The Immune System: Innate and Adaptive Body Defenses
Disclosure

- The material and the illustrations are adopted from the textbook “Human Anatomy and Physiology / Ninth edition/ Eliane N. Marieb 2013”
Immunity: Two Intrinsic Defense Systems

- **Innate (nonspecific)** system responds quickly and consists of:
  - **First line of defense** – intact skin and mucosae prevent entry of microorganisms
  - **Second line of defense** – antimicrobial proteins, phagocytes, and other cells
    - Inhibit spread of invaders throughout the body
    - Inflammation is its hallmark and most important mechanism
Immunity: Two Intrinsic Defense Systems

- Adaptive (specific) defense system
  - Third line of defense – mounts attack against particular foreign substances
    - Takes longer to react than the innate system
    - Works in conjunction with the innate system
Surface Barriers (*First Line of Defense*)

- **Skin**, mucous membranes, and their *secretions* make up the first line of defense

- Keratin in the skin:
  - Presents a formidable physical barrier to most microorganisms
  - Is resistant to weak acids and bases, bacterial enzymes, and toxins

- Mucosae provide similar mechanical barriers
Epithelial Chemical Barriers

- Epithelial membranes produce protective chemicals that destroy microorganisms
  - **Skin acidity** (pH of 3 to 5) inhibits bacterial growth
  - **Sebum** contains chemicals toxic to bacteria
  - Stomach mucosae secrete concentrated **HCl** and protein-digesting enzymes
  - **Saliva** and **lacrimal** fluid contain lysozyme
  - **Mucus** traps microorganisms that enter the digestive and respiratory systems
Respiratory Tract Mucosae

- Mucus-coated hairs in the nose trap inhaled particles
- Mucosa of the upper respiratory tract is ciliated
  - Cilia sweep dust- and bacteria-laden mucus away from lower respiratory passages
Internal Defenses *(Second Line of Defense)*

- The body uses **nonspecific** cellular and chemical devices to protect itself
  1. Phagocytes
  2. Natural killer (NK) cells
  3. Inflammatory response enlists macrophages, mast cells, WBCs, and chemicals
  4. Antimicrobial proteins in blood and tissue fluid

- Harmful substances are identified by surface carbohydrates unique to infectious organisms
1. Phagocytes

- **Macrophages** are the chief phagocytic cells
- Free macrophages wander throughout a region in search of cellular debris
- **Kupffer cells (liver)** and **microglia (brain)** are fixed macrophages
- **Neutrophils** become phagocytic when encountering infectious material
- **Eosinophils** are weakly phagocytic against parasitic worms
- Mast cells bind and ingest a wide range of bacteria
After division some cells remain stem cells.

Multipotent hematopoietic stem cell (hemocytoblast)

The remaining cell goes down one of two paths depending on the chemical signals received.

- **Myeloid stem cell**
  - Megakaryoblast
  - Proerythroblast
  - Myeloblast
  - Monoblast
  - Reticulocyte
  - Megakaryocyte
  - Erythrocyte
  - Basophil
  - Neutrophil
  - Eosinophil
  - Monocyte
  - Macrophage

- **Lymphoid stem cell**
  - Lymphoblast
  - Natural killer cell (Large granular lymphocyte)
  - Small lymphocyte
  - T lymphocyte
  - B lymphocyte
  - Plasma cell
2. Natural Killer (NK) Cells

- Cells that can lyse and kill cancer cells and virus-infected cells

- Natural killer cells:
  - Are a small, distinct group of large granular lymphocytes
  - React nonspecifically and eliminate cancerous and virus-infected cells
  - Kill their target cells by releasing perforins and other cytolytic chemicals
  - Secrete potent chemicals that enhance the inflammatory response
3. Inflammation: Tissue Response to Injury

- The inflammatory response is triggered whenever body tissues are injured
  - Prevents the spread of damaging agents to nearby tissues
  - Disposes of cell debris and pathogens
  - Sets the stage for repair processes
- The four common signs of acute inflammation are redness, heat, swelling, and pain
Inflammation Response

- Begins with a flood of inflammatory chemicals released into the extracellular fluid

