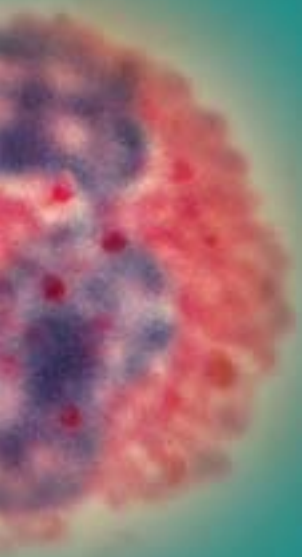
Selected Key Terms

The following terms and other boldface terms in the chapter are defined in the Glossary



allergy
anaphylaxis
antibody
antigen
antiserum
attenuated
autoimmunity
B cell
complement
gamma globulin
immunity
immunization
immunodeficiency
inflammation
interferon
interleukin
lymphocyte
macrophage
plasma cell
T cell
toxin
toxoid
transplantation
vaccine

Learning Outcomes

After careful study of this chapter, you should be able to:

1. List the factors that determine the occurrence of infection
2. Differentiate between nonspecific and specific body defenses and give examples of each
3. Briefly describe the inflammatory reaction
4. List several types of inborn immunity
5. Define *antigen* and *antibody*
6. Compare T cells and B cells with respect to development and type of activity
7. Explain the role of macrophages in immunity
8. Describe some protective effects of an antigen-antibody reaction
9. Differentiate between naturally acquired and artificially acquired immunity
10. Differentiate between active and passive immunity
11. Define the term *vaccine* and give several examples of vaccines
12. Define the term *immune serum* and give several examples of immune sera
13. List several disorders of the immune system
14. Explain the possible role of the immune system in preventing cancer
15. Explain the role of the immune system in tissue transplantation
16. Show how word parts are used to build words related to body defenses, immunity, and vaccines (see Word Anatomy at the end of the chapter)

chapter 17

Body Defenses, Immunity, and Vaccines

Chapter 5 presents a rather frightening list of harmful organisms that surround us in our environment. Fortunately, most of us survive contact with these invaders and even become more resistant to disease in the process. The job of protecting us from these harmful agents belongs in part to certain blood cells and to the lymphatic system, which together make up our **immune system.**

The immune system is part of our general body defenses against disease. Some of these defenses are **nonspecific;** that is, they are effective against any harmful agent that enters the body. Other defenses are referred to as **specific;** that is, they act only against a certain agent and no others.

Why Do Infections Occur?

Although the body is constantly exposed to pathogenic invasion, many conditions determine whether an infection will actually occur. Pathogens have a decided preference for certain body tissues and must have access to these tissues. Some viruses attack only nervous tissue. The poliovirus, for example, may be inhaled or swallowed in large numbers and therefore may come into direct contact with the mucous membranes lining the respiratory and digestive tracts, yet it causes no apparent disorder of these tissues. In contrast, the viruses that cause influenza and the common cold do attack these mucous membranes. HIV, the virus that causes AIDS, attacks a certain type of T cell (lymphocyte), which has surface receptors for the virus.

The **portal of entry** is an important condition influencing the occurrence of infection. The respiratory tract is a common entrance route for pathogens. Other important avenues of entry include the digestive system and the tubes that open into the urinary and reproductive systems. Any break in the skin or in a mucous membrane allows organisms such as staphylococci easy access to deeper tissues and may lead to infection, whereas unbroken skin or mucous membranes are usually not affected.

The **virulence** (VIR-u-lens) of an organism, or the organism's power to overcome its host's defenses, is another important factor. Virulence has two aspects: one may be thought of as "aggressiveness," or invasive power; the other is the organism's ability to produce **toxins** (poisons) that damage the body. Different organisms vary in virulence. The virulence of a specific organism also can change; the influenza virus, for example, can be more dangerous in some years than in others. Organisms may gain virulence as they pass from one infected host to another.

The **dose** (number) of pathogens that invade the body also is a determining factor in whether or not an infection develops. Even if the virulence of a particular organism happens to be low, infection may occur if a large number enter the body.

Finally, an individual's condition, or **predisposition,** to infection is also important. Disease organisms are around us all the time. Why does a person only occasionally get a cold, flu, or other infection? Part of the answer lies in the person's condition, as influenced by general physical and emotional health, nutrition, living habits, and age.

Checkpoint 17-1 What are some factors that influence the occurrence of infection?

Nonspecific Defenses

The features that protect the body against disease are usually considered as successive "lines of defense," beginning with the relatively simple or outer barriers and proceeding through progressively more complicated responses until the ultimate defense mechanism—immunity—is reached.

Chemical and Mechanical Barriers

Part of the first line of defense against invaders is the skin, which serves as a mechanical barrier as long as it remains intact. A serious danger to burn victims, for example, is the risk of infection as a result of skin destruction.

The mucous membranes that line the passageways leading into the body also act as barriers, trapping foreign material in their sticky secretions. The cilia in membranes in the upper respiratory tract help to sweep impurities out of the body.

Body secretions, such as tears, perspiration, and saliva, wash away microorganisms and may contain acids, enzymes, or other chemicals that destroy invaders. Digestive juices destroy many ingested bacteria and their toxins.

Certain reflexes aid in the removal of pathogens. Sneezing and coughing, for instance, tend to remove foreign matter, including microorganisms, from the upper respiratory tract. Vomiting and diarrhea are ways in which toxins and bacteria may be expelled.

Checkpoint 17-2 What tissues constitute the first line of defense against the invasion of pathogens?

Phagocytosis

Phagocytosis is part of the second line of defense against invaders. In the process of phagocytosis, white blood cells take in and destroy waste and foreign material (see Fig. 13-6 in Chapter 13). Neutrophils and macrophages are the main phagocytic white blood cells. Neutrophils are a type of granular leukocyte. Macrophages are derived from monocytes, a type of agranular leukocyte. Both types of cells travel in the blood to infection sites. Some of the macrophages remain fixed in the tissues, for example, in

the skin, liver, lungs, lymphoid tissue, and bone marrow, to fight infection and remove debris.

Natural Killer Cells

The **natural killer (NK) cell** is a type of lymphocyte different from those active in specific immunity, which are described later. NK cells can recognize body cells with abnormal membranes, such as tumor cells and cells infected with virus, and, as their name indicates, can destroy them on contact. NK cells are found in the lymph nodes, spleen, bone marrow, and blood. They destroy abnormal cells by secreting a protein that breaks down the cell membrane, but the way in which they find their targets is not yet completely understood.

Inflammation

Inflammation is the body's effort to get rid of anything that irritates it or, if this is not possible, to limit the harmful effects of the irritant. Inflammation can occur as a result of any irritant, not only microorganisms. Friction, fire, chemicals, x-rays, and cuts or blows all can be classified as irritants. If irritation is caused by pathogenic invasion, the resulting inflammation is termed an **infection.** With the entrance of pathogens and their subsequent multiplication, a whole series of defensive processes begins. This **inflammatory reaction** is accompanied by four classic symptoms: heat, redness, swelling, and pain, as described below.

When tissues are injured, **histamine** (HIS-tah-mene) and other substances are released from the damaged cells, causing the small blood vessels to dilate (widen). More blood then flows into the area, resulting in heat, redness, and swelling.

