



- *The Body's Defenses*

QOD

- Explain why organ transplants might be more successful in very young children



Lines of Defense

Nonspecific defense mechanisms		Specific defense mechanisms (immune system)
First line of defense	Second line of defense	Third line of defense
<ul style="list-style-type: none">• Skin• Mucous membranes• Secretions of skin and mucous membranes	<ul style="list-style-type: none">• Phagocytic white blood cells• Antimicrobial proteins• The inflammatory response	<ul style="list-style-type: none">• Lymphocytes• Antibodies

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Nonspecific Defense Mechanisms.....

Phagocytic and Natural Killer Cells

- **Neutrophils**

60-70% WBCs; engulf and destroy microbes at infected tissue

- **Monocytes**

5% WBCs; develop into....

- **Macrophages**

enzymatically destroy microbes

- **Eosinophils**

1.5% WBCs; destroy large parasitic invaders (blood flukes)

- **Natural killer (NK) cells**

destroy virus-infected body cells & abnormal cells



The Inflammatory Response

1- Tissue injury; release of chemical signals~

histamine (basophils/mast cells): causes Step 2...

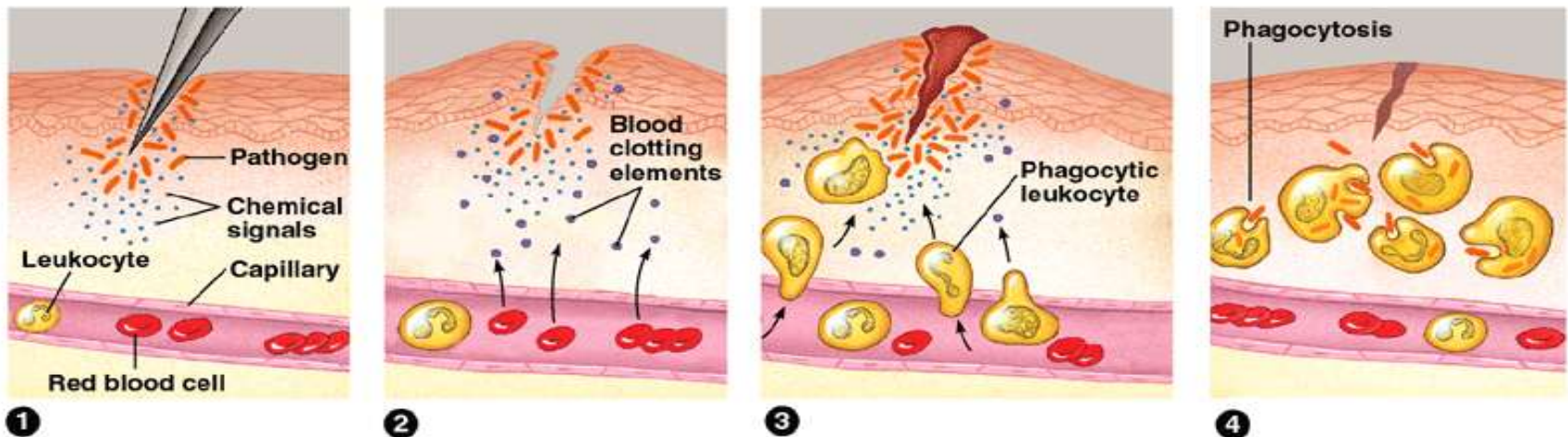
prostaglandins: increases blood flow & vessel permeability

2/3- Dilation and increased permeability of capillary~

chemokines: secreted by blood vessel endothelial cells mediates phagocytotic migration of WBCs

