Adaptive Defense System: Third Line of Defense

- Immune response is the immune system’s response to a threat
- Immunology is the study of immunity
- Antibodies are proteins that protect from pathogens

Three aspects of adaptive defense
- Antigen-specific—recognizes and acts against particular foreign substances
- Systemic—not restricted to the initial infection site
- Memory—recognizes and mounts a stronger attack on previously encountered pathogens

Types of Immunity
- Humoral immunity = antibody-mediated immunity
  - Provided by antibodies present in body fluids
- Cellular immunity = cell-mediated immunity
  - Targets virus-infected cells, cancer cells, and cells of foreign grafts

Antigens (nonself)
- Any substance capable of exciting the immune system and provoking an immune response
- Examples of common antigens
  - Foreign proteins (strongest)
  - Nucleic acids
  - Large carbohydrates
  - Some lipids
  - Pollen grains
  - Microorganisms
Adaptive Defense System: Third Line of Defense

- Self-antigens
  - Human cells have many surface proteins
  - These along form the major histocompatibility complex (MHC)
  - Our immune cells do not attack our own proteins
  - Our cells in another person’s body can trigger an immune response because they are foreign
  - Restricts donors for transplants

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Adaptive Defense System: Third Line of Defense

- Allergies
  - Delayed hypersensitivity
    - Many small molecules (called haptens or incomplete antigens) are not antigenic, but link up with our own proteins
    - Poison ivy
    - The immune system may recognize and respond to a protein-hapten combination
    - The immune response is harmful rather than protective because it attacks our own cells

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Adaptive Defense System: Third Line of Defense

- Immediate hypersensitivity
  - Non hapten. The antigen itself triggers immune response.
  - Pollen allergies
  - Body has developed antibodies against an irritant
    - Severe reactions can lead to anaphylactic shock
      - Intense severe swelling of tissues
      - Closure of airways

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Adaptive Defense System: Third Line of Defense

- Cells of the adaptive defense system
  - Lymphocytes respond to specific antigens
    - B lymphocytes (B cells)
    - T lymphocytes (T cells)
  - Macrophages help lymphocytes

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Adaptive Defense System: Third Line of Defense

- Immunocompetent—cell becomes capable of responding to a specific antigen by binding to it
- Cells of the adaptive defense system
  - Lymphocytes
    - Originates from hemocytoblasts in the red bone marrow
    - B lymphocytes become immunocompetent in the bone marrow (remember B for Bone marrow)
    - T lymphocytes become immunocompetent in the thymus (remember T for Thymus)
Cells of the adaptive defense system (continued)

A second exposure causes a rapid response

Arise from monocytes

Secrete cytokines (proteins important in the immune response)

Most B cells become plasma cells

A large number of clones are produced (primary humoral response)

Macrophages

- Arise from monocytes
- Become widely distributed in lymphoid organs
- Secrete cytokines (proteins important in the immune response)
- Tend to remain fixed in the lymphoid organs

Adaptive Defense System: Third Line of Defense

Humoral (Antibody-Mediated) Immune Response

- B lymphocytes with specific receptors bind to a specific antigen
- The binding event activates the lymphocyte to undergo clonal selection
- A large number of clones are produced (primary humoral response)

Humoral Immune Response

- Most B cells become plasma cells
  - Produce antibodies to destroy antigens
  - Activity lasts for 4 or 5 days
  - Some B cells become long-lived memory cells (secondary humoral response)

Secondary humoral responses

- Memory cells are long-lived
- A second exposure causes a rapid response
- The secondary response is stronger and longer lasting
Humoral Immune Response

Primary Response
- Initial encounter with antigen
- Antigen binding to a receptor on a specific B cell (lymphocyte)
- B cells with non-complementary receptors remain inactive
- Proliferation to form a clone of B lymphoblasts
- Plasma cells
- Secreted antibody molecules

Secondary Response
- Can be years later
- Memory B cells
- Plasma cells
- Secreted antibody molecules

Humoral Immune Response

Active Immunity
- Occurs when B cells encounter antigens and produce antibodies
- Active immunity can be:
  - Naturally acquired during bacterial and viral infections
  - Artificially acquired from vaccines

Passive Immunity
- Occurs when antibodies are obtained from someone else:
  - Conferred naturally from a mother to her fetus (naturally acquired)
  - Conferred artificially from immune serum or gamma globulin (artificially acquired)
- Immunological memory does not occur
- Protection provided by “borrowed antibodies”

Passive Immunity
- Monoclonal antibodies:
  - Antibodies prepared for clinical testing or diagnostic services
  - Produced from descendents of a single cell line
  - Examples of uses for monoclonal antibodies:
    - Diagnosis of pregnancy
    - Treatment after exposure to hepatitis and rabies
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Types of Acquired Immunity

Naturally acquired
- Active infection: contact with pathogen

Antibodies
- Passive
  - Antibodies pass from mother to fetus via placenta or to infant in her milk
  - Vaccine: dead or attenuated pathogens
  - Passive injection of immune serum (gamma globulin)

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Antibodies (Immunoglobulins or Igs)

- Soluble proteins secreted by B cells (plasma cells)
- Carried in blood plasma
- Capable of binding specifically to an antigen

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Antibodies (Immunoglobulins or Igs)