With the increased blood flow come a vast number of leukocytes. Then a new phenomenon occurs: the walls of the tiny blood vessels become "coarsened" in texture (as does a piece of cloth when it is stretched). Blood flow slows down, and the leukocytes move through these altered walls and into the tissue, where they can reach the irritant directly. Fluid from the blood plasma also leaks out of the vessels into the tissues and begins to clot.

When this response occurs in a local area, it helps prevent the spread of the foreign agent. The mixture of leukocytes and fluid, the **inflammatory exudate,** causes pressure on the nerve endings, which combined with the increased amount of blood in the vessels, causes the pain of inflammation.

As the phagocytes do their work, large numbers of them are destroyed, so that eventually the area becomes filled with dead leukocytes. The mixture of exudate, living and dead white blood cells, pathogens, and destroyed tissue cells is **pus.**

Meanwhile, the lymphatic vessels begin to drain fluid from the inflamed area and carry it toward the lymph nodes for filtration. The regional lymph nodes become enlarged and tender, a sign that they are performing their protective function by working overtime to produce phagocytic cells that "clean" the lymph flowing through them.

Fever

An increase in body temperature above the normal range can be a sign that body defenses are at work. When phagocytes are exposed to infecting organisms, they release substances that raise body temperature. Fever boosts the immune system in several ways. It stimulates phagocytes, increases metabolism, and decreases certain organisms' ability to multiply.

A common misperception is that fever is a dangerous symptom that should always be eliminated. Control of fever in itself does little to alter the course of an illness. Healthcare workers, however, should always be alert to fever development as a possible sign of a serious disorder and should recognize that an increased metabolic rate may have adverse effects on the hearts of weak patients.

Interferon

Certain cells infected with a virus release a substance that prevents nearby cells from producing more virus. This substance was first found in cells infected with influenza virus, and it was called **interferon** because it "interferes" with multiplication and spread of the virus. Interferon is now known to be a group of substances. Each is abbreviated IFN with a Greek letter, alpha (α), beta (β), or gamma (γ) to indicate the category of interferon and additional letters or numbers to indicate more specific types, such as α2a or β1b.

Pure interferons are now available in adequate quantities for treatment because they are produced by genetic engineering in microorganisms. They are used to treat certain viral infections, such as hepatitis. Interferons are also of interest because they act nonspecifically on cells of the immune system. They have been used with varying success to boost the immune response in the treatment of malignancies, such as melanoma, leukemia, and Kaposi sarcoma, a cancer associated with AIDS. Interestingly, interferon β is used to treat the autoimmune disorder multiple sclerosis (MS), because it stimulates cells that depress the immune response.

Checkpoint 17-3 What are some nonspecific factors that help to control infection?

Immunity

Immunity is the final line of defense against disease. Immunity to disease can be defined as an individual's power to resist or overcome the effects of a *particular* disease agent or its harmful products. In a broader sense, the im-

mune system will recognize *any* foreign material and attempt to rid the body of it, as occurs in tissue transplantation from one individual to another. Immunity is a selective process; that is, immunity to one disease does not necessarily cause immunity to another. This selective characteristic is called **specificity** (spes-ih-FIS-ih-te).

There are two main categories of immunity:

- **Inborn immunity** is inherited along with other characteristics in a person's genes.
- **Acquired immunity** develops after birth. Acquired immunity may be obtained by **natural** or **artificial** means; in addition, acquired immunity may be either **active** or **passive**.

Figure 17-1 summarizes the different types of immunity. Refer to this diagram as we investigate each category in turn.

Inborn Immunity

Both humans and animals have what is called a **species immunity** to many of each other's diseases. Although certain diseases found in animals may be transmitted to humans, many infections, such as chicken cholera, hog cholera, distemper, and other animal diseases, do not affect human beings. However, the constitutional differences that make human beings immune to these disorders also make them susceptible to others that do not affect different species. Such infections as measles, scarlet fever and diphtheria do not appear to affect animals who come in contact with infected humans.

Some members of a given group have a more highly developed **individual immunity** to specific diseases. For example, some people are prone to cold sores (fever blisters) caused by herpes virus, whereas others have never shown signs of this type of infection. Newspapers and magazines sometimes feature the advice of an elderly person who is asked to give his or her secret for living to a ripe old age. Some elderly people may say that they lived a carefully regulated life with the right amount of rest, exercise, and work, whereas others may boast of drinking alcohol, smoking, not exercising, and other kinds of unhealthy behavior. However, it is possible that the latter group resisted infection and maintained health despite their habits, rather than because of them, thanks to inherited resistance factors.

Acquired Immunity

Unlike inborn immunity, which is due to inherited factors, acquired immunity develops during a person's lifetime as that person encounters various specific harmful agents.

If the following description of the immune system seems complex, bear in mind that from infancy on, your immune system is able to protect you from millions of foreign substances, even synthetic substances not found in nature. All the while, the system is kept in check, so that it does not usually overreact to produce allergies or mistakenly attack and damage your own body tissues.

Checkpoint 17-4 What is the difference between inborn and acquired immunity?

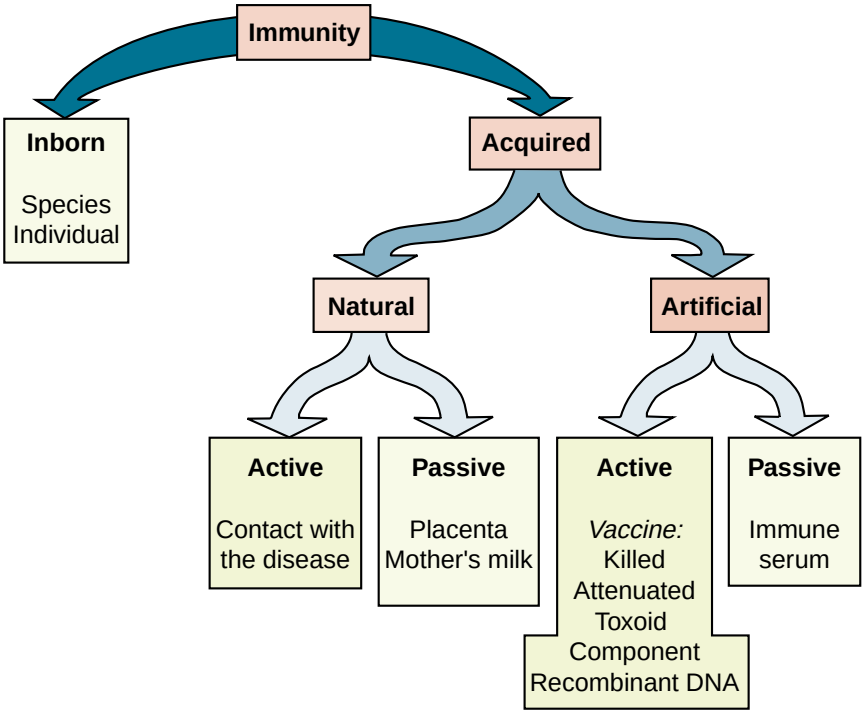


Figure 17-1 **Types of immunity.**

Antigens An **antigen** (AN-te-jen) (**Ag**) is any foreign substance that enters the body and induces an immune response. (The word is formed from *anti*body + *gen* because an antigen stimulates production of antibody.) Most antigens are large protein molecules, but carbohydrates and some lipids may act as antigens. Antigens may be found on the surface of pathogenic organisms, on the surface of red blood cells and tissue cells, on pollens, in toxins, and in foods. The critical feature of any substance described as an antigen is that it stimulates the activity of certain lymphocytes classified as T or B cells.

