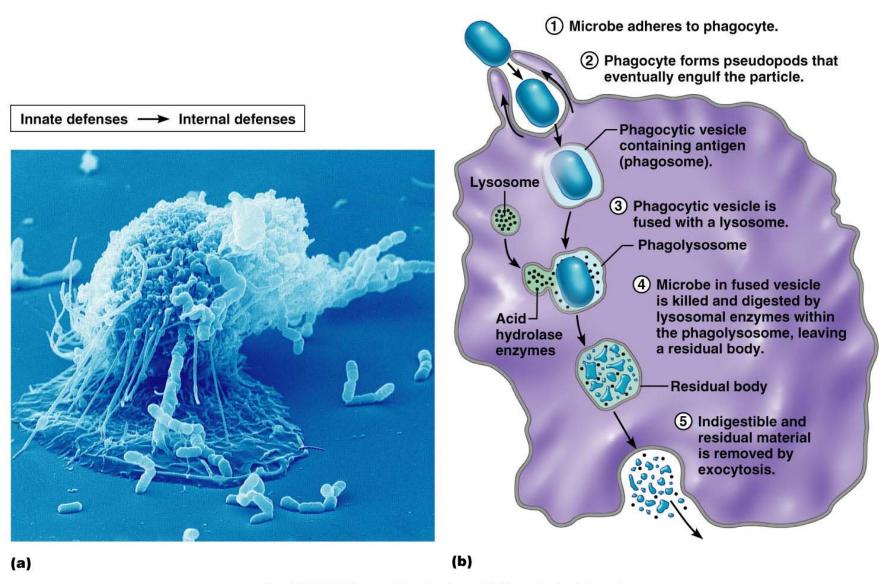
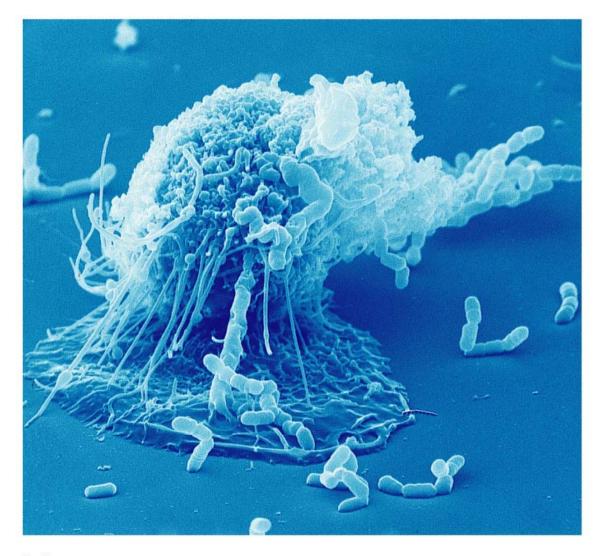


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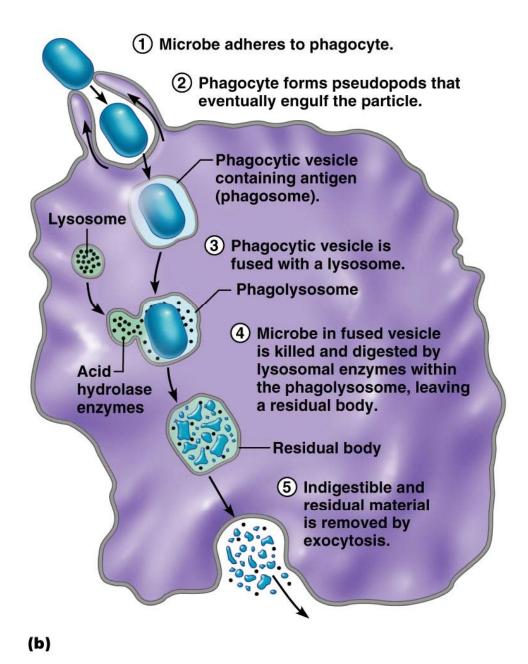


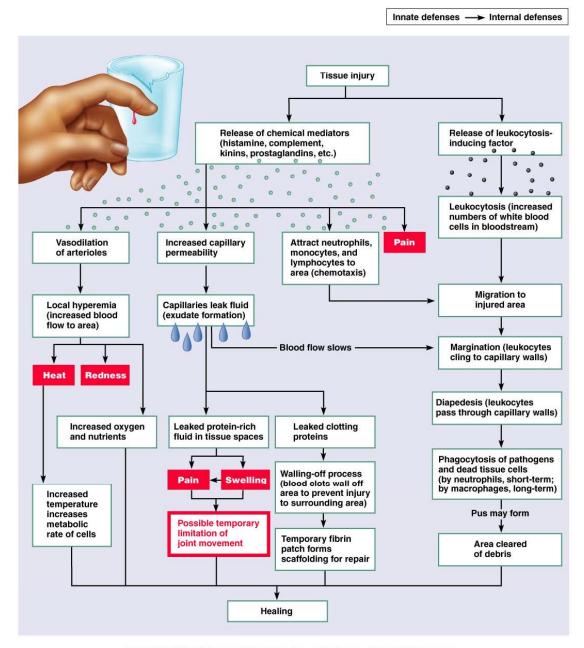
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Innate defenses → Internal defenses