- Inflammatory mediators (chemicals):
  - Released by injured tissue, phagocytes, lymphocytes, and mast cells
  - Include kinins, prostaglandins (PGs), complement, and cytokines
  - Cause local small blood vessels to dilate, resulting in hyperemia
Inflammatory Response: Vascular Permeability

- Chemicals liberated by the inflammatory response increase the permeability of local capillaries

- Exudate (fluid containing proteins, clotting factors, and antibodies):
  - Seeps into tissue spaces causing local edema (swelling), which contributes to the sensation of pain
Inflammatory Response: Edema

- The surge of protein-rich fluids into tissue spaces (edema):
  - Helps to dilute harmful substances
  - Brings in large quantities of oxygen and nutrients needed for repair
  - Allows entry of clotting proteins, which prevents the spread of bacteria
Inflammatory Response: Phagocytic Mobilization

- Occurs in four main phases:
  - **Leukocytosis** – neutrophils are released from the bone marrow in response to leukocytosis-inducing factors released by injured cells
  - **Margination** – neutrophils cling to the walls of capillaries in the injured area
  - **Diapedesis** – neutrophils squeeze through capillary walls and begin phagocytosis
  - **Chemotaxis** – inflammatory chemicals attract neutrophils to the injury site
**Inflammatory Response: Phagocytic Mobilization**

1. Neutrophils enter blood from bone marrow
2. Margination
3. Diapedesis
4. Positive chemotaxis

Inflammatory chemicals diffusing from the inflamed site act as chemotactic agents.

- Capillary wall
- Endothelium
- Basal lamina

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4. Antimicrobial Proteins

- Enhance the innate defenses by:
  - Attacking microorganisms directly
  - Hindering microorganisms’ ability to reproduce

- The most important antimicrobial proteins are:
  - Complement proteins
  - Interferon
Genes that synthesize IFN are activated when a host cell is invaded by a virus.

Interferon molecules leave the infected cell and enter neighboring cells.

- Interferon stimulates the neighboring cells to activate genes for PKR (an antiviral protein).

- PKR nonspecifically blocks viral reproduction in the neighboring cell.
Interferon (IFN)

Figure 21.4

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4 b. Complement

- 20 or so proteins that circulate in the blood in an inactive form
- Proteins include C1 through C9, factors B, D, and P, and regulatory proteins
- Provides a major mechanism for destroying foreign substances in the body
Complement

- Amplifies all aspects of the inflammatory response
- **Kills bacteria** and certain other cell types (our cells are immune to complement)
- Enhances the effectiveness of both nonspecific and specific defenses
Complement Pathways

- Complement can be activated by two pathways: classical and alternative

- Classical pathway is linked to the immune system
  - Depends on the binding of antibodies to invading organisms
  - Subsequent binding of C1 to the antigen-antibody complexes (complement fixation)

- Alternative pathway is triggered by interaction among factors B, D, and P, and polysaccharide molecules present on microorganisms
Complement Pathways

- Each pathway involves a cascade in which complement proteins are activated in an orderly sequence and where each step catalyzes the next
- Both pathways converge on C3, which cleaves into C3a and C3b
- C3b initiates formation of a membrane attack complex (MAC)
- MAC causes cell lysis by interfering with a cell’s ability to eject Ca^{2+}
- C3b also causes opsonization,
- C3a causes inflammation
Complement Pathways

**Classical pathway**
- Antigen–antibody complex + C1, C4, C2 Complex

**Alternative pathway**
- Microorganisms' cell wall polysaccharides + Factor B, Factor D, and Factor P (properdin)

**Opsonization:**
- Coats bacterial surfaces, which enhances phagocytosis

**Causes inflammation:**
- Stimulates histamine release, increased blood vessel permeability, chemotactic attraction of phagocytes, etc.

