The Body Defenses

Chapter Overview

The immune system contributes to homeostasis by providing a sophisticated highly effective defense system. The system is essential in defending against viruses and bacteria, removing "worn out" cell and tissue debris, and destroying mutant cells.

However, these benefits are not without cost. Inappropriate immune responses and tissue rejection are problems due to the efficacy of the immune system as a defense system.

The primary defensive cells are neutrophils, eosinophils, basophils, B lymphocytes, T lymphocytes and macrophages.

The methods of defense include phagocytizing, lysing secreting chemicals, marking for destruction, producing antibodies and inactivating the invaders. Also involved are memory and the transfer of information by cloning. The immunity derived from this system is either active, passive, or acquired. In most systems the cells function as part of a tissue or organ while in the immune system the defense is primarily from individual cells.

The skin and all surfaces that communicate with the external environment provide either physical and/or chemical defenses. Defense of the body begins at the environmental body interface and continues throughout the body. Thus, homeostasis is maintained for the survival of cells, which make up body systems, which maintain homeostasis.

Chapter Outline

INTRODUCTION

*The immune defense system provides protection against foreign and abnormal cells and removes cellular debris.*

- Immunity refers to the body's ability to resist or eliminate potentially harmful foreign materials or abnormal cells.
- The following activities are attributed to the immune defense system: (1) Defense against invading pathogens, (2) removal of "worn out" cells and tissue debris, (3) identification and destruction of abnormal or mutant cells that have originated in the body, (4) elicit inappropriate immune responses that lead either to allergies, or to autoimmune disease, and (5) rejection of tissue cells of foreign origin.

Pathogenic bacteria and viruses are the major targets of the immune defense system.

- Bacteria are nonnucleated, single-celled microorganisms self-equipped with all machinery essential for their own survival and reproduction.
- Pathogenic bacteria induce tissue damage and produce disease by releasing enzymes or toxins that injure or functionally disrupt cells and organs.
- Viruses are not self-sustaining cellular entities.
- Viruses consist only of nuclei acids enclosed in a protein coat
- Viruses invade a host cell and take over the cellular biochemical facilities for their own purposes.
Leukocytes are the effector cells of the immune defense system.
- Neutrophils are highly mobile phagocytic specialists that engulf and destroy unwanted materials.
- Eosinophils secrete chemicals that destroy parasitic worms and are involved in allergic manifestations.
- Basophils release histamine and heparin and also are involved in allergic manifestations.
- The B lymphocytes secrete antibodies that indirectly lead to the destruction of foreign material.
- The T lymphocytes are responsible for cell-mediated immunity involving direct destruction of virus-invaded cells and mutant cells through nonphagocytic means.
- Monocytes are transformed into macrophages, which are large, tissue-bound phagocytic specialists.

Immune responses may be either nonspecific or specific.
- Nonspecific immune responses are inherent defense responses that nonselectively defend against foreign or abnormal material of any type.
- Specific immune responses are selectively targeted against particular foreign material to which the body has previously been exposed.

Innate nonspecific defenses include inflammation, interferon, natural killer cells, and the complement system.
- Innate nonspecific defenses that come into play whether or not there has been prior experience with the offending agent include the following: inflammation, interferon, natural killer cells, and the complement system.

Inflammation is a nonspecific response to foreign invasion or tissue damage.
- The ultimate goal of inflammation is to bring to the invaded or injured area phagocytes and plasma proteins that can (1) isolate, destroy, or inactivate the invaders; (2) remove debris; and (3) prepare for subsequent healing and repair.
- Upon bacterial invasion, macrophages already present in the area immediately begin phagocytizing the foreign microbes.
- Almost immediately upon microbial invasion arterioles within the area dilate, increasing blood flow to the site of injury.
- Histamine is released in the area of tissue damage by mast cells.
- Released histamine increases the capillaries' permeability.
- Plasma proteins that normally are prevented from leaving the blood escape into the inflamed tissue.
- As the leaked plasma proteins accumulate in the interstitial fluid, they exert a colloid osmotic pressure.
- The elevation in local osmotic pressure, and the increased capillary blood pressure result in localized edema.
- Upon exposure to tissue thromboplastin in the injured tissue and to specific chemicals secreted by phagocytes on the scene, fibrinogen, the final factor in the clotting system, is converted into fibrin.
- Fibrin forms interstitial fluid clots in the spaces around the bacterial invaders and damaged cells.
- This walling off of the injured region from the surrounding tissues prevents or at least delays the spread of bacterial invaders and their toxic products.
- Within an hour after the injury, the area is teeming with leukocytes that have exited from the vessels.
- Neutrophils are the first to arrive.
- During the next eight to twelve hours, monocytes swell and mature into macrophages.
- Leukocyte emigration from the blood into the tissues involves the processes of margination, diapedesis, amoeboid movement and chemotaxis.
- Margination refers to the sticking of bloodborne leucocytes to the inner endothelium lining of capillaries.
- Cell adhesion molecules (CAM's) are important in the process of margination.
- Selectins, one type of CAM, cause leucocytes that are flowing by in the bloodstream to slow down.
• This slowing down allows the leucocytes enough time to check for local activating factors.
• The activating factors cause the leukocytes to adhere firmly to the endothelial lining by means of interaction with another type of CAM, the integrins.
• The adhered leukocytes start exiting by a mechanism known as diapedesis.
• Assuming amoeba-like behavior, an adhered leukocyte pushes a long, narrow projection through a capillary pore.
• Outside the vessel, the leukocyte moves in an amoeboid fashion toward the site of tissue damage and bacterial invasion.
• Phagocytic cells are guided in their direction of migration by attraction to certain chemical mediators, or chemotaxins.
• This process is referred to as chemotaxis.
• Within a few hours after the onset of the inflammatory response, the number of neutrophils in the blood may increase up to four or five times that of normal.
• Phagocytosis involves the engulfment and intracellular degradation of foreign particles and tissue debris.
• Dead tissue and many foreign materials have surface characteristics that differ from normal body cells.
• Foreign particles are deliberately marked for phagocytic ingestion by being coated with chemical mediators (opsonins) generated by the immune system.
• Microbe-stimulated phagocytes release many chemicals, which function as mediators of the inflammatory response.
• Macrophages secrete nitric oxide that is toxic to nearby microbes.
• Neutrophils secrete lactoferrin, a protein that lightly binds with iron, making it unavailable for use by invading bacteria.
• Phagocytic secretions stimulate the release or histamine from mast cells.
• Phagocytic secretions trigger both clotting and anticoagulating systems.
• Phagocytic secretions split kininogens into active kinins.
• Kinins activate nearby pain receptors.
• Kinins act as powerful chemotaxins to induce phagocyte migration to the affected area.
• Phagocytic secretions induce the development of fever by the release of endogenous pyrogen.
• Macrophages secrete a chemical mediator known as leukocyte endogenous mediator.
• Leukocyte endogenous mediator (LEM) causes a decrease in plasma concentration of iron by altering iron metabolism.
• The LEM stimulates granulopoiesis, the synthesis and release of neutrophils and other granulocytes by the bone marrow.
• The LEM also stimulates the release of acute-phase proteins from the liver.
• Macrophages secrete interleukin 1, which enhances the proliferation and differentiation of both B and T lymphocytes.
• The ultimate purpose of the inflammatory process is to isolate and destroy injurious agents and to clear the area for tissue repair.

