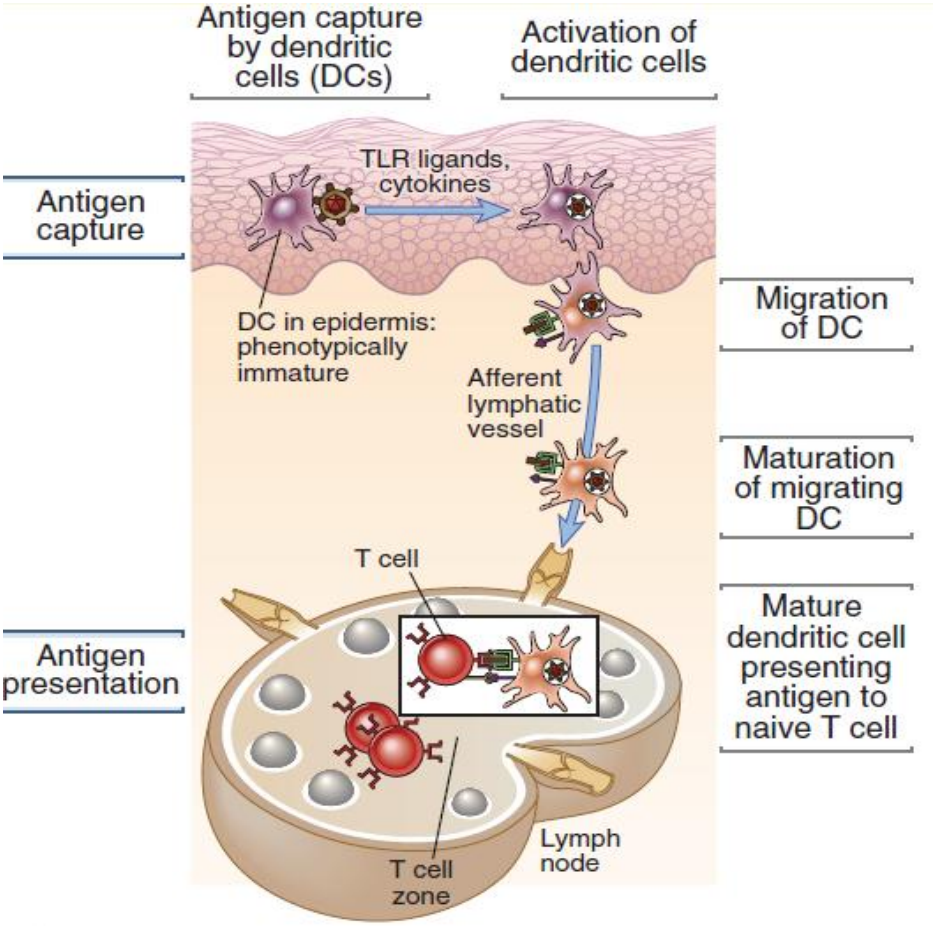
Capture and presentation of protein antigens by dendritic cells.

Immature dendritic cells in the epithelium (skin, as shown here, where the dendritic cells are called Langerhans cells) capture microbial antigens, **are activated**, and leave the epithelium. The dendritic cells **migrate to draining lymph nodes**, being attracted there by chemokines produced in the lymphatics and nodes. In response to signals induced by the microbe, such as Toll-like receptor (TLR) signals and cytokines, the dendritic cells mature and acquire the ability to present antigens to naive T lymphocytes in the lymph nodes. Dendritic cells at different stages of their maturation may express different membrane proteins. Immature dendritic cells express surface receptors that capture microbial antigens, whereas mature dendritic cells express high levels of major histocompatibility complex (MHC) molecules and costimulators, which function to stimulate T cells



Antigen Recognition in the Adaptive Immune System:

Antigen receptors serve critical roles in the maturation of lymphocytes from progenitors and in all adaptive immune responses. In adaptive immunity, naive lymphocytes recognize antigens to initiate responses, and effector T cells and antibodies recognize antigens to perform their functions. **B and T lymphocytes express different receptors that recognize antigens:membrane-bound antibodies on B cells and Tcell receptors (TCRs) on T lymphocytes.**

The principal function of cellular receptors in the immune system, as in other biologic systems, is to detect external stimuli (antigens, for the antigen receptors of the adaptive immune system) and trigger responses of the cells on which the receptors are expressed. To recognize a large variety of different antigens, the antigen

ADAPTIVE IMMUNITY

In contrast to innate immunity, there are other immune responses that are stimulated by exposure to infectious agents and increase in magnitude and defensive capabilities with each successive exposure to a particular microbe. Because this form of immunity develops as a response to infection and adapts to the infection, it is called **adaptive immunity** (also called **specific** or **acquired immunity**) Protective immunity against microbes is mediated by the early reactions of **innate immunity** and the later responses of adaptive

immunity. Innate immune responses are stimulated by molecular structures shared by groups of microbes and by molecules expressed by damaged host cells. **Adaptive immunity** is specific for different microbial and non-microbial antigens and is increased by repeated exposures to antigen (immunologic memory).

