

1. A Snapshot of the Immune System

The Immune System Recognizes and Eliminates Pathogens

- Immunology may be described as the summation of all those physiologic processes that endow the host with the capacity to recognize materials as foreign to itself and to neutralize, eliminate, or metabolize them with or without injury to its own tissue(s).
- This ability to differentiate “self” from “nonself” constitutes the basic hallmark of the immune response and the basis for an understanding of clinical immunology in health and disease.
- For ease of discussion, the possible outcome of an encounter of the host’s immune response with a foreign substance is shown schematically in **Figure 1**.
- If the foreign substance cannot be blocked by natural barriers such as skin and mucous secretions, the substance comes into contact with the immune system (**Figure 1**).

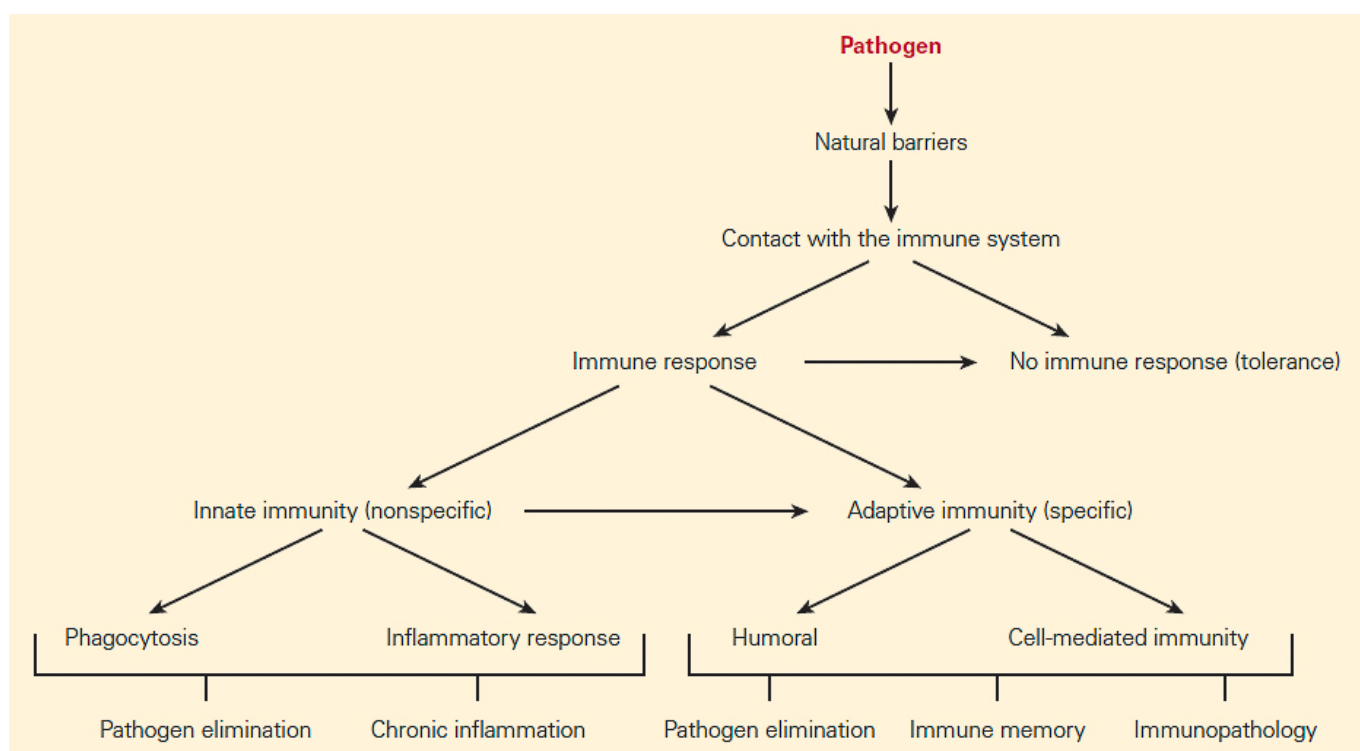


Figure 1. Possible outcomes of an encounter of the host with a foreign configuration. [Reproduced with permission from Bellanti, JA (Ed). Immunology IV: Clinical Applications in Health and Disease. I Care Press, Bethesda, MD, 2012].

- This encounter with a foreign substance can either lead to an immune response or to no response, a condition referred to as immune tolerance.