T Cells Both T and B cells come from hematopoietic (blood-forming) stem cells in bone marrow, as do all blood cells. The T and B cells differ, however, in their development and their method of action. Some of the imma-

ture stem cells migrate to the thymus and become T cells, which constitute about 80% of the lymphocytes in the circulating blood. While in the thymus, these T lymphocytes multiply and become capable of combining with specific foreign antigens, at which time they are described as **sensitized**. These thymus-derived cells produce an immunity that is said to be **cell-mediated** immunity.

There are several types of T cells, each with different functions. The different types of T cells and some of their functions are as follows:

- **Cytotoxic T cells** (T_c) destroy foreign cells directly.
- **Helper T cells** (T_h)release substances known as **interleukins** (in-ter-LU-kinz) (IL) that stimulate other lymphocytes and macrophages and thereby assist in the destruction of foreign cells. (These substances are so named because they act between white blood cells). There are several subtypes of these helper T cells, one of which is infected and destroyed by the AIDS virus (HIV). The HIV-targeted T cells have a special surface receptor (CD_4) to which the virus attaches.
- **Regulatory T cells** (T_{reg}) suppress the immune response in order to prevent overactivity. These T cells may inhibit or destroy active lymphocytes.
- **Memory T cells** remember an antigen and start a rapid response if that antigen is contacted again.

The T cell portion of the immune system is generally responsible for defense against cancer cells, certain viruses, and other pathogens that grow within cells (intracellular parasites), as well as for the rejection of tissue transplanted from another person.

The Role of Macrophages **Macrophages** are phagocytic white blood cells derived from monocytes (their name means "big eater"). They act as processing centers for foreign antigens. They ingest foreign proteins, such as disease organisms, and break them down within phagocytic vesicles (Fig. 17-2). They then insert fragments of the foreign antigen into their plasma membrane. The foreign antigens are displayed on the macrophage's surface in combination with antigens that a T cell can recognize as belonging to the "self." Self antigens are known as MHC (major histocompatibility complex) antigens because of their importance in cross-matching for tissue transplantation. They are also known as HLAs (human leukocyte antigens), because white blood cells are used in testing tissues for compatibility. Macrophages and other cells that present antigens to T cells are known as APCs (antigen-presenting cells).

For a T cell to react with a foreign antigen, that antigen must be presented to the T cell along with the MHC proteins. A special receptor on the T cell must bind with both the MHC protein and the foreign antigen fragment (see Fig. 17-2). The activated T_h then produces interleukins (ILs), which stimulate other leukocytes, such as B cells. There are many different types of interleukins, and they participate at different points in the immune response. They are produced by white cells and also by fibroblasts (cells in connective tissue that produce fibers) and by epithelial cells. Because ILs stimulate the cells active in immunity, they are used medically to boost the immune system.

Checkpoint 17-5 What is an antigen?

Checkpoint 17-6 List four types of T cells.

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B Cells and Antibodies An **antibody** (**Ab**), also known as an **immunoglobulin** (**Ig**), is a substance produced in response to an antigen. Antibodies are manufactured by **B cells** (B lymphocytes), another type of lymphocyte active in the immune system. These cells must mature in the fetal liver or in lymphoid tissue before becoming active in the blood.

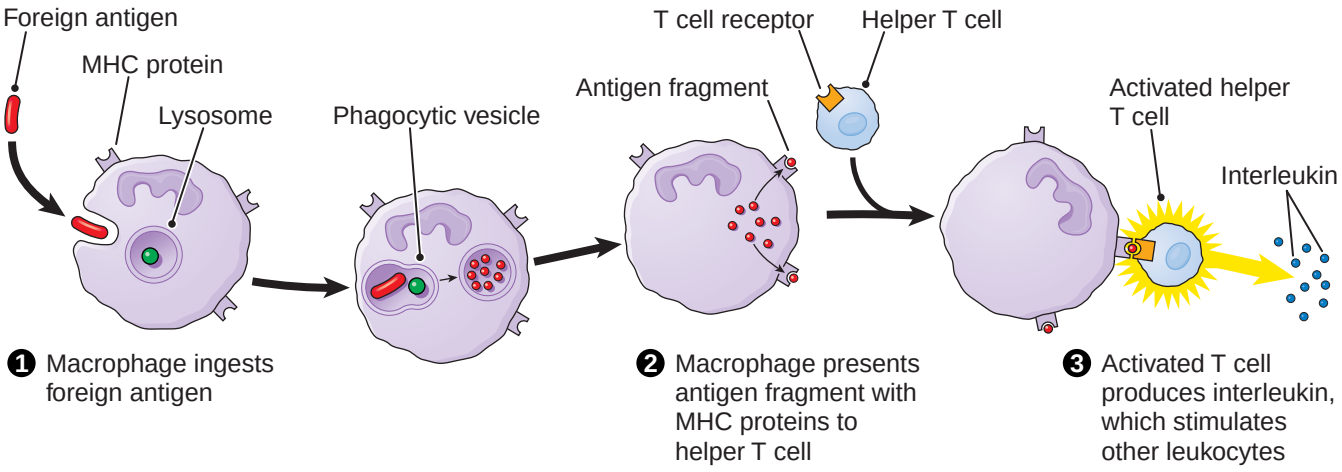

Figure 17-2 **Activation of a helper T cell by a macrophage (antigen-presenting cell).** *ZOOMING IN ✦ What is contained in the lysosome that joins the phagocytic vesicle?*

