CHAPTER

2

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Immunology

INTRODUCTION

The science of immunology studies the components of the immune system. A branch of immunology that studies the interactions between the immune system and cancer cells is referred to as cancer immunology. Immunological functioning impacts the development and management of cancer. For example, development of some cancers may contribute to a suppressed or inadequately functioning immune system. Certain cancers can also weaken the immune system by spreading to the bone marrow. Although the immune system may help fight cancer by recognizing cancer cells as abnormal and eradicating them, a suppressed immune system may not eradicate damaged cells, leading to an increased risk of cancer development. While the chemotherapeutic drugs and radiation therapy used to treat cancer induce immunosuppression, major advances in cancer immunology have occurred in terms of the development of immunotherapies for the treatment of cancer.

Oncology nurses must understand the cellular and molecular concepts of cancer immunology if they are to effectively manage patients with cancer diagnoses. This chapter reviews the various aspects of immunology, including components of the immune system, key immunologic processes, and clinical implications. **Table 2-1** provides a key for the numerous abbreviations that recur in the chapter.

TABLE 2-1

Immunology Abbreviation Key

Abbreviation	Term
APC	Antigen-presenting cell
CD	Clusters of differentiation
CRP	C-reactive protein
CSF	Colony-stimulating factor
IL	Interleukin
INF	Interferon
MALT	Mucosal-associated lymphoid tissue
MHC	Major histocompatibility complex
NK	Natural killer
Tc/CTL	Cytotoxic T cell/cytotoxic T lymphocyte
Th	T helper cell
Tm	T memory cell
TNF	Tumor necrosis factor
Treg	T regulator cell
Ts	T suppressor cell

OVERVIEW

Preventing or limiting infection and malignant disease is the primary function of the immune system. A complex arrangement of molecules, cells, tissues, and organs function collectively to provide immunity or protection against foreign organisms.[1] Each component of the system has a unique role to play in recognizing problems and communicating with other cells.

When the immune system recognizes foreign substances, it mounts an immune response to address the problem. Failure to recognize problems leads to infection or cancer. Allergic reactions and autoimmune diseases occur when the immune system become activated despite the lack of a problem or remains activated once the danger passes.[2] Therefore, maintaining homeostasis also serves as a main goal of the immune system.

COMPONENTS OF THE IMMUNE SYSTEM

Many different organs and tissues contribute to the functioning of the immune system, including the bone marrow, thymus, spleen, mucosal-associated lymphoid tissue (MALT), circulatory system, and lymphatic system. All of these organs and tissues work together to prevent infection. This section reviews the structure of the immune system, and examines the cells and proteins involved in immunity.

STRUCTURE OF THE IMMUNE SYSTEM

The immune system can be divided into two groups of organs and tissues based on their roles in defending the host (**Figure 2-1**). The primary organs and tissues are involved with lymphocyte production and differentiation. The bone marrow and thymus represent the primary lymphoid tissues that play key roles in immunocompetence.[1,3] The B cells mature in the bone marrow, whereas the T cells mature in the thymus. Systemic secondary organs include the spleen and lymph nodes. Secondary immune organs capture and process antigens.[1,3] The tonsils, Peyer's patches, and MALT constitute the secondary mucosal tissues. The spleen predominately responds to blood-borne antigens, the lymph nodes mount the immune response, and the mucosal tissues respond to antigens that penetrate the mucosal barriers.[4]

CELLS OF THE IMMUNE SYSTEM

Blood cells arise from hematopoietic stem cells that reside in the bone marrow. The pluripotent hematopoietic stem cells respond to the changing needs for blood cells in the body by replenishing cell types in the bone marrow. The majority

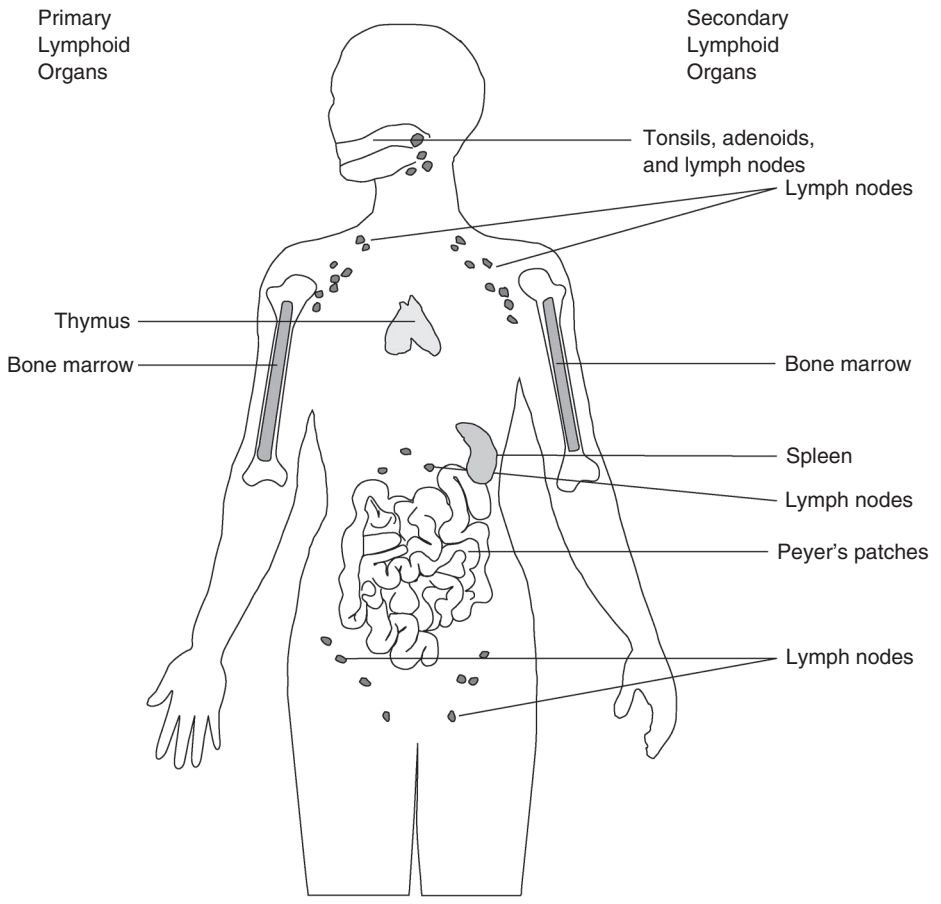

FIGURE 2-1

Primary and secondary lymphoid organs.

of cells produced by the hematopoietic system reside in the bone marrow microenvironment and have the capacity for self-renewal.[5] A subset of these cells differentiates into multipotent progenitor cells to form the myeloid or lymphoid cell lineage.[5,6] Hematopoietic stem cells express proteins on their cell membrane surface referred to as markers or clusters of differentiation (CD). These markers identify the type and function of the cell, and provide molecular signaling so that cells can communicate with one another.[6] Each lineage produces blood cells with specific functions (**Table 2-2**).[1,5] The next sections describe the lineages within the hematologic cascade illustrated in **Figure 2-2**.

Myeloid Immune Cells and Lineage

The myeloid cells give rise to two types of progenitors: the granulocyte–monocyte progenitor and the megakaryocyte–erythrocyte progenitor.[6] The granulocyte–monocyte produces the granulocyte lineage generating neutrophils, basophils, and eosinophils. Neutrophils—also referred to as polymorphonuclear leukocytes—are the most abundant of the circulating white blood cells. Granulocyte colony-stimulating factor (G-CSF) stimulates the production of neutrophils. The adult bone marrow rapidly produces neutrophils in volumes of more than 1×10^{11} neutrophils a day.[1] However, these cells circulate for only 6 hours or so, and for shorter periods in times of stress.[1] Neutrophils provide the body's first line of defense—hence the necessity for their rapid production.

