Immune response

- Memory cells that are formed remain in lymph node until same antigen is encountered.
- Once body infected with antigen, memory cells become activated, producing a rapid response; more antigens are produced, decline of antibodies is slower (longer-lasting).
- Requires less antigen than primary response.
- Reason why we do not usually suffer from same disease more than once.

Autoimmune Diseases:

Under normal conditions the body's immune system functions to recognize its own tissues and chemicals. It normally does not produce T cells or B cells against its own substances. At times, however, our immune system fails to recognize these materials as "self", this leads to an autoimmune disease. The immune system recognizes changes in certain tissues, causing them to be recognized as foreign antigens. Examples of such diseases includes *Type I diabetes, lupus, rheumatoid arthritis and multiple sclerosis.*