(a)



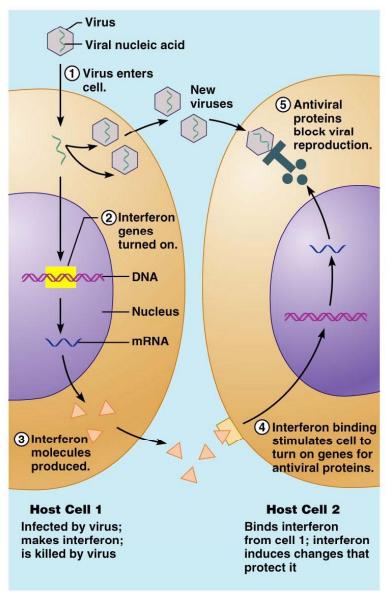


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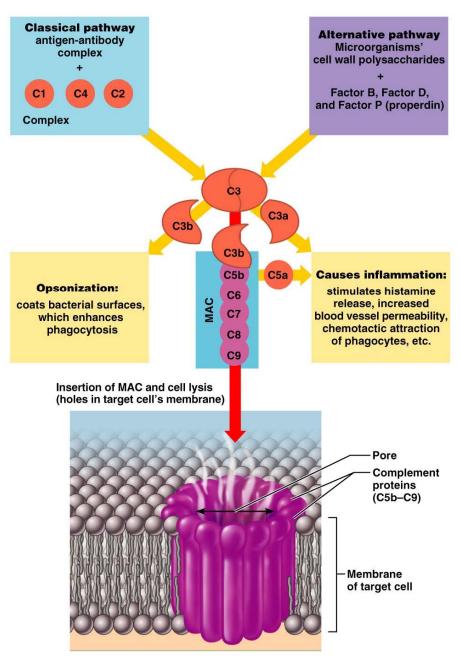
Innate defenses → Internal defenses (4) Positive chemotaxis Inflammatory chemicals diffusing from the inflamed site act as chemotactic agents 3 Diapedesis 1 Neutrophils enter blood from bone marrow 2 Margination Endothelium-Capillary wall-Basement membrane

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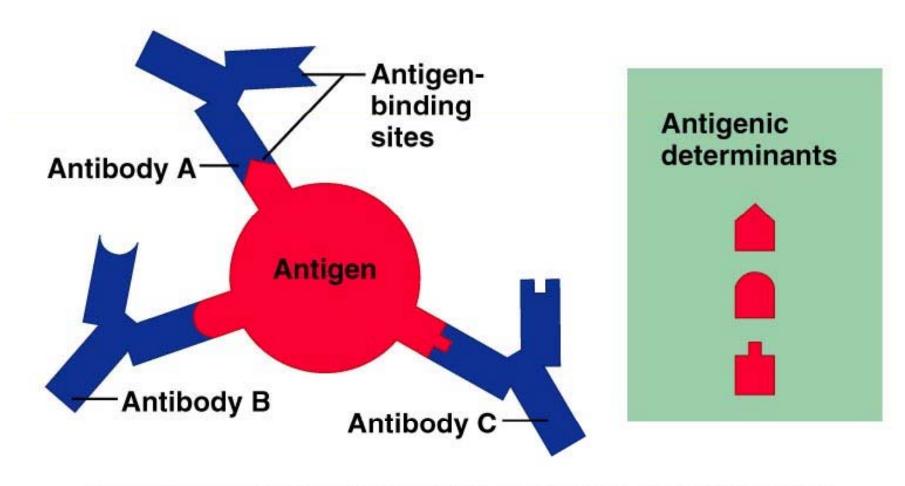
Innate defenses --> Internal defenses

