The Body's Defenses Against Disease and Injury

Part 3 Topics

- **The Immune System and Immune Response.**
- **Aging and the Immune Response.**
- **Inflammation Response.**
- **Variances in Immunity and Inflammation.**

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.

Infectious Agents

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 dies.**
- **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.

Other Agents of Infection (3 of 3)

- **Prions are the most recently recognized class of infectious agents. They are similar to viruses, but do not have protective capsids.**

Three Lines of Defense

Anatomic Barriers

- Epithelium
- Sebaceous glands
- Sweat, tears, saliva
- Mechanical responses—respiratory, urinary, gastrointestinal

Table 8-4 Three Lines of Defense against Infection and Injury

	External	Internal	Nonspecific	Specific
Anatomical Barriers	External		Nonspecific	
Inflammatory Response		Internal	Nonspecific	
Immune Response		Internal		Specific

Table 8-5 Characteristics of the Inflammatory and Immune Responses

	Inflammatory Response	Immune Response
Speed	Fast	Slow
Specificity	Nonspecific	Specific
Duration (Memory)	Transient (no memory)	Long-term (memory)
Involving Which Plasma Systems	Multiple plasma protein systems (complement, coagulation, kinin systems)	One plasma protein system (immunoglobulin)
Involving Which Cell Type	Multiple cell types (granulocytes, monocytes, macrophages)	One blood cell type (lymphocytes)

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;**
  - **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.**

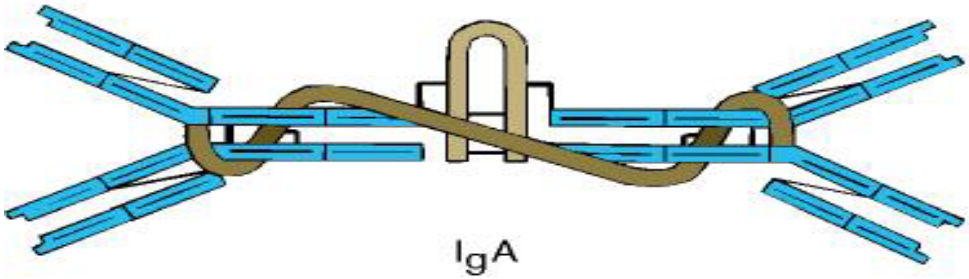
B Lymphocytes

- **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.**

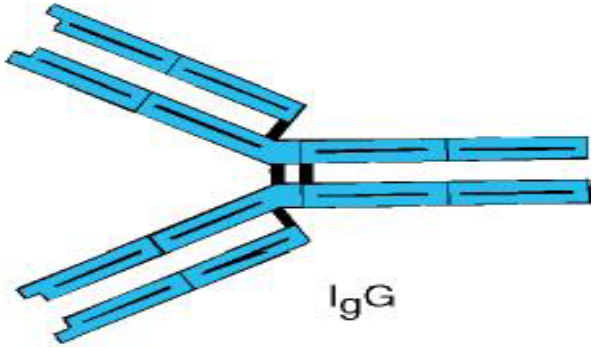
T Lymphocytes

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

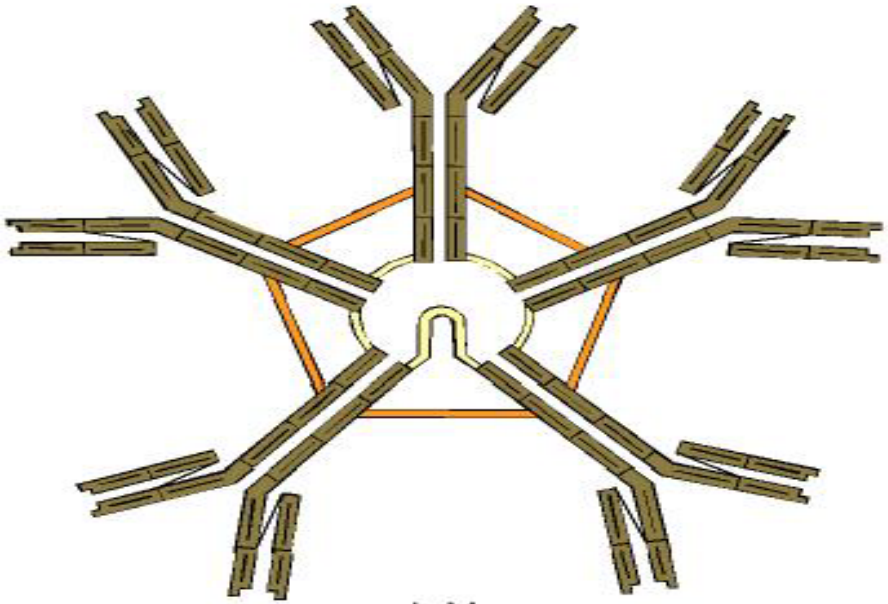
Some immunoglobulin (antibody) structures



IgA



IgG



IgM

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

- **The body recognizes if a substance is self or non-self 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 8-6 Blood Groups—ABO System

Blood Type	Antigen Present on Erythrocyte	Antibody Present in Serum
O	None	Anti-A, Anti-B
AB	A and B	None
B	B	Anti-A
A	A	Anti-B

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

Cells of Donor	Reaction with Serum of Recipient			
	AB	B	A	O
AB	−	+	+	+
B	−	−	+	+
A	−	+	−	+
O	−	−	−	−