Salicylates and glucocorticoid drugs suppress the inflammatory response.
• Numerous drugs can suppress the inflammatory response; the most effective are the salicylates and glucocorticoids.
• Salicylates interfere with the inflammatory response by decreasing histamine release, resulting in a reduction of swelling, redness, and pain.
• Salicylates reduce fever by inhibiting the production of prostaglandins.
• Glucocorticoids suppress almost every aspect of the inflammatory response.
• In addition, they destroy lymphocytes within lymphoid tissue and reduce antibody production.

Interferon transiently inhibits multiplication of viruses in most cells.
• A nonspecific defense mechanism is the release of interferon from virus-infected cells.
• Interferon binds with receptors on the plasma membranes of neighboring cells signaling these cells to prepare for the possibility of impending viral attack.
• Interferon triggers the production of viral-blocking enzymes by potential host cells.
• Binding with interferon induces these other cells to synthesize enzymes that can break down viral messenger RNA.
• Interferon exerts its effect by activating a heretofore unknown signal transduction pathway involving a newly identified class of intracellular chemicals known as Janus kinases within the cells to which it binds.
• Interferon markedly enhances the actions of cell-killing cells.
• Interferon also slows cell division and suppresses tumor growth.
• Through recombinant DNA technology, bacteria can be turned into interferon "factories" for large-scale commercial production of this valuable immune agent.
• Interferon has been approved for some forms of cancer, including one previously fairly rare form of leukemia and the AIDS-associated Kaposi's sarcoma, as well as for genital warts caused by papillomavirus.
• Interferon is also the first drug approved for treating multiple sclerosis.

**Natural killer cells destroy virus-infected cells and cancer cells upon first exposure to them.**
• Natural killer cells are naturally occurring, lymphocyte-like cells that nonspecifically destroy virus-infected cells and cancer cells by directly lysing their membranes.

**The complement system kills microorganisms directly both on its own and in conjunction with antibodies and augments the inflammatory response.**
• The system derives its name from the fact that it “complements” the action of antibodies.
• The complement system consists of plasma proteins that are produced by the liver and circulate in the blood in inactive form.
• Once the first component is activated, it activates the next component, and so on.
• The final five components assemble into a large protein complex, the membrane-attack complex (MAC), which attacks the surface membrane of nearby microorganisms by embedding itself, so that a large channel is created through the microbial surface membrane.

• The osmotic flux of water into the victim cell causes it to swell and burst.
• Complement-induced lysis is the major means of directly killing microbes without phagocytizing them.
• Complement components augment the inflammatory response by: (1) serving as chemotaxins, (2) acting as opsonins, (3) promoting vasodilation and increased vascular permeability; (4) stimulating the release of histamine; and (5) activating kinins.

**Adaptive immunity: General concepts**
Specific adaptive immune responses include antibody-mediated immunity accomplished by B lymphocyte derivatives and cell-mediated immunity accomplished by T lymphocytes.
• There are two classes of specific immune responses: antibody-mediated, or humoral, immunity involving the production of antibodies by B lymphocytes derivatives known as plasma cells, and cell-mediated immunity, involving the production of activated T lymphocytes, which directly attack unwanted cells.
• During fetal life and early childhood, some of the immature lymphocytes migrate through blood to the thymus, where they undergo further processing to become T lymphocytes.
• Lymphocytes that mature without benefit of "thymic education" become B lymphocytes.
• The thymus gradually atrophies and becomes less important as the individual matures.
• The thymus does, however, continue to produce thymosin, a hormone important in maintaining the T cell lineage.

**An antigen induces an immune response against itself.**
• Both B and T cells must be able to specifically recognize unwanted cells and other material to be destroyed or neutralized as being distinct from the body’s own normal cells.
• The presence of antigens enables them to make this distinction.
• Foreign proteins are the most common antigens.
• Haptens are low-molecular weight organic substances that are not antigens by themselves but can become antigens if they attach to body proteins.