**Insertion of MAC and cell lysis**
- Holes in target cell's membrane

**MAC**
- C3b, C5b, C6, C7, C8, C9

**Complement proteins**
- (C5b–C9)

**Lesion**
- Target cell
Fever

- Abnormally high body temperature in response to invading microorganisms
- The body’s thermostat is reset upwards in response to pyrogens, chemicals secreted by leukocytes and macrophages exposed to bacteria and other foreign substances
Fever

- High fevers are dangerous as they can **denature enzymes**

- Moderate fever can be beneficial, as it causes:
  - The liver and spleen to sequester iron and zinc (needed by microorganisms)
  - An **increase in the metabolic rate**, which speeds up tissue repair
Adaptive (Specific) Defenses (*Third Line of Defense*)

- The adaptive immune system is a functional system that:
  - Recognizes specific foreign substances
  - Acts to **immobilize, neutralize, or destroy** foreign substances
  - **Amplifies inflammatory** response and activates complement
Adaptive Immune Defenses

- The adaptive immune system is antigen-specific, systemic, and has memory

- It has two separate but overlapping arms
  - Humoral, or antibody-mediated (B Cell) immunity
  - Cellular, or cell-mediated (T Cell) immunity
Substances that can **mobilize the immune system** and provoke an immune response

The ultimate targets of all immune responses are **mostly large, complex molecules** not normally found in the body (nonself)

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**Antigens**
Self-Antigens: MHC Proteins

- Our cells are dotted with protein molecules (self-antigens) that are not antigenic to us but are strongly antigenic to others (reason for transplant rejection)

- One type of these, MHC proteins, mark a cell as self

- The two classes of MHC proteins are:
  - **Class I MHC proteins** – found on virtually all body cells (display fragments of non-self proteins from within the cell to Cytotoxic T Cells)
  - **Class II MHC proteins** – normally found only on antigen-presenting cells (APC) such as dendritic cells, mononuclear phagocytes and B cells. Extracellular proteins are endocytosed, digested in lysosomes, and the resulting epitopic peptide fragments are loaded onto MHC class II
Two types of lymphocytes

- **B lymphocytes** – oversee humoral immunity
- **T lymphocytes** – non-antibody-producing cells that constitute the cell-mediated arm of immunity

Antigen-presenting cells (APCs):

- Do not respond to specific antigens
- Play essential auxiliary roles in immunity
Lymphocytes

- Immature lymphocytes released from bone marrow are essentially identical

- Whether a lymphocyte matures into a B cell or a T cell depends on where in the body it becomes immunocompetent
  - B cells mature in the bone marrow
  - T cells mature in the thymus
B Cells

- B cells become immunocompetent and self-tolerant in bone marrow
- Some self-reactive B cells are inactivated (anergy) while others are killed
Immunocompetent B or T cells

- Display a unique type of receptor that responds to a distinct antigen
- Become immunocompetent before they encounter antigens they may later attack
- Are exported to secondary lymphoid tissue where encounters with antigens occur
- Mature into fully functional antigen-activated cells upon binding with their recognized antigen
- It is genes, not antigens, that determine which foreign substances our immune system will recognize and resist
Antigen-Presenting Cells (APCs)

- Major roles in immunity are:
  - To engulf foreign particles
  - To present fragments of antigens on their own surfaces, to be recognized by T cells
- Major APCs are dendritic cells (DCs), macrophages, and activated B cells
- The major initiators of adaptive immunity are DCs, which actively migrate to the lymph nodes and secondary lymphoid organs and present antigens to T and B cells
• Secrete soluble proteins that **activate T cells**

• Activated T cells in turn release chemicals that:
  • Rev up the maturation and mobilization of DCs
  • Stimulate macrophages to become activated macrophages, which are active phagocytes that secrete bactericidal chemicals
Antigen challenge – first encounter between an antigen and a naive immunocompetent cell

Takes place in the spleen or other lymphoid organ

If the lymphocyte is a B cell:

- The challenging antigen provokes a humoral immune response
  - Antibodies are produced against the challenger
A naive, immunocompetent B cell is activated when antigens bind to its surface receptors

**Stimulated B cell** growth forms clones bearing the same antigen-specific receptors

Antigen binding is followed by receptor-mediated endocytosis of the cross-linked antigen-receptor complexes

These activating events, plus T cell interactions, trigger clonal selection
Clonal Selection