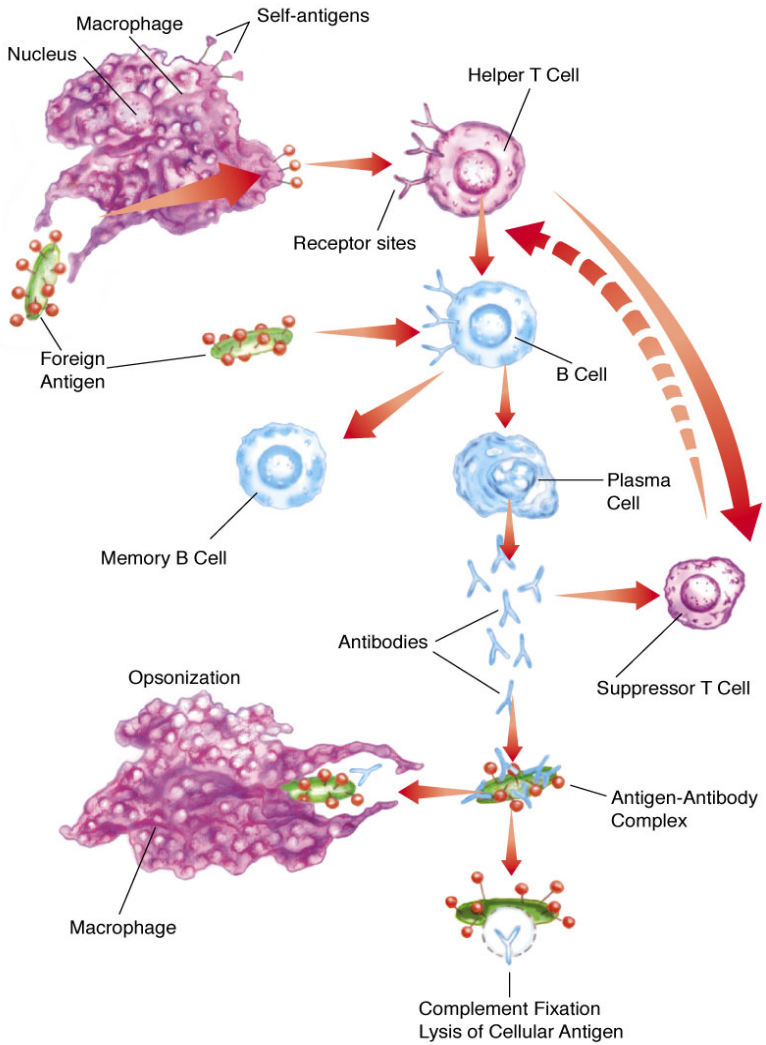
− = No reaction

+ = Reaction

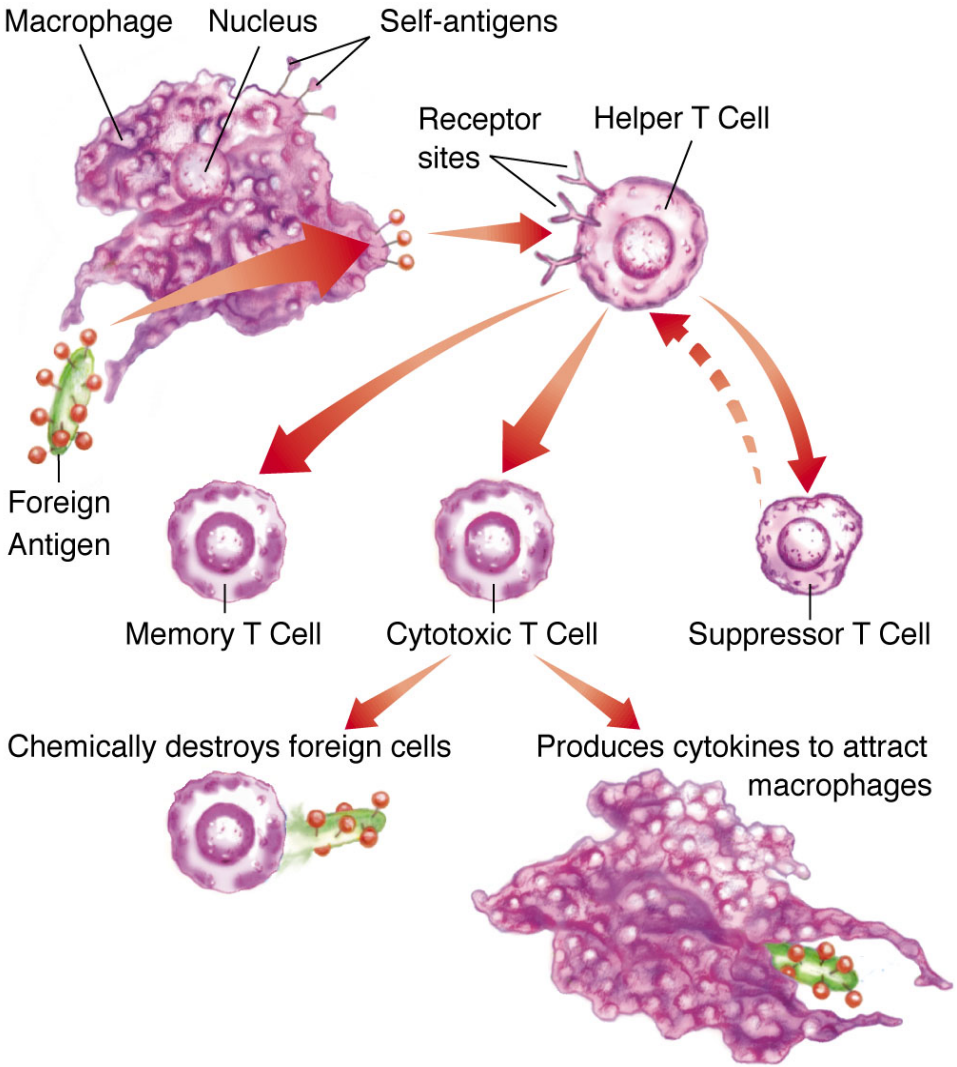
Humoral Immune Response (1 of 2)

- **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.**

Humoral Immune Response (2 of 2)



Cell-Mediated Immune Response



Lymphocytes

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

B cells specialize through process 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)

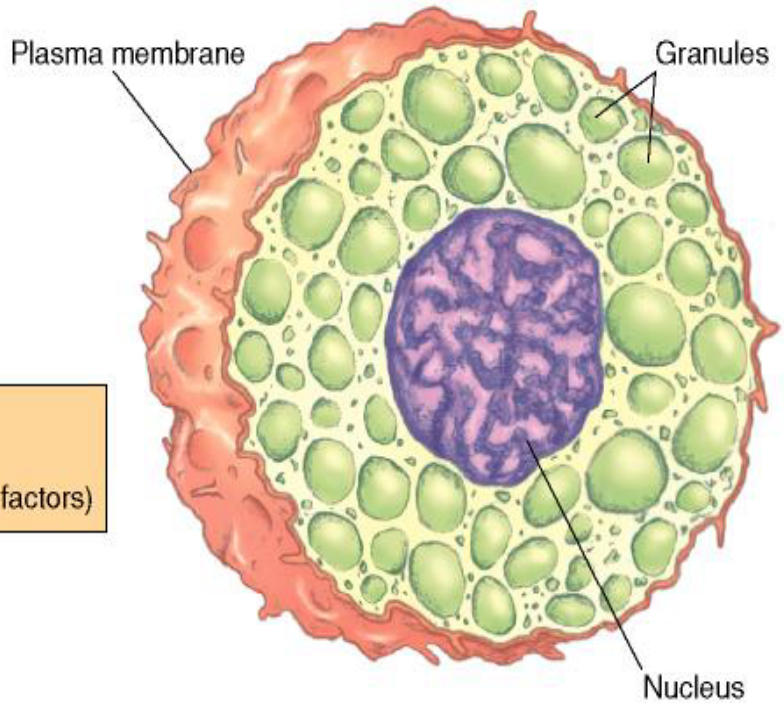
- **The end result is that mature B cells produce plasma cells that secrete immunoglobulin antibodies into the blood and secondary organs.**

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.**

Mast cell degradation and synthesis

Cause: Mast cell stimulated by:
- Physical injury (e.g., trauma, radiation, temperature extremes)
- Chemical agent (e.g., toxin, venom, enzyme, neutrophil-produced protein)
- Immunologic process (e.g., allergic reaction/IgE antibody, activated complement)