**B Lymphocytes: Antibody-Mediated Immunity**

*Antibodies amplify the inflammatory response to promote destruction of the antigen that stimulated their production.*

• In the case of B cells, binding with an antigen induces the cell to differentiate into a plasma cell, which produces antibodies that are able to combine with the specific antigen that stimulated the antibodies' production.
• Antibodies are secreted into the blood or lymph where they are known as gamma globulins or immunoglobulins.
• Antibodies are grouped into five subclasses.
• Antibody proteins in all five subclasses are composed of four interlinked polypeptide chains—arranged in the shape of a Y.
• Characteristics of the arm regions of the Y determine the specificity of the antibody.
• An antibody has two identical antigen-binding sites, one at the tip of each arm.
• These antigen-binding fragments (Fab) are unique for each different antibody.
• The tail portion of every antibody within each immunoglobulin subclass is identical.
• Immunoglobulins cannot directly destroy foreign organisms or other unwanted materials upon binding with antigens on their surfaces.
• Antibodies exert their protective influence in one of two general ways: physical hindrance of antigens and amplification of nonspecific immune responses.
• Antibodies mark or identify foreign material as targets for actual destruction by the complement system, phagocytes, or killer cells.

*Each antigen stimulates a different clone of B lymphocytes to produce antibodies.*

• Each B lymphocyte is preprogrammed to respond to only one of the millions of different antigens.
• The clonal selection theory proposes that diverse B lymphocytes are produced during fetal development, each capable of synthesizing an antibody against a particular antigen before ever being exposed to it.
• B cells remain dormant, not actually secreting their particular antibody product until they correct in contact with the appropriate antigen.
• Antigen binding causes the activated B cell clone to multiply and differentiate into two cell types—plasma cells and memory cells.
• Plasma cells switch to the production of IgG antibodies, which are secreted rather than remaining membrane bound.
• In the blood, the secreted antibodies combine with invading free antigen, marking it for destruction by the complement system, phagocytic ingestion, or other means.
• A small proportion of the new B lymphocytes become memory cells, which do not participate in the current immune attack against the antigen but instead remain dormant and expand the specific clone.
• During initial contact with a microbial antigen, the antibody response is delayed for several days until plasma cells are formed and does not reach its peak for a couple of weeks.
• This response is known as the primary response.
• After reaching the peak, the antibody levels gradually decline over a period of time.
• Long-term protection against the same antigen is primarily attributable to the memory cells.
• If the same antigen ever reappears, the long-lived memory cells launch a more rapid, more potent, and longer-lasting secondary response.
• This is the basis of long-term immunity against a specific disease.
• During vaccination, the individual is deliberately exposed to a pathogen that has been stripped of its disease-inducing capability, but can still induce antibody formation against it.

*Active immunity is self-generated; passive immunity is "borrowed."

• The production or antibodies as a result of exposure to an antigen is referred to as active immunity against that antigen.
• A second way in which an individual can acquire antibodies is by direct transfer of antibodies actively formed by another person (or animal).
• The transfer of antibodies is known as passive immunity.

Natural immunity is actually a special case of actively acquired immunity.
• Antibodies associated with blood types are the classic example of "natural antibodies".
• Accordingly, the plasma of type A blood contains anti-B antibodies, type B blood contains anti-A antibodies, and both anti-A and anti-B antibodies are present in type O blood.
• High levels of these antibodies are found in the plasma of individuals who have never been exposed to a different type of blood.
• It is now known that individuals are unknowingly exposed at an early age to small amounts of A- and B-like antigens associated with common intestinal bacteria.
• Because type O individuals do not have and A or B antigens, they are considered to be universal donors.
• Type O individuals can receive only type O blood.
• Type AB individuals are called universal recipients.
• Lacking both anti-A and anti-B antibodies, they can accept donor blood of any type.
• Individuals who possess the Rh factor (an erythrocyte antigen) are said to have Rh positive blood.
• Those lacking the Rh factor are considered to be Rh-negative.
• No naturally occurring antibodies develop against the Rh factor.

Lymphocytes respond only to antigens that have been processed and presented to them by macrophages.
• Invading organisms or other antigens are first engulfed by macrophages.
• During phagocytosis, the macrophage processes the raw antigen intracellularly and then exposes the processed antigen on the outer surface of the macrophage's plasma membrane in such a way that the adjacent B cells can recognize and be activated by it.
• When a macrophage engulfs a foreign microbe, it digests the microbe into antigenic peptides.
• Each antigenic peptide is then bound to an MHC molecule.
• An MHC molecule has a deep groove into which a variety of antigenic peptides can bind.
• Loading of the antigenic peptide onto an MHC molecule takes place in a newly discovered specialized organelle within antigen-presenting cells, the compartment for peptide loading or CPL.
• The MHC molecule then transports the bound antigen to the cell surface where it is presented to passing lymphocytes.
• Macrophages secrete interleukin 1 that enhances the differentiation and proliferation of the now-activated B cell clone.
• Interleukin 1 is also largely responsible for the fever and malaise accompanying many infections.
• Many antigens are similarly presented to T cells.
• Helper T cells help B cells upon being activated by macrophage-presented antigen.
• The helper T cells secrete a chemical mediator, B cell growth factor, which further contributes to B cell function in concert with the interleukin I secreted by macrophages.

