The body has powerful ways of defending and healing itself, and medical intervention is needed only on those occasions when the natural defense mechanisms are overwhelmed.

**Bacteria** (1 of 2)
- Single-cell organisms with a cell membrane and cytoplasm but no organized nucleus
- Cause many common infections, and usually respond to antibiotic treatment

**Bacteria** (2 of 2)
- Bacteria release toxins.
  - Exotoxins are secreted during bacteria growth.
  - Endotoxins are released when the bacteria die.
- The systemic release of toxins is septicemia, or sepsis.
Viruses  (1 of 2)

- Smaller than bacteria and cause most infections
- No organized cellular structure except a protein coat (capsid) surrounding the internal genetic material (RNA and DNA)

Viruses  (2 of 2)

- Viruses do not produce toxins.
  - They replicate and may cause a malignancy.
  - They may attack immune cells and destroy the ability to ward off infection.
- They are difficult to treat, and are usually treated symptomatically.

Other Agents of Infection  (1 of 3)

- Fungi don’t usually cause anything more serious than minor skin infections.

Other Agents of Infection  (2 of 3)

- Parasites are more common in developing nations than in the United States.
- Treatment depends on the organism and its location.

Three Lines of Defense

- Anatomic Barriers
  - Epithelium
  - Sebaceous glands
  - Sweat, tears, saliva
  - Mechanical responses—respiratory, urinary, gastrointestinal
Natural vs. Acquired Immunity

- Natural immunity is part of genetic makeup.
- Acquired immunity develops as an outcome of the immune response:
  - Active immunity is generated by the immune system after exposure to an antigen or immunizations.
  - Passive immunity is transferred to a person from an outside source.

Primary vs. Secondary Immune Responses

- Primary immune response is the initial development of antibodies in response to the first exposure to an antigen.
- Secondary immune response is the swift, strong response of the immune system to repeated exposures to an antigen.

Humoral vs. Cell-Mediated Immunity

- Humoral immunity is the long-term immunity to an antigen provided by antibodies produced by B lymphocytes.
- Cell-mediated immunity is short-term immunity to an antigen provided by T lymphocytes.

B Lymphocytes

- White blood cells
- Respond to antigens and produce antibodies that attack the antigen
- Develop a memory for the antigen
- Confer long-term immunity to specific antigens
**T Lymphocytes**

- White blood cells
- Do not produce antibodies
- Recognize the presence of a foreign antigen and attack it directly

**Lymphocytes and the Lymph System** (1 of 3)

- Lymphocytes are circulated throughout the body as part of the lymph system.
  - B lymphocytes, T lymphocytes, secretory lymphocytes
- Lymph consists primarily of interstitial fluid carrying proteins, bacteria, and other substances.

**Lymphocytes and the Lymph System** (2 of 3)

- Lymph is carried through lymphatic vessels that are parallel but separate from blood vessels.
- Two lymph ducts in thorax:
  - Right—the smaller drains the right arm, right head, and right side of thorax.
  - Thoracic duct—larger, in the left thorax, drains the rest of the body.

**Lymphocytes and the Lymph System** (3 of 3)

- The ducts drain lymph into the right and left subclavian veins.
- Lymph is returned from the blood through the tissues to the lymph system.

**Induction of the Immune Response**

- The immune response must be triggered, or induced.

**Antigens and Immunogens**

- Antigens that are able to trigger the immune response are immunogens.
- Not every antigen can trigger an immune response.
Characteristics of Antigenic Immunogenicity
- Sufficient foreignness
- Sufficient size
- Sufficient complexity
- Presence in sufficient amounts

Histocompatibility Locus Antigens (HLA)
- The body recognizes if a substance is self- or nonself-made as a result of certain antigens that are present on almost all cells of the body except red blood cells.
- This determines compatibility of tissues and organs that will be grafted or transplanted from a donor.

Blood Group Antigens
- More than 80 red cell antigens have been grouped into a number of different blood group systems.

The Rh System
- Present—Rh positive.
- Absent—Rh negative.
- Problems may occur with pregnancy.
  - Usually with the second pregnancy
  - Incompatibility can cause severe problems.
  - Hemolytic disease in infants

The ABO System
- The ABO blood group consists of only two antigens named A and B.
- People with blood type A carry A antigens.
- People with blood type B carry B antigens.
- People with blood type O carry neither antigen.