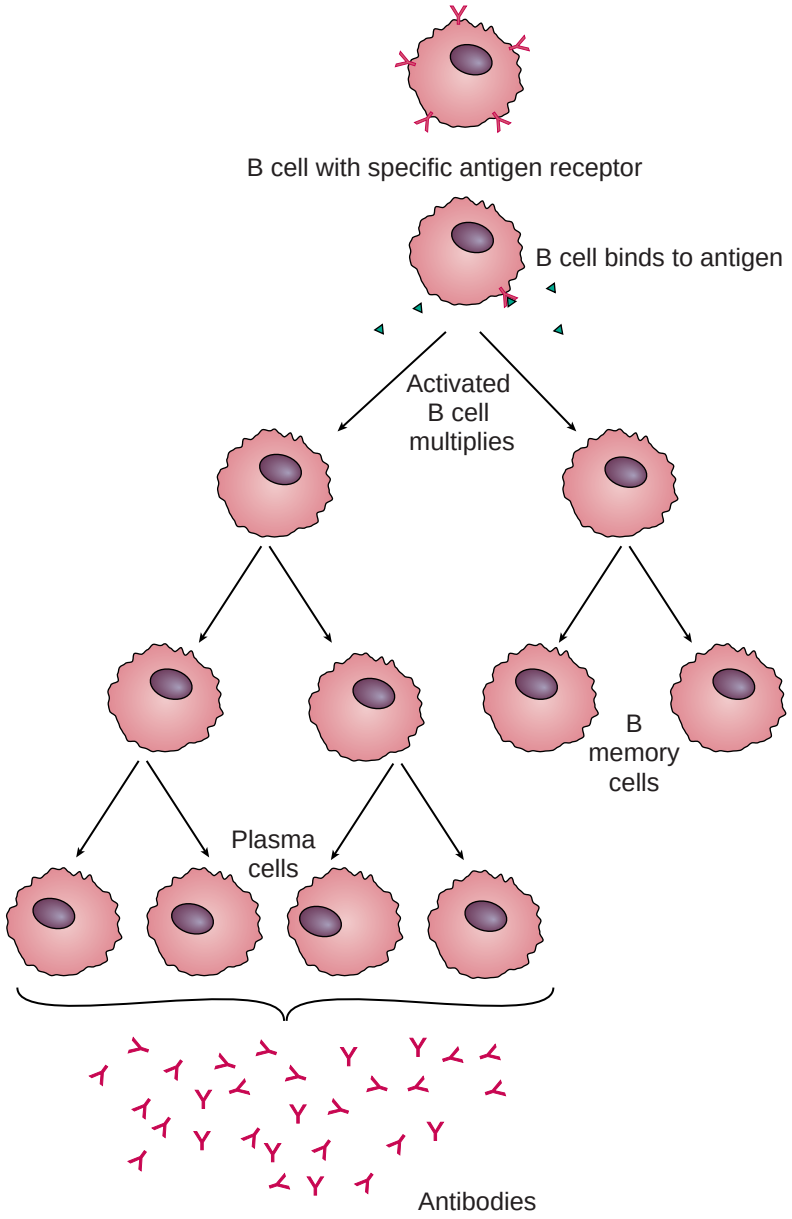

Figure 17-3 **Activation of B cells.** The B cell combines with a specific antigen. The cell divides to form plasma cells, which produce antibodies. Some of the cells develop into memory cells, which protect against reinfection. *ZOOMING IN ✦ What two types of cells develop from activated B cells?*

B cells have surface receptors that bind with a specific type of antigen (Fig. 17-3). Exposure to the antigen stimulates the cells to multiply rapidly and produce large numbers (clones) of **plasma cells**. Plasma cells produce antibodies against the original antigen and release these antibodies into the blood, providing the form of immunity described as **humoral immunity** (the term humoral refers to body fluids).

Humoral immunity generally protects against circulating antigens and bacteria that grow outside the cells (extracellular pathogens). All antibodies are contained in a portion of the blood plasma called the **gamma globulin** fraction. Box 17-1 provides further information about the different types of antibodies.

Some antibodies produced by B cells remain in the blood to give long-term immunity. In addition, some of the activated B cells do not become plasma cells but, like certain T cells, become memory cells. On repeated contact with an antigen, these cells are ready to produce antibodies immediately. Because of this "immunologic memory," one is usually immune to a childhood disease after having it.

Checkpoint 17-7 What is an antibody?

Checkpoint 17-8 What type of cells produce antibodies?

The Antigen–Antibody Reaction

The antibody that is produced in response to a specific antigen, such as a bacterial cell or a toxin, has a shape that matches some part of that antigen, much in the same way that the shape of a key matches the shape of its lock. The antibody can bind specifically to the antigen that caused its production and thereby destroy or inactivate it. Antigen–antibody interactions are illustrated and their protective effects are described in Table 17-1.

Complement The destruction of foreign cells sometimes requires the enzymatic activity of a group of nonspecific proteins in the blood, together called **complement**. Complement proteins are always present in the blood, but they must be activated by antigen–antibody complexes or by foreign cell surfaces. Complement is so named because it assists with immune reactions. Some of the actions of complement are:

- It coats foreign cells to help phagocytes recognize and engulf them.
- It destroys cells by forming complexes that punch holes in plasma membranes.
- It promotes inflammation by increasing capillary permeability.
- It attracts phagocytes to an area of inflammation.

Checkpoint 17-9 What is complement?

Box 17-1 A Closer Look

Antibodies: A Protein Army That Fights Disease

Antibodies are proteins secreted by plasma cells (activated B cells) in response to specific antigens. They are all contained in a fraction of the blood plasma known as gamma globulin. Because the plasma contains other globulins as well, antibodies have become known as immunoglobulins (Ig). Immunologic studies have shown that there are several classes of immunoglobulins that vary in molecular size and in function (see below). Studies of these antibody fractions can be helpful in making a diagnosis. For example, high levels of IgM antibodies, because they are the first to be produced in an immune response, indicate a recent infection.

CLASS	ABUNDANCE	CHARACTERISTICS AND FUNCTION
IgG	75%	Found in the blood, lymph, and intestines Enhances phagocytosis, neutralizes toxins, and activates complement Crosses the placenta and confers passive immunity from mother to fetus
IgA	15%	Found in glandular secretions such as sweat, tears, saliva, mucus, and digestive juices Provides local protection in mucous membranes against bacteria and viruses Also found in breast milk, providing passive immunity to newborn
IgM	5–10%	Found in the blood and lymph The first antibody to be secreted after infection Stimulates agglutination and activates complement
IgD	<1%	Located on the surface of B cells
IgE	<0.1%	Located on basophils Active in allergic reactions and parasitic infections

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Naturally Acquired Immunity

Immunity may be acquired naturally through contact with a specific disease organism, in which case, antibodies manufactured by the infected person's cells act against the infecting agent or its toxins. The infection that triggers the immunity may be so mild as to cause no symptoms (subclinical). Nevertheless, it stimulates the host's cells to produce an active immunity.

Each time a person is invaded by disease organisms, his or her cells manufacture antibodies that provide immunity against the infection. Such immunity may last for years, and in some cases for life. Because the host is actively involved in the production of antibodies, this type of immunity is called **active immunity**. See Box 17-2 for information on how stress affects the immune system.

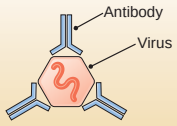
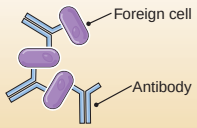
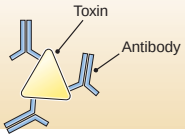
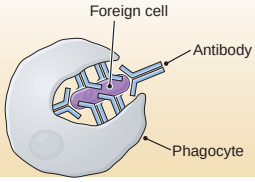
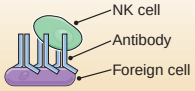
Immunity also may be acquired naturally by the passage of antibodies from a mother to her fetus through the placenta. Because these antibodies come from an outside source, this type of immunity is called **passive immunity**. The antibodies obtained in this way do not last as long as actively produced antibodies, but they do help protect the infant for about 6 months, at which time the child's own immune system begins to function. Nursing an infant can lengthen this protective period because of the presence of specific antibodies in breast milk and colostrum (the first breast secretion). These are the only known examples of naturally acquired passive immunity.

Checkpoint 17-10 What is the difference between the active and passive forms of naturally acquired immunity?