T LYMPHOCYTES: CELL-MEDIATED IMMUNITY
The three types of T cells are specialized to kill virus-infected host cells and to help or suppress other immune cells.
• Unlike B cells, T cells do not secrete antibodies.
• T cells must be in direct contact with their targets, a process known as cell-mediated immunity.
• Like B cells, T cells are clonal and exquisitely antigen-specific.
• T cells are activated by foreign antigen only when it is present on the surface of a cell that also carries a marker of the individual's own identity.
• There are three subpopulations of T cells, depending on their roles when activated by antigens: (1) cytotoxic T cells, (2) helper T cells, and (3) suppressor T cells.
• Like B cells, not all activated T cell progeny become effector T cells.
• A small proportion of them remain dormant, serving as a pool of memory T cells that are primed and ready to respond should the same foreign antigen ever reappear within a body cell.
• The targets of cytotoxic T cells most frequently are host cells infected with viruses.
• One means by which cytotoxic T cells and natural killer cells destroy a targeted cell is by releasing perforin molecules, which penetrate into the target cell's surface membrane and join together to form porelike channels.
• Cytotoxic T cells also induce these virus-infected cells to self-destruct, a process known as apoptosis.
• The virus released upon destruction of the host cell is then directly destroyed in the extracellular fluid by phagocytic cells, neutralizing antibodies, and the complement system.
• Virus-infected neurons are spared from extermination by the immune system.
• Antibodies not only target viruses for destruction in the extracellular fluid but can also eliminate viruses inside neurons.
• Helper T cells secrete B-cell growth factor, which enhances the antibody-secreting ability of the activated B-cell clone.
• Helper T cells secrete T cell growth factor, which augments the activity of cytotoxic T cells, suppressor T cells, and even other helper T cells responsive to the invading antigen.
• Some chemicals secreted by T cells act as chemotaxins to lure more neutrophils and macrophages-to-be to the invaded area.
• Macrophage-migration inhibition factor, another important cytokine released from helper T cells, keeps these large phagocytic cells in the region by inhibiting their outward migration.
• The AIDS virus selectively invades helper T cells, destroying or incapacitating the cells that normally orchestrate much of the immune response.
• The AIDS virus also invades macrophages.
• Recent studies have demonstrated the existence of two subsets of helper T cells, T helper 1 (TH 1) cells and T helper 2 (TH 2) cells.
• TH1 cells rally a cell-mediated response, whereas TH2 cells promote humoral immunity by B cells and rev up eosinophil activity.
• Helper T cells produced in the thymus are in a "naive" state until they encounter the antigen they are primed to recognize.
• Whether a naive helper T cell becomes a TH1 or TH2 cell depends on which cytokines are secreted by the macrophage as it presents the antigen to the naive T cell.
• Interleukin 12 drives a naive T cell specific for the antigen to become a TH1 cell, whereas interleukin 4 favors the development of a naive cell into a TH2 cell.
• Suppressor T cells limit the response of all other immune cells.

The immune system is usually tolerant of self-antigens.
• Suppressor T cells probably also play an important role in preventing the immune system from attacking the person's own tissues, a phenomenon known as tolerance.
• At least five different mechanisms appear to be involved in tolerance: (1) clonal deletion, (2) clonal energy, (3) inhibition by suppressor T cells, (4) antigen sequestering, and (5) granting of immune privilege.
• A condition in which the immune system fails to recognize and tolerate self-antigens associated with particular tissues is known as an autoimmune disease, of which myasthenia gravis is an example.
• Autoimmune disease may arise from a number of different causes: (1) A reduction in suppressor T cell activity or an imbalance in the ratio of suppressor to helper T cells specific for self-antigens; (2) normal self-antigens may be modified so that they are no longer recognized and tolerated by the immune system; (3) Exposure to normally inaccessible self-antigens sometimes induces an immune attack against these antigens; and (4) Exposure of the immune system to a foreign antigen structurally almost identical to a self-antigen.
The major histocompatibility complex is the code for surface membrane-enclosed self-antigens unique for each individual.

- The self-antigens, that the immune system learns to recognize as markers of a person's own cells, are plasma membrane-bound glycoproteins known as MHC molecules, because their synthesis is directed by a group of genes called the major histocompatibility complex or MHC.
- These are the same MHC molecules that escort engulfed foreign antigen to the cell surface for presentation by antigen-presenting cells.
- More than a hundred different MHC molecules have been identified in human tissue, but each individual has a code for only three to six of these possible antigens.
- The exact pattern of MHC molecules varies from one individual to another much like a "biochemical fingerprint."
- T cells bind with MHC self-antigens only when they are in association with a foreign antigen.
- T cells do bind with MHC antigens present on the surface of transplanted cells in the absence of foreign viral antigen.
- The ensuing destruction of the transplanted cells is responsible for rejection of transplanted or grafted tissues.
- To minimize the rejection phenomenon, the tissues of donor and recipient are matched according to MHC antigens.
- New therapeutic agents have become extremely useful in selectively depressing T cell.
- The natural function of MHC antigens lies in their ability to direct the responses of T cells, not in their artificial role in the rejection of transplanted tissue.
- Each individual has two main classes of MHC-encoded glycoproteins that are differentially recognized by cytotoxic T and helper T cells.
- Cytotoxic T cells are able to respond to foreign antigen only in association with class I MHC glycoproteins, which are found on the surface of virtually all nucleated cells.
- Class II MHC glycoproteins, which are recognized by helper T cells, are restricted to the surface of a few special types of immune cells, such as B cells, cytotoxic T cells, and macrophages.
- The class I and II markers serve as signposts to guide cytotoxic and helper T cells to precise cellular locations where their immune capabilities can be most effective.
- Essentially all cells display class I MHC glycoproteins, enabling cytotoxic T cells to attack any invaded host cell.
- Helper T cells can bind with foreign antigen only when it is found on the surfaces of immune cells bearing class II glycoproteins.
- These include macrophages, which present antigen to helper T cells, and B and T cells, whose activity is enhanced by helper T cells.
- Specific binding requirements for the various T cells help ensure the appropriate T cell responses.

Immune surveillance against cancer cells involves an interplay among cytotoxic T cells, natural killer cells, macrophages and interferon.