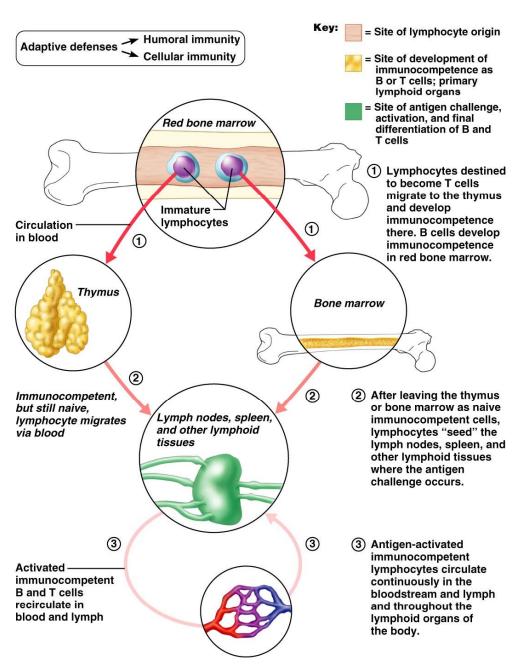


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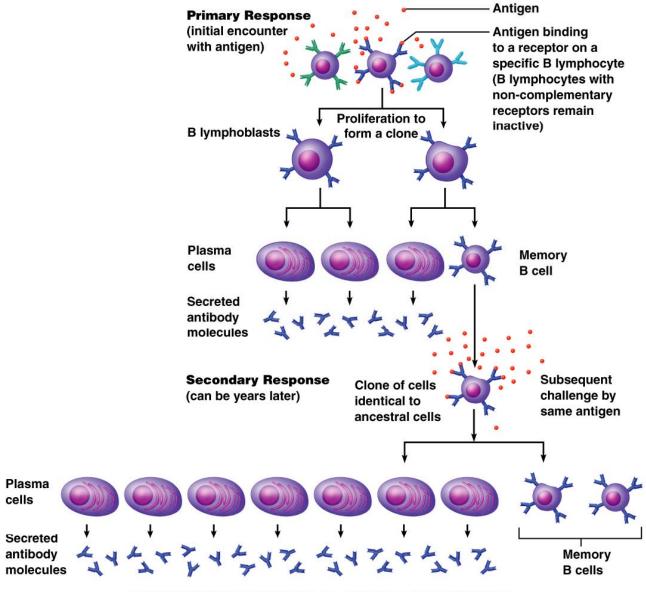


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Antigen-presenting Developing thymic cells T cells **Selection process** Results T cell Selfantigen receptor Positive selection – Eliminated (fails to recognize (apoptosis) self-MHC) MHC (a) Thymic cell T cell ➤ Positive selection — MHC restriction (binds MHC) of survivors (b) Thymic cell T cell ➤ Negative selection → Apoptosis; (binds MHC and surviving cells reacts vigorously are self-tolerant with self-antigen) (c) Thymic cell T cell