Basophils, eosinophils, and mast cells have cytoplasmic granules filled with various inflammatory and antimicrobial mediators.[1] Mast cells derive from the bone marrow, but they do not enter the bloodstream. Instead, they reside in connective tissue and present in the skin and mucosa filled with histamine, the compound that is responsible for producing allergy symptoms.[1] Like mast cells, basophils mature in the bone marrow, but they circulate in the blood. Although basophils account for less than 1% of the total volume of blood leukocytes, they play a key role in allergic responses.[1] Eosinophils express cytoplasmic granules that

are harmful to the parasitic cell walls that play a major role in inflammation.[1]

The granulocyte–monocyte progenitor also generates the monocyte–macrophage lineages. Monocytes have a primary role in phagocytosis as part of the mononuclear phagocyte system.[1,5,7] These cells enter the blood from the bone marrow prior to complete differentiation and migrate into tissues. After they enter the tissues, the monocytes mature and become macrophages. Examples of macrophages include the microglial cells in the central nervous system, the Kupffer cells that line the vascular sinusoids of the liver, the alveolar macrophages found in the pulmonary airways, and the multinucleate phagocytes found in osteoclasts of the bone.[1] Key functions of macrophages include ingesting and killing microbes as well as ingesting dead host cells to clean up after infections. Macrophages also secrete proteins referred to as cytokines, serve as antigen-presenting cells (APCs) to display antigens, activate T lymphocytes, and promote repair of damaged tissues through angiogenesis and fibrosis.[1,5,7]

Dendritic cells are also part of the myeloid lineage, arising from a precursor that can differentiate into monocytes, but not granulocytes.[1,5,7] Precursor dendritic cells in the blood and bone marrow have the ability to differentiate into various types. Once differentiated into an immature phase, they migrate and circulate in the tissues and peripheral blood, including in the skin, inner lining of the nose, lungs, stomach, and intestines.[8,9] Dendritic cells seek out and capture foreign antigens, and then migrate to the lymph nodes in search of T cells.[10] There, the dendritic cells are transformed into a mature state and present the antigen for destruction by the T cells.[10] In other words, a dendritic cell is a type of APC that becomes mobile so that it can migrate to lymph nodes and present a microbe to both B- and T-cell lymphocytes.

Although the megakaryocyte–erythrocyte progenitor does not produce leukocytes, erythrocytes are essential for moving oxygen and providing nutrients to the cells.[1,5] Megakaryocytes differentiate into platelets, which are necessary for forming blood clots. Following damage to endothelial cells, platelets adhere to and aggregate on the surface of the cells. Leukocytes migrate to the cell surface, activate the complement system, and stop blood flow.[1] Immune cells of the myeloid progenitor lineage have key functions in responding early to infection, contributing to allergic response and inflammation, engulfing and killing microbes, moving oxygen, and forming clots. Conversely, the lymphoid progenitor immune cells respond later in the immune response.

Lymphoid Immune Cells and Lineage

From the hematopoietic stem cell, the lymphoid progenitor differentiates into the B- and T-cell lymphocytes and the NK lineages. After macrophages present the APC to the lymphocytes in the lymphoid tissue, antigen development begins that is specific for B- or T-cell activation.[1,7] The B-cell lymphocytes mature in the bone marrow,

TABLE 2-2

Hematopoietic Cellular Types and Functions

Lineage	Cell Type	Function
Myeloid	Basophils	Type of granulocyte found in the blood that stores histamine for allergic reactions
	Dendritic cells	Present T cells to the immune cells
	Eosinophils	Type of granulocyte to combat parasites
	Erythrocytes	Form red blood cells that deliver oxygen to cells and tissues
	Granulocytes	Produce neutrophils, basophils, and eosinophils
	Monocytes	Enter tissues and mature into macrophages
	Macrophages	Ingest foreign materials and microbes
	Mast cells	Contain granules filled with histamine that is stored in tissues for allergic reaction
	Megakaryocytes	Fragment to form platelets
	Neutrophils	Most abundant granulocyte; first-line defense against infections
Lymphoid	B lymphocytes	Responsible for antibody production in humoral immunity
	T lymphocytes	Responsible for directly killing infected cells in innate immunity
	Natural killers	Large granular cells that rapidly migrate to site of inflammation and kill selected tumor cells without activating innate immunity
	NKT cells	T cells with NK marker that suppress or activate innate and adaptive immunity

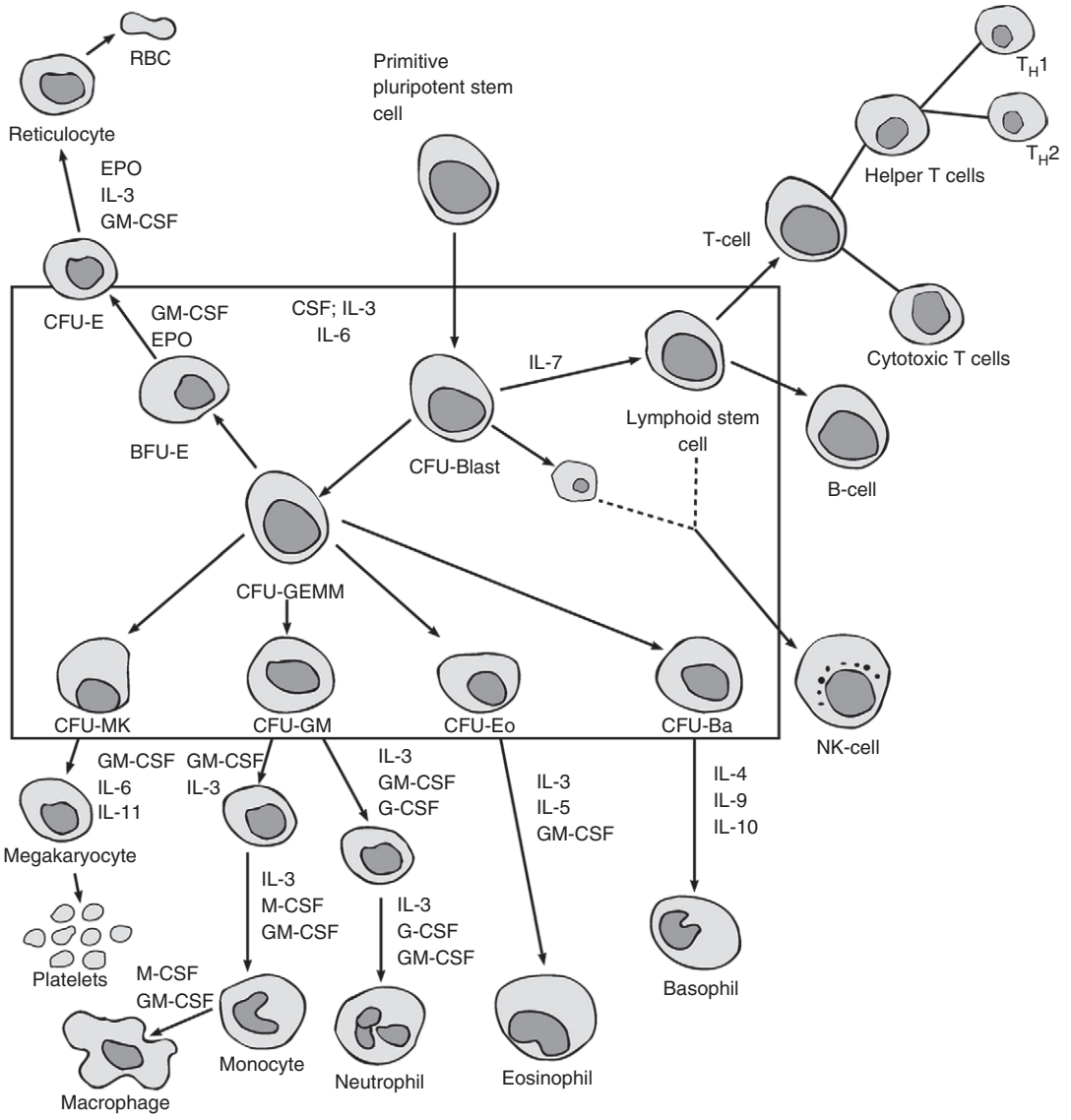

FIGURE 2-2

Hematologic cascade.

whereas the T-cell lymphocytes must leave the bone marrow, enter the bloodstream, and migrate to the thymus to mature.