- Another important function generally attributed to the T cell system is its role in recognizing and destroying newly arisen, potentially cancerous tumor cells before they have a chance to multiply and spread; this process is known as immune surveillance.
- Any normal cell may be transformed into a cancer cell if mutations occur within its genes responsible for controlling cell division and growth.
- Such mutations frequently occur by exposure to carcinogenic factors.
- A cell that has been transformed into a tumor cell defies the normal controls on its proliferation and position.
- Unrestricted multiplication of a single tumor cell results in a tumor.
- If the mass is slow growing and does not infiltrate into the surrounding tissue, it is considered a benign tumor.
- Invasive tumors are known as malignant tumors, commonly referred to as cancer.
- Often some of the cancer cells break away from the parent tumor and are transported through the blood to new territories.
- Metastasis is the term applied to this spread of cancer to other parts of the body.
• Cancer cells typically remain immature and do not become specialized, often resembling embryonic cells instead.
• Such dedifferentiated malignant cells lack the ability to perform the specialized functions of the normal cell type from which they mutated.
• Most mutations do not result in malignancy.
• Only a fraction of the mutations involve loss of control over the cell's growth and multiplication.
• A single mutation generally is not sufficient for a cell to become cancerous.
• Potentially cancerous cells that do arise are usually destroyed by the immune system early in their development.
• Immune surveillance against cancer depends on an interplay among three types of immune cells; cytotoxic T cells, natural killer cells, and macrophages.
• All three of these immune cell types secrete interferon.
• Interferon inhibits multiplication of cancer cells and increases the killing ability of the immune cells.
• Natural killer cells do not require prior exposure and sensitization to a cancer before being able to launch a lethal attack.
• Cytotoxic T cells are believed to be especially important in defending against the few kinds of virus-induced cancers.
• Natural killer cells and cytotoxic T cells release perforin and other toxic chemicals that destroy the targeted mutant cell.
• Macrophages are able to engulf and destroy cancer cells intracellularly.
• B cells, upon viewing a mutant cancer cell as an alien to normal self, may produce antibodies against it.
• The blocking antibodies are able to bind with the antigenic sites on the cancer cell, "hiding" these sites from recognition by cytotoxic T cells.

A regulatory loop appears to link the immune system and the nervous and endocrine systems.
• There are important links between the immune system and the body's two major control systems, the nervous and endocrine systems.
• The immune system both influences and is influenced by the nervous and endocrine systems.
• Interleukin 1 can turn on the stress response by activating a sequence of nervous and endocrine events that result in the secretion of cortisol.
• Cortisol mobilizes the body's nutrient stores so that metabolic fuel is readily available to keep pace with the body's energy demand at a time when the person is sick.
• Cortisol mobilizes amino acids to repair any tissue damage.
• Cytokines released by immune cells enhanced the neurally and hormonally controlled stress response, while cortisol suppresses the immune system.

IMMUNE DISEASES

Immune deficiency disease reduce resistance to foreign invaders.
• Abnormal functioning of the immune system can lead to immune diseases in two general ways: deficiency diseases and inappropriate immune attacks.
• Deficiency diseases occur when the immune system fails to respond adequately to foreign invasion.
• The most recent and tragically the most common acquired immune deficiency disease is AIDS, which is caused by HIV, a virus that invades and incapacitates the critical helper T cells.

Inappropriate immune attacks against harmless environmental substances are responsible for allergies.
• The other category of immune diseases involves inappropriate specific immune attacks that cause reactions harmful to the body.
• These include: (1) autoimmune responses, in which the immune system turns against one of the body's own tissues; (2) immune-complex diseases, which involve overexuberant antibody responses that "spill over" and damage normal tissues; and (3) allergies.
• An allergy is the acquisition of an inappropriate specific immune reactivity, or
hypersensitivity, to a normally harmless environmental substance.

- In immediate hypersensitivity, the allergic response appears within about twenty minutes after the sensitized individual is exposed to an allergen, whereas in delayed hypersensitivity, the reaction is not generally manifested until a day or so following exposure.

- The most common allergens that provoke immediate hypersensitivities are pollen grains, bee stings, penicillin, certain foods, molds, dust, feathers, and animal fur.

- These allergens bind to and elicit the synthesis of IgE antibodies rather than IgG antibodies.

- When an individual with an allergic tendency is first exposed to a particular allergen, compatible helper T cells secrete interleukin 4, which produces compatible B cells to synthesize IgE antibodies specific for the allergen.

- IgE antibodies do not freely circulate.

- Instead, their tail portions attach to mast cells and basophils.

- Binding of an appropriate allergen with the outreached arm regions of the IgE antibodies that are lodged tail first in a mast cell or basophil triggers the rupture of the cell's preformed granules.

- As a result, histamine and other chemical mediators spew forth into the surrounding tissue.

- The following are among the most important chemicals released during immediate allergic reactions: (1) histamine, (2) slow-reactive substance of anaphylactic, and (3) eosinophil chemotactic factor.

- If the reaction is limited to the upper respiratory passages, the released chemicals bring about the symptoms of hay fever.

- If the reaction is concentrated primarily within the bronchioles, asthma results.

- Localized swelling in the skin because of allergy-induced histamine release causes hives.

- When large amounts of these chemical mediators gain access to the blood, the extremely serious systemic reaction known as anaphylactic shock occurs, which is frequently fatal.

- Shared characteristics of the immune reactions to allergens and parasitic worms include the production of IgE antibodies and increased basophil and eosinophil activity.

- The inflammatory response in the skin could wall off parasitic worms attempting to burrow in.

- Coughing and sneezing could expel worms that migrated to the lungs.

- Diarrhea could help flush out worms before they could penetrate or attach to the digestive tract lining.

- Some allergens invoke delayed hypersensitivity, a T cell-mediated immune response.

- Among these allergens are poison ivy toxin and certain chemicals to which the skin is frequently exposed, such as cosmetics and household cleaning agents.

EXTERNAL DEFENSES
The skin consists of an outer protective epidermis and an inner connective tissue dermis.

- The epidermis consists of numerous layers of epithelial cells.

- Epidermal cells are tightly bound together by spot desmosomes, which interconnect with intracellular keratin filaments to form a strong, cohesive covering.

- The dermis is a connective tissue layer that contains many elastin fibers and collagen fibers, as well as an abundance of blood vessels and specialized nerve endings.

- Special infoldings of the epidermis into the underlying dermis form the skin's exocrine glands—the sweat glands and the sebaceous glands—as well as the hair follicles.

Specialized cells in the epidermis produce keratin and melanin and participate in immune defense.

- Melanocytes produce the pigment melanin.