- The mechanisms permitting recognition of foreign structures leading to an immune response can be broken down into two general categories:
 - Innate immunity
 - Adaptive immunity
- Innate immunity is a set of fixed responses activated by receptors that are encoded by genes in the host's germ line.
- These receptors recognize molecular patterns shared by many foreign substances that are not present in the mammalian host.
- Adaptive immunity is a set of responses to unique foreign structures (antigens or immunogens).
- Antigen receptors are encoded by relatively few gene elements that are somatically rearranged to result in the assembly of antigen-binding molecules with exquisite specificity for individual immunogens.
- These antigen-binding structures consist of both cell receptors located on specialized immune lymphoid cells (B and T lymphocytes) as well as extracellular secreted products known as antibodies (**Figure 2**).

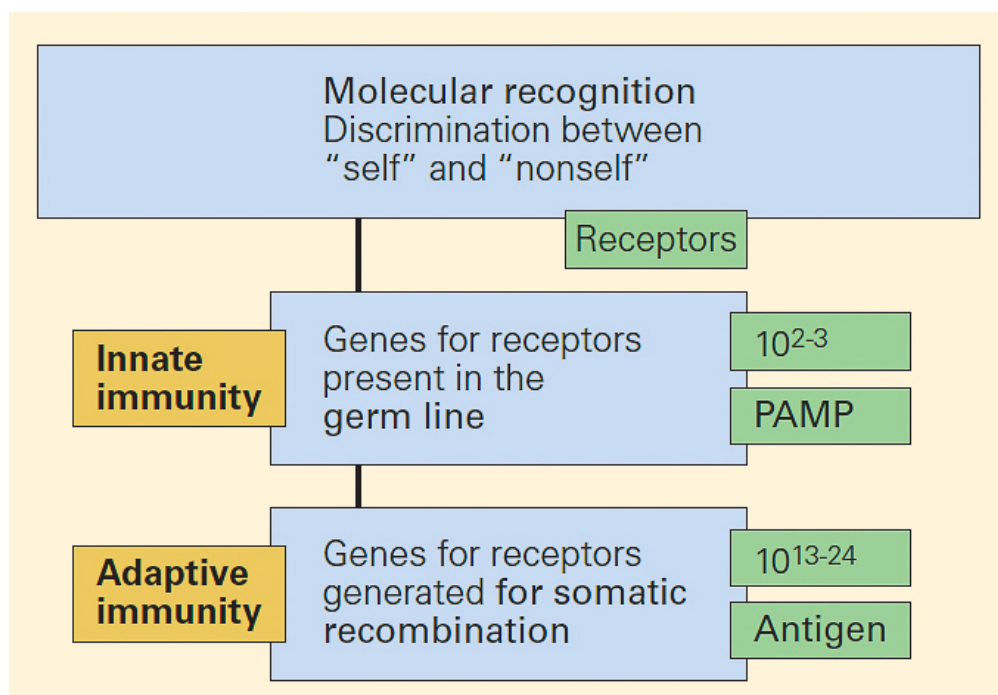


Figure 2. Characteristics of the immune response. [Reproduced with permission from Bellanti, JA (Ed). Immunology IV: Clinical Applications in Health and Disease. I Care Press, Bethesda, MD, 2012].

Anatomic Organization of the Immune System

- In order to carry out the functions of immunity, an ubiquitous system of cells and cell products has appeared within the vertebrates containing elements of both the innate and adaptive immune systems.
- For ease of discussion, this system can be divided into external and internal immune systems.
- Foreign substances that enter the body through the natural portals of entry, i.e., skin, respiratory, gastrointestinal, or genitourinary tracts, encounter components of the external immune system found in collections of lymphoid elements found at these sites.
- Since most of these organ systems are lined by mucosa, this system is referred to as the mucosa-associated lymphoid tissues (MALT).
- Foreign substances that penetrate these mucosal and skin-site barriers enter the body through the blood or lymphatics and encounter components of the internal immune system found in the lymph nodes, thymus, and spleen.

Mechanical Barriers and External Secretions

- Before the activation of the innate and adaptive immune systems takes place, there are a number of natural barriers consisting of anatomic structures and physiologic mechanisms that limit the access and progression of a foreign invader.
- The initial entry of an infectious agent or its secreted products first encounters the mechanical barriers provided by the skin, the largest external protective outer covering of the body, and the mucous membranes, which line all body passages that communicate with the external environment.
- The external secretions of the skin and mucous membranes contain a large number of substances that are detrimental to the growth of microorganisms (Table 1). These include a wide variety of metabolites, such as acids, peptides, and proteins.