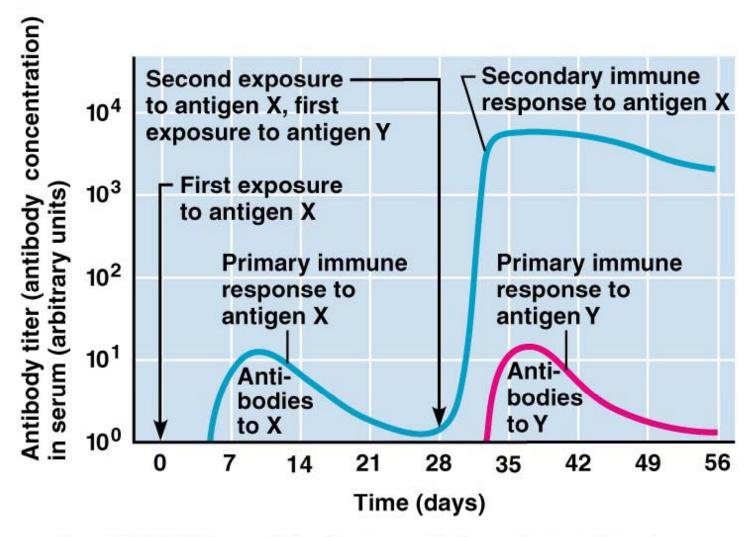
Adaptive defences -> Cellular immunity

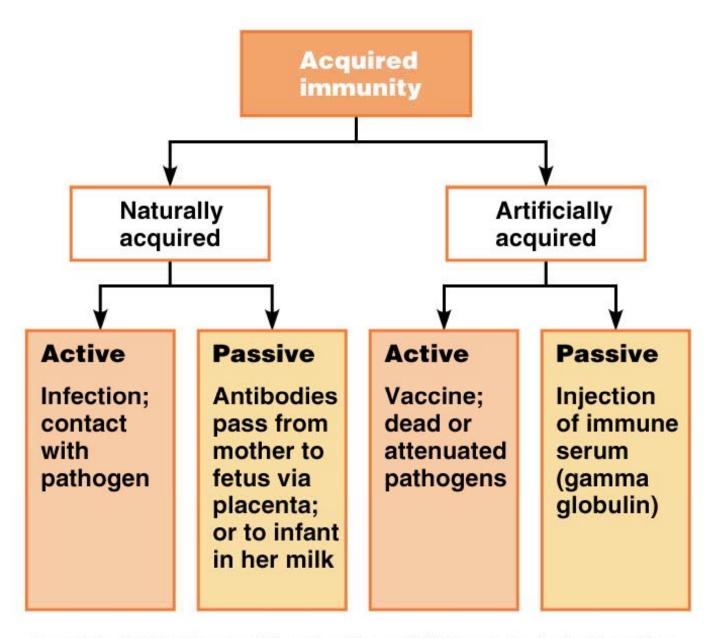
Adaptive defenses -- Humoral immunity



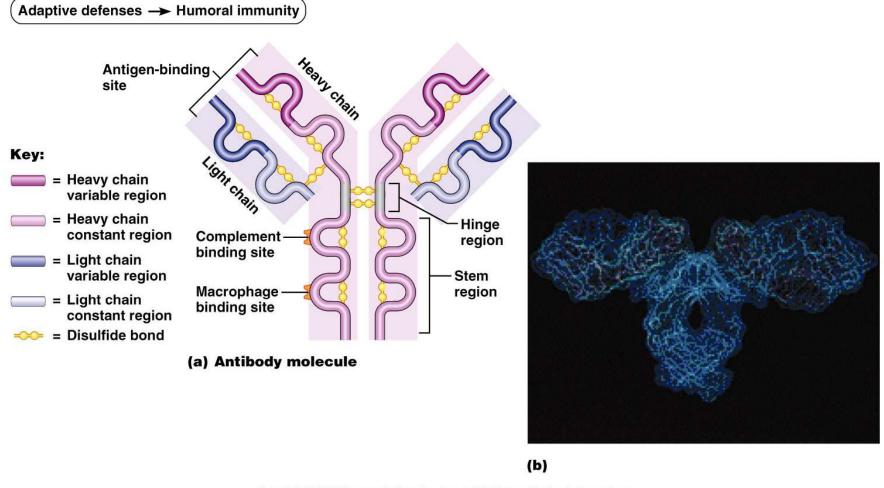
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Adaptive defenses --- Humoral immunity

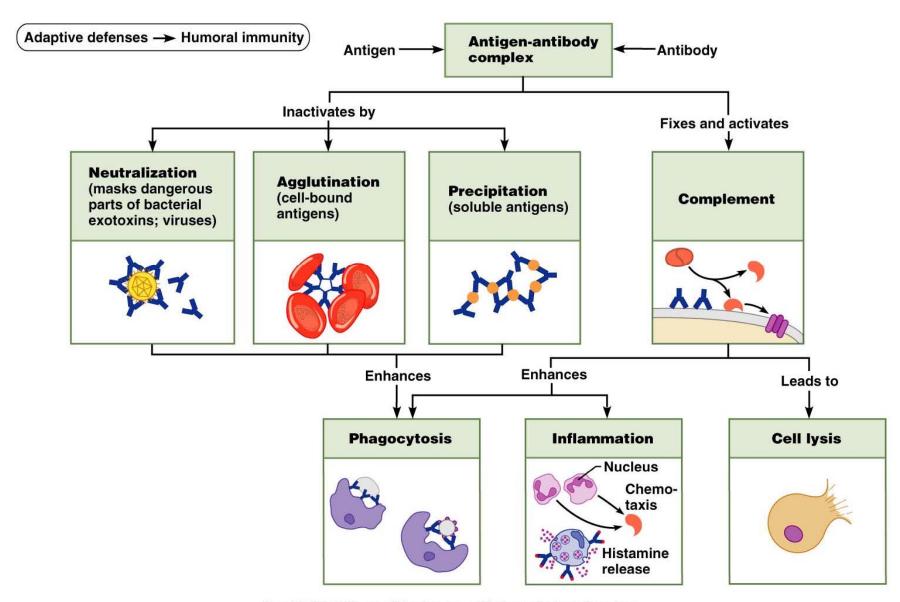




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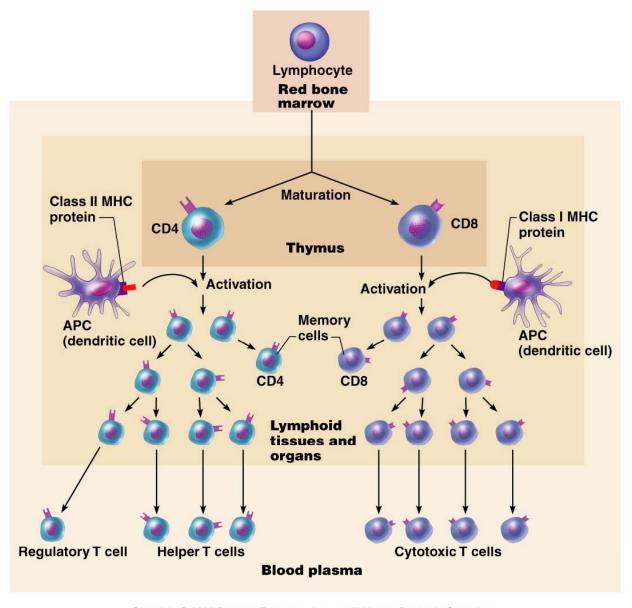


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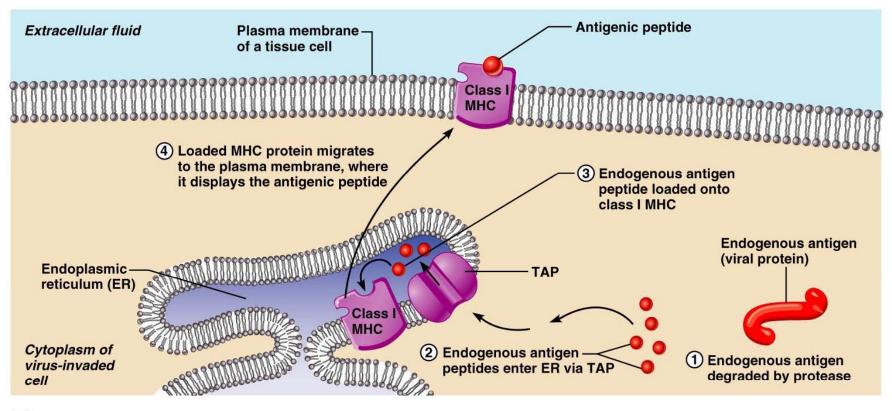