- The amount and type of melanin are responsible for the different shades of skin color of the various races.

- Melanin is produced through complex biochemical pathways in which the melanocyte enzyme tyrosinase plays a key role.
Two genetic factors prevent tyrosinase from functioning at full capacity: (1) much of the tyrosinase produced is in an inactive form, and (2) various inhibitors block tyrosinase action.

- Keratinocytes are specialists in keratin production.
- As they die, keratinocytes form the outer protective keratinized layer and are also responsible for generating hair and nails.
- Langerhans cells present antigen to helper T cells.
- Granstein cells interact with suppressor T cells, probably serving as a "brake" or skin-activated immune responses.
- The epidermis synthesizes vitamin D in the presence of sunlight.

**Protective measures within body cavities that communicate with the external environment discourage pathogen invasion into the body.**

- Saliva secreted into the mouth at the entrance of the digestive system contains an enzyme that lyses certain bacteria.
- Many of the surviving bacteria that are swallowed are killed by the strongly acidic gastric juice that they encounter in the stomach.
- Some bacteria do manage to survive and reach the large intestine.
- These harmless resident flora competitively suppress the growth or potential pathogens that have escaped the antimicrobial measures or earlier parts of the digestive tract.
- Within the genitourinary system, would-be invaders encounter hostile conditions in the acidic urine and acidic vaginal secretions.
- The genitourinary organs also produce a sticky mucus, which, like flypaper, entraps small invading particles.
- Large airborne particles are filtered out of the inspired air by hairs at the entrance of the nasal passages.
- The respiratory airways are coated with a layer of thick, sticky mucus secreted by epithelial cells within the airway lining.
- This mucus sheet, laden with any inspired particulate debris is constantly moved upward to the throat by ciliary action.
- Also contributing to defense against respiratory infections are antibodies secreted in the mucus.
- In addition, an abundance of phagocytic specialists called the alveolar macrophages scavenge within the air sacs or the lungs.
- Cigarette smoking suppresses these normal respiratory defenses.

**Key Terms**

- Active immunity
- Acquired immune deficiency syndrome (AIDS)
- Acute-phase proteins
- Adaptive (acquired) immune system
- Agglutination
- Allergen
- Allergy
- Anaphylactic shock
- Antigen
- Antiserum (antitoxin)
- Asthma
- Autoimmune disease
- Cell-mediated immunity
- Chemotaxis
- Complement system
- Clonal anergy
- Clonal selection theory
- Clone

- Cytotoxic T cells
- Dendritic cells
- Diapedesis
- Endogenous pyrogen
- Erythroblastosis fetalis (hemolytic disease of the newborn)
- Gut associated lymphoid tissue
- Gamma globulins (immunoglobulins)
- Granstein cells
- Granuloma
- Granulopoiesis
- Haptens
- Helper T cells
- Histamine
- Host cell
- Humoral immunity
- Hypersensitivity
- Immunity
Immune complex disease
Immune surveillance
Innate immune system
Interferon
Interleukin 1
Interleukin 2
Killer cells
Kininogens
Lactoferrin
Langerhans cells
Lymphoid cell
Margination
Major histocompatibility complex (MHC)
Melanin
Melanocytes
Membrane attack complex
Metastasis
Memory cells
MHC molecule
Mucous escalator
Opsonins
Passive immunity
Pathogens
Perforin
Phagocytosis
Plasma cell
Precipitation
Primary immune response
Psychoneuroimmunology
Recombinant DNA technology
Secondary immune response
Skin-associated lymphoid tissue (SALT)
Suppressor T cells
Transfusion reaction
Thymus
Thymosin
Virulence

Review Exercises
Answers are in the appendix.

True/False

1. Lymphocytes that mature without benefit of “thymic education” become T lymphocytes.
2. During fetal development some immature lymphocytes migrate to the thymus, where they undergo further processing to become T lymphocytes.
3. There are four classes of specific immune responses.
4. Foreign proteins are the most common antigens.
5. The thymus becomes less important as the individual matures.
6. Antibodies are secreted into the blood or lymph.
7. Antibodies are grouped into six subclasses.
8. IgD is present on the surface of many T cells, but its function is uncertain.
9. Immunoglobulins cannot directly destroy foreign organisms.
10. Each B lymphocyte is preprogrammed to respond to only one of the millions of different antigens.
11. An individual can acquire antibodies by the direct transfer of antibodies actively formed by another person or animal.
12. There are two naturally occurring antibodies developed against the Rh factor.

13. The most common allergens that provoke immediate hypersensitivities are pollen grains, bee stings, penicillin, certain foods, molds, dust, feathers, and animal fur.

14. Severe hypotension can lead to circulatory failure.

15. Immune complex disease is when the immune system turns against one of the body's own tissues.

16. In immediate hypersensitivity, the allergic response appears within about ten minutes after being exposed to an allergen.

17. A single mast cell may be coated with a number of different IgE antibodies.

18. T cells do not secrete antibodies.

19. Antibodies not only target viruses for destruction in the extracellular fluid but can also eliminate viruses inside neurons.

19. Helper T cells secrete B-cell growth factor.

20. The AIDS virus selectively invades cytotoxic T cells.


22. B cells typically bind with HLA self-antigens only when they are in association with a foreign antigen.

23. Most body cells undergo mutations that result in malignancy.

24. Epidermal cells are tightly bound together by spot desmosomes.

25. The epidermis has very little direct blood supply.

26. The keratinized layer is airtight, fairly waterproof, and impervious to most substances.

27. Epidermal enzymes are not able to convert many potential carcinogens into harmless compounds.

28. The dermal blood vessels have no control in temperature regulation.

29. Langerhans cells present antigen to helper T cells.

30. The epidermis synthesizes vitamin A in the presence of sunlight.

31. T lymphocytes secrete antibodies that indirectly lead to the destruction of foreign material.

32. Natural killer cells is a family of proteins that nonspecifically defend against viral infections.

33. Released histamine increases the capillaries permeability.
34. Neutrophils are the first to arrive at the site of an injury.