Artificially Acquired Immunity

A person who has not been exposed to repeated small doses of a particular organism has no antibodies against that organism and may be defenseless against infection. Therefore, medical personnel may use artificial measures to cause a person's immune system to manufacture antibodies. The administration of virulent pathogens obviously would be dangerous. Instead, laboratory workers treat the harmful agent to reduce its virulence before it is administered. In this way, the immune system is made to produce antibodies without causing a serious illness. This

Table 17•1 Antigen-Antibody Interactions and Their Effects

Interaction	Effects
Prevention of attachment 	A pathogen coated with antibody is prevented from attaching to a cell.
Clumping of antigen 	Antibodies can link antigens together, forming a cluster that phagocytes can ingest.
Neutralization of toxins 	Antibodies bind to toxin molecules to prevent them from damaging cells.
Help with phagocytosis 	Phagocytes can attach more easily to antigens that are coated with antibody.
Activation of complement 	When complement attaches to antibody on a cell surface, a series of reactions begins that activates complement to destroy cells.
Activation of NK cells 	NK cells respond to antibody adhering to a cell surface and attack the cell.

protective process is known as **vaccination** (vak-sin-A-shun), or **immunization,** and the solution used is called a **vaccine** (vak-SENE). Ordinarily, the administration of a vaccine is a preventive measure designed to provide protection in anticipation of invasion by a certain disease organism.

Originally, the word *vaccination* meant inoculation against smallpox. (The term even comes from the Latin word for *cow,* referring to cowpox, which is used to vaccinate against smallpox.) According to the World Health Organization, however, smallpox has now been eliminated as a result of widespread immunization programs. Mandatory vaccination has been discontinued because the chance of adverse side effects from the vaccine is thought to be greater than the probability of contracting the disease.

All vaccines carry a risk of adverse side effects and may be contraindicated in some cases. People who are immunosuppressed, for example, should not be given vaccines that contain live virus. Also pregnant women should not receive live virus vaccine because the virus could cross the placenta and harm the fetus.

Types of Vaccines Vaccines can be made with live organisms or with organisms killed by heat or chemicals. If live organisms are used, they must be nonvirulent for humans, such as the cowpox virus used for smallpox

Box 17-2 Clinical Perspectives

Too Much Stress Makes The Immune System Sick

The impact of stress on the immune system is the most wide-ranging and significant of its many effects on the body. Stressors such as trauma, infection, debilitating disease, surgery, pain, extreme environmental conditions, and emotional distress all hamper immune function. The mechanisms responsible for these changes are not yet fully understood. Scientists do know that stress causes the hypothalamus to promote the release of ACTH from the anterior pituitary. This hormone stimulates the adrenal cortex to release the hormone cortisol, which influences a person's immediate ability to overcome any challenge, even stress itself. However, the abnormally high levels of cortisol that appear during periods of intense stress can actually be harmful. Such levels can:

- inhibit histamine release from damaged tissues, thereby blocking inflammation and the arrival of phagocytic leukocytes.
- reduce phagocytosis in damaged tissues, thus preventing antigen presentation to (and activation of) both killer T cells and helper T cells.
- inhibit interleukin secretion from helper T cells, thus preventing the immune system from mounting a coordinated response to infection.

Box 12-3, Stress: Mechanisms for Coping, suggests some strategies for reducing stress.

immunization, or they must be treated in the laboratory to weaken them as human pathogens. An organism weakened for use in vaccines is described as **attenuated.** In some cases, just an antigenic component of the pathogen is used as a vaccine. Another type of vaccine is made from the toxin produced by a disease organism. The toxin is altered with heat or chemicals to reduce its harmfulness, but it can still function as an antigen to induce immunity. Such an altered toxin is called a **toxoid.**

The newest types of vaccines are produced from antigenic components of pathogens or by genetic engineering. By techniques of recombinant DNA, the genes for specific disease antigens are inserted into the genetic material of harmless organisms. The antigens produced by these organisms are extracted and purified and used for immunization. The hepatitis B vaccine is produced in this manner.

Boosters In many cases, an active immunity acquired by artificial (or even natural) means does not last a lifetime. Circulating antibodies can decline with time. To help maintain a high titer (level) of antibodies in the blood, repeated inoculations, called *booster shots,* are administered at intervals. The number of booster injections recommended varies with the disease and with an individual's environment or range of exposure. On occasion, epidemics in high schools or colleges may prompt recommendations for specific boosters. Table 17-2 lists the vaccines currently recommended in the United States for childhood immunizations. The number and timing of doses varies with the different vaccines.

Examples of Bacterial Vaccines Children are routinely immunized with vaccines against bacteria or their toxins. Because of whooping cough's seriousness in young infants, early inoculation with whooping cough, or **pertussis** (per-TUS-is), vaccine, is recommended. A new form of the vaccine containing pertussis toxoid causes fewer adverse reactions than older types that contained heat-killed organisms. This acellular (aP) vaccine usually is given in a mixture with diphtheria toxoid and tetanus toxoid. The combination, referred to as *DTaP,* may be given as early as the second month of life and should be followed by additional injections at 4, 6, and 15 months and again when the child enters day care, a school, or any other environment in which he or she might be exposed to one of these contagious diseases. Diphtheria and tetanus toxoid (Td) is given again at 11 to 12 years of age. A tetanus booster is given when there is a disease risk and the last booster was administered more than 10 years prior to exposure.

Routine inoculation against *Haemophilus influenzae* type B (Hib) has nearly eliminated the life-threatening meningitis caused by this organism among preschool children. Hib also causes pneumonia and recurrent ear infections in young children. Depending on the type used, the vaccine is given in either two doses or three doses beginning at 2 months of age.

Pneumococcal vaccine (PCV) protects against infection with pneumococcus, an organism that can cause pneumonia and meningitis. Four doses are given between the ages of 2 and 15 months.

Examples of Viral Vaccines Intensive research on viruses has resulted in the development of vaccines for an increasing number of viral diseases. The medical community has achieved spectacular results in eliminating poliomyelitis by the use of vaccines. The first of these was an inactivated polio vaccine (IVP) developed by Dr. Jonas Salk and made with killed poliovirus. A more convenient oral vaccine (OPV), made with live attenuated virus, was then developed by Dr. Albert Sabin. Both vaccine types are presently used in worldwide immunization programs, but IPV is preferred for routine childhood immunizations. A series of three doses is given between 2 and 18 months, and a fourth dose is given before entry into school.

MMR, made with live attenuated viruses, protects against measles (rubeola), mumps, and rubella (German measles). Rubella is a very mild disease, but it causes birth defects in a developing fetus (see Table 2 in Appendix 5). A first dose of MMR is given at 15 months and a second between 4 and 6 years of age.

Table 17•2 Childhood Immunizations*

VACCINE	DISEASE(S)	SCHEDULE
DTaP	Diphtheria, tetanus, pertussis (whooping cough)	2, 4, 6, and 15–18 months Booster at 4–6 years Diphtheria and tetanus toxoid (Td) at 11–12 years
Hib	*Haemophilus influenza* type b (spinal meningitis)	2 and 4 months or 2, 4, and 6 months depending on type used
PCV	Pneumococcus (pneumonia, meningitis)	2, 4, 6, and 12–15 months
MMR	Measles, mumps, rubella	15 months and 4–6 years
HBV	Hepatitis B	Birth, 1–2 months, 6–18 months
Polio vaccine (IPV)	Poliomyelitis	2 and 4 months, 6–18 months, and 4–6 years
Varicella	Chickenpox	12–18 months

**Recommended by the Advisory Committee on Immunization Practices (www.cdc.gov/nip/acip), the American Academy of Pediatrics (www.aap.org), and the American Academy of Family Physicians (www.aafp.org). Information available through the National Immunization Program website (www2a.cdc.gov/nip).*

Infants are now routinely immunized against hepatitis B, receiving the first of three shots just after birth and two more before the age of 18 months. The vaccine is also recommended for people at high risk of hepatitis B infection, including healthcare workers, people on kidney dialysis, people receiving blood clotting factors, injecting drug users, and those with multiple sexual partners. A vaccine against hepatitis A virus is recommended for travelers and others at high risk for infection.