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>Antigen Present on Erythrocyte</th>
<th>Antibody Present in Serum</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>None</td>
<td>Anti-A, Anti-B</td>
</tr>
<tr>
<td>AB</td>
<td>A and B</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>Anti-A</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>Anti-B</td>
</tr>
</tbody>
</table>
Type A and B Immune Responses
- An immune response will be activated if a person with blood type A receives type B blood.
- The same will occur if a person with type B blood receives type A blood.

Universal Donor and Recipient
- People with blood type O are universal donors since there are no antigens to trigger an immune response.
- People with blood type AB have both antigens and will not have a response. This is the universal recipient.

Table 8-7 Compatibility among ABO Blood Groups

<table>
<thead>
<tr>
<th>Cells of Donor</th>
<th>AB</th>
<th>B</th>
<th>A</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>B</td>
<td>-</td>
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<td>+</td>
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<tr>
<td>A</td>
<td>-</td>
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<td>+</td>
</tr>
<tr>
<td>O</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

- *No reaction
- *Reaction

Humoral Immune Response
- Long-lasting response provided by production in the bloodstream of antibodies and memory cells called B lymphocytes.
- This is also called the internal or systemic immune system.

Cell-Mediated Immune Response
- Includes T cells which recognize and act on antigens presented by MHC proteins on the cell surface.
Lymphocytes

- Lymphocytes are generated from stem cells in the bone marrow.
- These take one of two paths as they mature.
  - Through the thymus gland; mature into T lymphocytes.
  - Through a set of lymphoid tissues; mature into B lymphocytes.

B cells specialize through the processes of clonal diversity and clonal selection.

B Cells

- Clonal diversity is generated as the precursors of mature B cells develop in the bone marrow.
- The B cell precursor develops receptors for every possible type of antigen it may encounter.

Clonal Selection (1 of 3)

- Clonal selection is the process by which a specific antigen reacts with the appropriate receptor on the surface of immature B lymphocytes.

Clonal Selection (2 of 3)

- This activates the immature B cell, prompting it to proliferate and differentiate.

Clonal Selection (3 of 3)

- The end result is that mature B cells produce plasma cells that secrete immunoglobulin antibodies into the blood and secondary organs.
Immunoglobulins

- Antibodies are proteins secreted by plasma cells that are produced by B cells in response to an antigen.
- All antibodies are immunoglobulins, but it is undetermined if all immunoglobulins function as antibodies.

Antigen-Antibody Binding

- The shape of the antigen fits the shape of the antigen-binding site on the immunoglobulin (antibody) molecule like a key in a lock.

The Functions of Antibodies

- An antibody circulates in the blood or is suspended in body secretions until it meets and binds to a specific antigen.
- Antigen-antibody complexes form from the direct and indirect binding of antibodies and antigens.

Direct Effects of Antibodies on Antigens

- Agglutination
  - A soluble antibody combines with a solid antigen causing it to clump together.
Precipitation
- The antigen-antibody complex precipitates out of the blood and is carried away by body fluids.

Neutralization
- The antibody, in combining with the antigen, inactivates the antigen by preventing it from binding to receptors on the surface of cells.

Indirect Effects of Antibodies on Antigens

Enhancement of Phagocytosis
- Phagocytosis is one of the chief processes of inflammation in which certain types of white blood cells ingest and digest foreign substances.

Activation of Plasma Proteins
- Antibodies can activate plasma proteins of the complement system that attack and destroy antigens.

Functions of Antibodies
- Neutralization of bacterial toxins.
- Neutralization of viruses.
- Opsonization of bacteria.
- Activation of the inflammatory processes.
Classes of Immunoglobulins
- IgM—produced first
- IgG—has “memory”-80 to 85% of circ.
- IgA—involved in secretory immune responses
- IgE—involved in allergic reactions
- IgD—present in very low concentrations

Secretory Immune System
- Primary function is to protect the body from pathogens that are inhaled or ingested.