35. Phagocytic secretions stimulate the release of kininogens from the liver.

36. Salicylates reduce fever by inhibiting the production of prostaglandins.

**Fill in the Blank**

38. Antibodies are secreted into the blood or lymph, where they are known as ______________________

or ______________________.

39. ______________________ is the term applied to the process in which foreign cells, such as bacteria or mismatched transfused red blood cells, bind together a clump.

40. Antibodies mark or identify foreign material as targets for actual destruction by the ______________________, ______________________, or ______________________.

41. ______________________ remain dormant, not actually secreting their particular antibody product until they come into contact with the appropriate

42. The production of antibodies as a result of exposure to an antigen is referred to as ______________________ against that antigen.

43. Antigen-presenting macrophages secrete ______________________, a multipurpose chemical mediator that enhances the differentiation and proliferation of the now activated B-cell clone.

44. T-cells must be in direct contact with their targets, a process known as ______________________.

45. ______________________ destroy host cells bearing foreign antigen, such as body cells invaded by viruses, cancer cells, and transplanted cells.

46. Natural killer cells release ______________________ molecules, which penetrate into the target cell's surface membrane and join together to form porelike channels.

47. Helper T cells secrete T cell growth factor, also known as ______________________.

48. ______________________ are by far the most numerous of the T cells.

49. ______________________ is an example of an autoimmune disease.
50. The most recent and tragically the most common acquired immune deficiency disease is ________________.

51. A(n) ________________ is the acquisition of an inappropriate specific immune reactivity, or ________________ to a normally harmless environmental substance.

52. When large amounts of chemical mediators or allergens gain access to the blood, the extremely serious systemic reaction known as ________________ occurs.

53. ________________ refers to the body's ability to resist or eliminate potentially harmful foreign materials or abnormal cells.

54. ________________ refer collectively to the tissues that store, produce, or process lymphocytes.

55. Localized vasodilation is primarily induced by ________________ that has been released in the area of tissue damage from mast cells.

56. Upon exposure to tissue thromboplastin in the injured tissue and to specific chemicals secreted by phagocytes on the scene, ________________, the final factor in the clotting system, is converted into ________________.

57. Neutrophils secrete ________________, a protein that tightly binds with iron, making it unavailable for use by invading bacteria.

58. Such a more-or-less permanently walled-off structure in which nondestructible offending material is imprisoned is known as a(n) ________________

59. Numerous drugs can suppress the inflammatory process; the most effective are the ________________ and related compounds and ________________

60. There are two classes of specific immune responses: ________________ and ________________

61. The ________________ gradually atrophies and becomes less important as the individual matures. It does, however, continue to produce important in maintaining the T cell lineage.

62. ________________ are low-molecular-weight organic substances that are not antigenic by themselves but can become antigenic if they attach to body proteins.
63. In ________________, the allergic response appears within about twenty minutes after a
sensitized individual is exposed to an allergen.

64. Epidermal cells are tightly bound together by _________________.

65. The cells of the ____________________ produce an oily secretion known as _________________.

66. ________________ release a dilute salt solution through small openings,
______________ onto the surface of the body.

67. ________________ produce the pigment _________________.

68. The most abundant epidermal cells are the _________________.

69. ________________ present an antigen to helper T cells, thereby facilitating their
responsiveness to skin-associated antigens.

70. ________________ interact with suppressor T cells, probably serving as a "brake" on skin-
activated immune responses.

71. The ________________ synthesizes vitamin D in the presence of sunlight.

72. Phagocytic specialists called ________________ scavenge within the air sacs of the lungs.

---

Matching

Match the lymphoid tissue to the function.

a. thymus
b. spleen
c. bone marrow
d. lymph nodes, tonsils, adenoids, appendix, gut associated lymphoid tissue

____ 73. Exchanges lymphocytes with blood.
____ 74. Origin of all blood cells.
____ 75. Stores a small percentage of red blood cells.
____ 76. Secretes the hormone thymosin.
____ 77. Exchanges lymphocytes with lymph.
____ 78. Site of maturational processing for T lymphocytes.
79. Resident lymphocytes produce antibodies and sensitized T cells, which are released into the blood.

80. Site of maturational processing for B lymphocytes.

81. Resident macrophages remove microbes and other particulate debris from lymph.

82. Resident lymphocytes produce antibodies and sensitized cells, which are released into the lymph.

83. Resident macrophages remove microbes and other particulate debris, most notably worn-out red blood cells, from the blood.

Multiple Choice

84. Which of the following substances causes an inappropriate immune response?
   a. perforins
   b. opsonins
   c. endogenous pyrogens
   d. haptens
   e. allergens

85. Which of the following substances induces the development of fever
   a. perforins
   b. opsonins
   c. endogenous pyrogens
   d. haptens
   e. allergens

86. Which of the following substances is a secretory product of helper T cells?
   a. kallikrein
   b. interleukin 1
   c. haptens
   d. interleukin 2
   e. allergens

87. Which of the following substances make bacteria more susceptible to phagocytosis?
   a. allergens
   b. opsonins
   c. interleukin 1
   d. interleukin 2
   e. haptens

88. Which of the following substances are not antigenic by themselves but can become antigenic if they attach to body proteins?
   a. opsonins
   b. allergens
   c. perforins
   d. histamines
   e. haptens
89. Which of the following substances is secreted by neutrophils and binds tightly with iron?
   a. ferrokinogen
   b. lactoferrin
   c. endogenous pyrogen
   d. interleukin 1
   e. interferon

90. Which of the following substances is a secretory product of macrophages?
   a. interleukin 1
   b. interferon
   c. kallikrein
   d. interleukin 2
   e. perforin

91. Which of the following substances brings about vasodilation and increased capillary permeability?
   a. interferon
   b. histamine
   c. perforin
   d. interleukin 2
   e. kallikrein

