Immune System: is the defense system that has evolved to protect animals from invading pathogenic microorganisms and cancer.

It is able to generate an enormous variety of cells and molecules capable of specifically recognizing and eliminating an apparently limitless variety of foreign invaders.

These cells and molecules act together in a dynamic work.

Functionally, an immune response can be divided into two related activities, recognition and response.

1. Immune recognition is remarkable for its specificity, of which it is able to discriminate between foreign molecules and the body's own cells and proteins.

2. Immune response, as a foreign organism has been recognized, the immune system recruits a variety of cells and molecules to mount an appropriate response, called an **effector response,** to eliminate or neutralize the organism. In this way the system is able to convert the initial recognition event into a variety of effector responses, each uniquely suited for eliminating a particular type of pathogen.

Later exposure to the same foreign organism induces a **memory response,** characterized by a more rapid and heightened immune reaction that serves to eliminate the pathogen and prevent disease.

The Immune System Includes Innate and Adaptive Components

Innate immunity: less specific component**,**provides the first line of defense against infection.

Most components of innate immunity are present before the onset of infection and constitute a set of disease-resistance mechanisms that are not specific to a particular pathogen but include cellular and molecular components that recognize classes of molecules peculiar to frequently encountered pathogens.

Phagocytic cells, such as macrophages and neutrophils, barriers such as skin, and a variety of antimicrobial compounds synthesized by the host, all play important roles in innate immunity.

Adaptive immunity: is the specific component of immune system and it does not come into play until there is an antigenic challenge to the organism.

It responds to the challenge with a high degree of specificity as well as the remarkable property of "**memory**."

Typically, there is an adaptive immune response against an antigen within five or six days after the initial exposure to that antigen. Exposure to the same antigen in the future results in a memory response.

The immune response to the second challenge occurs more quickly than the first, is stronger, and is often more effective in neutralizing and clearing the pathogen.

The major agents of adaptive immunity are lymphocytes and the antibodies as well as other molecules they produce.

Innate immunity includes:

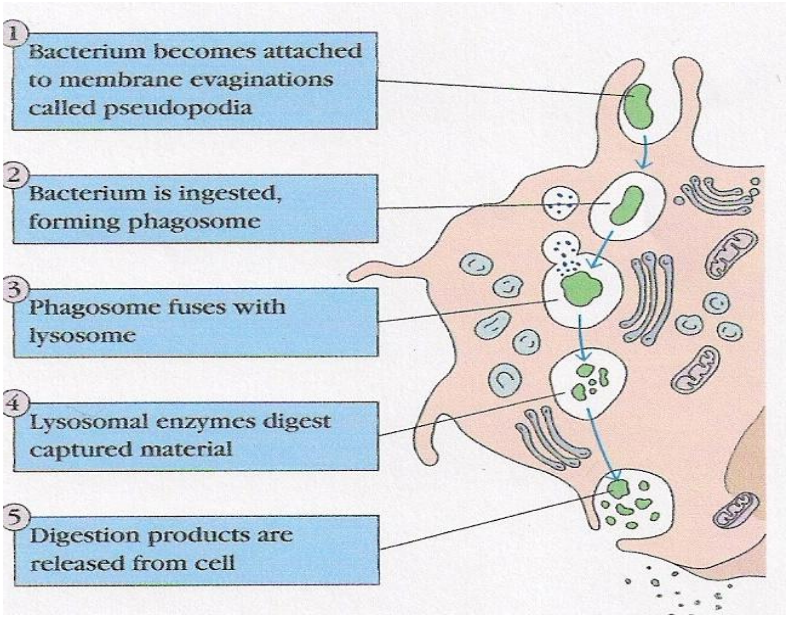
A. Physiologic Barriers to Infection Include General Conditions and Specific Molecules

1. **Temperature:** many species are not susceptible to certain diseases simply because their normal body temperature inhibits growth of the pathogens. Chickens, for example, have innate immunity to anthrax because their high body temperature inhibits the growth of the bacteria.
2. **pH as Gastric acidity:** very few ingested microorganisms can survive the low pH of the stomach contents. One reason newborns are susceptible to some diseases that do not afflict adults is that their stomach contents are less acid than those of adults.
3. **Soluble factors**, such as ***Lysozyme,** a hydrolytic enzyme found in mucous secretions and in tears, is able to cleave the peptidoglycan layer of the bacterial cell wall.