Features of Adaptive Immune Responses:

All humoral and cell-mediated immune responses to foreign antigens have a number of fundamental properties that reflect the properties of the lymphocytes that mediate these responses:

Feature	Functional Significance
Specificity	Ensures that the immune response to a microbe (or nonmicrobial antigen) is targeted to that microbe (or antigen)
Diversity	Enables the immune system to respond to a large variety of antigens
Memory	Increases the ability to combat repeat infections by the same microbe
Clonal expansion	Increases the number of antigen-specific lymphocytes to keep pace with microbes
Specialization	Generates responses that are optimal for defense against different types of microbes
Contraction and homeostasis	Allows the immune system to recover from one response so that it can effectively respond to newly encountered antigens
Nonreactivity to self	Prevents injury to the host during responses to foreign antigens

Cardinal Features of Adaptive Immune Responses

1. **Specificity and diversity**. Immune responses are specific for distinct antigens and, in fact, for different portions of a single complex protein, polysaccharide, or other macromolecule The parts of such antigens that are specifically recognized by individual lymphocytes are called **epitopes**

2. **Memory**. Exposure of the immune system to a foreign antigen enhances its ability to respond again to that antigen. Responses to second and subsequent exposures to the same antigen, called secondary immune responses, are usually more rapid, larger, and often qualitatively different from the first, or primary, immune response to that antigen.

3. **Clonal expansion.** Lymphocytes specific for an antigen undergo considerable proliferation after exposure to that antigen. The term clonal expansion refers to an increase in the number of cells that express identical receptors for the antigen and thus belong to a clone.

4. **Specialization**. As we have already noted, the immune system responds in distinct and special ways to different microbes, maximizing the effectiveness of antimicrobial defense mechanisms.

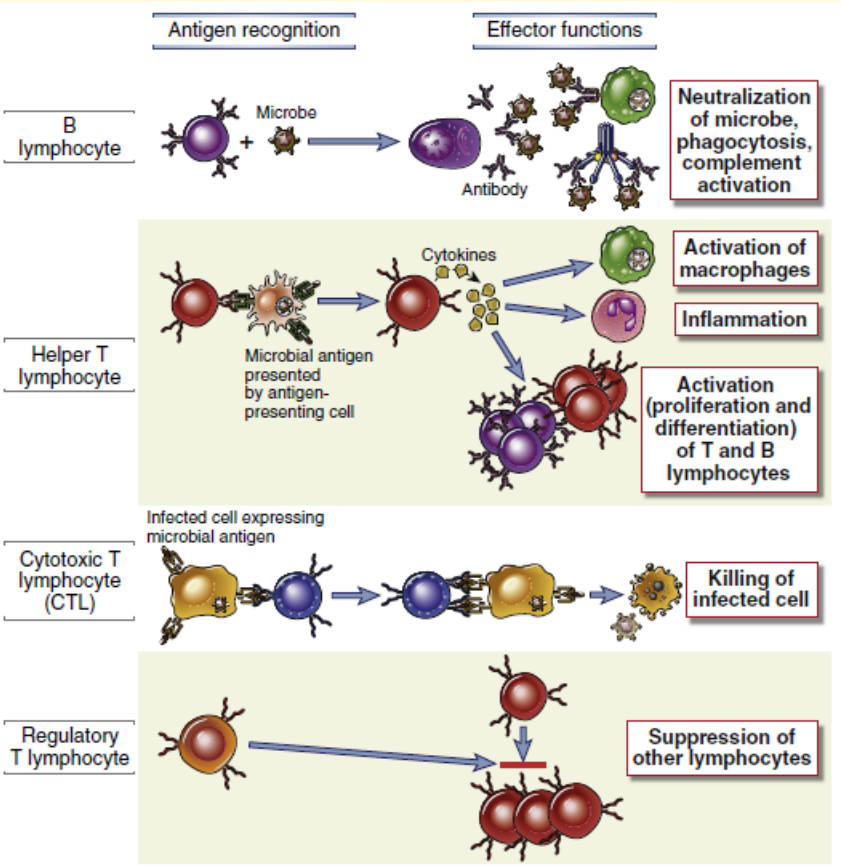
5. **Contraction and homeostasis**. All normal immune responses wane with time after antigen stimulation, thus returning the immune system to its resting basal state, a state called **homeostasis.** This contraction of immune responses occurs largely because responses that are triggered by antigens function to eliminate the antigens, thus eliminating an essential stimulus for lymphocyte survival and activation.