Cell-Mediated Immune Response

Types of Mature T Cells
- Memory cells—secondary immune responses
- T_d cells—delayed hypersensitivity
- T_c cells—cytotoxic, attack infected or pathogenic cells
- T_h cells—helpers, induce antibody production with B lymphocytes and activate cytotoxic T cells
- T_s cells—suppressors

The Physiology of Cytotoxic T cells

Cellular Interactions in Immune Response
- Antigen-presenting (macrophages) interact with T_h (helper) cells.
- T_h (helper) cells interact with B cells.
- T_h (helper) cells interact with T_c (cytotoxic) cells.
Cytokines

- Messengers of the immune response.
- Help regulate cell functions during the inflammatory and immune functions.
- Monokines are released by a macrophage.
- Lymphokines are released by a lymphocyte.

Interferons

- Important messengers, but are host specific rather than antigen-specific as infected cells secrete them, inhibit replication of many viruses, and have anti-tumor effects.

Processes Necessary for Immune Response

- Antigen processing (by macrophages)
- Antigen presentation (by macrophages)
- Antigen recognition (by T cells or B cells)

Antigen Processing

- The recognition, ingestion, and breakdown of a foreign antigen

Antigen Presentation

- Following antigen processing, antigen fragments are expressed by the macrophage and presented on its surface with its own antigens.

Antigen Recognition

- Helper T cells recognize foreign and self antigens, and the helper T cells are activated.
Some immune response capabilities are developed in utero, but most of the immune response system is not fully developed.

To protect the child in utero and during the first few months after birth, maternal antibodies cross the placenta into the fetal circulation.

Trophoblasts actively transport immunoglobulin cells from maternal to fetal circulation.

At birth antibodies begin to drop until the immune system matures.

As the human body ages, immune functions begin to deteriorate.

T cells are primarily affected.

Immune vs. Inflammatory

<table>
<thead>
<tr>
<th>Immune</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develops slowly</td>
<td>Develops swiftly</td>
</tr>
<tr>
<td>Targets specific antigens</td>
<td>Non-specific</td>
</tr>
<tr>
<td>Long-lasting—has “memory”</td>
<td>Temporary—days to weeks</td>
</tr>
<tr>
<td>Involves one type of white blood cell</td>
<td>Involves many types of white blood cells and platelets</td>
</tr>
<tr>
<td>One type of plasma protein—antibodies</td>
<td>Several plasma proteins—complement, coagulation, kinin</td>
</tr>
</tbody>
</table>
**Phases of Inflammation**
- Phase 1: acute inflammation healing
  - If healing doesn't take place, moves to phase 2
- Phase 2: chronic inflammation healing
  - If healing doesn't take place, moves to phase 3
- Phase 3: granuloma formation
- Phase 4: healing

**Functions of Inflammation**
- Destroy and remove unwanted substances
- Wall off infected and inflamed area
- Stimulate the immune response
- Promote healing

**The Inflammatory Response**

**The Acute Inflammatory Response**

**Mast Cells**
- Chief activators of the inflammatory response
- Activate the inflammatory response through granulation and synthesis

**Degranulation**
- Process by which mast cells empty granules from their interior into the extracellular environment.
- Occurs when the mast cell is stimulated by one of the following:
  - Physical injury
  - Chemical agents
  - Immunologic and direct processes
Biochemical Agents Released During Degranulation

- Vasoactive amines
- Chemotactic factors

Synthesis

- Mast cells construct substances that play important roles in inflammation:
  - Leukotrienes
  - Prostaglandins

Mast Cell Degranulation and Synthesis

Plasma Protein Systems

Complement System

- 11 proteins that are dormant until activated
- Assist in destroying or limiting the damage of an invading organism

Alternative Pathway

- Activated without an intervening antigen-antibody complex formed by the immune response
- Much faster than the classic pathway
- Acts as part of the first line of inflammatory defense
The Complement Cascade

- The classic pathway is activated at C1 while the alternative pathway is activated at C3.

The Coagulation System

- The clotting system.
- Fibrin is formed that stops the spread of infectious and inflammatory agents.
- Forms a clot that stops bleeding.