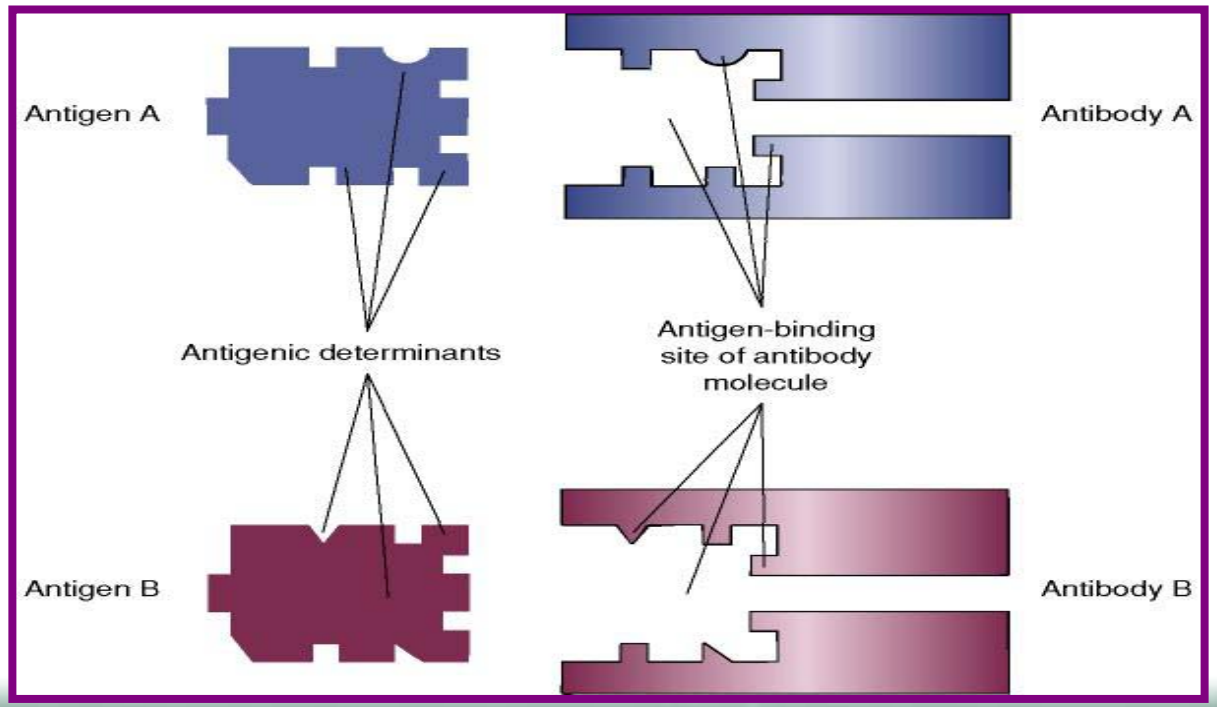


Result: Degranulation
(release of histamine, serotonin, and chemotactic factors)

Result: Synthesis
(construction of leukotrienes and prostaglandins)

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.”
- IgA—involved in secretory immune responses.
- IgE—involved in allergic reactions.
- IgD—present in very low concentrations.

Human Antibody Classifications

- **Isotypic—same with same species.**
- **Allotypic—differ between members of same species.**
- **Idiopathic—differ within the same individual.**

Secretory Immune System

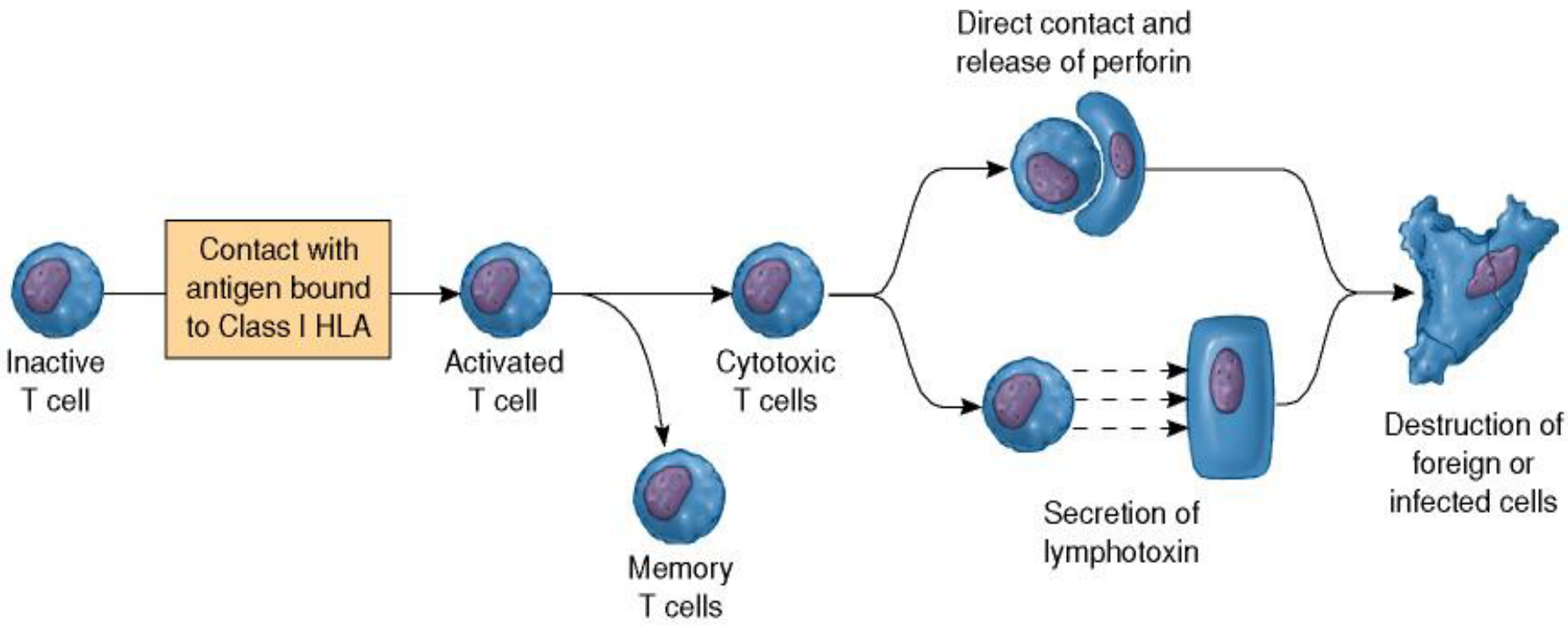
- **Primary function is to protect the body from pathogens that are inhaled or ingested.**

Cell-Mediated Immune Response

Types of Mature T Cells

- **Memory cells—secondary immune responses.**
- **T_d cells—delayed hypersensitivity.**
- **T_c cells—cytotoxic.**
- **T_h cells—helpers.**
- **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.**