   ***Interferon,**comprises a group of proteins produced by virus-infected cells & have the ability to bind to nearby cells and induce a generalized antiviral state.

   ***Complement,** is a group of serum proteins that circulate in an inactive state.
4. **Pattern recognition** are the property of many molecules that involved in innate immunity with the ability to recognize a given class of molecules. Molecules with pattern recognition ability may be soluble, like lysozyme and the complement components, or they may be cell-associated receptors, which are called **toll-like receptors (TLRs),** foreg; TLR2 recognizes the lipopolysaccharide (LPS) found on Gram-negative bacteria.

B. Ingestion of extracellular particulate material by phagocytosis.
Phagocytosis is one type of **endocytosis,** the general term for the uptake (by a cell) of material from its environment. In phagocytosis, a cell's plasma membrane expands around the particulate material, to form large vesicles called **phagosomes**.



Comparison between innate and adaptive immunity

	Innate	Adaptive
Response time	Hours	Days
Specificity	Limited and fixed	Highly diverse, improves during the course of immune response
Response to repeat infection	Identical to primary response	Much more rapid than primary response

Inflammatory response

Inflammatory response has three major events:

1. Vasodilation, an increase in the diameter of blood vessels of nearby capillaries. The engorged capillaries are responsible for tissue redness (erythema) and an increase in tissue temperature.
2. An increase in capillary permeability facilitates an influx of fluid and cells from the engorged capillaries into the tissue. Accumulation of exudate contributes to tissue swelling **(edema).**
3. Influx of phagocytes from the capillaries into the tissues is facilitated by the increased permeability of the capillaries. The emigration of phagocytes is a multistep process that includes adherence of the cells to the endothelial wall of the blood vessels **(margination),** followed by their emigration between the capillary endothelial cells into the tissue **(diapedesis or extravasation),** and, finally, their migration through the tissue to the site of the invasion **(chemotaxis).**

The events in the inflammatory response are initiated by a complex series of events involving a variety of chemical mediators derived from invading microorganisms, some are released from damaged cells in response to tissue injury and some are products of various white blood cells participating in the inflammatory response.

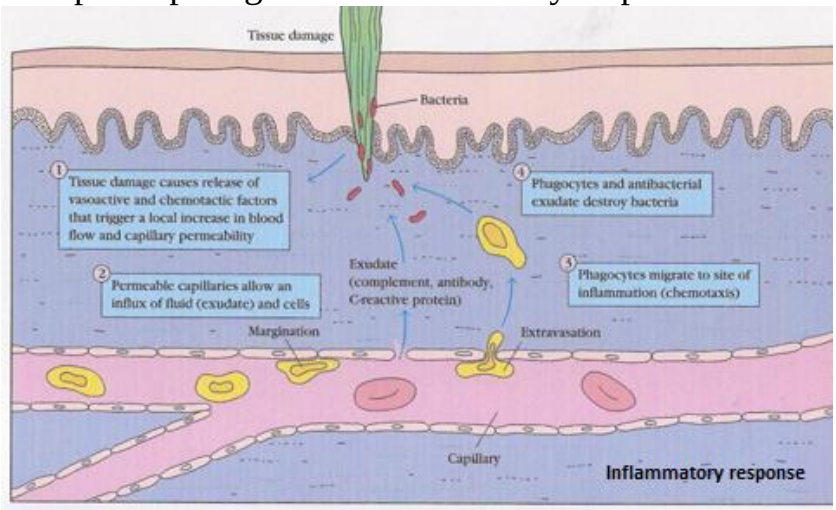


FIGURE 1-4 Major events in the inflammatory response. A bacterial infection causes tissue damage with release of various vasoactive and chemotactic factors. These factors induce increased blood flow to the area, increased capillary permeability, and an influx of white blood cells, including phagocytes and lymphocytes, from the blood into the tissues. The serum proteins contained in the exudate have antibacterial properties, and the phagocytes begin to engulf the bacteria, as illustrated in Figure 1-3.