6.Nonreactivity to self: One of the most remarkable properties of every normal individual's immune system is its ability to recognize, respond to, and eliminate many foreign (non-self) antigens while not reacting harmfully to that individual's own (self) antigenic substances. Immunologic unresponsiveness is also called **tolerance.**

Cellular components of the adaptive immune system:

Classes of lymphocytes. B lymphocytes recognize soluble antigens and develop into antibody-secreting cells. Helper T lymphocytes recognize antigens on the surfaces of antigen-presenting cells and secrete cytokines, which stimulate different mechanisms of immunity and inflammation. Cytotoxic T

lymphocytes recognize antigens on infected cells and kill these cells. Regulatory T cells suppress and prevent immune responses (e.g., to self-antigens).



The strategies of adaptive immune response:

The adaptive immune system uses three main strategies to combat most microbes.

1.**Antibodies**. Secreted antibodies bind to extracellular microbes, block their ability to infect host cells, and promote their ingestion and subsequent destruction by phagocytes.

2.**Phagocytosis**. Phagocytes ingest microbes and kill them, and antibodies and helper T cells enhance the microbicidal abilities of the phagocytes.

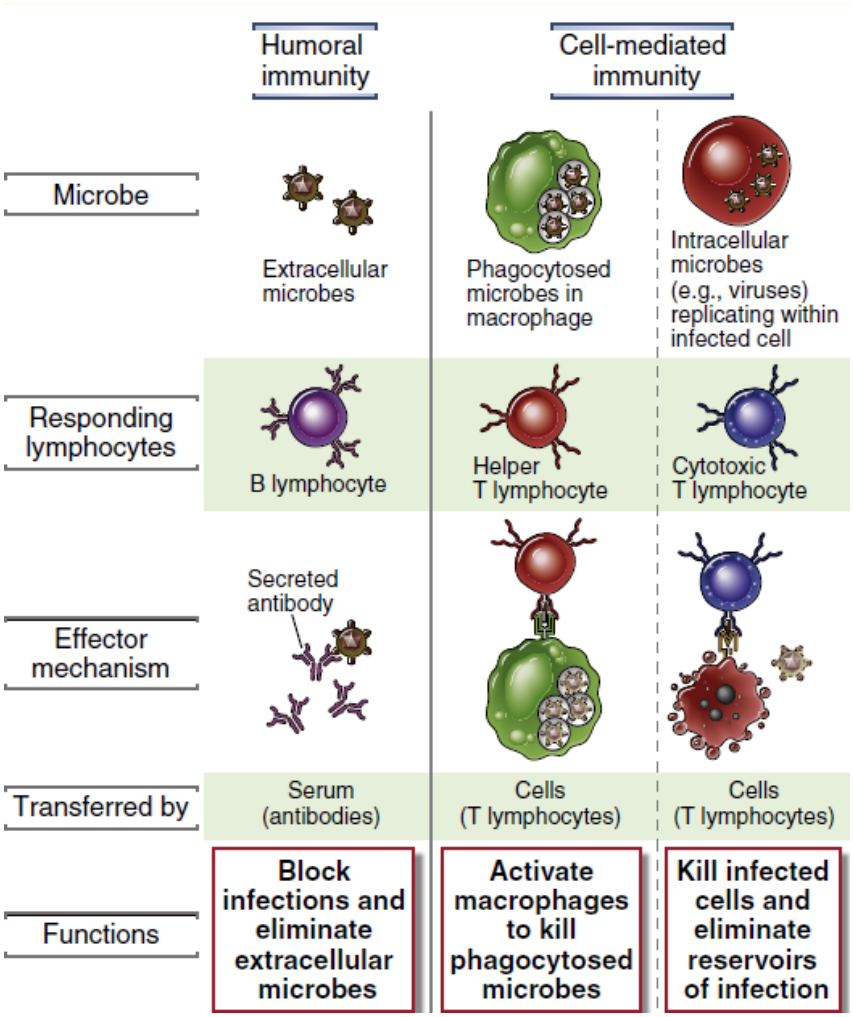
3.Cell killing. Cytotoxic T lymphocytes (CTLs) destroy cells infected by microbes that are inaccessible to antibodies and phagocytic destruction.

