

Chapter 22 The Immune System



- Wisdom of the body: distinguish self from non-self
 - Each human is biologically unique.
 - Proteins embedded in membrane of body cells are recognized as self.
 - Any other cell enters the body without this protein is non-self and is destroyed.
 - Foreign proteins = antigens (“antibody generator”)
 - Immune system uses antigens as a point of attack.

NONSPECIFIC RESISTANCE: INNATE DEFENSES

First Line of Defense: Skin and Mucous Membranes

- *Nonspecific resistance* refers to a wide variety of body responses against a wide range of pathogens (disease producing organisms) and their toxins.
- *Mechanical protection* includes the intact epidermis layer of the skin (Figure 5.1), mucous membranes, the lacrimal apparatus, saliva, mucus, cilia, the epiglottis, and the flow of urine. Defecation and vomiting also may be considered mechanical processes that expel microbes.
- *Chemical protection* is localized on the skin, in loose connective tissue, stomach, and vagina.
- The skin produces *sebum*, which has a low pH due to the presence of unsaturated fatty acids and lactic acid.
- *Lysozyme* is an enzyme component of sweat that also has antimicrobial properties.
- *Gastric juice* renders the stomach nearly sterile because its low pH (1.5-3.0) kills many bacteria and destroys most of their toxins; *vaginal secretions* also are slightly acidic.

Second Line of Defense: Internal Defenses

- The *second line of defense* involves internal antimicrobial proteins, phagocytic and natural killer cells, inflammation, and fever.

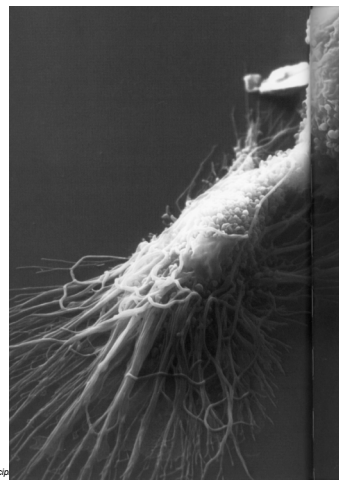
Internal Defenses

- Antimicrobial proteins discourage microbial growth
 - Interferons
 - Causes other cells to produce antiviral proteins (stops replication of viruses)
 - Can stimulate NK cells to attack virus-infected cells.
 - Use in treating diseases (Hep C)
 - complement proteins (“complement” the immune response)
 - Punch holes in membranes of bacteria
 - Cause mast cells to release histamines
 - Attract phagocytes to the site
 - Adhere to microbes and then attach to phagocytes (opsonization)

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Phagocytes



Princip

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Phagocytes

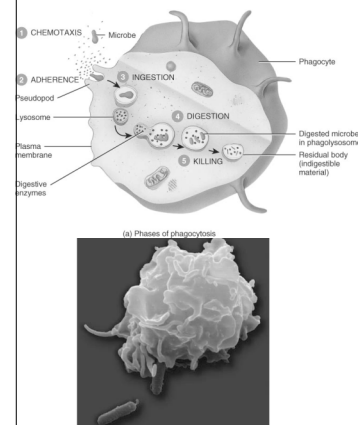
Phagocytes (neutrophils & macrophages)

- ingest microbes or particulate matter
- macrophages developed from monocytes
 - fixed macrophages stand guard in specific tissues
 - histiocytes in the skin, kupffer cells in the liver, alveolar macrophages in the lungs, microglia in the brain & macrophages in spleen, red marrow & lymph nodes
 - wandering macrophages in most tissue

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Phagocytosis



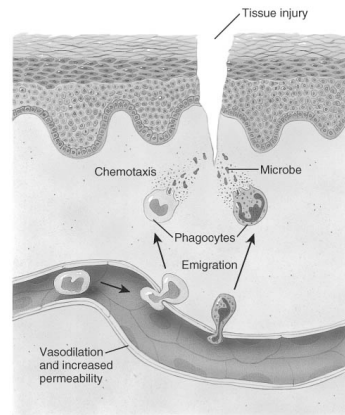
(a) Phagocyte (white blood cell) engulfing a microbe. Principles of human anatomy and physiology, 11e