The Kinin System

- Produces bradykinin which causes:
  - Vasodilation
  - Extravascular smooth muscle contraction
  - Increased permeability
  - Possibly chemotaxis
- Acts more slowly than histamine.
- Plasma kinin cascade is triggered by factors associated with the coagulation cascade.

The Coagulation Cascade

Cellular Components of Inflammation

Control and Interaction of Plasma Protein Systems

- Control of the plasma protein systems is important for two reasons:
  - The inflammatory response is essential to protect from unwanted invaders.
  - The inflammatory processes are powerful and potentially very damaging to the body.
Sequence of Events in Inflammation
1. Vascular response
2. Increased permeability
3. Exudation of white cells

Cellular Products
- Cytokines:
  - Lymphokines
  - Monokines
  - Interleukins
  - Macrophage-activating factor (MAF)
  - Interferon

Systemic Inflammatory Responses of Acute Inflammation
- Fever
- Leukocytosis
- Increased circulating plasma proteins

Chronic Inflammatory Responses
- Neutrophils degranulate and die.
- Lymphocytes infiltrate.
- Fibroblasts secrete collagen.
- Pus is produced and self-digested.
- A granuloma may form.
- Tissue repair.
- Scar formation.

Local Inflammatory Responses
- Vascular changes
- Exudation:
  - Dilutes toxins released by bacteria and toxic products of dying cells
  - Brings plasma proteins and leukocytes to the site to attack the invaders
  - Carries away the products of inflammation, e.g., toxins, dead cells, pus

Resolution and Repair
- Resolution
  - Complete restoration of normal function and structure if damage was minor and tissue is capable of regeneration.
- Repair
  - Scarring takes place if the wound is large, an abscess or granuloma has formed, or fibrin remains in the tissue.
Reconstruction

- Initial response
- Granulation
- Epithelialization
- Contraction

Maturation

- Scar tissue is remodeled.
- Blood vessels disappear.
- Scar tissue becomes stronger.

Causes of Dysfunctional Wound Healing

- Disease states
- Hypoxemia
- Nutritional deficiencies
- Use of certain drugs

Aging and the Mechanisms of Self-Defense

- Newborns and the elderly are particularly susceptible to problems of insufficient immune and inflammatory responses.

Variances in Immunity and Inflammation

Types of Hypersensitivity

- Allergy
- Autoimmunity
- Isoimmunity
Mechanisms of Hypersensitivity Reaction

- **Type I: IgE-mediated reactions**
- **Type II: tissue-specific reactions**
- **Type III: immune complex-mediated reactions**
- **Type IV: cell-mediated reactions**

**Type I – IgE Reactions**

- Upon re-exposure to an allergen, the allergen binds to the IgE on the mast cell.
- Degranulation of the mast cell occurs.
- Histamine is released.
- The inflammatory response is triggered.

**Clinical Indications of IgE-Mediated Responses** (1 of 2)

- **Skin**—flushed, itching, hives, edema
- **Respiratory system**—breathing difficulty, laryngeal edema, laryngospasm, bronchospasm
- **Cardiovascular system**—vasodilation and increased permeability, increased heart rate, increased blood pressure

**Clinical Indications of IgE-Mediated Responses** (2 of 2)

- **GI system**—nausea, vomiting, cramping, diarrhea
- **Nervous system**—dizziness, headache, convulsions, tearing

**Type II – Tissue-Specific Reactions**

- Immune response against some antigens present on only some body tissues

**Type III – Immune Complex-Mediated Reactions** (1 of 3)

- Result from antigen-antibody complexes that are formed when antibodies circulating in the blood or suspended in body secretions meet and bind to a specific antigen.
Type III – Immune Complex-Mediated Reactions (2 of 3)

- The organ affected has very little connection with where or how the antigen or the immune complex originated.