**Primary Response** (initial encounter with antigen)

- B lymphoblasts
- Plasma cells
- Secreted antibody molecules

**Secondary Response** (can be years later)

- Clone of cells identical to ancestral cells
- Plasma cells
- Secreted antibody molecules

**Antigen**

- Antigen binding to a receptor on a specific B lymphocyte (B lymphocytes with non-complementary receptors remain inactive)

**Proliferation to form a clone**

**Memory B cell**

**Subsequent challenge by same antigen**

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Figure 21.9
Fate of the Clones

- Most clone cells become antibody-secreting plasma cells
- Plasma cells secrete specific antibody at the rate of 2000 molecules per second
Fate of the Clones

- Secreted **antibodies**:
  - Bind to free antigens
  - Mark the antigens for destruction by specific or nonspecific mechanisms
- Clones that do not become plasma cells become **memory cells** that can mount an immediate response to subsequent exposures of the same antigen
Immunological Memory

- **Primary immune response** – cellular differentiation and proliferation, which occurs on the first exposure to a specific antigen
  - Lag period: 3 to 6 days after antigen challenge
  - Peak levels of plasma antibody are achieved in 10 days
  - Antibody levels then decline
Immunological Memory

- Secondary immune response – re-exposure to the same antigen
  - Sensitized memory cells respond within hours
  - Antibody levels peak in 2 to 3 days at much higher levels than in the primary response
  - Antibodies bind with greater affinity, and their levels in the blood can remain high for weeks to months
Primary and Secondary Humoral Responses

Figure 21.10

Second exposure to antigen x, first exposure to antigen y

Secondary immune response to antigen x

Primary immune response to antigen x

Antibodies to x

Antibodies to y
Active Humoral Immunity

- B cells encounter antigens and produce antibodies against them
  - Naturally acquired – response to a bacterial or viral infection
  - Artificially acquired – response to a vaccine of dead or attenuated pathogens
    - Vaccines – spare us the symptoms of disease, and their weakened antigens provide antigenic determinants that are immunogenic and reactive
Passive Humoral Immunity

- Differs from active immunity in the antibody source and the degree of protection
  - B cells are not challenged by antigens
  - Immunological memory does not occur
  - Protection ends when antibodies naturally degrade in the body
- Naturally acquired – from the mother to her fetus via the placenta
- Artificially acquired – from the injection of serum, such as gamma globulin
Types of Acquired Immunity

Acquired immunity

Naturally acquired

Active
Infection; contact with pathogen

Passive
Antibodies pass from mother to fetus via placenta; or to infant in her milk

Artificially acquired

Active
Vaccine; dead or attenuated pathogens

Passive
Injection of immune serum (gamma globulin)
Antibodies

• Also called immunoglobulins
  • Constitute the gamma globulin portion of blood proteins
  • Are soluble proteins secreted by activated B cells and plasma cells in response to an antigen
  • Are capable of binding specifically with that antigen
• There are five classes of antibodies: IgD, IgM, IgG, IgA, and IgE
Complement Fixation and Activation

- Complement fixation is the main mechanism used against cellular antigens
- Antibodies bound to cells change shape and expose complement binding sites
- This triggers complement fixation and cell lysis
- Complement activation:
  - Enhances the inflammatory response
  - Uses a positive feedback cycle to promote phagocytosis
  - Enlists more and more defensive elements
Other Mechanisms of Antibody Action

- Neutralization – antibodies bind to and block specific sites on viruses or exotoxins, thus preventing these antigens from binding to receptors on tissue cells

- Agglutination – Cell-bound antigens are cross-linked, causing clumping (agglutination)

- Precipitation – soluble molecules are cross-linked into large insoluble complexes
Mechanisms of Antibody Action

Antigen-antibody complex

Antigen

Antibody

Inactivates by

Neutralization (masks dangerous parts of bacterial exotoxins; viruses)

Agglutination (cell-bound antigens)

Precipitation (soluble antigens)

Fixes and activates

Complement

Enhances

Phagocytosis

Inflammation

Chemotaxis

Histamine release

Leads to

Cell lysis

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Since antibodies are useless against **intracellular antigens**, cell-mediated immunity is needed.