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.**

Fetal and Neonatal Immune Function (1 of 2)

- **Some immune response capabilities are developed *in utero*, but most of the immune response system is not fully developed.**

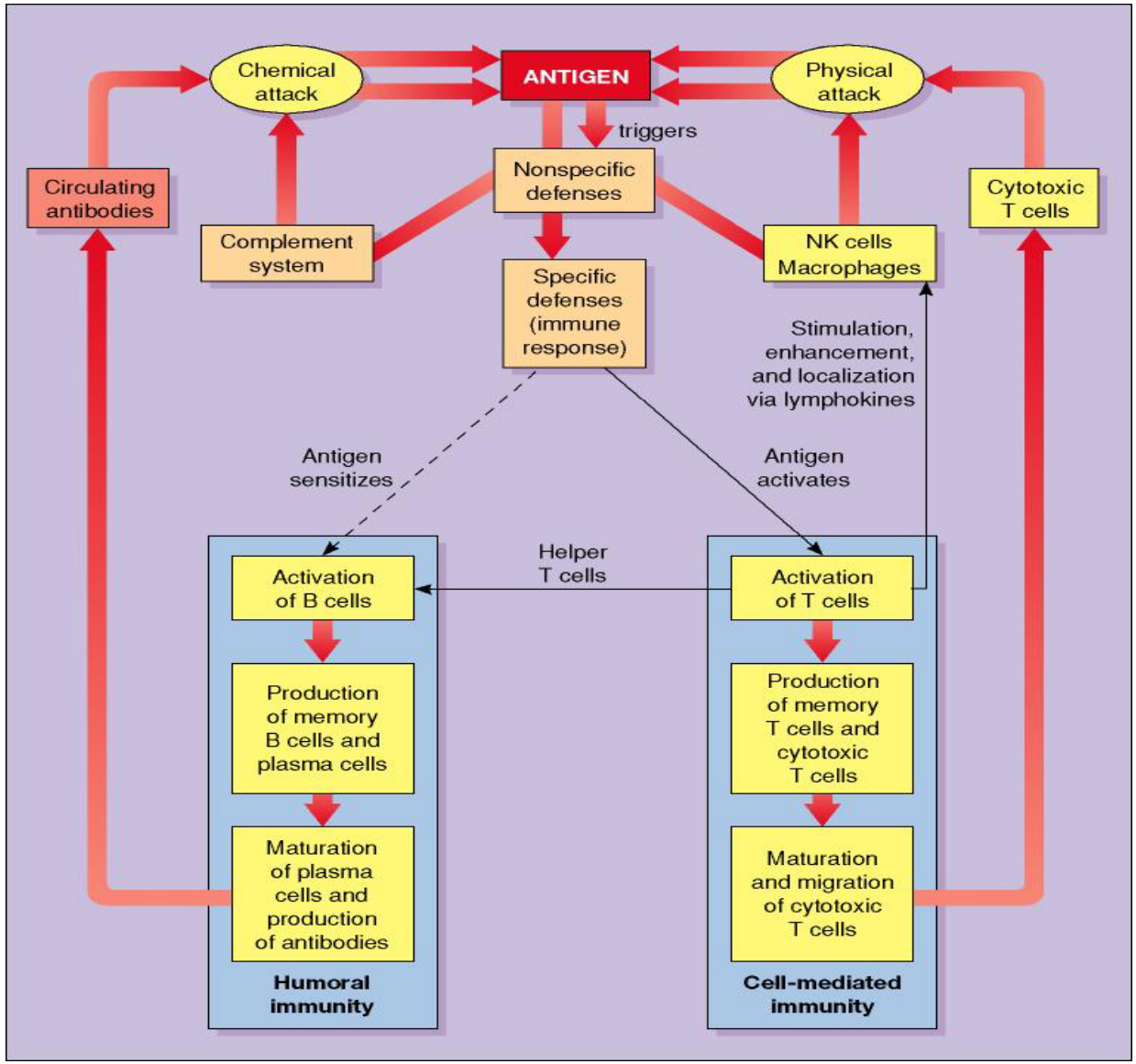
Fetal and Neonatal Immune Function (2 of 2)

- **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 fetal to maternal circulation.**
- **At birth antibodies begin to drop until the immune system matures.**

Aging and the Immune Response

- **As the human body ages, immune functions begin to deteriorate.**
- **T cells are primarily affected.**

Summary of the Immune response



Inflammation

Immune vs. Inflammatory

Immune	Inflammation
Develops slowly	Develops swiftly
Targets specific antigens	Non-specific
Long-lasting—has "memory"	Temporary—days to weeks
Involves one type of white blood cell	Involves many types of white blood cells and platelets
One type of plasma protein—antibodies	Several plasma proteins—complement, coagulation, kinin