B-Cell Lymphocytes

The B-cell lymphocytes play an important role in adaptive immunity through the production of antibodies; they also contain memory cells.[1,11] The antibodies produced are referred to as immunoglobulin (Ig). Each antibody is Y-shaped, consisting of three fragments and four polypeptide chains (**Figure 2-3**). The two identical light chains have two identical fragments for antigen binding (Fab).[4] The two identical heavy chains at the lower tail of the antibody have the crystalline fragment (Fc) needed to activate complement.[4] Antibodies use the Fab and Fc fragments to form a bridge between the antigen and the phagocyte to facilitate antigen destruction.[1] Once activated, B-cell lymphocytes become antibody-secreting plasma cells.[4]

Plasma cells are B-cell lymphocytes that actively produce antibodies against antigens that they have been exposed to and that secrete immunoglobulin.[4] Five types of immunoglobulin have been identified, each with unique functions (**Table 2-3**).[1,6,11] Plasma cells release antibody until the antigen is destroyed.

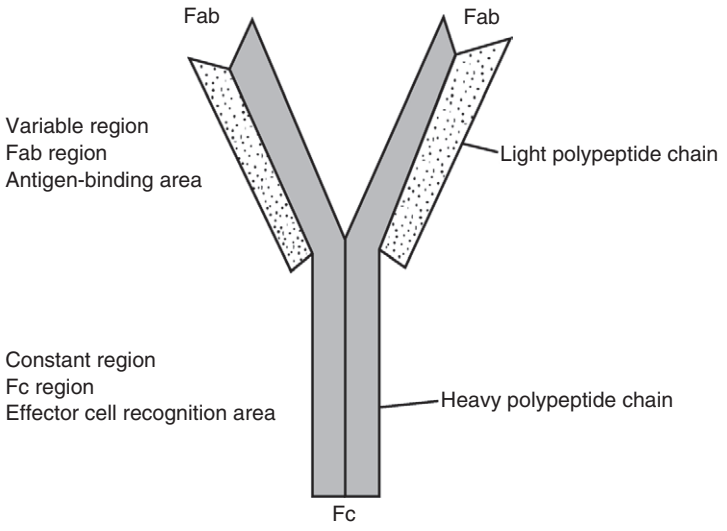

FIGURE 2-3

Antibody molecule.

Source: Data from Buchsel and DeMeyer.[8]

Both B- and T-cell lymphocytes have distinct phenotype and functional subsets. The B cell lymphocyte subsets include follicular, marginal zone, and B-1 cells within lymphoid tissues.[11] Tumors of plasma cells such as those found in multiple myeloma produce antibodies of a single specificity—that is, monoclonal antibodies.[1] Monoclonal antibodies have several practical applications, including defining CD markers for cell types, diagnosing infectious and systemic diseases with immunoassays, detecting specific tumors, and targeting cells and molecules in the pathogenesis of diseases.[1] The principal functions of B-cell lymphocytes include making antibodies against antigens, functioning as APCs, developing into memory cells, and releasing cytokines. Conversely, T-cell lymphocytes specialize in recognizing protein antigens.

T-Cell Lymphocytes

Unlike the B-cell lymphocytes, which can recognize antigens as stand-alone entities, the T-cell lymphocytes recognize antigens only when the antigens are directly presented

TABLE 2-3

Types of Immunoglobulins

Immunoglobulin	Actions
IgA	Serves as mucosal immunity Found in body secretions Offers natural protection against nonspecific foreign antigens
IgD	Regulates cell activation on B-cell membranes
IgE	Essential role in Type I hypersensitivity and allergic responses Located on basophils and mast cells for inflammatory and immune responses
IgG	Major immunoglobulin in the blood and extracellular fluid Responsible for opsonization, complement activations, and cell-mediated cytotoxicity Essential roles in Type II and III hypersensitivity reactions Primary mediator for secondary immune response against bacteria and viruses
IgM	Largest antibody in circulatory system produced in the spleen Activates complement Neutralizes circulating pathogens

to them. The principal functions of T-cell lymphocytes include eradicating infection and activating cells such as macrophages and B-cell lymphocytes.[1,5]

Antigen-presenting cells are specialized cells that capture and display antigens, thereby activating the T lymphocytes.[1,10] An antigen moves through the body after entering the host, is filtered in the spleen, and enters the lymphatic system. Once macrophages ingest the antigen, a portion of the antigen is expressed on the plasma membrane, where it is presented to B and T cells.[10] Formation of this antigen–phagocyte complex is required to induce the majority of immune responses.[1,10] Although dendritic cells derive from the myeloid lineage, they are also an example of an APC that captures antigens and migrates to lymphoid organs. This process maximizes the chance of locating a specific antigen.

Another key component in ensuring that T-cell lymphocytes interact only with host cells, and not microbes, is the major histocompatibility complexes (MHCs). Two classes of MHCs are distinguished that display the host cells' associated antigens, rather than the microbes.[1,3] Class I displays peptides to recognize CD8+ T cells. Class II display peptides to CD4+ T cells.[1,5] The T-cell lymphocytes recognize antigens only in the form of these peptides and display them for subsequent recognition by antigen-specific T lymphocytes.[1]

The T-cell lymphocytes also have molecules on their surface that are similar to an antibody, referred to as T-cell receptors (TcR).[12] These molecules recognize peptide fragments presented with human leukocyte antigen (HLA).[1,3] HLA is found on the surface of APCs. The T-cell lymphocytes may also release antibodies from activated B cells into the peripheral blood, thereby contributing to cell-mediated immune responses.[1,3] Several subsets of T-cell lymphocytes exist, including helper T cells (Th); cytotoxic T cells (Tc), also called cytotoxic T lymphocytes (CTL); regulatory T cells (Treg); memory T cells (Tm); and natural killer cells (NK). Each of these lymphoid progenitor subsets has a distinctive function, but all collectively serve as effectors and regulators of the immune response.[12–15]

Effector Cells (Tc and Tm)

The Tc cells are also referred to as CD8+ T cells because they express the CD8 protein on their cell surface. The Tc cells eradicate viral infections and may also play roles in autoimmunity and allogeneic organ rejection.[5,15] Unlike the Th cells, the Tc cells recognize their targets by binding to antigens associated with MHC class I molecules.[1,5]

The Tm cells include both central and effector memory cells.[16] The Tm cells are sensitized to specific antigens and cloned to remember the antigen.[16] The central memory cells are involved in the secondary immune response and long-term protection. The effector memory cells contribute to immediate protection.[1,5,15]

Regulatory Cells (Th and Ts)

The Th cells initiate responses geared toward providing specific immunity, including the maturation of B cells and the activation of Tc cells and macrophages.[5,13] The APC cells express a class II MHC molecule on their surface, and the Th cells become activated when presented with peptide antigens by the MHC.[5,15] These cells also express the CD4 cell surface molecule.[13,15] Once activated, the Th cells divide rapidly into Th1 and Th2, which then secrete cytokines that regulate or assist in activating the immune response.[14] The Th1 cells produce interferon (IFN), interleukin-12 (IL-12), and tumor necrosis factor (TNF) pro-inflammatory cytokines that activate macrophages, NK cells, and Tc cells to kill antigen-containing cells.[12–14] The Th1 cells regulate cell-mediated immunity. The Th2 cells produce IL-4, IL-5, IL-6, IL-10, and IL-13 anti-inflammatory cytokines that activate B cells to produce antibody and regulate humoral immunity.[12–14] The Th and Ts regulatory cells maintain immunologic homeostasis.