A vaccine against chicken pox (varicella) has been available since 1995. Children who have not had the disease by 1 year of age should be vaccinated. Although chicken pox is usually a mild disease, it can cause encephalitis, and infection in a pregnant woman can cause congenital malformation of the fetus. Because varicella is the same virus that causes shingles, vaccination may prevent this late-life sequel.

A number of vaccines have been developed against influenza, which is caused by a variety of different viral strains. Laboratories produce a new vaccine each year to combat what they expect will be the most common strains in the population. The elderly, the debilitated, and children with certain risk factors, including asthma, heart disease, sickle cell disease, HIV infection, and diabetes, should be immunized yearly against influenza.

The rabies vaccine is an exception to the rule that a vaccine should be given before invasion by a disease organism. Rabies is a viral disease transmitted by the bite of wild animals such as raccoons, bats, foxes, and skunks. Mandatory vaccination of domestic animals has practically eliminated this source of rabies in some countries, including the United States, but worldwide, a variety of wild and domestic animals are host to the virus. There is no cure for rabies; it is fatal in nearly all cases. The disease develops so slowly, however, that affected people vaccinated after transmission of the organism still have time to develop an active immunity. The vaccine may be given preventively to people who work with animals.

Checkpoint 17-11 What are some bacterial diseases for which there are vaccines?

Checkpoint 17-12 What are some viral diseases for which there are vaccines?

Passive Immunization

It takes several weeks to produce a naturally acquired active immunity and even longer to produce an artificial active immunity through the administration of a vaccine. Therefore, a person who receives a large dose of virulent organisms and has no established immunity to them is in great danger. To prevent illness, the person must quickly receive counteracting antibodies from an outside source. This is accomplished through the administration of an **immune serum,** or **antiserum.** The "ready-made" serum gives short-lived but effective protection against the invaders in the form of an artificially acquired passive immunity. Immune sera are used in emergencies, that is, in situations in which there is no time to wait until an active immunity has developed.

Preparation of Antisera Immune sera often are derived from animals, mainly horses. It has been found that the horse's tissues produce large quantities of antibodies in response to the injection of organisms or their toxins. After repeated injections, the horse is bled according to careful sterile technique; because of the animal's size, it is possible to remove large quantities of blood without causing injury. The blood is allowed to clot, and the serum is removed and packaged in sterile containers.

Injecting humans with serum derived from animals is not without its problems. The foreign proteins in animal sera may cause an often serious sensitivity reaction, called **serum sickness.** To avoid this problem, human antibody in the form of gamma globulin may be used.

Checkpoint 17-13 What is an immune serum and when are immune sera used?

Examples of Antisera Some immune sera contain antibodies, known as **antitoxins,** that neutralize toxins but have no effect on the toxic organisms themselves. Certain antibodies act directly on pathogens, engulfing and destroying them or preventing their continued reproduction. Some antisera are obtained from animal sources, others from human sources. Examples of immune sera are:

- Diphtheria antitoxin, obtained from immunized horses.
- Tetanus immune globulin, effective in preventing lockjaw (tetanus), which is often a complication of neglected wounds. Because tetanus immune globulin is of human origin, it carries less risk of adverse reactions than do sera obtained from horses.
- Immune globulin (human) is given to people exposed to hepatitis A, measles, polio, or chickenpox. It is also given on a regular basis to people with congenital (present at birth) immune deficiencies.
- Hepatitis B immune globulin, used after hepatitis B exposure, is given principally to infants born to mothers who have hepatitis.
- The immune globulin $Rh_o(D)$ (trade name RhoGAM), a concentrated human antibody given to prevent an Rh-negative mother from forming Rh antibodies. It is given during pregnancy if maternal antibodies develop and after the birth of an Rh-positive infant (or even after a miscarriage of a presumably Rh-positive fetus) (see Chapter 13). It is also given when Rh transfusion incompatibilities occur.
- Anti–snake bite sera, or **antivenins** (an-te-VEN-ins) are used to combat the effects of certain poisonous snake bites.
- Botulism antitoxin, an antiserum from horses offers the best hope for botulism victims, although only if given early.

- Rabies antiserum, from humans or horses, is used with the vaccine to treat victims of rabid animal bites.

Disorders of the Immune System

Immune system disorders may result from overactivity or underactivity. Allergy and autoimmune diseases fall into the first category; hereditary, infectious, and environmental immune deficiency disease fall into the second.

Allergy

Allergy involves antigens and antibodies, and its chemical processes are much like those of immunity. Allergy—a broader term for which is **hypersensitivity**—can be defined informally as a tendency to react unfavorably to certain substances that are normally harmless to most people.

These reaction-producing substances are called **allergens** (AL-er-jens), and like most antigens, they are usually proteins. Examples of typical allergens are pollens, house dust, animal dander (*dander* is the term for the minute scales that are found on hairs and feathers), and certain food proteins. Many drugs can induce allergy, particularly aspirin, barbiturates, and antibiotics (especially penicillin).

When a susceptible person's tissues are repeatedly exposed to an allergen—for example, exposure of the nasal mucosa to pollens—those tissues become **sensitized**; that is, antibodies are produced in them. When the next exposure to the allergen occurs, there is an antigen–antibody reaction. Normally, this type of reaction takes place in the blood without harm, as in immunity. In allergy, however, the antigen–antibody reaction takes place within the cells of the sensitized tissues, with results that are disagreeable and sometimes dangerous. In the case of the nasal mucosa that has become sensitized to pollen, the allergic manifestation is **hay fever**, with symptoms much like those of the common cold.

The antigen–antibody reaction in sensitive individuals promotes the release of excessive histamine. Histamine causes dilation and leaking from capillaries as well as contraction of involuntary muscles (*e.g.*, in the bronchi). Antihistamines are drugs that counteract histamine and may be effective in treating the symptoms of certain allergies. Sometimes, it is possible to desensitize an allergic person by repeated intermittent injections of the offending allergen. Unfortunately, this form of protection does not last long.

Serum sickness is an example of an allergic manifestation that may occur in response to various sera. People who are allergic to the proteins in serum from a horse or some other animal show such symptoms as fever, vomiting, joint pain, enlargement of the regional lymph nodes, and **urticaria** (ur-tih-KA-re-ah), also called hives. This type of allergic reaction can be severe but is rarely fatal.

Anaphylaxis

Anaphylaxis (an-ah-fih-LAK-sis) is a severe, life-threatening allergic response in a sensitized individual. (The term actually means excess "guarding," in this case, immune protection, from the Greek word *phylaxis*.) Any allergen can result in an anaphylactic response, but common causes are drugs, insect venom, and foods. Symptoms appear within seconds to minutes after contact and include breathing problems, swelling of the throat and tongue, urticaria, edema, and decreased blood pressure with cardiovascular shock. Anaphylaxis is treated with injectable epinephrine, antihistamine, administration of oxygen, and plasma expanders to increase blood volume. People subject to severe allergic reactions must avoid contact with known allergens. They should be sensitivity tested before administration of a new drug and should also carry injectable epinephrine and wear a medical bracelet identifying their allergy.