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Adaptive defenses → Cellular immunity

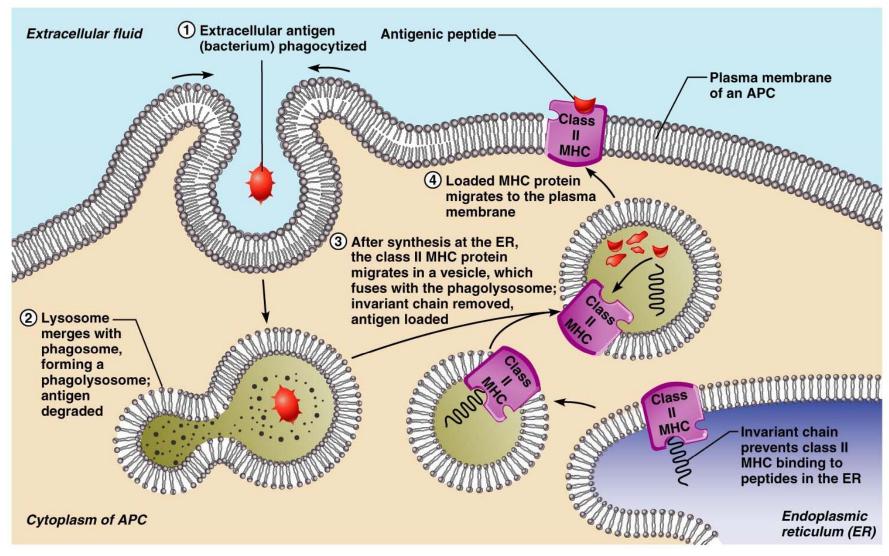


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(a)

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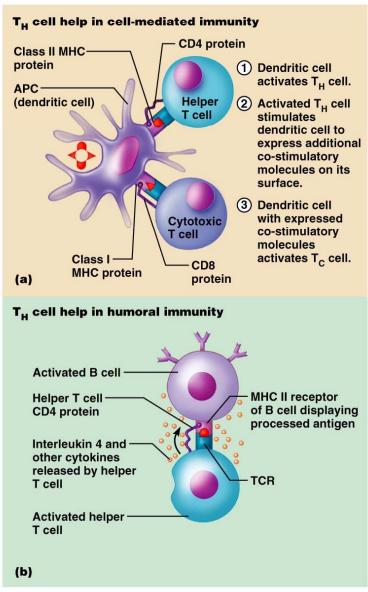


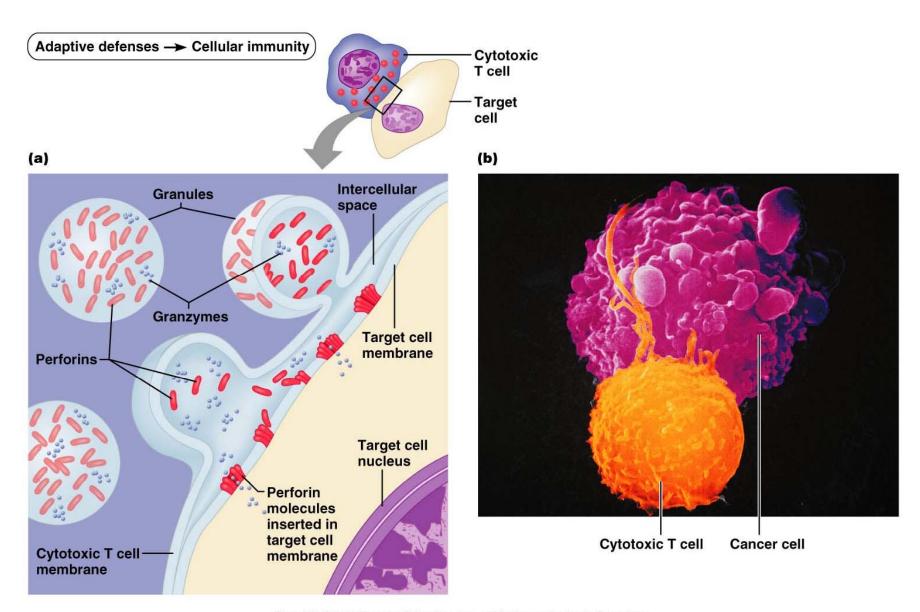
(b)

Adaptive defenses → Cellular immunity Viral antigen internalized by APC Processed viral antigen (peptide) presented in combination with class II MHC protein Class II MHC **Dendritic** protein cell CD4 protein Immunocompetent Dendritic helper T cell cell presenting antigenic peptide T cell receptor recognized by (TCR) helper T cell Clone formation **Activated** helper **Helper T** T cells memory cell