The goal of the adaptive response is to activate one or more of these defense mechanisms against diverse microbes that may be in different anatomic locations, such as the intestines or airways, the circulation, or inside cells. All adaptive immune responses develop in sequential steps, each of which corresponds to particular reactions of lymphocytes. We start this overview of adaptive immunity with the first step, which is the recognition of antigens.

Types of adaptive immune responses:

- **Active immunity**

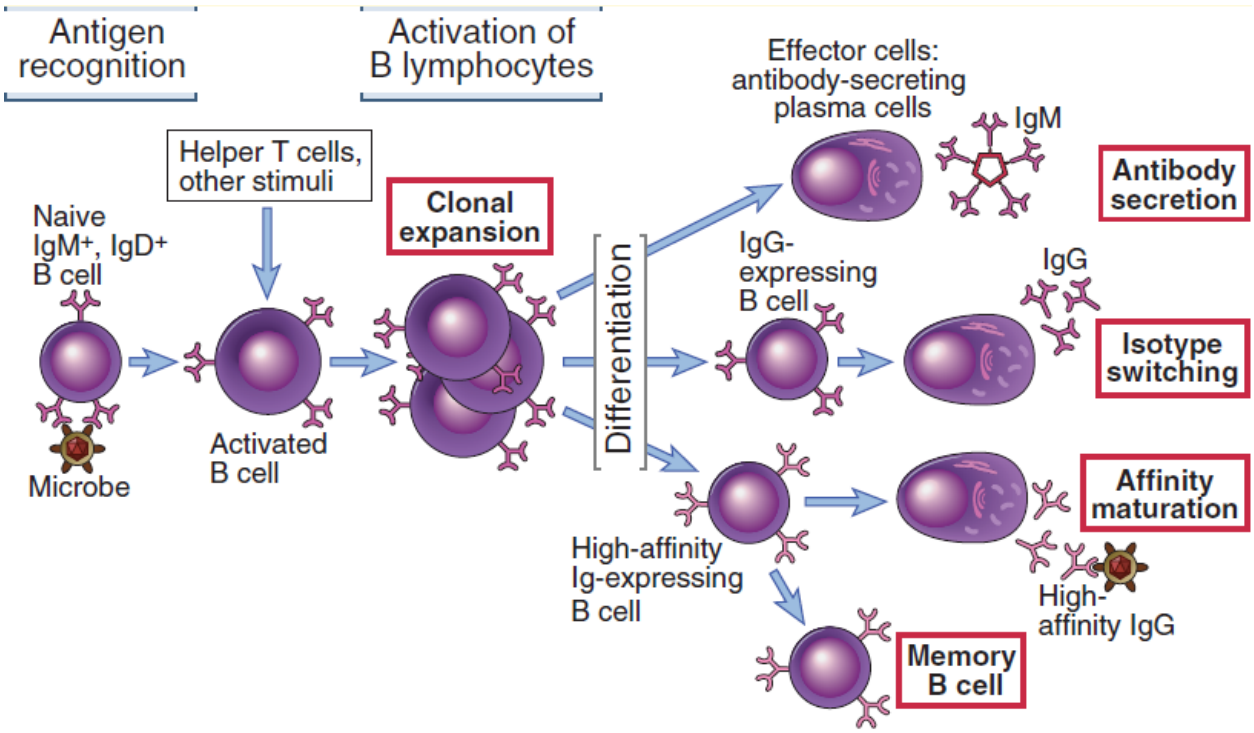
Protective immunity against a microbe is usually induced by the host's response to the microbe .The form of immunity that is induced by exposure to a foreign antigen is called active immunity **active immunity** because the immunized individual plays an active role in responding to the antigen.
There are two types of adaptive immune responses, called **humoral immunity** and **cell-mediated** immunity that are mediated by different components of the immune system and function to eliminate different types of microbes:



Types of adaptive immunity. In humoral immunity, B lymphocytes secrete antibodies that prevent infections and eliminate extracellular microbes. In cell-mediated immunity, helper T lymphocytes activate macrophages to kill phagocytosed microbes, or cytotoxic T lymphocytes directly destroy infected cells

