Chapter 4
Immunity, Hypersensitivity, Allergy, and Autoimmune Diseases

Learning Objectives (1 of 2)
• Differentiate cell-mediated versus humoral immunity
• Compare immunity and hypersensitivity
• List and differentiate five classes of antibodies

Learning Objectives (2 of 2)
• Hypersensitivity reaction
  – Describe pathogenesis
  – Role of IgA in allergy
  – Methods of treatment
• Autoimmune diseases
  – Summarize theories of pathogenesis
  – Clinical manifestations
  – Methods of treatment

The Body’s Defense Mechanisms (1 of 2)
• Two separate mechanisms function together to protect us from disease
  – Inflammatory reaction: nonspecific response, phagocytosis of material by neutrophils and macrophages
  – Acquired immunity: develops after contact with pathogenic microorganism; depends on immune system; associated with stage of altered reactivity to foreign material (hypersensitivity)

The Body’s Defense Mechanisms (2 of 2)
• Two types of acquired immunity
  – Humoral immunity
    • Production of antibodies
    • Main defense against bacteria and bacterial toxins
  – Cell-mediated immunity
    • Formation of a population of lymphocytes that attack and destroy foreign material
    • Main defense against viruses, fungi, parasites, and some bacteria
    • Mechanism by which the body rejects transplanted organs
    • Means of eliminating abnormal cells that arise spontaneously in cell division

Hypersensitivity
• An individual who displays hypersensitivity to an organism or its products usually possesses some degree of immunity as well
• Many diseases are associated with the development of an acquired immunity without demonstrable hypersensitivity
• Normally, a person develops an immune response only against foreign antigens (non-self antigens) because the body has developed a tolerance to self antigens present in an individual’s cells and tissues
Autoantibodies

• In autoimmune diseases, a patient forms antibodies against his or her own cells and tissues (autoantibodies).
• These antibodies may injure or destroy the patient’s cells or tissue components.

Acquired Immunity: Role of Lymphocytes

• Respond to foreign antigens
  – Cytokines: general term for chemical messengers involved in the immune process
  – Lymphokines: soluble proteins secreted by lymphokines that act as chemical messengers to exert their effects and to communicate with various cells of the immune system
  – Interferon: interferes with the multiplication of viruses within the cell
  – Interleukin: sends regulatory signals between cells of the immune system
  – Tumor necrosis factor: destroys foreign or abnormal cells and tumor cells.

Lymphatic System (1 of 3)

• Precursor cells are formed initially from stem cells in the bone marrow, eventually developing into either of two groups:
  – T lymphocyte, thymus-dependent: Precursor cells that migrated from the marrow to the thymus
  – B lymphocyte, bone marrow: Precursor cells that remained within the bone marrow
• T and B cells need time to be activated and function effectively
• Natural killer cells: can destroy target cells as soon as they are encountered.

Lymphatic System (2 of 3)

• Before birth, precursor cells of T and B lymphocytes migrate into spleen, lymph nodes, and other sites to proliferate and form masses of mature lymphocytes that will populate the various lymphoid organs
• Lymphocytes vary in lifespan
• Lymphocytes do not remain localized within lymphoid organs but circulate between bloodstream and lymphoid tissues
  – T lymphocytes = 2/3 of circulating lymphocytes
  – B lymphocytes = rest of circulating lymphocytes
  – Natural killer cells = 10%–15%; have neither T or B lymphocyte receptors; major targets are virus-infected cells and cancer cells

Lymphatic System (3 of 3)

• Each programmed lymphocyte develops antigen receptors on its cell membranes, allowing it to “recognize” and respond to a specific antigen
• Programming process allows T and B cells to be programmed to recognize and respond to a different antigen.