- Chemotaxis
 - attraction to chemicals from damaged tissues, complement proteins, or microbial products
- Adherence
 - attachment to plasma membrane of phagocyte
- Ingestion
 - engulf by pseudopods to form phagosome
- Digestion & killing
 - merge with lysosome containing digestive enzymes & hydrogen peroxide
 - exocytosis residual body

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Inflammation

- Damaged cell initiates
- Signs of inflammation
 - redness
 - heat
 - swelling
 - pain
 - *Loss of function* may be a fifth symptom, depending on the site and extent of the injury.
- Function is to trap microbes, toxins or foreign material & begin tissue repair



Phagocytes migrate from blood to site of tissue injury

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Stages of Inflammation

- Vasodilation & increased permeability of vessels
 - caused by histamine from mast cells, kinins from precursors in the blood, prostaglandins from damaged cells, and leukotrienes from basophils & mast cells
 - occurs within minutes producing heat, redness & edema
 - pain can result from injury, pressure from edema or irritation by toxic chemicals from organisms
 - blood-clotting factors leak into tissues trapping microbes
- Phagocyte emigration
 - within an hour, neutrophils and then monocytes arrive and leave blood stream (emigration)
- Tissue repair

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Abscesses and Ulcers

- Pus is dead phagocytes, damaged tissue cells & fluid
- Abscess is accumulation of pus in a confined space not open to the outside
 - pimples & boils
- Ulcer is an open sore
- People with poor circulation (diabetics with advanced atherosclerosis)
 - stasis ulcers in tissues of legs due to poor oxygen & nutrient supply to tissues

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Fever

- Abnormally high body temperature that occurs because the hypothalamic thermostat is reset
- Occurs during infection & inflammation
- Benefits
 - intensifies effects of interferons, inhibits bacterial growth, speeds up tissue repair
 - Reduces amount of iron in circulation.

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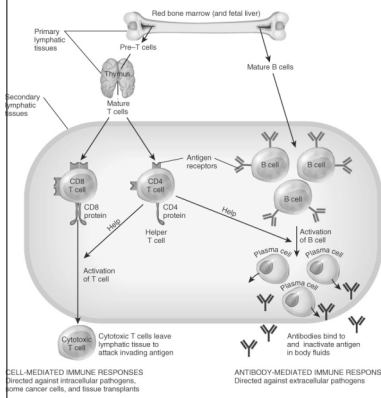
Review

- Table 22.1 summarizes the components of nonspecific resistance.

SPECIFIC RESISTANCE: IMMUNITY

- *Immunity* is the ability of the body to defend itself against specific invading agents.
 - bacteria, toxins, viruses, cat dander, etc.
- Differs from nonspecific defense mechanisms
 - specificity----recognize self & non-self
 - memory----2nd encounter produces even more vigorous response
- *Antigens* are substances recognized as foreign by the immune responses.