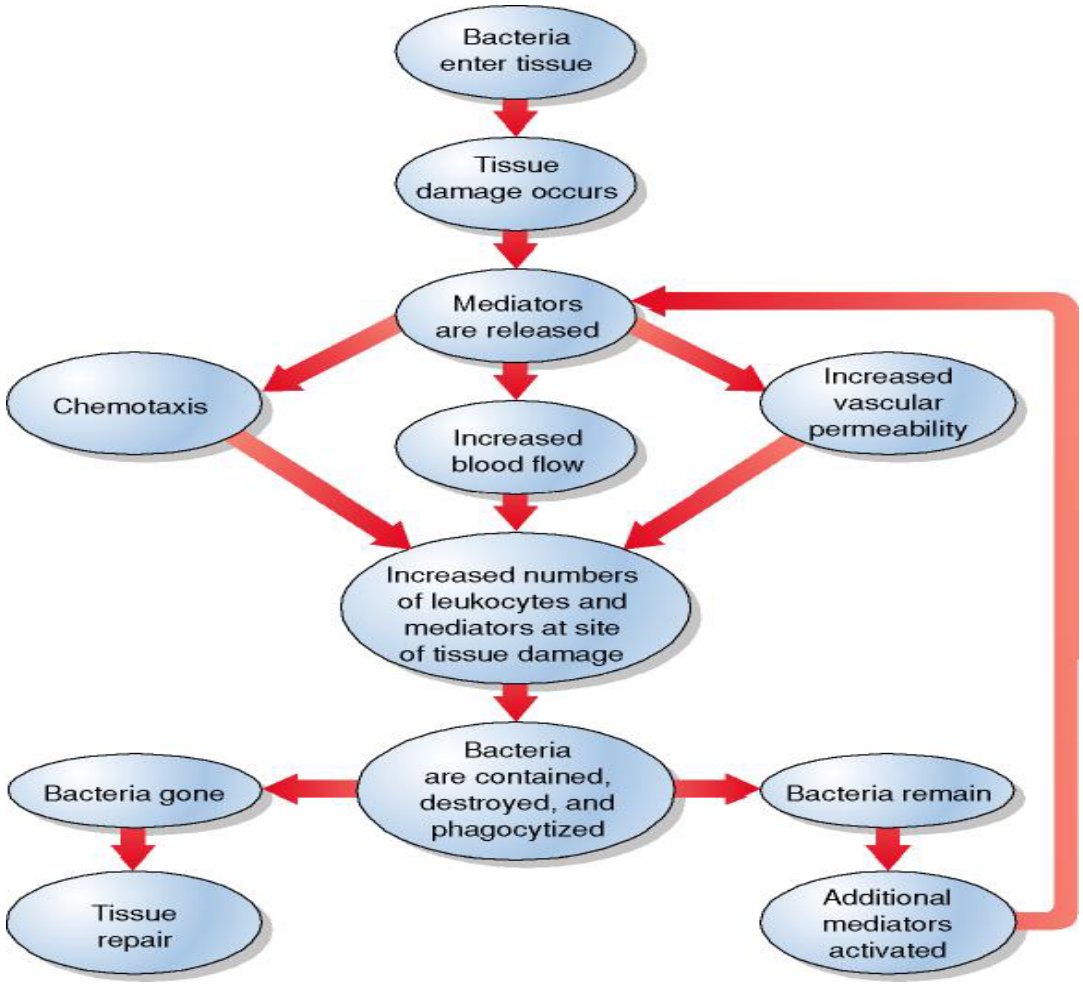
Phases of Inflammation

- **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**

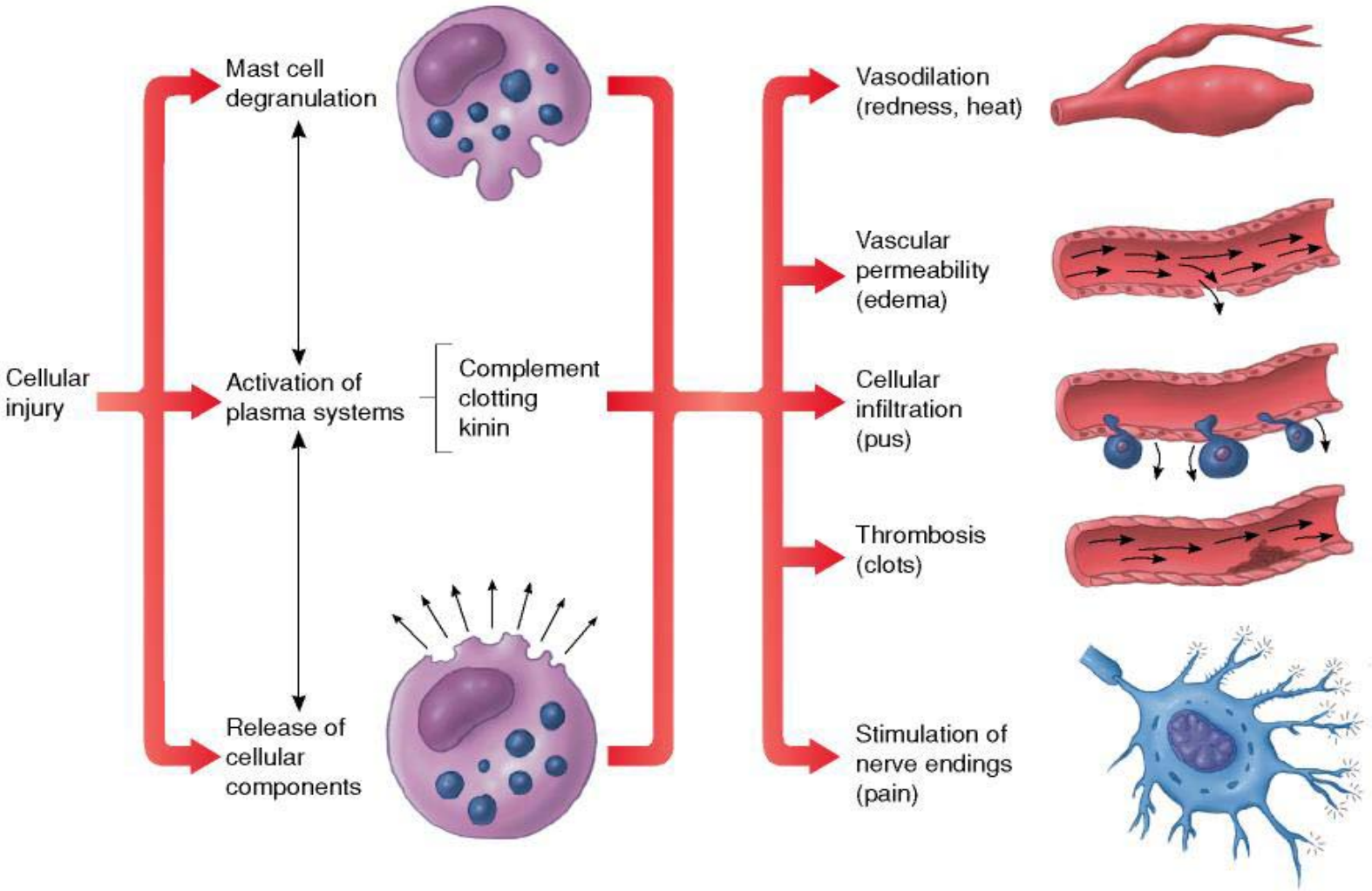
Functions of Inflammation

- Destroy and remove unwanted substances.
- Wall of 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

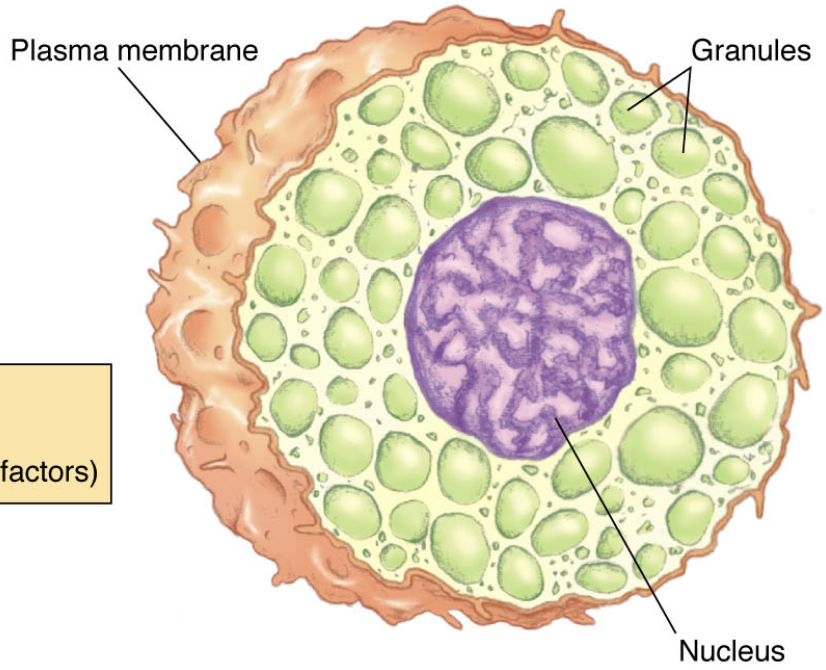
- **Vasoactive amines.**
- **Chemotactic factors.**