The Treg cells, which were formerly referred to as suppressor T cells (Ts), suppress T-cell–mediated immunity and autoreactive T cells that escape maturation in the thymus.[5,12] The Treg cells produce a soluble factor that suppresses cytotoxic responses by the effector cells and inhibits antibody production.[12]

In addition to distinct functionality, the T-cell subsets have different surface antigens. As noted earlier, these surface antigens are referred to as clusters of differentiation (CD). The Th cells express the surface protein CD4 that are referred to as CD4+ T cells. The Tc cells express the surface protein CD8 and are referred to as CD8+ T cells. The CD4+ T cells recognize antigens combined with HLA class II molecules. Conversely, the CD8+ T cells recognize HLA class I molecules.[14] There is a growing interest in the potential therapeutic benefits of these actions in the treatment of autoimmune diseases, chronic inflammatory disease, infectious disease, and cancer immunotherapy because the Treg cells express CD4, CD8, and CD25.[5,12]

The NK cells directly kill tumors and viral-infected cells. These cells have a unique attribute: They recognize cells in the absence of MHC molecules and antibodies.[1] They also do not require activation, which facilitates faster recognition and shorter reaction times. The T-cell lymphocytes have a central role in cell-mediated immunity and support the body's mechanism for intracellular attack on pathogens located inside the host cells.[14]

SOLUBLE MEDIATORS OF THE IMMUNE RESPONSE

Soluble mediators such as C-reactive protein (CRP), complement, and cytokines also play an important role in positive and negative regulations of immune responses. Cell-to-cell communication occurs due to the production and secretions of soluble mediators. The concentrations of

a number of proteins—known as acute-phase proteins—increase rapidly during infection.[4] CRP and complement are the two key serum proteins increased during infections.

CRP has the ability to bind and coat bacteria, thereby promoting phagocytosis.[4] This protein binds to a molecule expressed on dead and dying cells, which then activates the complement system. The complement system consists of approximately 20 serum proteins that function to control inflammation.[4] Both the alternative and classical pathways activate the complement system. The alternative pathway relies on CRP as part of an innate immune defense to activate the complement system.[3,4] When this occurs, the microorganism becomes coated with the complement molecules, triggering phagocytosis.[3,4] The classical pathway involves a specific adaptive response activated by antibodies bound to the pathogen surface.[3,4] Activating the complement system produces four effects: (1) opsonization of microorganisms for phagocytosis; (2) attraction of phagocytes to the site of infection (chemotaxis); (3) increased vascularity and permeability to the activation site and plasma molecules leading to lysis; and (4) release of inflammatory mediators from mast cells.[3,4]

Cytokines comprise a large, heterogeneous group of secreted proteins produced by many different cell types.[1] Endothelial cells, macrophages, fibroblasts, lymphocytes, and mast cells produce these chemical messengers.[17,18] Under normal conditions, cytokines are released to act during processes of cellular proliferation and migration, apoptosis, and inflammation.[18] All cytokines are proteins or glycoproteins involved in cell signaling during immune responses. The various categories of cytokines include lymphokines, chemokines, tumor necrosis factor, and transforming growth factors. **Table 2-4** provides an overview of the more common cytokines.[4,19]

Lymphocytes produce lymphokines as protein mediators to attract macrophages and other lymphocytes to sites of infection in preparation for the immune response.[20] Lymphokines also help B-cell lymphocytes make antibodies. Examples of lymphokines include interleukin (IL), interferon (INF), and colony-stimulating factor (CSF).[17] Interferons limit the spread of certain viral infections, whereas interleukins have a variety of functions and also cause other cells to divide and differentiate.[17] CSF directs the differentiation of bone marrow stem cells; it has the

TABLE 2-4

Cytokines: Sources and Major Functions

Type	Source	Major Functions
Interleukins (ILs)		
IL-1	Macrophages, endothelial cells, Th2, some epithelial cells	Activates B and T cells, pro-inflammatory cytokines, crosses blood–brain barrier, ↑ glucocorticoids, ↓ dopamine and serotonin, causes fevers
IL-2	Th1, NK cells	↑ T-cell proliferation and differentiation, ↑ cytolytic activity of NK and LAK cells, activates B cells to ↑ immunoglobulin
IL-3	Th1, Th2	↑ production and differentiation of hematopoietic progenitor cells
IL-4	Th2, T cells, macrophages, mast cells, B cells, basophils	Induces proliferation and differentiation of B cells, differentiation of Th1 and Th2
IL-6	Th2, monocytes, macrophages, fibroblasts, endothelial cells	Activates hematopoietic progenitor cells, proliferation of antibody-producing cells, synthesis of acute-phase proteins
IL-7	Bone marrow stromal cells	↑ proliferation and cytotoxic activity of Tc and LAK cells, support growth of pre-B cells and proliferation of T cells
IL-8	Monocytes, macrophages, endothelial cells	↑ chemotactic activity of neutrophils, T cells, and basophils, ↑ phagocytic activity of neutrophils
IL-10	Th2, Treg, macrophages, B cells	↑ pro-inflammatory cytokine release of macrophages, inhibits Th1, ↑ B-cell proliferation and immunoglobulin production, inhibition of IL-12 production and expression of class II MHC molecules
IL-12	Macrophages, B cells, dendritic cells	Initiates cell-mediated immunity, Th1 differentiation, ↑ growth and activity NK and Tc cells, IFN-γ synthesis
IL-15	Macrophages, others	Proliferates NK cells and T cells (CD8+ cells)
IL-18	Macrophages	Proliferates NK and T cells, IFN-γ synthesis

TABLE 2-4

Cytokines: Sources and Major Functions (*continued*)

Type	Source	Major Functions
IL-23	Macrophages, dendritic cells	Maintains IL-17–producing T cells
IL-27	Macrophages, dendritic cells	Th1 differentiation, inhibits Th1 and NK cells, IFN-γ synthesis
Interferons (IFNs)		
IFN-α	Macrophages, B and T cells	Antiviral activity, ↑ class I MHC expression, ↓ B-cell proliferation, ↓ macrophage activity and production of IL-8
IFN-β	Fibroblasts, epithelial cells	Antiviral activity, ↑ IL-6, ↓ IL-8, activates NK cells
IFN-γ	Th1, T, NK cells	Activates NK cells, ↑ MHC class I and II expression on macrophages, ↑ B-cell differentiation, ↑ macrophage activity
Tumor Necrosis Factors (TNFs)		
TNF-α (cachetin)	Th1 cells, activated lymphocytes	↑ macrophage activity, ↑ cytokines from NK cells, inflammatory mediators, synthesis of acute-phase proteins
TNF-β (lymphotoxin)	NK cells, fibroblasts, endothelial cells, malignant cells, macrophages	
Colony-Stimulating Factors (CSFs)		
Granulocyte CSF (G-CSF)	T cells, macrophages, neutrophils, fibroblasts, endothelial cells	↑ differentiation and activation of neutrophils
Granulocyte–macrophage CSF (GM-CSF)	Macrophages, T cells, polymorphs, endothelial cells	↑ growth and differentiation of multi-potential progenitor cells, stimulates all cells of the myeloid lineage

ability to stimulate and enhance NK cells, monocytes, neutrophils, and dendritic cells.[8,9]

Signaling proteins secreted by cells referred to as chemokines induce chemotaxis in responsive cells.[1] Some chemokines are pro-inflammatory, whereas others are homeostatic, acting to control migration of cells.[21] They are located on target cell surfaces and direct the movement of leukocytes around the body from the blood and into the tissues.

Activated macrophages, CD4+ lymphocytes, NK cells, neutrophils, mast cells, and eosinophils produce TNF.[17,19] The primary role of TNF involves regulating immune cells. TNF induces fevers, causes apoptotic cell death, and mediates inflammations and cytotoxic reactions.[17,19] Transforming growth factor (TGF) controls cell division and tissue repair.[4] Once the body identifies the antigen, an immune response initiates.

Learning the structure, cells, and soluble mediators of the immune system provides a foundation for understanding how the immune system mounts an immune response.

IMMUNE RESPONSE

The immune response serves as the body's defense against foreign substances in the cells and molecules of the immune system.[1,20] An immune response involves both innate and adaptive immunity. Innate immunity occurs early in the response, whereas adaptive immunity occurs in later stages that involves more specific immune cells. The following sections describe the processes involved with innate and acquired immune responses. **Figure 2-4** provides a schematic representation of the innate and acquired responses.

INNATE IMMUNITY

Innate immunity, often referred to as natural immunity, provides the first line of defense. Innate cells respond quickly to foreign substances and contain components including physical and chemical barriers, phagocyte cells, dendritic cells, NK cells, blood proteins, and cytokines.[1,22] The innate immunity recognizes by-products of damaged and dead cells, and eliminates these substances to initiate tissue repair.[1,23] When microbes break through these barriers, they encounter cells of innate immunity generating either an inflammatory or antiviral defense reaction.[1,22]

The inflammation process recruits leukocytes and plasma proteins to bind and ingest the microbes and respond to injury.[20] Neutrophils are the most abundant leukocytes, followed by monocytes, which evolve into macrophages.