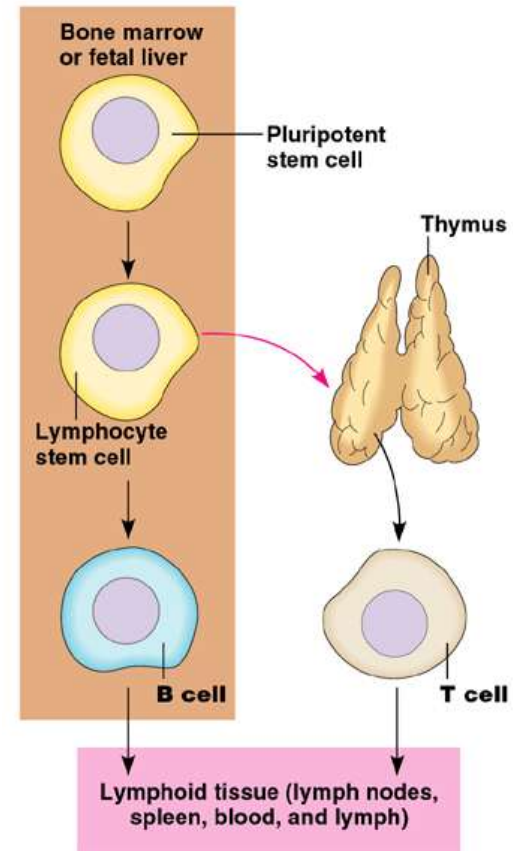
4- Phagocytosis of pathogens~

fever & pyrogens: leukocyte-released molecules increase body temperature



Specific Immunity

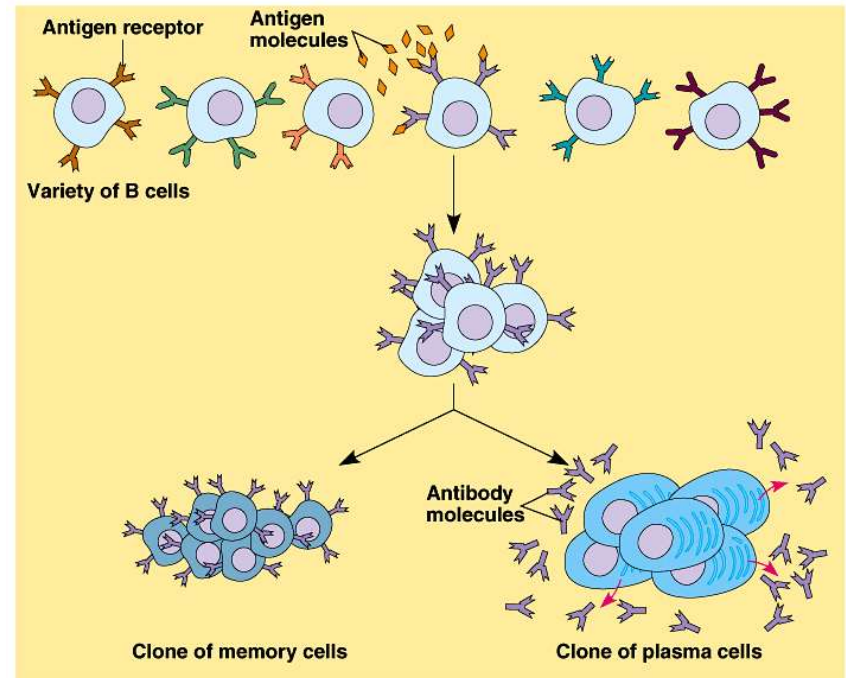
- Lymphocytes
 - pluripotent stem cells...
 - B Cells (bone marrow)
 - T Cells (thymus)
- Antigen: a foreign molecule that elicits a response by lymphocytes (virus, bacteria, fungus, protozoa, parasitic worms)
- Antibodies: antigen-binding immunoglobulin, produced by B cells
- Antigen receptors: plasma membrane receptors on B and T cells



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Clonal selection

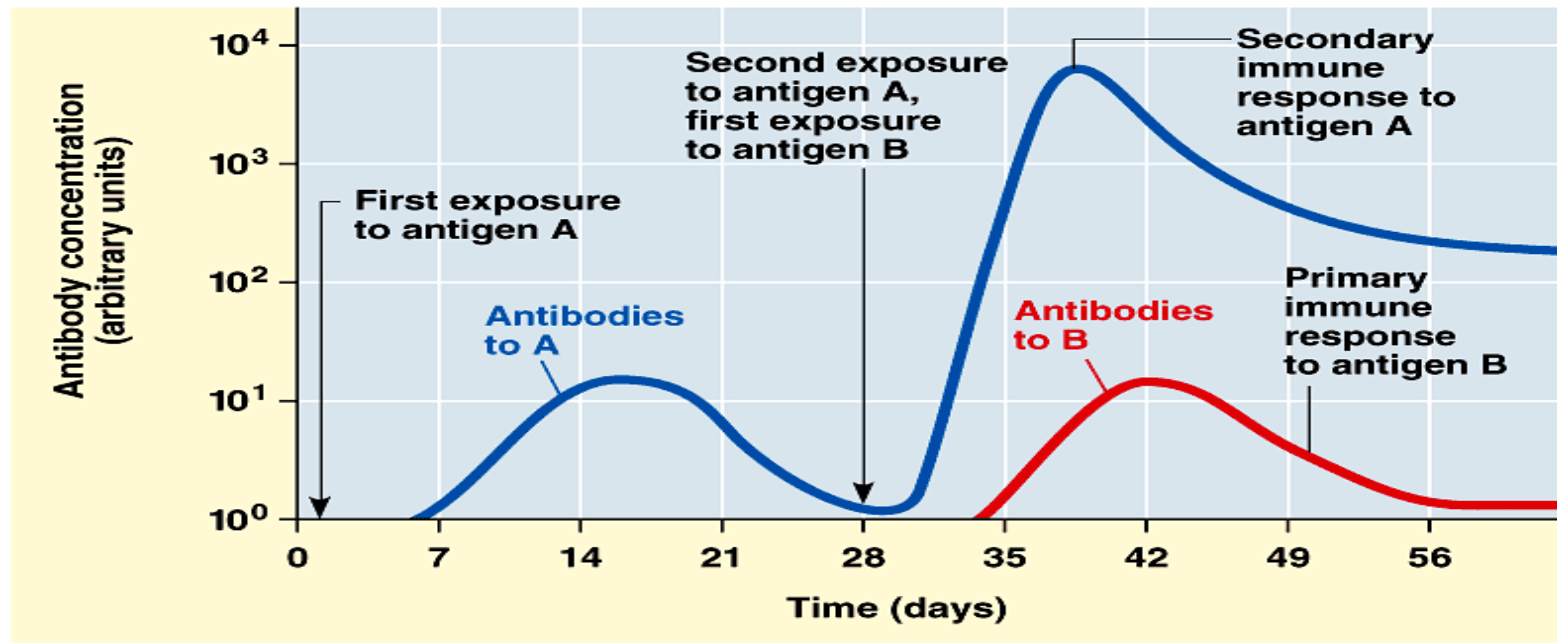
- Effector cells: short-lived cells that combat the antigen
- Memory cells: long-lived cells that bear receptors for the antigen
- Clonal selection: antigen-driven cloning of lymphocytes
- ***“Each antigen, by binding to specific receptors, selectively activates a tiny fraction of cells from the body’s diverse pool of lymphocytes; this relatively small number of selected cells gives rise to clones of thousands of cells, all specific for and dedicated to eliminating the antigen.”***