Maturation of T and B Cells



T cell mature in thymus

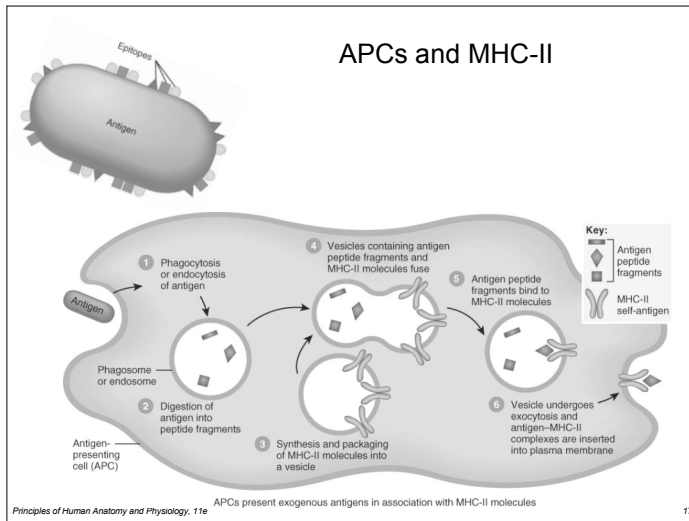
- cell-mediated response
 - killer cells attack antigens
 - helper cells costimulate T and B cells
- effective against fungi, viruses, parasites, cancer, and tissue transplants

B cells in bone marrow

- antibody-mediated response
 - plasma cells form antibodies
- effective against bacteria

Types of Immune Response

- *Cell-mediated immunity* (CMI) refers to destruction of antigens by T cells.
 - particularly effective against intracellular pathogens, such as fungi, parasites, and viruses; some cancer cells; and foreign tissue transplants.
 - CMI always involves cells attacking cells.
- *Antibody-mediated (humoral) immunity* (AMI) refers to destruction of antigens by antibodies.
 - works mainly against antigens dissolved in body fluids and extracellular pathogens, primarily bacteria, that multiply in body fluids but rarely enter body cells.
- Often a pathogen provokes both types of immune response.



- ### Antigens
- Molecules or bits of foreign material
 - entire microbes, parts of microbes, bacterial toxins, pollen, transplanted organs, incompatible blood cells
 - Required characteristics to be considered an antigen
 - immunogenicity = ability to provoke immune response
 - reactivity = ability to react to cells or antibodies it caused to be formed
 - Get past the bodies nonspecific defenses
 - enter the bloodstream to be deposited in spleen
 - penetrate the skin & end up in lymph nodes
 - penetrate mucous membrane & lodge in associated lymphoid tissue
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- ### Diversity of Antigen Receptors
- Immune system can recognize and respond to a billion different epitopes -- even artificially made molecules
 - Explanation for great diversity of receptors is genetic recombination of few hundred small gene segments
 - Each B or T cell has its own unique set of gene segments that codes its unique antigen receptor in the cell membrane
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- ### Pathways of Antigen Processing
- B and T cells must recognize a foreign antigen before beginning their immune response
 - B cells can bind to antigen in extracellular fluid
 - T cells can only recognize fragments of antigens that have been processed and presented to them as part of a MHC molecule
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Processing of Endogenous Antigens

- Endogenous antigens are synthesized within the body and include viral proteins or proteins produced by cancer cells
- Most of the cells of the body can process endogenous antigens
- The antigen complex moves to the cell's surface where it alerts T cells.

CELL-MEDIATED IMMUNITY

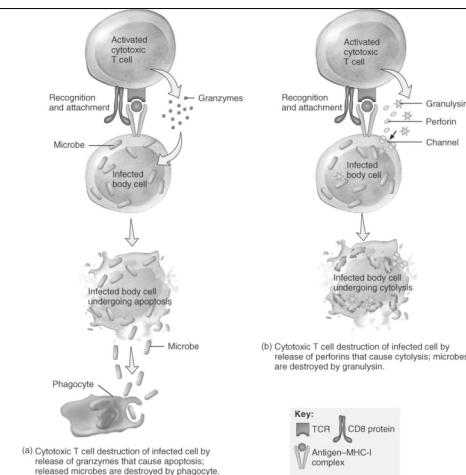
- Begins with activation of T cell by a specific antigen
- Result is T cell capable of an immune attack
 - elimination of the intruder by a direct attack
- Move out and directly attack the offending pathogens.