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Antibodies

- Antibody structure
  - Four amino acid chains linked by disulfide bonds
  - Two identical amino acid chains are linked to form a heavy chain
  - The other two identical chains are light chains
  - Specific antigen-binding sites are present

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Antibody Structure
Antibodies

- Antibody classes
  - Antibodies of each class have slightly different roles
  - Five major immunoglobulin classes (MADGE)
    - IgM—can fix complement
    - IgA—found mainly in mucus
    - IgD—important in activation of B cell
    - IgG—can cross the placental barrier and fix complement
    - IgE—involved in allergies

Immunoglobin Classes

Antibodies

- Antibody function
  - Antibodies inactivate antigens in a number of ways
    - Complement fixation
    - Neutralization
    - Agglutination
    - Precipitation

Cellular (Cell-Mediated) Immune Response

- Antigens must be presented by macrophages to an immunocompetent T cell (antigen presentation)
- T cells must recognize nonself and self (double recognition)
- After antigen binding, clones form as with B cells, but different classes of cells are produced
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Cellular (Cell-Mediated) Immune Response

- Macrophage
- Antigen
- "Presented" antigen
- T cell antigen receptor
- Cytosine
- B cell
- Helper T cell
- Helper T cell receptor

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Cellular (Cell-Mediated) Immune Response

- T cell clones
  - Cytotoxic (killer) T cells
    - Specialize in killing infected cells
    - Insert a toxic chemical (perforin)
  - Helper T cells
    - Recruit other cells to fight the invaders
    - Interact directly with B cells

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Cellular (Cell-Mediated) Immune Response

Helper T Cells

Cytotoxic T Cells

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Cellular (Cell-Mediated) Immune Response

- T cell clones (continued)
  - Regulatory T cells
    - Release chemicals to suppress the activity of T and B cells
    - Stop the immune response to prevent uncontrolled activity
  - A few members of each clone are memory cells

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Functions of Cells and Molecules Involved in Immunity

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helper T cell</td>
<td>Recruit other cells to fight the invaders</td>
</tr>
<tr>
<td>Cytotoxic T cell</td>
<td>Specialize in killing infected cells</td>
</tr>
<tr>
<td>Regulatory T cell</td>
<td>Release chemicals to suppress the activity of T and B cells</td>
</tr>
<tr>
<td>Memory cell</td>
<td>A few members of each clone are memory cells</td>
</tr>
</tbody>
</table>
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Functions of Cells and Molecules Involved in Immunity

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Summary of Adaptive Immune Response

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Summary of Adaptive Immune Response

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Summary of Adaptive Immune Response

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Organ Transplants and Rejection

- Major types of grafts
  - Autografts—tissue transplanted from one site to another on the same person
  - Isografts—tissue grafts from an identical person (identical twin)
  - Allografts—tissue taken from an unrelated person
  - Xenografts—tissue taken from a different animal species
Organ Transplants and Rejection

- Autografts and isografts are ideal donors
- Xenografts are never successful
- Allografts are more successful with a closer tissue match

Disorders of Immunity: Allergies (Hypersensitivity)

- Abnormal, vigorous immune responses
- Types of allergies
  - Immediate hypersensitivity
    - Triggered by release of histamine from IgE binding to mast cells
    - Reactions begin within seconds of contact with allergen
    - Anaphylactic shock—dangerous, systemic response
  - Delayed hypersensitivity
    - Triggered by the release of lymphokines from activated helper T cells
    - Symptoms usually appear 1–3 days after contact with antigen

Allergy Mechanisms

1. Antigen (allergen) binds to IgE
2. Plasma cells produce large amounts of IgE antibodies against antigen
3. IgE activates when it binds to mast cells in body, triggering histamine release
Disorders of Immunity: Immunodeficiencies
- Production or function of immune cells or complement is abnormal
- May be congenital or acquired
- Includes AIDS (Acquired Immune Deficiency Syndrome)

Disorders of Immunity: Autoimmune Diseases
- The immune system does not distinguish between self and nonself
- The body produces antibodies and sensitized T lymphocytes that attack its own tissues

Examples of autoimmune diseases
- Multiple sclerosis—white matter of brain and spinal cord are destroyed
- Myasthenia gravis—impairs communication between nerves and skeletal muscles
- Type 1 diabetes mellitus—destroys pancreatic beta cells that produce insulin
Disorders of Immunity:
Autoimmune Diseases
- Examples of autoimmune diseases
  - Rheumatoid arthritis—destroys joints
  - Systemic lupus erythematosus (SLE)
    - Affects kidney, heart, lung and skin
  - Glomerulonephritis—impairment of renal function

Self Tolerance Breakdown
- Inefficient lymphocyte programming
- Appearance of self-proteins in the circulation that have not been exposed to the immune system
  - Eggs
  - Sperm
  - Eye lens
  - Proteins in the thyroid gland

Self Tolerance Breakdown
- Cross-reaction of antibodies produced against foreign antigens with self-antigens
  - Rheumatic fever

Developmental Aspects of the Lymphatic System and Body Defenses
- Except for thymus and spleen, the lymphoid organs are poorly developed before birth
- A newborn has no functioning lymphocytes at birth, only passive immunity from the mother
- If lymphatics are removed or lost, severe edema results, but vessels grow back in time