Response of Lymphocytes to Foreign Antigens

• Entry of a foreign antigen into the body triggers a chain of events
  – Recognition of foreign antigen
  – Proliferation of lymphocytes that are programmed to respond to the antigen form a large group (clone) of cells
  – Destruction of foreign antigen by the responding lymphocytes.
Interaction of Cell-Mediated and Humoral Immunity

- Antigen must first be “processed” and displayed on the cell membrane of the antigen processing cell before the immune response can be set in motion
- Lymphocytes interact with the antigen they are programmed to recognize

Interaction of Cell-Mediated and Humoral Immunity (2 of 3)

- When appropriately stimulated:
  - B lymphocytes proliferate and mature into antibody-forming plasma cells
  - T lymphocytes proliferate to form a diverse population of cells that regulate the immune response and generate a cell-mediated immune reaction to eliminate antigen
- Initial contact with a foreign antigen is followed by a lag phase of a week or more before an immune response is demonstrated

Types of Responding T Cells

- Regulator T cells: helper T cells that regulate immune system by establishing a balance between promoting and inhibiting the immune response
- Effector T cells: involved in delayed hypersensitivity reactions
- In AIDS, the virus attacks and destroys helper T lymphocytes

Classification and Function of Immune System Cells (1 of 3)

<table>
<thead>
<tr>
<th>Cell Function</th>
<th>Cell Type</th>
<th>Action of Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen Processing</td>
<td>Macrophages, B Lymphocytes, Dendritic cells</td>
<td>Process antigen and present to lymphocytes</td>
</tr>
<tr>
<td>Regulate immune response</td>
<td>Helper T cells (CD4+)</td>
<td>Cytokines regulate immune system activity</td>
</tr>
<tr>
<td>Promote cytotoxic immune response</td>
<td>Cytotoxic T cells (CD8+)</td>
<td>Produce cytokines that destroy foreign or abnormal cells displaying antigen fragments combined with MHC Class I antigens</td>
</tr>
</tbody>
</table>
Classification and Function of Immune System Cells (2 of 3)

<table>
<thead>
<tr>
<th>Cell Function</th>
<th>Cell Type</th>
<th>Action of Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Promote delayed hypersensitivity</td>
<td>Delayed</td>
<td>Respond to antigen processing cells presenting foreign antigen fragments combined with MHC Class II antigens; produce cytokines that activate and stimulate macrophages, cytotoxic T cells, and NK cells</td>
</tr>
<tr>
<td>response</td>
<td>hypersensitivity</td>
<td></td>
</tr>
<tr>
<td>T cells (CD4+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Destroy virus-infected cells and</td>
<td>NK cells</td>
<td>Cytokine-mediated cell destruction; no previous contact with antigen required</td>
</tr>
<tr>
<td>cancer cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Classification and Function of Immune System Cells (3 of 3)

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<thead>
<tr>
<th>Cell Function</th>
<th>Cell Type</th>
<th>Action of Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Produce</td>
<td>Plasma Cells</td>
<td>Antigen processed by B lymphocytes and presented to responding T cells stimulates B lymphocytes to mature into plasma cells and make antibodies</td>
</tr>
<tr>
<td>antibodies</td>
<td></td>
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</tr>
</tbody>
</table>

Immune Response Genes

- Closely related to the HLA complex on chromosome 6
- Control the immune response by regulating T and B cell proliferation
- Influence resistance to infection and tumors
- Influence likelihood of acquiring an autoimmune disease

Antibody Types

- Immunoglobulin G (IgG)
- Immunoglobulin A (IgA)
- Immunoglobulin M (IgM)
- Immunoglobulin E (IgE)
- Immunoglobulin D (IgD)

Antibodies (1 of 3)

- Globulins produced by plasma cells
- Can react only with the specific antigen that induced its formation

Antibodies (2 of 3)

- IgG
  - Smaller antibody
  - Principal antibody molecule in response to majority of infectious agents
- IgM
  - Large antibody, a macroglobulin
  - Very efficient combining with fungi
- IgE
  - Found in minute quantities in blood; concentration is increased in allergic individuals
Antibodies (3 of 3)

• IgA
  – Produced by antibody-forming cells located in the respiratory and gastrointestinal mucosa
  – Combines with harmful ingested or inhaled antigens, forming antigen-antibody complexes that cannot be absorbed, preventing antigens from inducing sensitization