Overview of Mature T Cells

1. *Helper T (T_H) cells,*
2. *Cytotoxic T (T_C) cells,*
3. *Memory T cells* are programmed to recognize the original invading antigen, allowing initiation of a much swifter reaction should the pathogen invade the body at a later date.
4. *Suppressor T cells:* inhibit cytotoxic and helper T cells.
5. *Delayed hypersensitivity T cells:* key factor in delayed allergic response and transplant rejection.
6. *Amplifier T cells:* stimulate T and B cells to higher activity.

Elimination of Invaders

- Cytotoxic T cells migrate to site of infection or tumor formation
- Recognize, attach & attack
- Effective for virus infected cells, some tumors.



Immunological Surveillance

- Cancerous cell displays unusual surface antigens (tumor antigens)
- Surveillance = immune system finds, recognizes & destroys cells with tumor antigens
 - done by cytotoxic T cells, macrophages & natural killer cells
 - most effective in finding tumors caused by viruses
- Transplant patients taking immunosuppressive drugs suffer most from viral-induced cancers

Antibody-Mediated Immunity

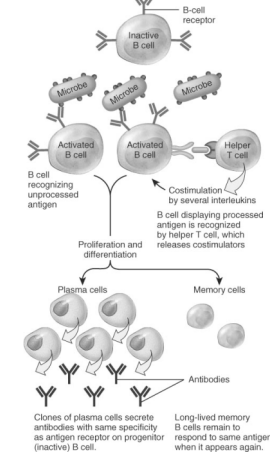
- The body contains not only millions of different T cells but also millions of different *B cells*, each capable of responding to a specific antigen.
- B cells sit still and let antigens be brought to them
 - stay put in lymph nodes, spleen or peyer's patches
- Once activated, differentiate into plasma cells that secrete antibodies
- Antibodies circulate in lymph and blood
 - combines with epitope on antigen similarly to key fits a specific lock

Activation, Proliferation, and Differentiation of B Cells

- During activation of a B cell, an antigen binds to antigen receptors on the cell surface (Figure 22.16).
- B cell antigen receptors are chemically similar to the antibodies that will eventually be secreted by their progeny.
- Some antigen is taken into the B cell, broken down into peptide fragments and combined with the MHC-II self-antigen, and moved to the B cell surface.
- Helper T cells recognize the antigen-MHC-II combination and deliver the costimulation needed for B cell proliferation and differentiation.
- Some activated B cells become antibody-secretion plasma cells. Others become memory B cells.

Activation, Proliferation, & Differentiation of B Cells

- B cell receptors bind to antigen -- response more intense if on APC
- Helper T cell costimulates
- Rapid cell division & differentiation occurs
 - long-lived memory cells
 - clone of plasma cells
 - produce antibody at 2000 molecules/sec for 4-5 days
 - secrete only one kind antibody
- Antibody enters the circulation to attack antigen



Antibody Structure

Based on chemistry and structure, antibodies are grouped into five principal classes each with specific biological roles.

IgG: 75%; works against blood-borne antigens.

IgM: stimulates macrophages and activates complement system.

IgA: found in body secretions and works against inhaled or ingested antigens.

IgD: Unknown function.

IgE: Mediates allergic reactions. Specialized for parasites.

Antibody Actions

- Neutralization of antigen by blocking effects of toxins or preventing its attachment to body cells
- Immobilize bacteria by attacking cilia/flagella
- Agglutinate & precipitate antigens by cross-linking them causing clumping & precipitation
- Complement activation which releases proteins to digest the pathogen, coat it, or increase the inflammation response.