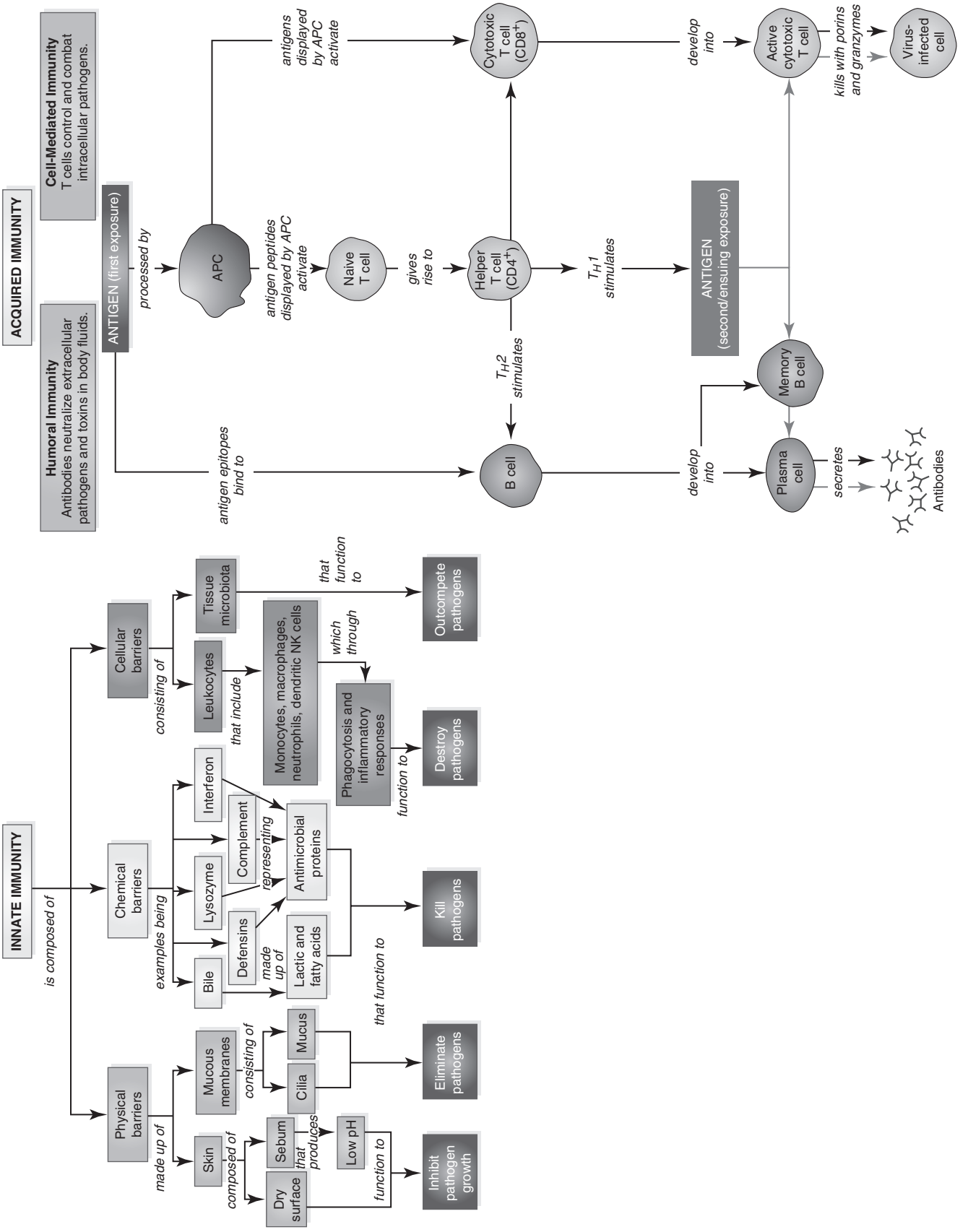

FIGURE 2-4

Schematic representation of the innate and acquired immunity.

Complement proteins and antibodies are the plasma proteins that enter inflammatory sites.[20] Acute inflammation develops in minutes to hours, whereas chronic inflammation develops when the infection is not eliminated or with prolonged tissue injury.[1]

A cytokine-mediated reaction occurs as part of the antiviral defense, in which NK cells kill the virus-infected cells.[1] The innate immune system induces expression of type I interferons to inhibit viral replication.[4] Type I interferons constitute a large family of structurally related cytokines that mediate the early innate immune response to viral infections.[4] These interferons activate gene transcription to create an antiviral state, sequester lymphocytes to maximize microbial encounters, increase the cytotoxicity of NK cells, and upregulate expression of MHC to eradicate viral infections.[4]

Despite the importance of the innate immune response, it has notable negative consequences. Although innate immunity includes a variety of feedback inhibition mechanisms that are intended to limit the potential damage to tissues, it has the potential to cause injury and disease such as autoimmune disorders.[1] Additionally, despite innate cells' rapid response, they are not able to differentiate among the various types of infection. Adaptive immunity, often referred to as acquired immunity, involves more specialized cells that develop in response to an infection.

ADAPTIVE IMMUNITY

In contrast to the cells associated with innate immunity, the adaptive cells have the unique ability to remember and respond to repeated exposure to the same pathogen.[1,22] In other words, the immune system builds a defense against a specific antigen. Adaptive immunity responses include two types: (1) humoral immunity and (2) cell-mediated immunity. Antibodies produced by B-cell lymphocytes mediate humoral immunity. The T-cell lymphocytes mediate cell-mediated immunity. Although the humoral and cell-mediated immune responses involve both B- and T-cell lymphocytes, they function interdependently under the domain of adaptive immunity.[4]

Humoral Immunity

Antibodies are the only mechanism of adaptive immunity that prevents infections from becoming established in the body.[1] Antibodies in the blood and mucosal secretions mediate humoral immunity as the principal defense mechanism against extracellular microbes.[1] Elements in the humoral immunity response attack microbes by binding to the microbes, thereby preventing them from infecting cells. In humoral immunity, the antibodies may activate different effector mechanisms such as phagocytosis and the release of inflammatory mediators.[1,22] This process involves the binding of antibodies to antigens. The B-cell lymphocytes proliferate and differentiate into cells when activated, and they secrete different classes of antibodies with distinct functions. For example, the response of B-cell lymphocytes to protein antigens requires help from the CD4+ cells. Some of the expanded B-cell lymphocytes differentiate into antibody-secreting plasma cells.

The complement system serves as one of the major effector mechanisms of both humoral and innate immunity. Serum and cell surface proteins interact with one another and with other molecules in a highly regulated manner to generate products that eliminate microbes.[1] Antibodies attach to antigens to activate one of the three major pathways of the complement system: (1) classical, (2) alternative, or (3) lectin. The classical pathway is activated by antigen–antibody complexes.[1,3] In the absence of antibody, the alternative pathway is activated on microbial surfaces.[1,3] The lectin pathway is initiated by collectins binding to antigens.[1,3] These three pathways result in the generation of enzyme complexes that can cleave the most abundant complement protein, C3.[1,3] No matter how the complement pathway is activated, the biologic functions involved include opsonization of organism and immune complexes, followed by phagocytic clearance, and activation of inflammatory cells.[1,3]

Cell-Mediated Immunity

The T-cell lymphocytes mediate cellular immunity. Viruses and some bacteria may survive the initial immune response and proliferate as intracellular microbes. When this occurs, the microbes are inaccessible to circulating antibodies.[1] Cell-mediated immunity promotes the intracellular destruction of these microbes. Activated CD4+ T-cell lymphocytes proliferate and differentiate into effector cells that secrete different cytokines.[1,16,24] The growth factor interleukin-12 (IL-12) also acts on the antigen-activated lymphocytes early in the process to stimulate proliferation of other cytokines.[1] A vast number of effector cells leave the lymphoid organs and migrate to sites of infection and inflammation. When the differentiated effectors encounter cell-associated microbes again, they eliminate the microbes.[1]

Effector CD4+ cells contribute to cell-mediated immunity in a variety of ways, including secreting cytokines to recruit leukocytes, stimulating phagocytosis to kill microbes, and triggering the production of antibodies.[1,16,24] The effector CD4+ cells also activate eosinophils to kill oversized parasites that were missed during the phagocytosis process, and some remain in the lymphoid organs to stimulate B-cell responses.[1] Activated CD8+ lymphocytes proliferate and differentiate into Tc cells, which then kill microbes harbored by the cytoplasm, thereby eliminating

reservoirs of infection.[1,14] In other words, antibodies neutralize microbial infections and promote the elimination of microbes through phagocytosis and activation of the complement system.