Autoimmunity

The term **autoimmunity** refers to an abnormal reactivity to one's own tissues. In autoimmunity, the immune system reacts to the body's own antigens, described as "self," as if they were foreign antigens, or "nonself." Normally, the immune system learns before birth to ignore (tolerate) the body's own tissues by eliminating or inactivating those lymphocytes that will attack them. Some factors that might result in autoimmunity include:

- A change in "self" proteins, as a result of disease, for example.
- Loss of immune system control, as through loss of regulatory T cell activity, for example.
- Cross-reaction of antibodies with "self" antigens. This reaction occurs in rheumatic fever, for example, when antibodies to streptococci damage the valves of the heart.

Autoimmunity is involved in a long list of diseases, including rheumatoid arthritis, multiple sclerosis, lupus erythematosus, psoriasis, inflammatory bowel diseases, Graves disease, glomerulonephritis, and Type I diabetes. All of these diseases probably result to varying degrees from the interaction of individual genetic makeup with environmental factors, including infections. Autoimmune diseases are three times more prevalent in women than in men, perhaps related to hormonal differences.

Autoimmunity is treated with drugs that suppress the immune system and with antibodies to lymphocytes. Pure antibodies, such as these, are prepared in the laboratory and are known as *monoclonal antibodies*. A newer approach uses chemotherapy to destroy immune cells followed by their replacement with healthy stem cells from bone marrow.

Immune Deficiency Diseases

An immune deficiency is some type of failure of the immune system. This failure may involve any part of the

system, such as T cells, B cells, or the thymus gland, and it may vary in severity. Such disorders may be congenital (present at birth) or may be acquired as a result of malnutrition, infection, or treatment with x-rays or certain drugs.

The disease **AIDS** (acquired immunodeficiency syndrome) is a devastating example of an infection that attacks the immune system. It is caused by **HIV** (human immunodeficiency virus), which destroys the specific helper T cells that have a receptor (CD_4) for the virus. Its first appearance in the United States in the early 1980s was among homosexual men and injecting drug users. It now occurs worldwide in heterosexual populations of all ages. AIDS is considered to be a pandemic, especially in sub-Saharan Africa and in some parts of Asia. It is spread through unprotected sexual activity and the use of contaminated injection needles. It can also be transmitted from a mother to her fetus. The testing of donated blood has virtually eliminated the spread of AIDS through blood transfusions.

Diagnosis of HIV infection is based on the presence of HIV antibodies, the virus, or viral components in the blood. The disease is monitored with CD4+ T cell counts and measurement of HIV RNA in the blood. (See Box 17-3 for information on the type of virus that causes AIDS.)

Patients with AIDS succumb easily to disease, including rare diseases such as parasitic (*Pneumocystis*) pneumonia and an especially malignant skin cancer, **Kaposi** (*KAP-o*-se) **sarcoma**.

Drugs active against HIV stop viral growth at different stages of replication. These drugs, often used in combination, can slow the progress of AIDS, but so far, do not cure it. An obstacle to the development of a vaccine against HIV is the tremendous variability of the virus.

Multiple Myeloma

Multiple myeloma is a cancer of the blood-forming cells in bone marrow, mainly the plasma cells that produce antibodies. These cells produce an excess of a particular antibody, but the antibody is not effective. The disease causes loss of resistance to infection, anemia, bone pain, and weakening of the bones, owing to production of a factor that accelerates loss of bone tissue. High blood levels of calcium and proteins secreted by the plasma cells often lead to kidney failure. Multiple myeloma is treated with chemotherapy. A new approach is high-dose chemotherapy combined with bone marrow transplants. Blood-forming stem cells in the bone marrow replace cells killed by the chemotherapy. This treatment is expensive, and stem cell transplants in themselves are dangerous, but this combined treatment has improved survival rates.

Checkpoint 17-14 What are some disorders of the immune system?

The Immune System and Cancer

Cancer cells differ slightly from normal body cells and therefore the immune system should recognize them as "nonself." The fact that people with AIDS and other immune deficiencies develop cancer at a higher rate than normal suggests that this is true. Cancer cells probably form continuously in the body but normally are destroyed by NK cells and the immune system, a process called **immune surveillance** (sur-VAY-lans). As a person ages, cell-mediated immunity declines and cancer is more likely to develop.

Some efforts are being made to treat cancer by stimulating the patient's immune system, a practice called **immunotherapy.** In one approach, T cells have been removed from the patient, activated with interleukin, and then reinjected. This method has given some positive results, especially in treatment of melanoma, a highly malignant form of skin cancer. In the future, a vaccine against cancer may become a reality. Vaccines that target specific proteins

Box 17-3 A Closer Look

Retroviruses: Working Backward to Cause Disease

HIV, the virus that causes AIDS, belongs to a group of viruses that is unique in its method of reproduction. The group's name, **retroviruses**, which means "backward viruses," refers to the way in which the viruses reverse the typical order of genetic action. Retroviruses have RNA instead of DNA as their genetic material. Unlike other RNA viruses, however, they transcribe (copy) the RNA into DNA to reproduce inside the host. To accomplish this unusual feat, the virus has an enzyme called **reverse transcriptase**.

The DNA formed using reverse transcriptase enters the nucleus of the host cell and becomes part of the genetic material. There, it may direct the formation of more viruses or lie dormant and undetected for long periods, even years, before being triggered to multiply and cause disease. Some retroviruses can transform the DNA of the host cell and produce cancer. These viruses have been associated with leukemia in both humans and animals and with other types of tumors in animals.

Some drugs that are used against retroviruses like HIV act by inhibiting reverse transcriptase and interrupting the replication cycle of the virus. The drug AZT is one such example. While drugs like AZT can slow the rate of HIV replication, they do not cure or prevent HIV infection or AIDS.

produced by cancer cells have already been tested in a few forms of cancer.

Transplantation and the Rejection Syndrome

Transplantation is the grafting to a recipient of an organ or tissue from an animal or other human to replace an injured or incompetent part of the body. Much experimental work preceded transplantation surgery in humans. Tissues that have been transplanted include: bone marrow, lymphoid tissue, skin, corneas, parathyroid glands, ovaries, kidneys, lungs, heart, and liver.

The natural tendency of every organism to destroy foreign substances, including tissues from another person or any other animal, has been the most formidable obstacle to complete success. This normal antigen–antibody reaction has, in this case, been called the **rejection syndrome.**

In all cases of transplantation or grafting, the tissues of the donor, the person donating the part, should be typed in much the same way that blood is typed when a transfusion is given. Blood type antigens are much fewer in number than tissue antigens; thus, the process of obtaining matching blood is much less involved than is the process of obtaining matching tissues. Laboratories do tissue typing in an effort to obtain donors whose tissues contain relatively few antigens that might cause transplant rejection in a recipient, the person receiving the part. (One exception to the need for careful cross-matching is corneal transplantation in the eye. Corneal proteins don't enter the circulation to stimulate an immune response.)