92. Which of the following substances triggers the production of viral-blocking enzymes by potential host cells?
   a. perforin
   b. interleukin 2
   c. interleukin 1
   d. ferrokinogen
   e. interferon

93. Which of the following substances is released by cytotoxic T cells and binds to a target cell's surface membrane?
   a. perforin
   b. interferon
   c. interleukin 1
   d. interleukin 2
   e. ferrokinogen

**Modified Multiple Choice**

*Indicate whether the characteristic applies to active immunity or passive immunity by writing the appropriate letter in the blank using the following answer code.*

A = applies to active immunity
B = applies to passive immunity
C = applies to both active and passive immunity

94. _____ exposure to antigen required for immunity to develop
95. _____ antibodies produced by a source other than one's own body
96. _____ often confers long-lasting immunity
97. ______ resistance to antigen exposure immediate upon injection of antibodies
98. ______ natural immunity is actually a special case of this type of immunity

Indicate which type of T cell is being described by writing the appropriate letter in the blank using the answer code below.

A = applies to cytotoxic T cells
B = applies to helper T cells
C = applies to suppressor T cells
D = applies to both helper T cells and suppressor T cells
E = applies to all three types of T cells

99. ______ destroys host cells bearing foreign antigen
100. ______ suppresses both T-cell and B-cell activity
101. ______ secretes B cell growth factor
102. ______ enhances the development of antigen-stimulated B cells into antibody-secreting cells
103. ______ called regulatory T cells
104. ______ secretes interleukin 2
105. ______ releases perforin
106. ______ secretes macrophage-migration inhibition factor
107. ______ attacked by the AIDS virus
108. ______ most numerous of the T cells
109. ______ serves to limit immune reactions
110. ______ believed to play a role in tolerance
111. ______ recognizes class I MHC glycoproteins
112. ______ recognizes class II MHC glycoproteins

Points to Ponder

1. With the current social views in this country, do you feel that the eradication of AIDS is possible?
2. In that part of the body defenses involving B cells and T cells, cellular memory plays a major role. When and how is this memory lost?
3. Do animal rights activists hinder our fight against viral diseases?
4. How does exercise strengthen the immune system?
5. If you have an allergy, will your children inherit it? Explain why or why not.
6. A drug has been discovered that destroys all mast cells. How might this drug help prevent allergies? Would there be any negative side effects by taking this drug?
7. How does an elevated body temperature help an infection caused by a virus?
8. What is the difference between a nonspecific host defense mechanism and a specific defense mechanism? Give examples.
9. How does the clonal selection theory explain the ability of the immune response to distinguish between self and nonself?

10. What is the basis of immunological memory?

Clinical Perspectives

1. What is the significance of a "booster shot"?

2. This summer you will direct a biological field trip to the remote areas of the Chihuahuan Desert. The students and yourself will spend a month living in tents as you study the desert. With regard to this chapter, what precautions should you take before you begin this trip?

3. Why don’t we become immune to the cold virus?

4. Why do most children outgrow common food allergies?

5. Why is cortisone and its analogues used clinically in patients who have a transplanted organ?

6. While painting the house, you get stung by a bee. This is the first time you have ever been bitten by a bee. You develop an itchy rash which is not relieved by antihistamines prescribed by your physician. The physician then tries cortisone which alleviated the rash. Several weeks latter, you get stung again by a bee; however, unlike the first time, you respond well to the antihistamines. Why did this occur?

7. The tuberculin skin test and poison ivy are both type IV hypersensitivities. What does this mean? Explain the common mechanism involved.

8. How does hemolytic disease of the newborn develop?

9. What is the immunological basis behind blood transfusions?

10. In desensitization procedures, the allergist injects more of the same allergen to which the person is allergic. How can this be beneficial?
Chapter 12: The Body Defenses

True/False

1. False—Lymphocytes.
2. True
4. True
5. True
6. True
7. False—Five.
8. False—B cells.
9. True
10. True
11. True
12. False—No naturally occurring antibodies.
13. True
14. True
15. False—Autoimmune responses.
16. False—20 minutes.
17. False—IgE antibodies.
18. True
19. True
20. True
22. True
23. False—T cells.
24. False—Do not result in malignancy.
25. True
26. False—Has no direct blood supply.
27. True
28. False—Are able to convert.
29. False—Does have control.
30. True
31. False—Vitamin D.
32. False—B lymphocytes.
33. False—Interferon.
34. True
35. True
37. True

Fill in the Blank

38. Gamma globulins, immunoglobulins
39. Agglutination
40. Complement system, phagocytes, killer cells
41. B cells, antigen
42. Active immunity
43. Interleukin 1
44. Cell-mediated immunity
45. Cytotoxic T cells
46. Perforin
47. Interleukin 2
48. Helper T cells
49. Myasthenia gravis
50. AIDS
51. Allergy, hypersensitivity
52. Anaphylactic shock
53. Immunity
54. Lymphoid tissue
55. Histamine
56. Fibrinogen, fibrin
57. Lactoferrin
58. Granuloma
59. Salicylates, glucocorticoids
60. Antibody-mediated, cell-mediated
61. Thymus, thymosin
62. Haptens
63. Immediate hypersensitivity
64. Spot desmosomes
65. Sebaceous glands, sebum
66. Sweat glands, the sweat pores
67. Melanocytes, melanin
68. Keratinocytes
69. Langerhans cells
70. Granstein cells
71. Epidermis
72. Alveolar macrophages

Matching

73. b
74. c
75. b
76. a
77. d
78. a
79. b
80. c
81. d
82. d
83. b

Multiple Choice

84. e
85. e
86. d
87. b
88. e
89. b
90. a
91. b
92. e
93. a
94. a
95. b
96. a
97. b
98. a
99. a
100. c
101. b
102. b
103. d
104. b
105. a
106. b
107. b
108. b
109. c
110. c
111. a
112. b