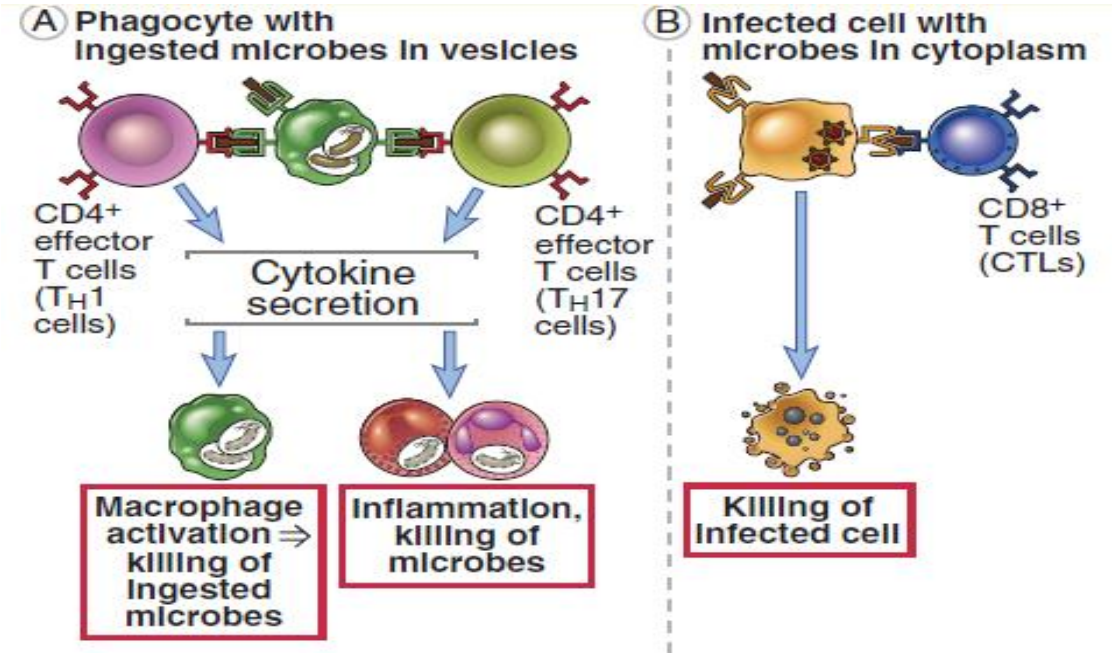
1. **Humoral immunity** is mediated by molecules in the blood and mucosal secretions, called antibodies, which are produced by cells called B lymphocytes (also called B cells). Antibodies recognize microbial antigens, neutralize the infectivity of the microbes, and target microbes for elimination by various effector mechanisms. Humoral immunity is the principal defense mechanism against extracellular microbes and their toxins because secreted antibodies can bind to these microbes and toxins and assist in their elimination. Antibodies themselves are specialized and may activate different mechanisms to combat microbes (**effector mechanisms)**. For example, different types of antibodies promote the ingestion of microbes by host cells (phagocytosis), bind to and trigger the release of inflammatory mediators from cells, and are actively transported into the lumens

of mucosal organs and through the placenta to provide defense against ingested and inhaled microbes and against infections of the newborn, respectively.



Phases of humoral immune responses. Naive B lymphocytes recognize antigens, and under the influence of helper T cells and other stimuli (not shown), the B cells are activated to proliferate, giving rise to clonal expansion, and to differentiate into antibody-secreting plasma cells. Some of the activated B cells undergo heavy-chain isotype switching and affinity maturation, and some become long-lived memory cells.