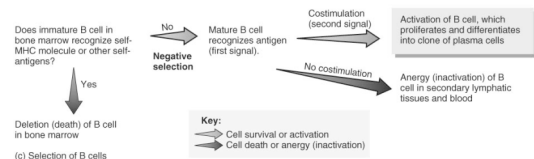
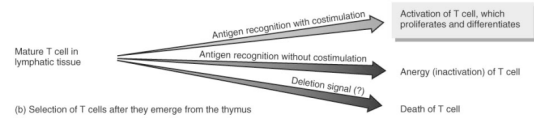
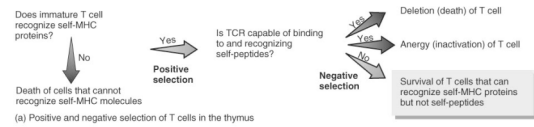
Active v. Passive Immunity

- Active: immunity developed naturally or artificially through immunization.
 - Body actively produces its own antibodies
 - Memory cells are created
 - Can last for years (vaccines) or a lifetime
- Passive: antibodies produced outside of the body and introduced orally or through an injection.
 - No memory cells
 - Only lasts a few months
 - Placenta or breast feeding.

Clinical Application

- Monoclonal antibodies are important in measuring levels of a drug in a patient's blood
- Diagnosis of pregnancy, allergies, and diseases such as hepatitis, rabies, and some sexually transmitted diseases.
- They have also been used in early detection of cancer and assessment of extent of metastasis.
- They may be useful in preparing vaccines to counteract transplant rejection, to treat autoimmune diseases, and perhaps to treat AIDS.

Development of Self-Recognition & Immunological Tolerance



Aging

- With advancing age, the immune system functions less effectively.
- Individuals become more susceptible to infections and malignancies
- Response to vaccines is decreased
- Produce more autoantibodies
- Reduced immune system function
 - T cells less responsive to antigens
 - age-related atrophy of thymus
 - decreased production of thymic hormones
- B cells less responsive
 - production of antibodies is slowed

AIDS: Acquired Immunodeficiency Syndrome

- *AIDS* is a condition in which a person experiences a telltale assortment of infections as a result of the progressive destruction of immune cells by the *human immunodeficiency virus (HIV)*.

HIV

- HIV enters T cells where it sheds its protein coat.
- New HIV DNA is produced in the T cell along with new protein coats and then released.
- The T cells are ultimately destroyed.
- Common signs and symptoms of infection are fever, fatigue, rash, headache, joint pain, sore throat, and swollen lymph nodes. The infected individual ultimately develops antibodies to HIV.
- Progression to AIDS occurs because of reduced numbers of T cells and resulting immunodeficiency. AIDS lowers the body's immunity by decreasing the number of helper T cells; the result is progressive collapse of the immune system, making the person susceptible to opportunistic infections (invasion of normally harmless microorganisms that now proliferate wildly because of the defective immune system).

Hypersensitivity Reactions

- A person who is overly reactive to a substance that is tolerated by most others is said to be *hypersensitive* (*allergic*). Whenever an allergic reaction occurs, there is tissue injury. The antigens that induce an allergic reaction are called *allergens*.
- Allergens can be pollens, foods, drugs, venoms, cosmetics, dust, mold, antibiotics, etc.
- Anaphylaxis can be fatal.
- Poor self-knowledge?

Auto-Immune Disease

- In an *autoimmune disease* the immune system fails to display self-tolerance and attacks the person's own tissue.
- Diseases include:
 - Rheumatoid arthritis, multiple sclerosis, myasthenia gravis, lupu, type II diabetes, mononucleosis, rheumatic fever.

Transplant Rejections

- When tissue is transplanted from another person, the host immune system recognizes it as "non-self" and activates immune response against it.
- Drugs and x-rays are used to destroy host's T-cells to prevent the immune response.
 - Cyclosporine halts early T-cell activation.
- This suppression of the immune system can make person more susceptible to other pathogens and cancer growth.
- Three areas of the body that accept foreign tissues:
 - Brain
 - Cornea
 - Uterus

Severe Combined Immunodeficiency Disease

- No B or T cells at all.
- Clinical presentation of SCID includes recurrent severe infection, failure to thrive, developmental delay, or absence of lymphadenopathy (or tonsillar tissue) despite serious infections.
- Treatment with bone marrow transplant, gene therapy and immunoglobulin replacement therapy.