Type III – Immune Complex-Mediated Reactions (3 of 3)

- Systemic immune complex diseases are called serum sickness:
  - Raynaud’s disease
- Local immune complex diseases are arthus reactions:
  - Skin reactions following inoculation
  - GI reaction to wheat products

Type IV – Cell-Mediated Tissue Reactions

- Activated directly by T cells and do not involve antibody
- Examples: graft rejection, contact allergic reaction—poison ivy

Targets of Hypersensitivity

<table>
<thead>
<tr>
<th>Type of Hypersensitivity</th>
<th>Targeted Antigen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergy</td>
<td>Environmental antigens</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>Self antigens</td>
</tr>
<tr>
<td>Isoimmunity</td>
<td>Other person’s antigens</td>
</tr>
</tbody>
</table>

Autoimmune and Isoimmune Diseases

- Grave’s disease
- Rheumatoid arthritis
- Myasthenia gravis
- Immune thrombocytopenia purpura
- Isoimmune neutropenia
- Systemic lupus erythematosus
- Rh and ABO isoimmunization

Deficiencies in Immunity and Inflammation
### Congenital Immune Deficiencies
- Develops if the development of lymphocytes in the fetus or embryo is impaired or halted:
  - DiGeorge syndrome
  - Bruton agammaglobulinemia
  - Bare lymphocyte syndrome
  - Wiskott-Aldrich syndrome
  - Selective IgA deficiency
  - Chronic mucocutaneous candidiasis

### Acquired Immune Deficiencies
- Nutritional deficiencies
- Iatrogenic deficiencies
- Deficiencies caused by trauma
- Deficiencies caused by stress
- AIDS

### Replacement Therapies for Immune Deficiencies
- Gamma-globulin therapy
- Transplantation and transfusion
- Gene therapy

### Disorders of Immunity

### Autoimmune Disease
- Clinical disorder produced by immune response to normal tissue component of patient's body

### Graves’ Disease
- Antibody stimulates thyroid hormone over production
- Produces hyperthyroidism
- Antibody, disease can be passed through placenta
Juvenile Rheumatoid Arthritis

- Idiopathic chronic inflammatory diseases affecting joints and connective tissues in children
- Approximately 1 in 1000 children are diagnosed with arthritis
- 80-90% will outgrow, and satisfactorily recover from having arthritis, 10% of children may require Meds, PT, Joint Replacement if progresses to adulthood

## Pathophysiology

- Cause is unknown, but linked to genetic, environmental, and immunologic factors
- Immunogenetic susceptibility along with external trigger, viral or bacterial, both necessary to start the inflammatory process in genetically targeted body cells

Rheumatoid Arthritis

- Antibody reaction to collagen in joints
- Causes inflammation, destruction of joints

Myasthenia Gravis

- Antibodies destroy acetylcholine receptors on skeletal muscle
- Produce episodes of severe weakness
- Antibodies can cross placenta, affect newborn

## Psychosocial

- Growth
- Emotional
- Physical
- Functional Impairments
Immune Thrombocytopenic Purpura
- Antibodies destroy platelets
- Produces clotting disorders, hemorrhaging
- Antibodies can cross placenta, affect newborn

Other Autoimmune Diseases
- Type I diabetes mellitus
- Rheumatic fever
- Crohn’s disease
- Ulcerative colitis
- Systemic Lupus Erythematosus (SLE)

SLE
- Chronic, multi-system auto-immune disease
- Highest incidence
  - Women, 20-40 years of age
  - Black, Hispanic women
- Mortality after diagnosis averages 5% per year

SLE
- Antibody against nucleic acid components (ANA, anti-nuclear antibody)
- Immune complex precipitates in tissues, causes widespread destruction
- Especially affected are renal system, blood vessels, heart

SLE
- Signs/Symptoms
  - Facial rash/skin rash triggered by sunlight exposure
  - Oral/nasopharyngeal ulcers
  - Fever
  - Arthritis

SLE
- Signs/Symptoms
  - Serositis (pleurisy, pericarditis)
  - Renal injury/failure
  - CNS involvement with seizures/psychosis
  - Peripheral vasculitis/gangrene
  - Hemolytic anemia
SLE

- Chronic management
  - Anti-inflammatory drugs
    - Aspirin
    - Ibuprofen
    - Corticosteroids
  - Avoidance of emotional stress, physical fatigue, excessive sun exposure

Immunodeficiency Disease

- Patient unable to fight off infection
- Hallmarks
  - Repeated infections
  - Opportunistic infections

Immunizations

Immunizations

Catch-Up

Catch-Up