Because it is impossible to match all of a donor's antigens with those of the recipient, physicians give the recipient drugs that will suppress an immune response to the transplanted tissue. These include drugs that suppress synthesis of nucleic acids, drugs or antibodies that inhibit lymphocytes, and adrenal glucocorticoid hormones, such as cortisol, that suppress immunity. These drugs cause a variety of adverse side effects, such as hypertension, kidney damage, and osteoporosis (glucocorticoids). Most importantly, they reduce a patient's ability to fight infection. Because T cells cause much of the reaction against the foreign material in transplants, scientists are trying to use drugs and antibodies to suppress the action of these lymphocytes without damaging the B cells. B cells produce circulating antibodies and are most important in preventing infections. Success with transplantation will increase when methods are found to selectively suppress the immune attack on transplants without destroying the recipient's ability to combat disease.

Checkpoint 17-15 What is the greatest obstacle to tissue transplantation from one individual to another?

17

Word Anatomy

Medical terms are built from standardized word parts (prefixes, roots, and suffixes). Learning the meanings of these parts can help you remember words and interpret unfamiliar terms.

WORD PART	MEANING	EXAMPLE
Factors in the Occurrence of Infection		
tox	poison	A *toxin* is a substance that is poisonous.
Disorders of the Immune System		
erg	work	In cases of *allergy*, the immune system overworks.
ana-	excessive	*Anaphylaxis* is a life-threatening condition that results from an excessive immune reaction.
myel/o	marrow	Multiple *myeloma* is a cancer (-oma) of blood-forming cells in bone marrow.

Summary

I. Factors in the occurrence of infection

A. Tissue preference of pathogen
B. Portal of entry of pathogen
C. Virulence of pathogen
   1. Invasive power
   2. Production of toxins (poisons)
D. Dose (number) of pathogens
E. Predisposition of host

II. Nonspecific defenses

A. Chemical and mechanical barriers
   1. Skin
   2. Mucous membranes
   3. Body secretions
   4. Reflexes—coughing, sneezing, vomiting, diarrhea
B. Phagocytosis—mainly by neutrophils and macrophages
C. Natural killer (NK) cells—attack tumor cells and virus-infected cells

D. Inflammation
E. Fever
F. Interferon
   1. Substances released from virus-infected cells
   2. Prevent virus production in nearby cells
   3. Stimulate the immune response nonspecifically

III. Immunity—specific defense against disease

A. Inborn immunity
   1. Inherited
   2. Types: species, individual
B. Acquired immunity—develops after birth
   1. Antigens—stimulate immune response by lymphocytes
   2. T cells (T lymphocytes)
      a. Processed in thymus
      b. Types: cytotoxic, helper, regulatory, memory
      c. Involved in cell-mediated immunity
   3. Macrophages
      a. Derived from monocytes
      b. Present antigen to T cells in combination with MHC ("self") proteins
      c. Stimulate the release of interleukins (IL)
   4. B cells (B lymphocytes)
      a. Mature in lymphoid tissue
      b. Develop into plasma cells
         (1) Produce circulating antibodies
         (2) Antibodies counteract antigens
      c. Also develop into memory cells
      d. Involved in humoral immunity
C. The antigen–antibody reaction
   1. Shape of antibody matches shape of antigen
   2. Results
      a. Prevention of attachment
      b. Clumping of antigen
      c. Neutralization of toxins
      d. Help in phagocytosis
      e. Activation of complement
      f. Activation of NK cells
   3. Complement
      a. Group of proteins in blood
      b. Actions
         (1) Coats foreign cells
         (2) Damages plasma membranes
         (3) Promotes inflammation
         (4) Attracts phagocytes
D. Naturally acquired immunity
   1. Active—acquired through contact with the disease
   2. Passive—acquired from antibodies obtained through placenta and mother's milk
E. Artificially acquired immunity
   1. Active—immunization with vaccines
      a. Types: live (attenuated), killed, toxoid, recombinant DNA
      b. Boosters—keep antibody titers high
      c. Examples of bacterial vaccines
      d. Examples of viral vaccines
   2. Passive—administration of immune serum (antiserum)

IV. Disorders of the immune system

A. Allergy—hypersensitivity to normally harmless substances (allergens)
   1. Anaphylaxis—severe, life-threatening allergic response
B. Autoimmunity—abnormal response to body's own tissues
C. Immune deficiency disease—failure in the immune system
   1. Congenital (present at birth)
   2. Acquired (*e.g.*, AIDS)
D. Multiple myeloma—cancer of blood-forming cells in bone marrow

V. The immune system and cancer

A. Immune surveillance—ability of immune system to find and destroy abnormal cells (*e.g.*, cancer cells)
B. Immunotherapy—stimulating the immune system to treat cancer

VII. Transplantation

A. Grafting of an organ or tissue to replace injured or incompetent part
B. Requirements
   1. Tissue typing
   2. Suppression of immune system

Questions for Study and Review

Building Understanding

Fill in the blanks

1. The power of the organism to overcome its host's defenses is called _____.
2. Heat, redness, swelling, and pain are classic signs of _____.
3. Any foreign substance that enters the body and induces an immune response is called a(n)_____.
4. All antibodies are contained in a portion of the blood plasma termed the _____.
5. Substances capable of inducing a hypersensitivity reaction are called _____.

Matching

Match each numbered item with the most closely related lettered item.

___ 6. Destroy foreign cells directly.
___ 7. Release interleukins, which stimulate other cells to join the immune response.
___ 8. Suppress the immune response in order to prevent overactivity.
___ 9. Remember an antigen and start a rapid response if the antigen is contacted again.
___ 10. Manufacture antibodies when activated by antigens

a. regulatory T cells
b. memory T cells
c. cytotoxic T cells
d. B cells
e. helper T cells

Multiple choice

___ 11. All of the following are part of the first line of defense against invaders *except*
a. tears
b. saliva
c. neutrophils
d. skin

___ 12. Damaged cells release a vasodilator substance called
a. interleukin
b. interferon
c. histamine
d. complement

___ 13. Which of the following cells mature in the thymus?
a. T cell
b. B cell
c. plasma cell
d. natural killer cell

___ 14. Sensitivity to animal-derived immune serum may lead to a serious condition called
a. serum sickness
b. hay fever
c. Kaposi sarcoma
d. rejection syndrome

___ 15. An abnormal reactivity to one's own tissues is called
a. allergy
b. autoimmunity
c. anaphylaxis
d. rejection

Understanding Concepts

16. Describe four factors that influence the occurrence of infection.
17. What causes the symptoms of inflammation?
18. Differentiate between the terms in each of the following pairs:
a. interferon and interleukin
b. antibody and complement
c. inborn immunity and acquired immunity
d. cell-mediated immunity and humoral immunity
e. active immunization and passive immunization
f. attenuated vaccine and toxoid
19. Describe the events that must occur for a T cell to react with a foreign antigen. Once activated, what do the T cells do?
20. What role do antibodies play in immunity? How are they produced? How do they work?
21. Compare and contrast the four types of acquired immunity.
22. What is an immune serum? Give examples. Define antitoxin.
23. Define allergy. How is the process of allergy like that of immunity, and how do they differ?
24. What is meant by rejection syndrome, and what is being done to offset this syndrome?

Conceptual Thinking

25. While in the garden with his father Alek, a 4-year old Caucasian boy was, in his own words, "kicked by a bee." Shortly afterward, Alek developed hives near the affected area, which he began to scratch. About ten minutes later, Alek's father noticed that his son was wheezing. What is happening to Alek? Describe the inflammatory events that are occurring in his body. How should Alek's father respond?
26. Why is HIV's attack on helper T cells so devastating to the entire immune system?