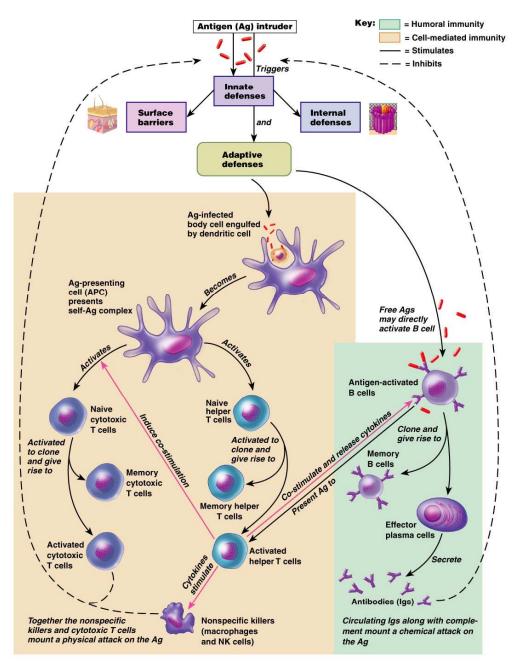
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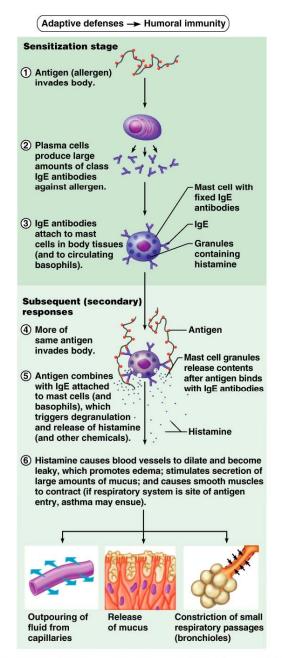




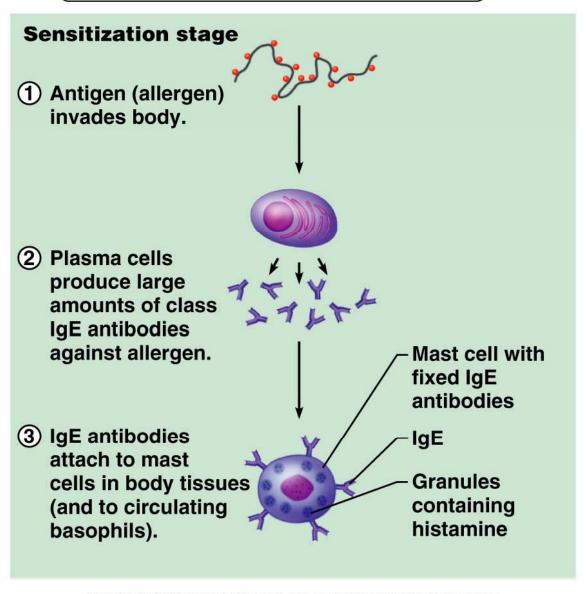
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Adaptive defenses → Humoral immunity)



Adaptive defenses -- Humoral immunity Subsequent (secondary) responses (4) More of Antigen same antigen invades body. Mast cell granules release contents (5) Antigen combines after antigen binds with IgE attached with IgE antibodies to mast cells (and basophils), which triggers degranulation and release of histamine Histamine (and other chemicals). (6) Histamine causes blood vessels to dilate and become leaky, which promotes edema; stimulates secretion of large amounts of mucus; and causes smooth muscles to contract (if respiratory system is site of antigen entry, asthma may ensue). **Outpouring of** Constriction of small Release fluid from of mucus respiratory passages capillaries (bronchioles)

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CHEMICAL	SOURCE	PHYSIOLOGICAL EFFECTS
CHEWICAL	SOURCE	PHISIOLOGICAL EFFECTS
Histamine	Granules of basophils and mast cells; released in response to mechanical injury, presence of certain microorganisms, and chemicals released by neutrophils	Promotes vasodilation of local arterioles; increases permeability of local capillaries, promoting exudate formation
Kinins (bradykinin and others)	A plasma protein, kininogen, is cleaved by the enzyme kallikrein found in plasma, urine, saliva, and in lysosomes of neutrophils and other types of cells; cleavage releases active kinin peptides	Same as for histamine; also induce chemotaxi of leukocytes and prompt neutrophils to release lysosomal enzymes, thereby enhancing generation of more kinins; induce pain
Prostaglandins	Fatty acid molecules produced from arachidonic acid—found in all cell membranes; generated by enzymes of neutrophils, basophils, mast cells, and others	Sensitize blood vessels to effects of other in- flammatory mediators; one of the intermediate steps of prostaglandin generation produces fre radicals, which themselves can cause inflam- mation; induce pain
Platelet-derived growth factor (PDGF)	Secreted by platelets and endothelial cells	Stimulates fibroblast activity and repair of damaged tissues
Complement	See Table 21.2 (p. 796)	
Cytokines	See Table 21.4 (pp. 817–818)	