Two major populations of **T cells** mediate cellular immunity:

- **CD4 cells** (T4 cells) are primarily **helper T cells** ($T_H$)
- **CD8 cells** (T8 cells) are **cytotoxic T cells** ($T_C$) that destroy cells harboring foreign antigens

Other types of T cells are:

- **Suppressor T cells** ($T_S$)
- **Memory T cells**
Major Types of T Cells

Figure 21.14
Importance of Humoral Response

- Soluble antibodies
  - The simplest ammunition of the immune response
  - Interact in extracellular environments such as body secretions, tissue fluid, blood, and lymph
Importance of Cellular Response

- T cells recognize and respond only to processed fragments of antigen displayed on the surface of body cells.

- T cells are best suited for cell-to-cell interactions, and target:
  - Cells infected with viruses, bacteria, or intracellular parasites
  - Abnormal or cancerous cells
  - Cells of infused or transplanted foreign tissue

- Both types of MHC proteins are important to T cell activation.
Antigen Recognition

- Provides the key for the immune system to recognize the presence of intracellular microorganisms
- MHC proteins are ignored by T cells if they are complexed with self protein fragments
If MHC proteins are complexed with endogenous or exogenous antigenic peptides, they:

- Indicate the presence of intracellular infectious microorganisms
- Act as antigen holders
T Cell Activation: Step One – Antigen Binding

- Viral antigen
- Processed viral antigen (peptide) presented in combination with class I MHC protein
- Class I MHC protein
- CD8 protein
- Immunocompetent cytotoxic T cell
- T cell receptor (TCR)
- Infected tissue cell presenting antigenic peptide recognized by cytotoxic T cell
- Clone formation
- Cytotoxic T memory cell
- Mature cytotoxic T cells
T Cell Activation: Step Two – Co-stimulation

- T cells that are activated:
  - Enlarge, proliferate, and form clones
  - Differentiate and perform functions according to their T cell class
Primary T cell response peaks within a week after signal exposure.

- T cells then undergo apoptosis between days 7 and 30.
- Effector activity wanes as the amount of antigen declines.
- The disposal of activated effector cells is a protective mechanism for the body.
- Memory T cells remain and mediate secondary responses to the same antigen.
Mediators involved in cellular immunity, including hormonelike glycoproteins released by activated T cells and macrophages

Some are co-stimulators of T cells and T cell proliferation

Interleukin 1 (IL-1) released by macrophages co-stimulates bound T cells to:

- Release interleukin 2 (IL-2)
- Synthesize more IL-2 receptors
Cytokines

- IL-2 is a key growth factor, which sets up a positive feedback cycle that encourages activated T cells to divide
  - It is used therapeutically to enhance the body’s defenses against cancer
- Other cytokines amplify and regulate immune and nonspecific responses
Examples include:

- Perforin and lymphotoxin – cell toxins
- Gamma interferon – enhances the killing power of macrophages
- Inflammatory factors
Helper T Cells ($T_H$)

- Regulatory cells that play a *central role in the adaptive immune response*

- Once primed by APC presentation of antigen, they:
  - Chemically or directly stimulate proliferation of other T cells
  - Stimulate B cells that have already become bound to antigen

- Without $T_H$, there is no immune response
Helper T Cells ($T_H$)
- $T_H$ cells interact directly with B cells that have antigen fragments on their surfaces bound to MHC II receptors
- $T_H$ cells **stimulate B cells to divide** faster and begin antibody formation
- Most antigens, require $T_H$ co-stimulation to activate B cells
- Cytokines released by $T_H$ amplify nonspecific defenses
Helper T Cells

Activated B cell

Helper T cell CD4 protein

Interleukins 13 and 4 released by helper T cell

Activated helper T cell

MHC II receptor of B cell displaying processed antigen

TCR
Cytotoxic T Cell (T\textsubscript{c})