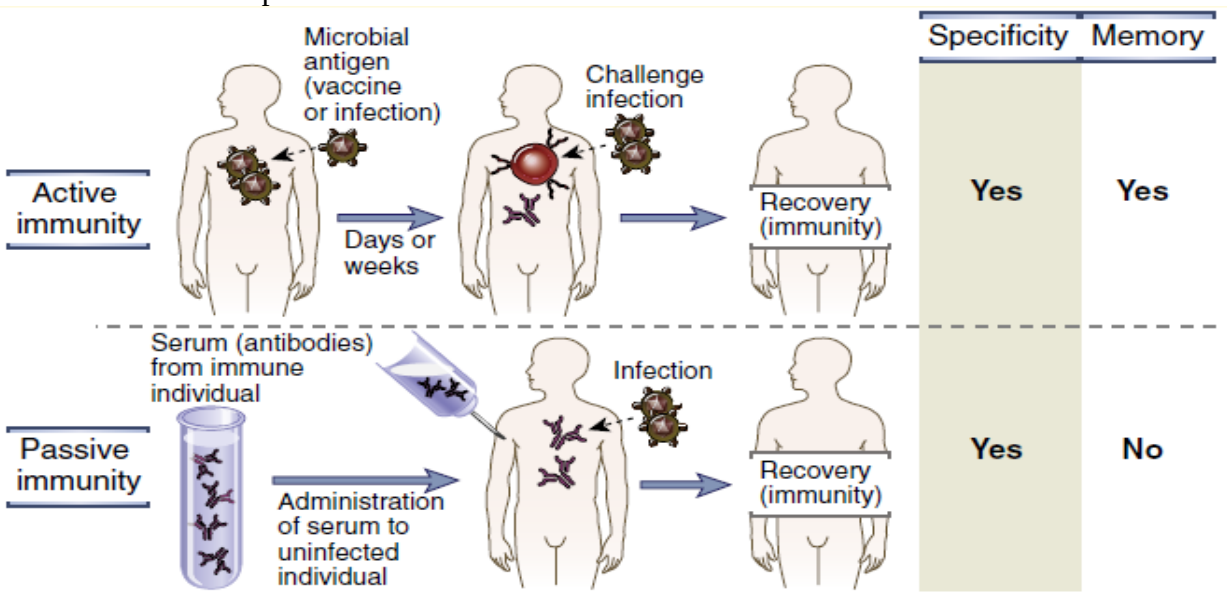
2. **Cell-mediated immunity**, also called **cellular immunity**, is mediated by T lymphocytes (also called T cells). Intracellular microbes, such as viruses and some bacteria, survive and proliferate inside phagocytes and other host cells, where they are inaccessible to circulating antibodies. Defense against such infections is a function of cell-mediated immunity, which promotes the destruction of microbes residing in phagocytes or the killing of infected cells to eliminate reservoirs of infection. Some T lymphocytes also contribute to eradication of extracellular microbes by recruiting leukocytes that destroy these pathogens and by helping B cells make effective antibodies. Protective immunity against a microbe is usually induced by the host's response to the microbe Individuals and lymphocytes that have not encountered a particular antigen are said to be naive,implying that they are immunologically inexperienced.Individuals who have responded to a microbial antigen and are protected from subsequent exposures to that microbe are said to be immune.



Cell-mediated immunity against intracellular microbes. **A,** Effector T helper cells of the CD4+ TH1 and TH17 subsets recognize microbial antigens and secrete cytokines that recruit leukocytes (inflammation) and activate phagocytes to kill the microbes. CD8+ T cells also produce cytokines that induce inflammation and activate macrophages (not shown). **B,** CD8+ cytotoxic T lymphocytes (CTLs) kill infected cells with microbes in the cytoplasm.

- **passive immunity**

Passive immunization is a useful method for conferring resistance rapidly, without having to wait for an active immune response to develop. A physiologically important example of passive immunity is the transfer of maternal antibodies through the placenta to the fetus, which enables newborns to combat infections before they develop the ability to produce antibodies themselves Immunity can also be conferred on an individual by transferring serum or lymphocytes from a specifically immunized individual in experimental situations, a process known as adoptive transfer



Active and passive immunity. Active immunity is conferred by a host response to a microbe or microbial antigen, whereas passive immunity is conferred by adoptive transfer of antibodies or T lymphocytes specific for the microbe. Both forms of immunity provide resistance to infection and are specific for microbial antigens, but only active immune responses generate immunologic memory. Therapeutic passive transfer of antibodies, but not lymphocytes, is done routinely and also occurs during pregnancy (from mother to fetus).

Phases of adaptive immune responses.

Adaptive immune responses consist of distinct phases, the first three being the recognition of antigen, the activation of lymphocytes, and the elimination of antigen (the effector phase). The response contracts (declines) as antigen-stimulated lymphocytes die by apoptosis, restoring homeostasis, and the antigen-specific cells that survive are responsible for memory. The duration of each phase may vary in different immune responses. The y-axis represents an arbitrary measure of the magnitude of the response. These principles apply to humoral immunity (mediated by B lymphocytes) and cell-mediated immunity (mediated by T lymphocytes).