TABLE 21.2 Summary of Nonspecific Body Defenses

CATEGORY/ASSOCIATED

ELEMENTS PROTECTIVE MECHANISM

FIRST LINE OF DEFENSE: SURFACE MEMBRANE BARRIERS

Intact skin epidermis	Forms mechanical barrier that prevents entry of pathogens and other harmful substances into body
Acid mantle	Skin secretions (perspiration and sebum) make epidermal surface acidic, which inhibits bacterial growth; sebum also contains bactericidal chemicals
Keratin	Provides resistance against acids, alkalis, and bacterial enzymes
Intact mucous membranes	Form mechanical barrier that prevents entry of pathogens
Mucus	Traps microorganisms in respiratory and digestive tracts
Nasal hairs	Filter and trap microorganisms in nasal passages
Cilia	Propel debris-laden mucus away from lower respiratory passages
 Gastric juice 	Contains concentrated hydrochloric acid and protein-digesting enzymes that destroy pathogens in stomach
 Acid mantle of vagina 	Inhibits growth of most bacteria and fungi in female reproductive tract
Lacrimal secretion (tears); saliva	Continuously lubricate and cleanse eyes (tears) and oral cavity (saliva); contain lysozyme, an enzyme that destroys microorganisms
Urine	Normally acid pH inhibits bacterial growth; cleanses the lower urinary tract as it flushes from the body

TABLE 21.2 Summary of Nonspecific Body Defenses (continued)

CATEGORY/ASSOCIATED

ELEMENTS PROTECTIVE MECHANISM

SECOND LINE OF DEFENSE: INNATE, CELLULAR AND CHEMICAL DEFENSES

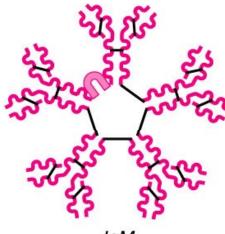
Phagocytes	Engulf and destroy pathogens that breach surface membrane barriers; macrophages also contribute to immune response
Natural killer (NK) cells	Promote apoptosis (cell suicide) by direct cell attack against virus-infected or cancerous body cells; do not require specific antigen recognition; do not exhibit a memory response
Inflammatory response	Prevents spread of injurious agents to adjacent tissues, disposes of pathogens and dead tissue cells, and promotes tissue repair; chemical mediators released attract phagocytes (and immunocompetent cells) to the area
Antimicrobial proteins • Interferons (α, β, γ)	Proteins released by virus-infected cells and certain lymphocytes that protect uninfected tissue cells from viral takeover; mobilize immune system
Complement	Lyses microorganisms, enhances phagocytosis by opsonization, and intensifies inflammatory and immune responses
Fever	Systemic response initiated by pyrogens; high body temperature inhibits microbial multiplication and enhances body repair processes

TABLE 21.3

Immunoglobulin Classes



IgD (monomer) IgD is virtually always attached to the external surface of a B cell, where it functions as the antigen receptor of the B cell; important in B cell activation.

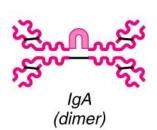


IgM (pentamer) IgM exists in monomer and pentamer (five united monomers) forms. The monomer, which is attached to the B cell surface, serves as an antigen receptor. The pentamer (illustrated) circulates in blood plasma and is the first Ig class released by plasma cells during the primary response. (This fact is diagnostically useful because presence of IgM in plasma usually indicates current infection by the pathogen eliciting IgM's formation.) Because of its numerous antigen-binding sites, IgM is a potent agglutinating agent and readily fixes and activates complement.

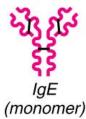
TABLE 21.3 Immunoglobulin Classes (continued)



IgG is the most abundant and diverse antibody in plasma, accounting for 75–85% of circulating antibodies. It protects against bacteria, viruses, and toxins circulating in blood and lymph, readily fixes complement, and is the main antibody of both secondary and late primary responses. It crosses the placenta and confers passive immunity from the mother to the fetus.



IgA monomer exists in limited amounts in plasma. The dimer (illustrated), referred to as secretory IgA, is found in body secretions such as saliva, sweat, intestinal juice, and milk, and helps prevent attachment of pathogens to epithelial cell surfaces (including mucous membranes and the epidermis).



IgE is slightly larger than the IgG antibody. It is secreted by plasma cells in skin, mucosae of the gastrointestinal and respiratory tracts, and tonsils. Its stem region becomes bound to mast cells and basophils, and when its receptor ends are triggered by an antigen, it causes the cells to release histamine and other chemicals that mediate inflammation and an allergic reaction. Typically only traces of IgE are found in plasma, but levels rise during severe allergic attacks or chronic parasitic infections of the gastrointestinal tract.