TUMOR IMMUNITY

Cancer arises from uncontrolled proliferation and spread of malignant cells. Malignant tumors have the ability to resist apoptotic death, invade host tissues, and metastasize to distant sites. A large body of research in tumor immunology focuses on the possibility that cancer cells might be eradicated by specific tumor responses.[25–30] The theory or concept of immune surveillance, for example, has existed since the 1950s. It proposes that the immune system should recognize and destroy clones of transformed cells before they grow into tumors, and kill tumors after they are formed.[1,31] Although the theory of immune surveillance remains controversial, recently it has been established that innate and adaptive immunity does react against many tumors.[31] The most recent studies have also led to recommendations that information gleaned from evaluation of the immune response in and around the tumor should be included in prognostic evaluation and treatment decisions.[31] This section describes the types of antigen expressed by malignant tumors, the way in which the immune system recognizes and responds to these antigens, the means by which tumors evade the host immune response, and the application of immunologic approaches to the treatment of cancer.

Antigens expressed on tumor cells but not on normal cells are referred to as tumor-specific antigens.[1,31] Conversely, tumor antigens expressed on normal cells are referred to as tumor-associated antigens.[1,31] The identification of antigens expressed on tumors represents a major advance in tumor immunology. Examples of mutated tumor antigens include oncogene products such as *Ras* mutations and the *Bcr/Abl* rearrangement.[30] A tumor suppressor gene product such as mutated *P53* is another example of a mutated tumor antigen. Although not mutated, the HER2/neu oncogene is overexpressed in breast and other carcinomas as a tumor antigen. Normal cellular proteins are abnormally expressed on tumor cells, eliciting an immune response. Tumors stimulate specific innate and adaptive immune responses, including specificity and memory shown to kill tumor cells.[3,31] Histopathology shows that many tumors and lymph nodes that drain tumors are surrounded by mononuclear cell infiltrates consisting of T-cell lymphocytes, NK cells, and macrophages.[1,31] For example, NK cells kill many types of tumor cells, including virally infected cells and hematopoietic tumors.[1] Macrophages inhibit and promote tumor growth depending on the activation state.[1] CD8+ and Tc cells also elicit T-cell–mediated and humoral immune responses in which the CD8+ and Tc cells kill tumor cells.[14,31] Thus, the Tc CD8+ cells are critical in establishing antitumor activity.

Despite these immune responses, many cancers develop mechanisms to evade antitumor immune responses. Several intrinsic mechanisms enable tumors to escape host defenses—for example, downregulation of MHC molecular expression, lack of tumor antigen expression on cells, and production of immunosuppressive substances.[1] Immune responses also fail to prevent the growth of tumors because tumor cells are derived from host cells and resemble normal cells.[31] As a consequence, tumors tend to be weakly immunogenic. Tumors may also grow rapidly and spread quickly, overwhelming the capacity of the immune system to control and eradicate the tumor. This process has become a major focus of tumor immunology research designed to elucidate the immune evasion mechanism of tumors.

The increased body of knowledge related to immunology and tumor immunity has led to a new era in cancer immunology, in which the immune system is being used to treat cancer. The theory that cancer cells have different surface molecules or tumor antigens supports the development of immunotherapy treatment for cancer. Three main groups of cancer immunotherapy treatments have emerged: (1) cell-based therapies or cancer vaccines, (2) monoclonal antibodies directed at cell surface receptors as targets, and (3) cytokines that enhance antitumor activity in the immune system.[32] Tumor immunotherapy augments active immune responses against the tumor or delivers tumor-specific immune effectors.[1] Although great strides have already been made in terms of identifying cancer treatment options, more work is required to recognize and target cancer cells while sparing healthy cells.

TRANSPLANT IMMUNITY

Solid-organ and tissue transplantation to a nonidentical recipient leads to a rejection immune response. The alloantigens involved in the transplant elicit both cellular and humoral immune responses. Allogeneic class I and II MHC molecules are the major molecular targets in allograft rejection.[1] In such a reaction, the allogeneic MHC molecules may be presented on the donor APCs to the recipient T cells, or the alloantigens may be picked up by host APCs and presented to T cells as peptides.[1] Graft rejection is mediated by T cells. The Tc cells kill graft cells; the Th cells cause cytokine-mediated inflammation.[1,33] Acute rejection occurs when alloreactive T cells and antibodies produced by the graft damage the blood vessel walls and cause parenchymal cell death.[1,33] Conversely, chronic rejection is characterized by fibrosis and vascular abnormalities causing T-cell– and cytokine-mediated inflammatory reactions in the walls of the arteries.[1,33]

Hematopoietic stem cell and bone marrow transplant rejection involves adaptive immunity and NK cells. The T lymphocytes in the bone marrow graft respond to alloantigens of the host, causing graft-versus-host disease (GVHD).[34] Epithelial cell death in the skin, liver, and gastrointestinal tract occurs in acute GVHD. Clinical manifestations include rash, jaundice, and diarrhea. Conversely, chronic GVHD is characterized by fibrosis and atrophy of one or more organs.

In both solid-organ and stem cell/bone marrow transplant, immunosuppression of T-cell responses with cytotoxic drugs, immunosuppressive agents, or anti-T-cell antibodies can prevent graft rejection. These therapies are often combined with anti-inflammatory agents such as corticosteroids to inhibit the cytokine synthesis by macrophages and other cells.[33,34] For example, thymoglobulin mediates T-cell suppression, FK506 (tacrolimus) and cyclosporine inhibit the transcription of certain genes in T cells, rapamycin (sirolimus) inhibits growth factor–mediated T-cell proliferation, mycophenolate mofetil (MMF) kills proliferating T cells, and intravenous immune globulin (IVIG) treats antibody-mediated and inflammatory diseases.[33,34]

HYPERSENSITIVITY

Hypersensitivity produces an abnormal or pathologic immune reaction caused by repeated antigen exposure.[1,35] It involves the innate immune response, antibodies, T lymphocytes, various effector cells, and mediators of inflammation.[1] Disorders caused by immune responses are referred to as hypersensitivity diseases. Hypersensitivity diseases result when antibodies bind to cells or tissues, circulating immune complexes are deposited in tissues, or reactive T-cell lymphocytes bind with antigens in tissues.[1] The effector mechanisms of antibody-mediated tissue injury or T-cell–mediated tissue injury induced by cytokines contribute to acute and delayed hypersensitivity.[1,16]

Four types of hypersensitivity reactions are distinguished. Type I involves an immediate or anaphylactic reaction that is mediated by a rapid release of IgE and mast cells.[34] Upon subsequent exposure to the antigen, the target-fixed antibodies react to the antigen immediately, causing a release of histamine, leukotrienes, and prostaglandin into the periphery.[34,35] This flood of substances elicits a cell-mediated vascular and smooth muscle response that is amplified by platelets, neutrophils, and eosinophils. An excessive Th2 response also occurs. As a whole, the Type I reaction may involve a range of symptoms such as urticaria and bronchospasm; it may occur within 15 to 30 minutes after exposure to the antigen, or may be delayed up to 12 hours.[35–37]

The antibody-mediated Type II hypersensitivity reaction affects organs and tissues. This reaction results when the antibodies are directed against antigens on the surface of tissues and cells. This results in the release of IgM or IgG, complement, phagocytes, and NK cells, causing inflammation, opsonization, and phagocytosis.[1,18] The reaction time ranges from minutes to hours, and symptoms can occur in the blood and tissues such as the skin, nerves, or thyroid. Examples of Type II reactions include hemolytic anemia, drug-induced hemolysis, and idiopathic thrombocytopenic purpura.