Adaptive Immunity: It is capable of recognizing and selectively eliminating specific foreign microorganisms and molecules (i.e., foreign antigens). It displays four characteristic attributes:

- Antigenic specificity.
- Diversity.
- Immunologic memory.
- Self/nonself recognition.

An effective immune response involves two major groups of cells: *T lymphocytes and antigen-presenting cells.* lymphocytes mediate the defining immunologic attributes of specificity, diversity, memory, and self/nonself recognition.

The two major populations of lymphocytes, **B lymphocytes (B cells) and T lymphocytes (T cells).**

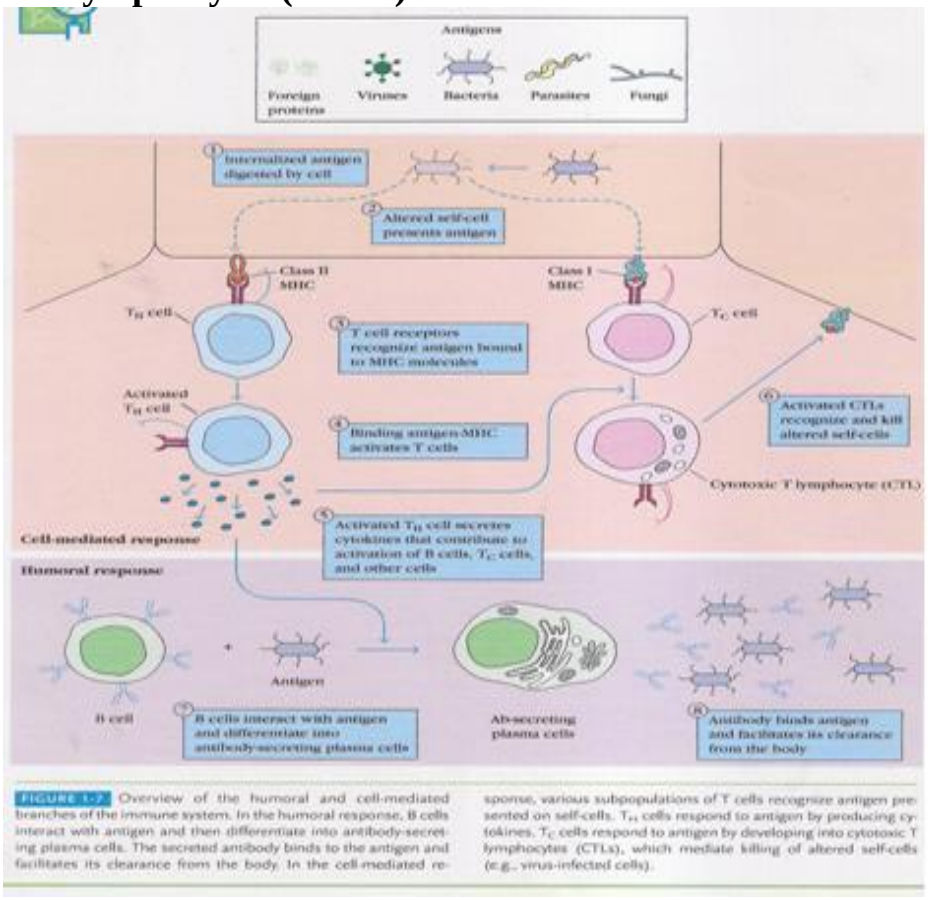


FIGURE 1-7 Overview of the humoral and cell-mediated branches of the immune system. In the humoral response, B cells interact with antigen and then differentiate into antibody-secreting plasma cells. The secreted antibody binds to the antigen and facilitates its clearance from the body. In the cell-mediated response, various subpopulations of T cells recognize antigen presented on self-cells. T_H cells respond to antigen by producing cytokines. T_C cells respond to antigen by developing into cytotoxic T lymphocytes (CTLs), which mediate killing of altered self-cells (e.g., virus-infected cells).