Hypersensitivity Reactions (1 of 5)

• Antibody-mediated hypersensitivity
  – Type I: anaphylactic (immediate)
  – Type II: cytotoxic
  – Type III: immune complex

Hypersensitivity Reactions (2 of 5)

• Type I: anaphylactic (immediate)
  – Sensitizing antigen circulates throughout the body, triggers widespread mediator release from Ig-coated mast cells and basophils
  – May lead to anaphylaxis: severe generalized IgE-mediated reaction (fall in blood pressure, severe respiratory distress)
  – Prompt treatment required with epinephrine, other appropriate agents

Hypersensitivity Reactions (3 of 5)

  – Antihistamine drugs often relieve many of the allergic symptoms; histamine is one of the mediators released from IgE-coated cells
  – Later contact with same antigen triggers release of mediators (histamine) and related clinical manifestations
    • Ex: Localized response: hay fever, food allergy (peanuts)
    • Systemic response: bee sting, penicillin allergy
  – Atopic person: allergy-prone individual
  – Allergen: sensitizing antigen

Hypersensitivity Reactions (4 of 5)

• Type II: cytotoxic
  – Antibody combines to cell or tissue antigen resulting in complement-mediated lysis of cells or other membrane damage
  – Ex: Autoimmune hemolytic anemia, blood transfusion reactions, RH hemolytic disease, some types of glomerulonephritis

• Type III: immune complex
  – Ag-Ab immune complexes deposited in tissues activate complements; PMNs attracted to site, causing tissue damage
  – Ex: rheumatoid arthritis, systemic lupus erythematosus (SLE), some types of glomerulonephritis

Hypersensitivity Reactions (5 of 5)

• Type IV: delayed hypersensitivity or cell-mediated hypersensitivity
  – T lymphocytes are sensitized and activated on second contact with same antigen
  – Lymphokines induce inflammation and activate macrophages
  – Ex: Tuberculosis, fungal and parasitic infections, contact dermatitis
Suppression of Immune Response

- Reasons for suppression
  - Prevent undesirable effects
  - May be directed against individual’s own cells or tissue components leading to autoimmune diseases
  - Responsible for rejection of transplanted organs
  - May lead to Rh hemolytic disease in newborn infants

Methods of Immune Suppression

- Main immunosuppressive agents
  - Radiation
  - Immunosuppressive drugs that impede cell division or cell function
  - Adrenal corticosteroid hormones
    - Suppress inflammatory reaction
    - Impair phagocytosis
    - Inhibit protein synthesis
  - Gamma globulin preparations contain potent antibodies preventing body from responding to corresponding antigen

Autoimmune Diseases (1 of 2)

- Pathogenesis
  - Alteration of patient’s own (self) antigens causing them to become antigenic, provoking an immune reaction
  - Formation of cross-reacting antibodies against foreign antigens that also attack patient’s own antigens
  - Defective regulation of the immune response by regulator T lymphocyte
- Treatment: corticosteroids, cytotoxic drugs

Autoimmune Diseases (2 of 2)

- Examples
  - Systemic lupus erythematosus
    - Systemic manifestations in various organs
  - Rheumatic fever
    - Inflammation in heart and joints
  - Glomerulonephritis
    - Inflammation in renal glomeruli
  - Autoimmune blood diseases: anemia, leukopenia, thrombocytopenia
  - Thyroiditis (hypothyroidism)
  - Diffuse toxic goiter (hyperthyroidism)

Discussion (1 of 2)

- Which of the following does NOT characterize an active acquired immunity?
  A. Requires repeated contact or exposure to the same antigen
  B. Host produces own antibodies
  C. Slow onset of action
  D. Short-lived immunity
  E. None of the above

Discussion (2 of 2)

- The first antibody formed in response to an antigenic stimulation is
  A. IgM
  B. IgG
  C. IgE
  D. IgA
  E. IgD