The immune-complex–mediated Type III hypersensitivity occurs when antibody and antigen complexes are deposited in the vascular walls and tissues.[1,18] The excess of antigen causes an inflammatory response characterized by tissue damage similar to that seen with Type II reactions, owing to the release of IgM and IgG. The reaction occurs 3 to 10 hours after exposure and is mediated by soluble immune complexes. Examples of such reactions include serum sickness and systemic lupus erythematosus.

Type IV reactions involve cell-mediated or delayed type hypersensitivities.[1,15,36] This type of hypersensitivity results from inappropriate or excessive immune reaction. Type IV reactions occur in autoimmune diseases, dermatitis, and infectious diseases such as tuberculosis. The Tc cells cause direct damage in response to the antibody, and the Th1 cells secrete cytokines in response to the damage.[15] In turn, this response activates Tc cells, macrophages, and monocytes, causing even more damage.[15] This process evolves over 24 to 72 hours, ultimately resulting in blood vessel permeability with fluid and protein accumulation into the tissues.[15]

AUTOIMMUNITY

Autoimmunity results from a failure of the self-tolerance mechanism in B or T cells. This failure may lead to lymphocyte activation and control mechanism imbalance. General factors associated with autoimmune reactions include defects in B- or T-cell deletion during maturation, number and function of regulatory T cells, and self-reactive lymphocyte apoptosis.[1] Autoimmune reactions also activate APCs that overcome regulatory mechanisms, resulting in excessive T-cell activation.[1] Genetic susceptibly and environmental triggers (i.e., infections and local tissue injury) also contribute to autoimmunity development.[38,39]

Autoimmune diseases may be either systemic or organ specific, depending on the distribution of autoantigens recognized.[1] For example, formation of circulating immune complexes composed of specific antibodies typically leads to systemic disease. In contrast, autoantibody or T-cell responses against self-antigens lead to organ-specific disease.[1] The majority of autoimmune diseases are complex and polygenic, with numerous susceptibility genes contributing to the disease development process.[38,39] The MHC

genes are the greatest contributors; they may present a particular self-peptide and activate pathogenic T cells.[1] Other potential theories and hypotheses about the origin of autoimmunity focus on tissue inflammation and hormonal influences.[40]

Autoimmunity remains one of the most challenging scientific and clinical immunologic problems. With the rapid technical advances in this area and better understanding of self-tolerance, more definitive answers to questions about autoimmunity are expected to be obtained in the future.

VACCINES

Vaccines achieve immune memory without the individual experiencing an actual infection, leaving the body primed to respond to a virus or bacteria that subsequently enter the body.[20] Effective vaccines activate both innate and adaptive responses. Vaccines use an immunogen to activate the body's adaptive response so that specific memory cells are generated.[20] Adjuvants or immunostimulatory molecules can also be added to vaccines to activate innate immunity, thereby increasing recognition of a broader range of pathogens.[20] Cancer vaccines use adjuvants such as CSF, IL-2, and interferon to lure dendritic cells and immune cells to the injection site or to trick the immune system into mounting a response against the carrier protein.[8] In other words, vaccines activate B cells to remember pathogens, and sensitize T cells to increase cell kill.

Although vaccines are most effective if the infectious agent does not establish latency, does not undergo much antigenic variation, and does not interfere with the host immune response, this behavior continues to be an area of research in tumor cells.[1] Cancer vaccines can be administered for either prevention or treatment purposes.

Cancer vaccines work by presenting a target antigen to the dendritic cell. The vaccine can be made from general tumor antigens or from antigen-specific patient tumors.[30] Dendritic cell vaccines involve exposing immature dendritic cells to tumor antigens, followed by administration of the sensitized dendritic cell for antigen presentation to T cells.[8,9] The dendritic cells respond by upregulating the molecules to interact with T cells and migrate to lymph nodes.[32] If the T cell recognizes the cognate antigen, then it is activated.[32] Once activated, the CD4+ cells produce cytokines to help CD8+ cells to mature.[32] After the CD8+ cells are fully mature, they migrate throughout the body, acting as a tumor antigen to lyse cells, potentially mediating an antitumor response.[32] **Figure 2-5** illustrates cancer vaccines' mechanism of action.

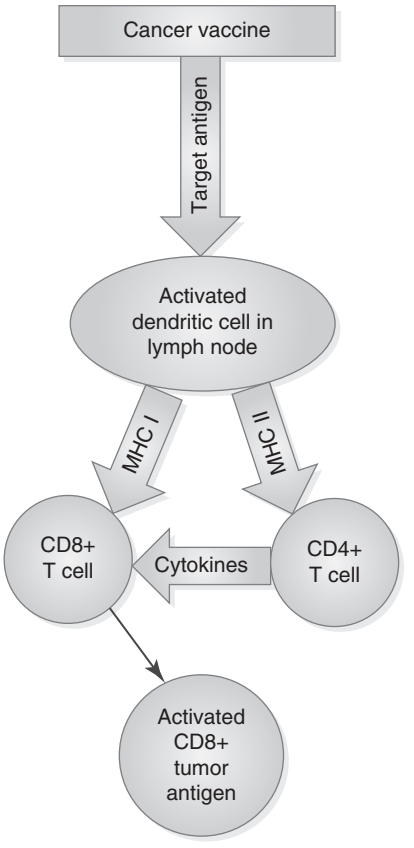

FIGURE 2-5

Cancer vaccine mechanism of action.

FACTORS AFFECTING IMMUNE RESPONSE

The actions of the immune system may lead to either positive or negative outcomes. While attempting to maintain homeostasis, rid the body of foreign organisms, and fight cancer, the stimulated immune responses may cause tissue inflammation and damage to both healthy and unhealthy cells. Studies have shown that certain factors, such as the environment, stress, aging, alcohol, tobacco, hormones, exercise, and sleep, may affect the immune system both positively and negatively. Increasing NK cell activity, lymphocyte proliferation, and pro-inflammatory cytokines to increase phagocytosis has demonstrated positive effects on the immune system.[9,21] Conversely, decreasing NK cell activity, lymphocyte proliferation, and pro-inflammatory cytokines may result in downregulation of the immune system.

ENVIRONMENT

Environmental factors affect the immune system through the formation of free radicals. The term "free radical" refers

to any of a family of compounds that are highly reactive due to the presence of unpaired electrons in the outer orbital of the atoms making up the compound.[21] Free radicals include reactive oxygen species (ROS) such as superoxide anion (O_2), hydroxyl radical (OH), and hydrogen peroxide (H_2O_2), as well as reactive nitrogen species (RNS) including nitric oxide (NO) and peroxynitrite (ONOO).[21] The protective function of the immune system vis-à-vis free radicals depends on two components of the cell membrane: fluid and oxidation.[21] Cell membranes are rich in phospholipids, and the immune system is sensitive to oxidative stress.[21] Therefore, if the cell membrane becomes perioxidized, it may lose its integrity and have altered fluidity.[21] These changes result in impairment of cellular functioning and signaling.