B lymphocytes:

It mature within the bone marrow; when they leave it, each expresses a unique antigen-binding receptor on its membrane. This antigen-binding or B-cell receptor is a membrane-bound **antibody molecule.** When a naive B cell (one that has not previously encountered antigen) first encounters the Ag that matches its membrane bound Ab, such a binding

causes the cell to divide rapidly; its progeny differentiate into **memory B cells and effector B cells called plasma cells.**

Memory B cells have a longer life span than naive cells, and they express the same membrane-bound Ab as their parent B cell.

Plasma cells produce the Ab in a form that can be secreted and have little or no membrane-bound Ab. Although plasma cells live for only a few days, they secrete enormous amounts of Ab during this time.

T lymphocytes:

1. It also arise in the bone marrow. Then it migrate to the thymus gland to mature. During its maturation within the thymus, the T cell comes to express a unique Ag-binding molecule, called the **T-cell receptor,** on its membrane.

2. T-cell receptors can recognize only Ag that is bound to cell-membrane proteins called **major histocompatibility complex (MHC) molecules.**

3. There are two well-defined subpopulations of T cells: **T helper (TH) and T cytotoxic (TC) cells.** T helper and T cytotoxic cells can be distinguished from one another by the presence of either **CD4 or CD8 membrane glycoproteins on their surfaces.**

4. After T-cell activation, it becomes an effector cell that secretes various growth factors known collectively as **cytokines.** The secreted cytokines play an important role in activating B cells, TC cells, macrophages, and various other cells that participate in the immune response.

5. Differences in the pattern of cytokines produced by activated TH cells result in different types of immune response.

6. Under the influence of TH-derived cytokines, a TC cell that recognizes an Ag–MHC class I molecule complex proliferates and differentiates into an effector cell called a **cytotoxic T lymphocyte (CTL).** In contrast to the TC cell, the CTL generally does not secrete many cytokines and instead exhibits cell-killing or cytotoxic activity.

Ag-presenting cells(APC):

These specialized cells, which include macrophages, B lymphocytes, and dendritic cells, are distinguished by <u>two properties</u>:

(1) they express class II MHC molecules on their membranes.
(2) they are able to deliver a co-stimulatory signal that is necessary for TH-cell activation.

APC first internalize Ag, either by phagocytosis or by endocytosis, and then display a part of that Ag on their membrane bound to a class II MHC molecule. The TH cell recognizes and interacts with the Ag–class II MHC molecule complex on the membrane of the APC. An additional co-stimulatory signal is then produced by the APC, leading to activation of the TH cell.

Antigens, which are generally very large and complex, are not recognized in their entirety by lymphocytes. Instead, both B and T lymphocytes recognize discrete sites on the Ag called **antigenic determinants, or epitopes. Epitopes** are the immunologically active regions on a complex Ag, the regions that actually bind to B-cell or T-cell receptors.

The humoral branch (B cells) recognizes an enormous variety of epitopes: those displayed on the surfaces of bacteria or viral particles, as well as those displayed on soluble proteins, glycoproteins, polysaccharides, or lipopolysaccharides that have been released from invading pathogens.

The cell-mediated branch (T cells) recognizes protein epitopes displayed together with MHC molecules on self-cells.

Thus, **four** related but distinct cell-membrane molecules are responsible for Ag recognition by the immune system:

1. Membrane-bound Ab on B cells.
2. T-cell receptors.
3. Class I MHC molecules.
4. Class II MHC molecules.

The role of Ag becomes critical when it interacts with and activates mature, antigenically committed T and B lymphocytes, bringing about expansion of the population of cells with a given antigenic specificity. In this process of **clonal selection,** an antigen binds to a particular T or B cell and stimulates it to divide repeatedly into a clone of cells with the same antigenic specificity as the original parent cell.

Immunologic memory also is a consequence of clonal selection. During clonal selection, the number of lymphocytes specific for a given Ag is greatly amplified. Moreover, many of these lymphocytes, referred to as memory cells, appear to have a longer life span than the naive lymphocytes from which they arise. The initial encounter of a naive immunocompetent lymphocyte with an Ag induces a **primary**

response; a later contact of the host with Ag will induce a more rapid and heightened **secondary response.**

The amplified population of memory cells accounts for the rapidity and intensity that distinguishes a secondary response from the primary response.