Table 1: Soluble factors in secretions and sweat

Factors	Locations	Functions
Acidic pH	Skin, stomach, vagina	Inhibit bacterial growth
Fatty acids	Sweat	Inhibit bacterial growth
Mucins and agglutinins	Secretions	Aggregate bacteria
Peroxidases	Secretions	Catalyze oxidation of lipid membranes of bacteria

Factors	Locations	Functions
Protease inhibitors	Secretions	Inhibit bacterial function by inhibiting protease activity
Lysozymes	Sweat and secretions	Destroy bacteria by hydrolyzing the polysaccharide component of the cell wall.
Lactoferrin	Secretions	Inhibit bacterial growth by binding iron
Histidine-rich proteins (histatins)	Saliva	Exert antifungal properties by disrupting mitochondrial function
Cationic proteins	Sweat and secretions	Exert antibacterial activity by binding to lipid cellular membranes
Defensins and other antibacterial peptides	Secretions	Secreted by leukocytes and active against bacteria, fungi, and enveloped viruses

Innate Immunity Responds Quickly to Conserved Pathogen Structure

- The first set of responses to foreign substances are called innate immune responses because they are present without the requirement for specific induction and are present upon initial and subsequent encounters with a foreign substance.
- The innate immune responses are primitive, stereotyped, and lack the form of memory associated with adaptive immunity or the ability to respond in an enhanced manner upon subsequent encounters with the same foreign substance.
- The innate immune system recognizes certain structures on a foreign substance—referred to as pathogen-associated molecular patterns (PAMPs) that are mediated utilizing receptors called pattern recognition receptors (PRRs) located on the surfaces of a variety of cells of the innate immune system
- Macrophages and dendritic cells are examples of cells bearing these receptors.
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- **phagocytosis:** the ability of certain cells to ingest foreign substances;
- **inflammation:** the body's response to injury;
- **cytotoxicity:** the elimination of infected or transformed cells via apoptosis, a cellular process involving a genetically controlled series of events leading to noninflammatory programmed cell death.

Adaptive Immunity Is More Specific and Generates Immune Memory

- The adaptive immune system includes a complex set of genetically controlled, interdependent, and interactive responses, and is also referred to as acquired (specific) immunity.
- In contrast to the innate immune system, the adaptive immune system is more expansive and diverse and is characterized by:
 - **Specificity:** The recognition of the foreign substance (i.e., antigen or immunogen) by antigen-recognition molecules on the surfaces of lymphocytes in a highly precise and selective manner;
 - **Heterogeneity:** The cells and cell products that comprise the adaptive immune system consist of a variety of different types; and
 - **Memory:** The ability to recognize an antigen upon subsequent encounters with the foreign substance in a more rapid and highly augmented fashion.
- Because the adaptive immune system is composed of relatively small numbers of cells with specificity to recognize an individual immunogen, the responding cells must proliferate, forming a cell clone, and differentiate into effector cells
- After encountering a foreign substance, the effector cells attain sufficient numbers to mount an effective response commensurate with the quantity of the foreign agent being presented.
- Thus, the adaptive immune response generally expresses itself temporally, usually several days after the innate response, in the encounter with foreignness.
- A key feature of the adaptive immune response is that it produces large quantities of long-lived cells (i.e., memory cells) that persist in an apparently dormant state, but that can re-express effector functions rapidly after subsequent encounters with the same antigen.
- This provides the adaptive immune response with the ability to manifest immune memory, permitting it to contribute to a more effective host response against specific pathogens when they are encountered a second time, even decades after the initial sensitizing encounter.

Humoral and Adaptive Immunity

- The two major components of the adaptive immune response are
 - humoral immunity and

- cell-mediated immunity (CMI).
- Humoral immunity is a process carried out by antibodies (immunoglobulins), produced B lymphocytes in response to and capable of reacting with antigen (Table 2)
- Cell-mediated immunity is the other arm of the adaptive immune response carried out by T lymphocytes (Table 2)

Table 2: The two major components of the adaptive immune system

Type	Effector cells	Effector mechanism(s)	Outcome
Humoral	B cells	Antibody	Neutralization of foreign antigen and coating substances for opsonization
Cell-mediated	T cells	Cytokines, cell-cell interaction & Cytotoxic activity	Promotion or inhibition of inflammation, and/or humoral function & Lysis of infected cells

- Antibodies are proteins produced by and secreted from B cells and specifically bind extracellular antigen.
- In humans, there are five major classes (i.e., isotypes) of immunoglobulins: IgM, IgG, IgA, IgD, and IgE, each differing in physical, chemical, and biologic properties.
- The primary function of antibody is to directly bind with the foreign substance/pathogen.
- As will be described subsequently, there are a number of other interactions of antibody with other cells and components of the innate immune system.
- T cells are capable of recognizing intracellular infections (viruses and bacteria that can survive inside the cells that have ingested them).
- Cell-mediated immunity is a process carried out by T cells through the production of cell-regulating molecules (cytokines) or through inducing cell death (cytotoxicity) without the participation of antibody.

Quiz

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