TABLE 21.4 Cells and Molecules of the Adaptive Immune Response	
ELEMENT	FUNCTION IN IMMUNE RESPONSE
CELLS	
B cell	Lymphocyte that matures in bone marrow. Induced to replicate by antigen binding, usually followed by helper T cell interactions in lymphoid tissues. Its progeny (clone members) form memory cells and plasma cells
Plasma cell	Antibody-producing "machine"; produces huge numbers of antibodies (immunoglobulins) with the same antigen specificity. Specialized B cell clone descendant
Helper T cell (T _H)	A CD4 T cell that is central to both humoral and cellular immunity. After binding with a specific antigen presented by an APC, it stimulates production of cytotoxic T cells and B cells to help fight invader, activates macrophages, and acts both directly and indirectly by releasing cytokines
Cytotoxic T cell (T _C)	A CD8 cell; also called a cytolytic (CTL) T cell. Activated by antigen presented by an antigen- presenting cell, often with helper T cell involvement. Its specialty is killing virus-invaded body cells and cancer cells; also involved in rejection of foreign tissue grafts
Regulatory T cell (T _{Reg})	Formerly called suppressor T cell; slows or stops activity of immune system. Thought to be important in controlling autoimmune diseases; likely several different populations exist
Memory cell	Descendant of activated B cell or any class of T cell; generated during initial immune response (primary response); may exist in body for years after, enabling it to respond quickly and efficiently to subsequent infections or meetings with same antigen
Antigen-presenting cell (APC)	Any of several cell types (dendritic cell, macrophage, B cell) that engulfs and digests antigens that it encounters, presenting parts of them on its plasma membrane (bound to an MHC protein) for recognition by T cells bearing receptors for same antigen. This function, antigen presentation, is essential for normal cell-mediated responses. Macrophages also release chemicals (cytokines) that activate T cells

ELEMENT	FUNCTION IN IMMUNE RESPONSE
MOLECULES	
Antibody (immunoglobulin)	Protein produced by B cell or by plasma cell. Antibodies produced by plasma cells are released into body fluids (blood, lymph, saliva, mucus, etc.), where they attach to antigens, causing complement fixation, neutralization, precipitation, or agglutination, which "mark" the antigens for destruction by complement or phagocytes
Perforin, granzymes	Released by $T_{\rm C}$ cells. Perforin creates large pores in the target cell's membrane, allowing entry of apoptosis-inducing granzymes
Complement	Group of bloodborne proteins activated after binding to antibody-covered antigens or certain molecules on the surface of microorganisms; enhances inflammatory response and causes lysis of some microorganisms
Antigen	Substance capable of provoking an immune response. Typically a large complex molecule (e.g., protein or modified protein) not normally present in the body
CYTOKINES	
Interferons (IFNs)	
 Alpha (α) and beta (β) 	Secreted by leukocytes, fibroblasts, and other cells; antiviral effects; activate macrophages and NK cells
Gamma (γ)	Secreted by lymphocytes; activates macrophages; stimulates synthesis and expression of more class and II MHC proteins; promotes differentiation of T_H cells into T_H 1
Interleukins (ILs)	
■ IL-1	Secreted by activated macrophages; promotes inflammation and T cell activation; causes fever (a pyrogen that resets the thermostat of the hypothalamus)
■ IL-2	Secreted by T cells; stimulates proliferation of T cells; activates NK cells
■ IL-3	Stimulates production of leukocytes and mast cells

TABLE 21.4 Cells and Molecules of the Adaptive Immune Response (continued)

FUNCTION IN IMMUNE RESPONSE

CTIORINES	
Interleukins (ILs)	
■ IL-4	Secreted by T_H cells; promotes differentiation to T_H2 ; promotes B cell activation; switches antibody production to IgE
■ IL-5	Secreted by some T_H cells and mast cells; attracts and activates eosinophils; causes plasma cells to secrete IgA antibodies
■ IL-6	Induces lymphocyte activation and increases antibody production; stimulates liver to secret C-reactive protein, which binds certain bacteria, resulting in complement activation and opsonization
■ IL-7	Induces lymphocyte proliferation and maturation
 IL-8 (also called CXCL8) 	Stimulates chemotaxis of neutrophils, basophils, and T cells; promotes angiogenesis
■ IL-10	Inhibits macrophages and dendritic cells; turns down cellular and innate immune response
■ IL-12	Secreted by dendritic cells and macrophages; stimulates T_C and NK cell activity; promotes $T_H 1$ differentiation

Migration inhibitory Inhibit factor (MIF) Inhibit a num

Secreted by T_H cells; switches antibody production to IgE Inhibits macrophage migration and keeps them in the area of antigen deposition; a generic term for

a number of cytokines

Suppressor factors

A generic term for a number of cytokines that suppress the immune system, for example TGF- β and

IL-10

Transforming growth factor beta (TGF-β)

A suppressor factor similar to IL-10

Tumor necrosis factors (TNFs)

■ IL-13

ELEMENT

CYTOKINES

Produced by lymphocytes and in large amounts by macrophages. Enhance nonspecific killing; slow tumor growth by selectively damaging tumor blood vessels; enhance granulocyte chemotaxis; help activate T cells, phagocytes, and eosinophils; promote cell death by apoptosis



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