During inflammatory processes, the phagocyte activity promotes a multicomponent flavoprotein, NADPH oxidase, that catalyzes the production of the superoxide anion radical (O_2) in high amounts.[21] Neutrophils and macrophages also produce superoxide free radicals and H_2O_2.[21] Free radicals are generated as a result of cellular metabolic activity and the immune system's elimination of microbes.[21] Subsequently, these free radicals cause breaks in the DNA strands that may potentially lead to mistakes in repair and tumor cell generation.[41] Furthermore, long-chain lipids are more susceptible to free radical attacks that lead to oxidative destruction of fatty acids (lipid peroxidation).[21] Indeed, this is a key consequence of oxidative stress. When oxidation exceeds the control mechanisms, oxidative stress arises. In contrast, antioxidant defense systems neutralize the generation of free radicals or attempt to intercept the detected free radicals.[21] Adequate amounts of antioxidants can protect the cells from oxidative stress and prevent damage to the immune cells.[21]

STRESS

Stress places demands on the body that threaten homeostasis by altering the adhesive properties of leukocytes.[41] Levels of circulating white blood cells and cytokines increase during times of stress. Stress activates the hypothalamic–pituitary–adrenal (HPA) axis and initiates sympathetic arousal, which in turn leads to a release of glucocorticoids and catecholamines; their production increases the level of inflammation and shifts the immune system from cellular to humoral immunity.[21]

When chronic stress is present, the stress response system does not "turn off." The ongoing response can disrupt many of the body's processes, leading to molecular damage and increasing the individual's risk of developing anxiety, depression, cardiovascular disease, sleep disorders, and chronic diseases.[21,41,42]

AGING

Aging also impacts the immune system. Several components contribute to decreased immune system function with aging. The thymus gland shrinks with age, thereby changing the functions of T cells and potentially leading to malfunction of immune cells.[43] Levels of IL-6 increase with age, contributing to cognitive decline and decreased functional status.[44] Recent studies have also discovered effects on white blood cells related to aging.[43,45] Each time the body recovers from an immune insult, a certain percentage of white cells become deactivated.[43,45] Over time, the immune defenses may become weakened as a result of the dwindling population of white blood cells.

ALCOHOL

Studies have found that light to moderate intake of alcohol enhances nonspecific immunity and increases populations of leukocytes, neutrophils, lymphocytes, and basophils.[46] However, extensive alcohol intake suppresses a wide range of immune responses. Research suggests that excessive alcohol exposure impairs both B- and T-cell lymphocyte functioning, NK cells, and cytokine production.[46] Chronic alcohol ingestion also causes abnormal ROS involved with oxidation.[46]

SMOKE

Exposure to cigarette and wood smoke weakens the body's innate defenses, alters antigen presentation, and promotes autoimmunity.[47] Inhalation of both primary and secondhand smoke promotes the release of pro-inflammatory cytokines such as TNF, IL-1, IL-6, and IL-8 and decreases the activity of anti-inflammatory cytokines.[48] Smoke exposure also activates macrophages and dendritic cells, resulting in increased levels of IgE, which then contribute to hypersensitivity reactions.[47,48]

HORMONES

Changes in the levels of estrogen, progesterone, and testosterone in the body also impact the immune system. Recent studies have shown that these hormones influence cytokine production, suppress lymphocytes, decrease NK cell activity, and depress cellular immunity.[49] Many autoimmune disorders are exacerbated by the presence of higher levels of hormones, particularly estrogens (but not androgens).[50] Higher levels of estrogens favor immune processes involving CD4+, Th2, and B cells, whereas higher levels of

androgens support the activities of CD4+, Th1, and CD8+ cells.[49,50] These differences are believed to contribute to the higher incidence of autoimmune diseases in women compared to men.[50] Hormone depletion reduces populations of B and T cells, Th-cell cytokines, and monocytes, and impairs responses to viral infections.[49]

EXERCISE AND SLEEP

Exercise and sleep are also suspected to influence immune functions. Studies involving exercise and the immune system have not produced definitive proof of this relationship, however.[51,52] Although studies suggest that regular moderate levels of exercise enhance immune function by increasing NK cell activity, concern has arisen that such exercise might decrease the CD4/CD8 ratio and increase levels of pro-inflammatory cytokines such as IL-6 and TNF.[52,53] Furthermore, studies have shown that excessive amounts of exercise might impair immune function by depressing lymphocyte proliferation and antigen presentation.[51–53]

Sleep and the circadian cycle affect the immune system as well. Sleep restores the immune function. During sleep, immune cells reach their peak in terms of differentiation, immune cells migrate, and melatonin stimulates cytokine production, thereby enhancing phagocytosis and increasing NK cellular activity.[54–56] Prolonged sleep deprivation increases chemokine production and pro-inflammatory cytokines.[54-57]

NUTRITION AND ANTIOXIDANTS

Nutritional status contributes to both immunocompetence and development of infection. Nutritional deficiencies negatively affect cell-mediated immunity, phagocyte activity, cytokine production, and antibody synthesis.[41] Conversely, dietary antioxidants, vitamins, and trace elements protect cells and improve immune function.[41,58]

Dietary antioxidants include vitamin C, vitamin E, and beta-carotene. Vitamin C serves as a major water-soluble chain-breaking antioxidant against oxidative damage, particularly in leukocytes.[41,59] This nutrient increases neutrophil chemotaxis, NK cell activity, and T-lymphocyte proliferation.[41,59] Vitamin E acts as an antioxidant in cellular membranes necessary in infection and inflammation.[41,59] This chain-breaking lipid-soluble antioxidant reduces damage to the membrane during infection.[41] Supplementing vitamin E increases lymphocyte proliferation, IL-2 production, and NK cell activity.[41,58]

Minerals such as selenium, zinc, copper, and iron also act as antioxidants. Selenium and copper increase lymphocyte proliferation and enhances Th1 immune responses.[41,58] Zinc defends against oxidative stress by increasing phagocytosis, NK cell activity, and antibody response.[41,58] Iron contributes to numerous immune functions, including T-lymphocyte, NK cell, monocyte, and macrophage differentiation and proliferation.[41,58]

Although trace elements do not act directly as antioxidants, they are critical components of antioxidant enzymes. Other natural antioxidants contained in foods such as olive oil, tea, curcumin, and red wines modulate immune system functions and eliminate toxins.[41,58]

In recent years, vitamin D insufficiency has become a global issue with widespread health consequences. In particular, the role of this steroid hormone in the immune response has drawn critical attention. Studies indicate that vitamin D influences both innate and acquired immunity.[59] In terms of innate immunity, vitamin D modulates the cytokine response and peptide production.[60] Additionally, vitamin D influences B- and T-cell lymphocyte activation, and boosts macrophage and monocyte activation.[60] Vitamin D also impacts the development of Treg cells and the maturation of antigen-presenting dendritic cells.[59] Low levels of vitamin D (less than 30 ng/mL) have been linked to an increased risk of cancer.[60,61]

IMPLICATIONS FOR NURSING PRACTICE

Breakthroughs in immunology are having a profound impact across the healthcare realm, affecting immunotherapy, antiviral development, and gene therapy, among other areas. Immunology involves a complex coordination of cells and tissues to acquire, maintain, and regulate resistance to diseases. It has a pivotal role in the pathogenesis of cancer and inflammatory diseases. Nurses are at the forefront of therapy administration, toxicity management, education, and follow-up in regard to immunotherapy. Methods for enhancing the immune system have moved from bench to bedside, requiring nurses to keep abreast of the changing knowledge based related to immunology and cancer immunotherapy. In particular, many new cancer staging systems and therapies are based on cellular and molecular immunology functions. Strategies for targeting cancer cells also rely on an understanding of these mechanisms.

Oncology nurses need education on pathophysiology of cancer so that they will understand the traditional chemotherapy and radiation treatment options, but they also must receive cellular and molecular immunology education so that they can effectively manage patients receiving novel targeted therapies. Tumor immunology requires that oncology nurses caring for patients with cancer acquire knowledge of the immunology complexity, cellular and molecular biology, and tumor immunology. Practitioners are challenged to understand the treatment plans, rationales, administration techniques, symptom management, and follow-up with these approaches. Moreover,

immune-related side effects and management differ from traditional chemotherapy side effects due to the different mechanism of action—that is, one centered in the immune system. Advancing knowledge on the normal processes and complex components will assist in the understanding of the treatment plan and outcomes.

CONCLUSION

The immune system consists of complex, interdependent functions involving hematopoiesis, cellular proliferation and differentiation, innate and adaptive immunity, and soluble mediators. Immune responses may be overactive, inappropriate, or deficient, all of which may cause immune system disorders. For example, an overactive immune system can trigger autoimmune diseases and cause organ rejection. Allergies develop as a result of inappropriate immune responses. Under-activity of the immune system may result in immunodeficiency disorders. Although great strides have been made that advanced the science of immunology, more unraveling of these complexities is required to understand the interactions among genetics, hormones, environmental and behavioral factors, tumor immunity, autoimmunity, and hypersensitivity in the science of immunology.

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