- T\textsubscript{c} cells, or killer T cells, are the **only T cells that can directly attack and kill other cells**
- They circulate throughout the body in search of body cells that **display the antigen** to which they have been sensitized
- Their targets include:
  - Virus-infected cells
  - Cells with intracellular bacteria or parasites
  - Cancer cells
  - Foreign cells from blood transfusions or transplants
Cytotoxic T Cells

- Bind to self-antiself complexes on all body cells
- Infected or abnormal cells can be destroyed as long as appropriate antigen and co-stimulatory stimuli (e.g., IL-2) are present
- Unlike Tc, Natural killer cells activate their killing machinery when they bind to MICA receptor
- MICA receptor – MHC-related cell surface protein in cancer cells, virus-infected cells, and cells of transplanted organs
Mechanisms of $T_c$ Action

- In some cases, $T_c$ cells:
  - Bind to the target cell and release perforin into its membrane
    - In the presence of $Ca^{2+}$ perforin causes cell lysis by creating transmembrane pores
  - Other $T_c$ cells induce cell death by:
    - Secreting lymphotoxin, which fragments the target cell’s DNA
    - Secreting gamma interferon, which stimulates phagocytosis by macrophages
Mechanisms of $T_c$ Action
Summary of the Primary Immune Response

Figure 21.19
The four major types of grafts are:

- **Autografts** – graft transplanted from one site on the body to another in the same person
- **Isografts** – grafts between identical twins
- **Allografts** – transplants between individuals that are not identical twins, but belong to same species
- **Xenografts** – grafts taken from another animal species
Prevention of Rejection

- Prevention of tissue rejection is accomplished by using immunosuppressive drugs

- However, these drugs depress patient’s immune system so it cannot fight off foreign agents
Immunodeficiencies

- **Congenital** or **acquired** conditions in which the function or production of immune cells, phagocytes, or complement is abnormal
Severe Combined Immunodeficiency (SCID)

- SCID – severe combined immunodeficiency (SCID) syndromes; genetic defects that produce:
  - A marked deficit in B and T cells
  - Abnormalities in interleukin receptors
  - Defective adenosine deaminase (ADA) enzyme
    - Metabolites lethal to T cells accumulate
- SCID is fatal if untreated; treatment is with bone marrow transplants
Acquired Immunodeficiencies

- **Hodgkin’s disease** – cancer of the lymph nodes leads to immunodeficiency by depressing lymph node cells

- **Acquired immune deficiency syndrome (AIDS)** – cripples the immune system by interfering with the activity of helper T (CD4) cells
  - Characterized by severe weight loss, night sweats, and swollen lymph nodes
  - Opportunistic infections occur, including pneumocystis pneumonia and Kaposi’s sarcoma
Caused by human immunodeficiency virus (HIV) transmitted via body fluids – blood, semen, and vaginal secretions

HIV enters the body via:

- Blood transfusions
- Contaminated needles
- Intimate sexual contact

HIV:

- Destroys $T_H$ cells
- Depresses cell-mediated immunity
- HIV multiplies in lymph nodes throughout the asymptomatic period
- Symptoms appear in a few months to 10 years
- Attachment
  - HIV’s coat protein (gp120) attaches to the CD4 receptor
  - A nearby protein (gp41) fuses the virus to the target cell
HIV enters the cell and uses reverse transcriptase to produce DNA from viral RNA.

This DNA (provirus) directs the host cell to make viral RNA (and proteins), enabling the virus to reproduce and infect other cells.
• HIV reverse transcriptase is not accurate and produces frequent transcription errors
  • This high mutation rate causes resistance to drugs
• Treatments include:
  • Reverse transcriptase inhibitors (AZT)
  • Protease inhibitors (saquinavir and ritonavir)
  • New drugs currently being developed that block HIV’s entry to helper T cells
Autoimmune Diseases

- Loss of the immune system’s ability to distinguish self from nonself
- The body produces autoantibodies and sensitized $T_C$ cells that destroy its own tissues
- Examples include:
  - multiple sclerosis
  - myasthenia gravis
  - Graves’ disease
  - Type I (juvenile) diabetes mellitus
  - systemic lupus erythematosus (SLE)
  - Glomerulonephritis
  - rheumatoid arthritis
Ineffective lymphocyte programming – self-reactive T and B cells that should have been eliminated in the thymus and bone marrow escape into the circulation