Synthesis

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

Mast cell degranulation and synthesis

Cause: **Mast cell stimulated by:**
- Physical injury (e.g., trauma, radiation, temperature extremes)
- Chemical agent (e.g., toxin, venom, enzyme, neutrophil-produced protein)
- Immunologic process (e.g., allergic reaction/IgE antibody, activated complement)



Result: **Degranulation**
(release of histamine, serotonin, and chemotactic factors)

Result: **Synthesis**
(construction of leukotrienes and prostaglandins)

Plasma Protein Systems

Complement System

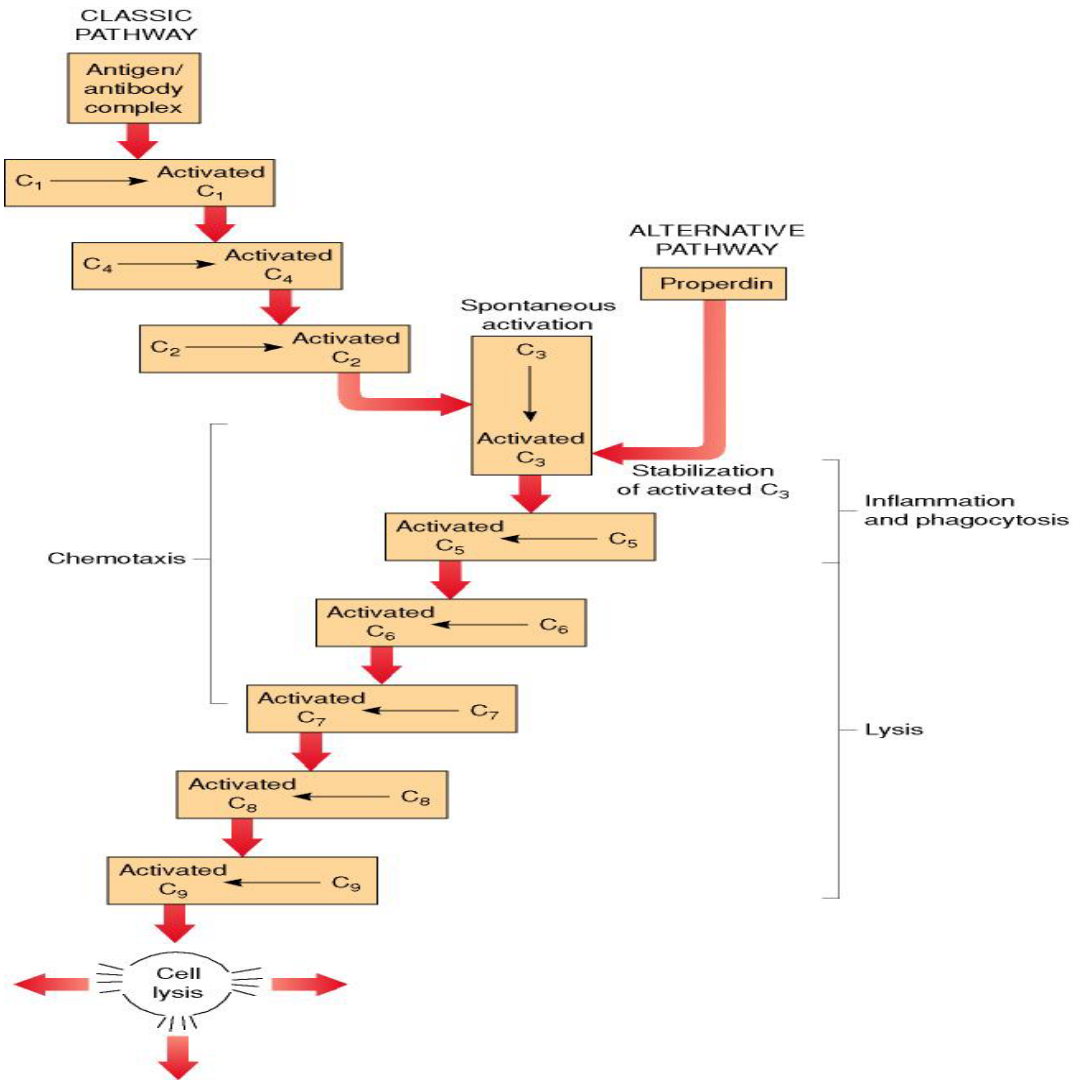
- **11 proteins that are dormant until activated.**
- **Assist in destroying or limiting the damage of an invading organism.**

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.