New self-antigens appear, generated by:

- Gene mutations that cause new proteins to appear
- Changes in self-antigens by hapten attachment or as a result of infectious damage
If the determinants on foreign antigens resemble self-antigens:

- Antibodies made against foreign antigens cross-react with self-antigens
Hypersensitivity

- Immune responses that cause tissue damage

- Different types of hypersensitivity reactions are distinguished by:
  - Their time course
  - Whether antibodies or T cells are the principle immune elements involved

- Antibody-mediated allergies are immediate and subacute hypersensitivities

- The most important cell-mediated allergic condition is delayed hypersensitivity
Immediate Hypersensitivity

- **Acute (type I) hypersensitivities** begin in **seconds** after contact with allergen

- **Anaphylaxis** – initial allergen contact is asymptomatic but sensitizes the person
  - Subsequent exposures to allergen cause:
    - Release of histamine and inflammatory chemicals
    - Systemic or local responses
Immediate Hypersensitivity

- The mechanism involves IL-4 secreted by T cells
- IL-4 stimulates B cells to produce IgE
- IgE binds to mast cells and basophils causing them to degranulate, resulting in a flood of histamine release and inducing the inflammatory response
Acute Allergic Response

**Sensitization stage**

1. Antigen (allergen) invades body
2. Plasma cells produce large amounts of class IgE antibodies against allergen
3. IgE antibodies attach to mast cells in body tissues (and to circulating basophils)

**Subsequent (secondary) responses**

4. More of same antigen invades body
5. Antigen combines with IgE attached to mast cells (and basophils), which triggers degranulation and release of histamine (and other chemicals)
6. Histamine causes blood vessels to dilate and become leaky, which promotes edema; stimulates secretion of large amounts of mucus; and causes smooth muscles to contract (if respiratory system is site of antigen entry, asthma may ensue)

Outpouring of fluid from capillaries
Release of mucus
Constriction of small respiratory passages (bronchioles)
Anaphylaxis

- Reactions include *runny nose, itching reddened skin, and watery eyes*

- If allergen is inhaled, *asthmatic symptoms* appear – constriction of bronchioles and restricted airflow

- If allergen is ingested, cramping, vomiting, or diarrhea occur

- *Antihistamines counteract* these effects
Anaphylactic Shock

- Response to allergen that directly enters the blood (e.g., insect bite, injection)
- Basophils and mast cells are enlisted throughout the body
- Systemic histamine releases may result in:
  - Constriction of bronchioles
  - Sudden vasodilation and fluid loss from the bloodstream
  - Hypotensive shock and death
- Treatment – epinephrine is the drug of choice
Subacute Hypersensitivities

- Caused by IgM and IgG, and transferred via blood plasma or serum
  - Onset is slow (1–3 hours) after antigen exposure
  - Duration is long lasting (10–15 hours)
- Cytotoxic (type II) reactions
  - Antibodies bind to antigens on specific body cells, stimulating phagocytosis and complement-mediated lysis of the cellular antigens
  - Example: mismatched blood transfusion reaction
Subacute Hypersensitivities

- **Immune complex (type III) hypersensitivity**
  - Antigens are widely distributed through the body or blood
  - Insoluble antigen-antibody complexes form
  - Complexes cannot be cleared from a particular area of the body
  - **Intense inflammation**, local cell lysis, and death may result
  - Example: **systemic lupus erythematosus (SLE)**
Delayed Hypersensitivities (Type IV)

- Onset is slow (1–3 days)
- Mediated by mechanisms involving delayed hypersensitivity T cells and cytotoxic T cells
- Cytokines from activated $T_C$ are the mediators of the inflammatory response
- Antihistamines are ineffective and corticosteroid drugs are used to provide relief
Example: allergic contact dermatitis (e.g., poison ivy)

Involved in protective reactions against viruses, bacteria, fungi, protozoa, cancer, and rejection of foreign grafts or transplants