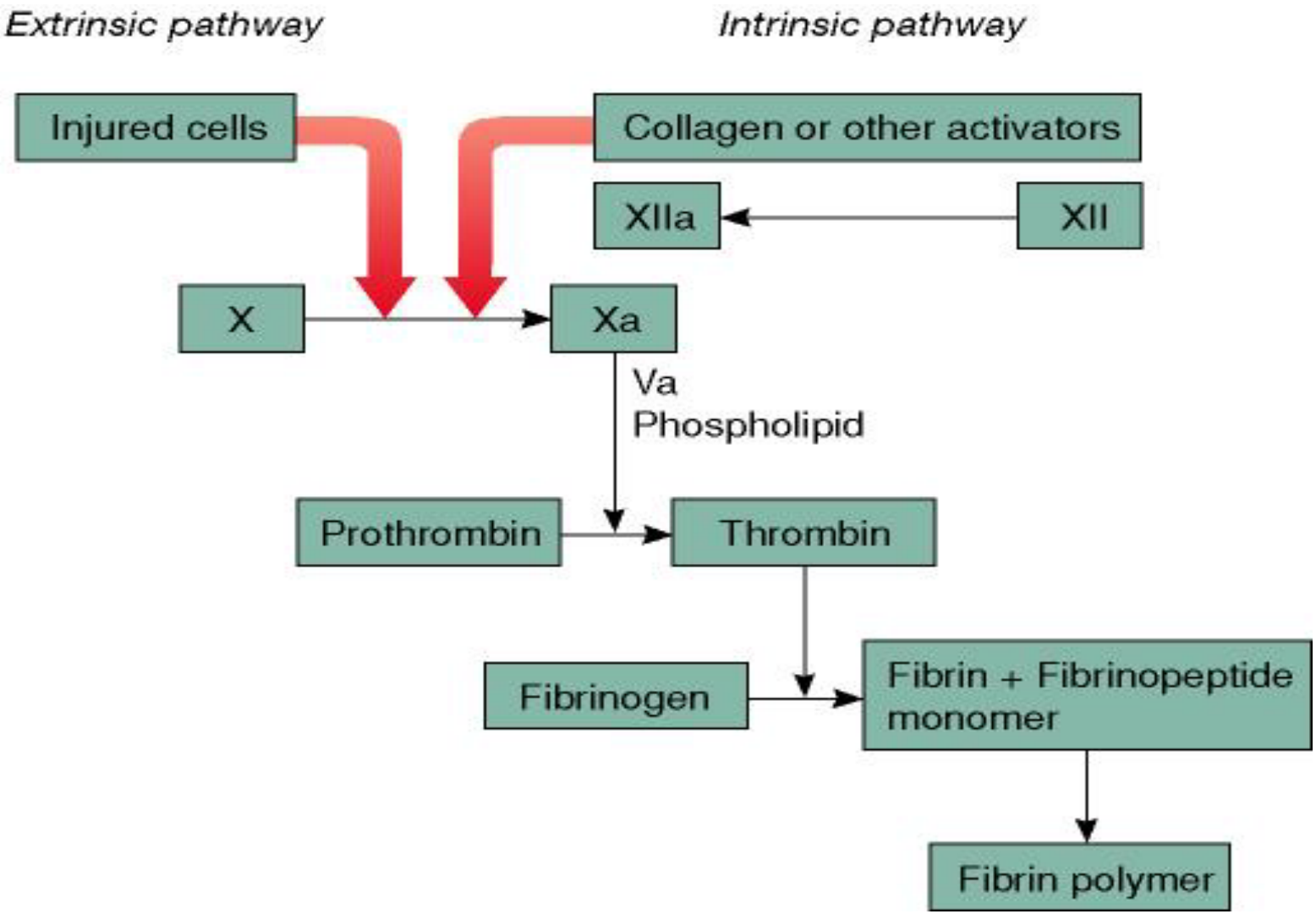
The Coagulation System

- **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 triggered by factors associated with the coagulation cascade.**

The Coagulation Cascade



Control and Interaction of Plasma Protein Systems

- **Control of the plasma protein systems is important for two reasons:**
  1. **The inflammatory response is essential to protect from unwanted invaders.**
  2. **The inflammatory processes are powerful and potentially very damaging to the body.**

Cellular Components of Inflammation

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 allergen 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

- **An immune response against *some* antigens present on only *some* body tissues.**

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

- **Results 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 arthrus 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

Type of Hypersensitivity	Targeted Antigen
Allergy	**Environmental antigens**
Autoimmunity	**Self antigens**
Isoimmunity	**Other person's antigens**

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
- Latrogenic deficiencies
- Deficiencies caused by trauma
- Deficiencies caused by stress
- AIDS

Replacement Therapies for Immune Deficiencies

- **Gamma-globulin therapy**
- **Transplantation and transfusion**
- **Gene therapy**

Stress and Disease

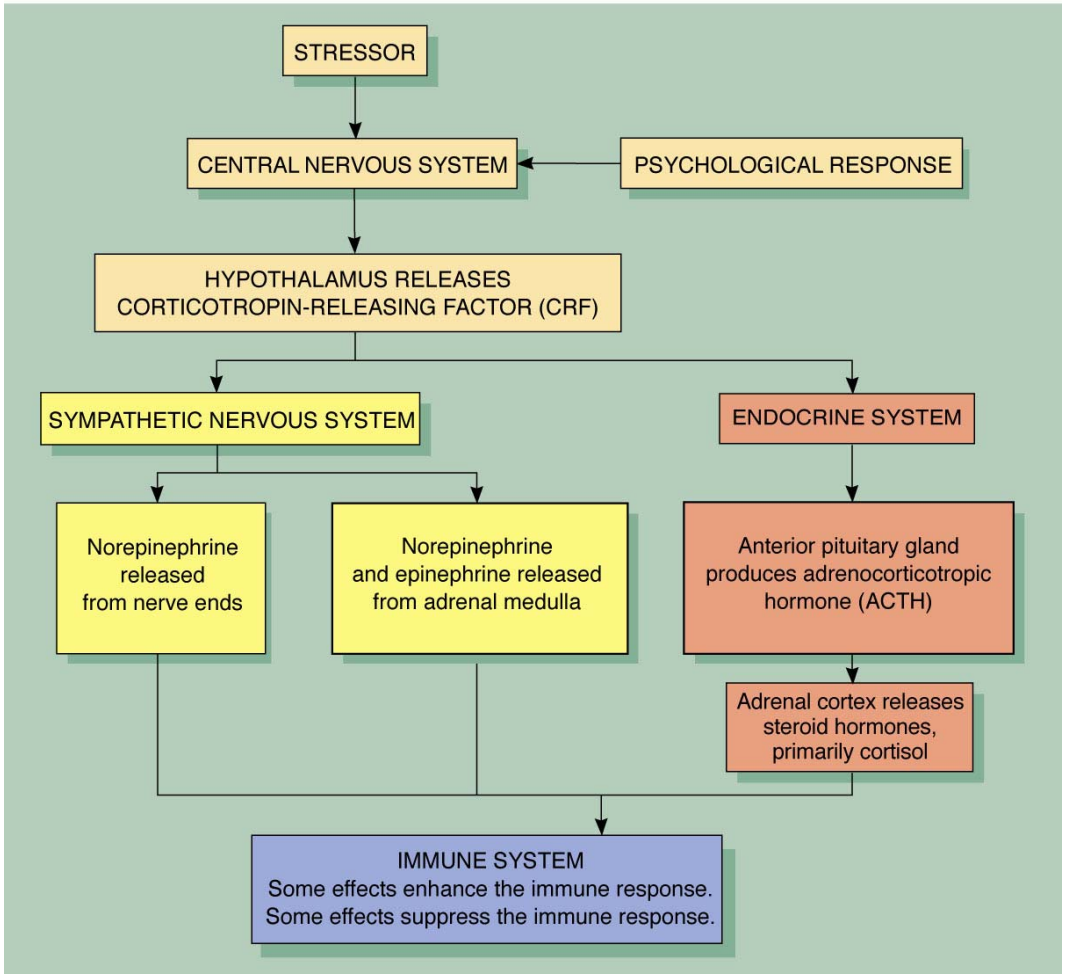
Stress is a state of physical or psychological arousal to stimulus.

General Adaptation Syndrome

- **Stage I – Alarm**
- **Stage II – Resistance or adaptation**
- **Stage III – Exhaustion**

Stressors cause a series of reactions that alter the dynamic steady state of homeostasis.

The Stress Response:
Effects on the Sympathetic Nervous, Endocrine, and Immune Systems.



Neuroendocrine Regulation

- **Sympathetic nervous system is stimulated by corticotropin-releasing factor.**
- **This stimulates the release of catecholamines, cortisol, and other hormones.**

Table 8–9 Physiological Effects of Catecholamines

Organ	Effects
Brain	Increased blood flow Increased glucose metabolism
Cardiovascular system	Increased contractile force and rate Peripheral vasoconstriction
Pulmonary system	Increased ventilation Bronchodilation Increased oxygen supply
Liver	Increased glucose production Increased gluconeogenesis Increased glycogenolysis Decreased glycogen synthesis
Gastrointestinal and genitourinary tracts	Decreased protein synthesis
Muscle	Increased glycogenolysis Increased contraction Increased dilation of skeletal muscle vasculature
Skeleton	Decreased glucose uptake and utilization (insulin release decreased)
Adipose (fatty) tissue	Increased lipolysis Increased fatty acids and glycerol
Skin	Decreased blood flow
Lymphoid tissue	Increased protein breakdown (shrinkage of lymphoid tissue)

Table 8-10 Physiological Effects of Cortisol

Function	Effects
Carbohydrate metabolism	Diminished peripheral uptake/use of glucose; promotes gluconeogenesis; elevates blood glucose levels
Protein metabolism	Increases protein synthesis in liver; depresses protein synthesis in other tissues; depresses immunoglobulin production
Inflammatory effects	Decreases blood levels of lymphocytes, macrophages, eosinophils; decreases leukocytes at inflammation site; delays healing/promotes wound infection
Lipid metabolism	Increases lipolysis in extremities, lipogenesis in face and trunk
Immune reserves	Decreases lymphoid tissue mass; decreases circulation white cells; inhibits production of interleukin-1 and interleukin-2; blocks cell-mediated immunity and generation of fever.
Digestive function	Promotes gastric secretions; at high levels causes ulceration
Urinary function	Enhances production of urine
Connective tissue function	Decreases proliferation of fibroblasts (delays healing)
Muscle function	Maintains normal contractility and work output for skeletal and cardiac muscle
Bone function	Decreases bone formation
Cardiovascular function	Maintains normal blood pressure; assists arteriole constriction; supports myocardial function
Central nervous system function	Modulates perceptual/emotional functioning and daytime arousal

Other Hormones

- **Regulate ACTH secretion.**
- **Inhibit CRF secretion.**
- **Growth hormone released.**
- **Prolactin released.**
- **Testosterone decreased.**

Interactions among the nervous, endocrine, and immune systems.

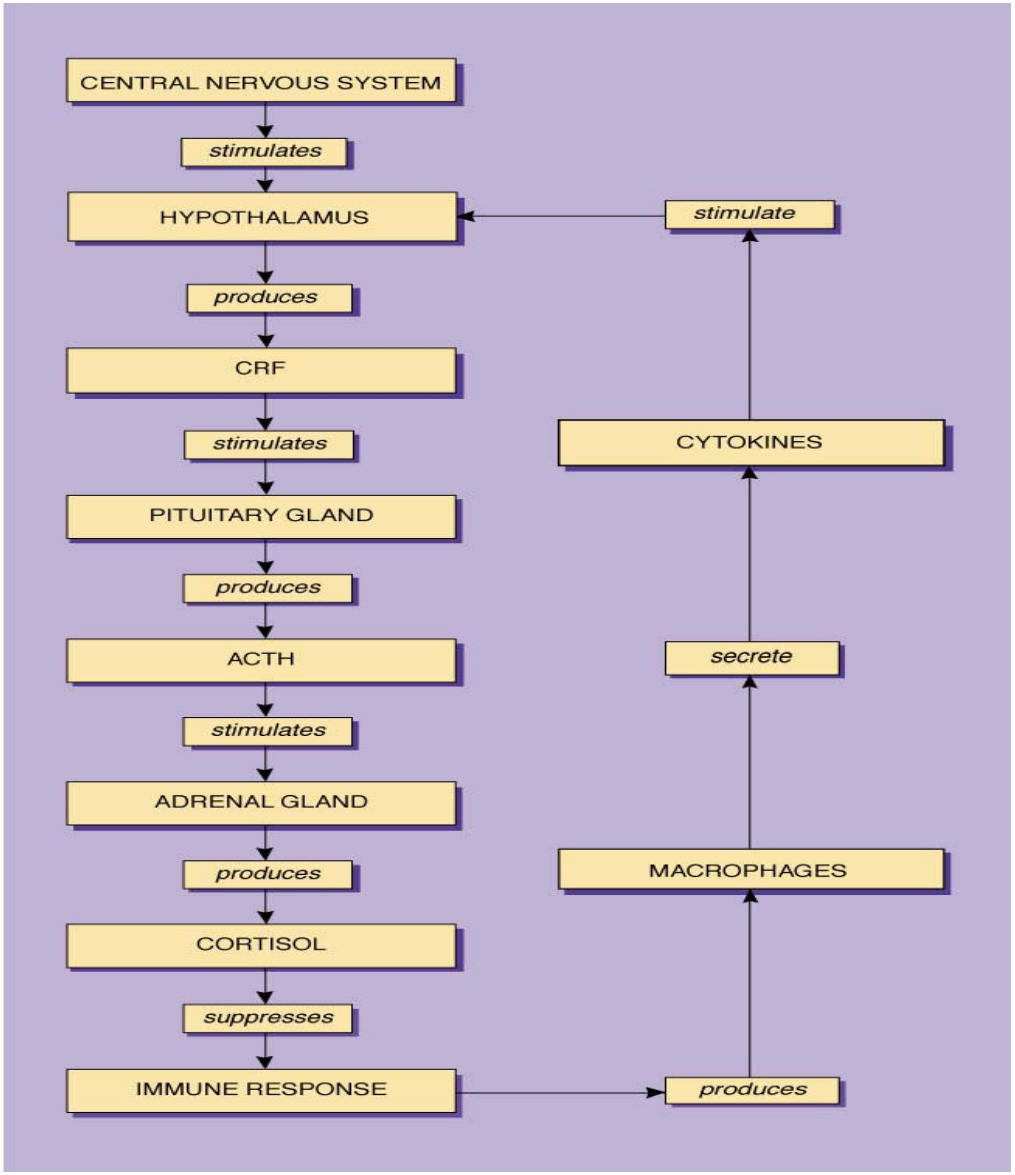


Table 8-11 Stress- and Immune-Related Diseases and Conditions

Target Organ	Diseases and Conditions
Cardiovascular system	Coronary artery disease Hypertension Stroke Dysrhythmias
Muscles	Tension headaches Muscle-related backaches
Connective tissues	Rheumatoid arthritis
Pulmonary system	Asthma Hay fever
Immune system	Immunosuppression or immune deficiency
Gastrointestinal system	Ulcer Irritable bowel syndrome Ulcerative colitis
Genitourinary system	Diuresis Impotence
Skin	Eczema Acne
Endocrine system	Diabetes mellitus
Central nervous system	Fatigue Depression Insomnia

Part 3 Summary

- **The immune system and immune response**
- **Aging and the immune response**
- **Inflammation response**
- **Variances in immunity and inflammation**