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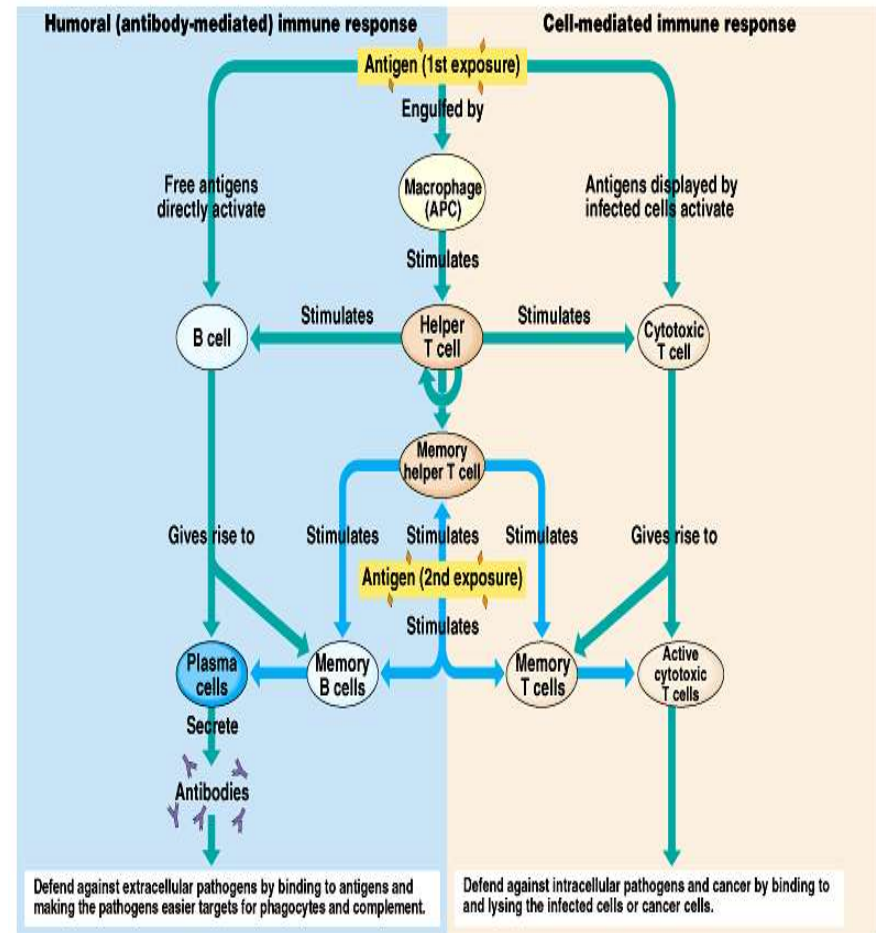
Induction of Immune Responses

- Primary immune response: lymphocyte proliferation and differentiation the 1st time the body is exposed to an antigen
- Plasma cells: antibody-producing effector B-cells
- Secondary immune response: immune response if the individual is exposed to the same antigen at some later time ~ Immunological memory



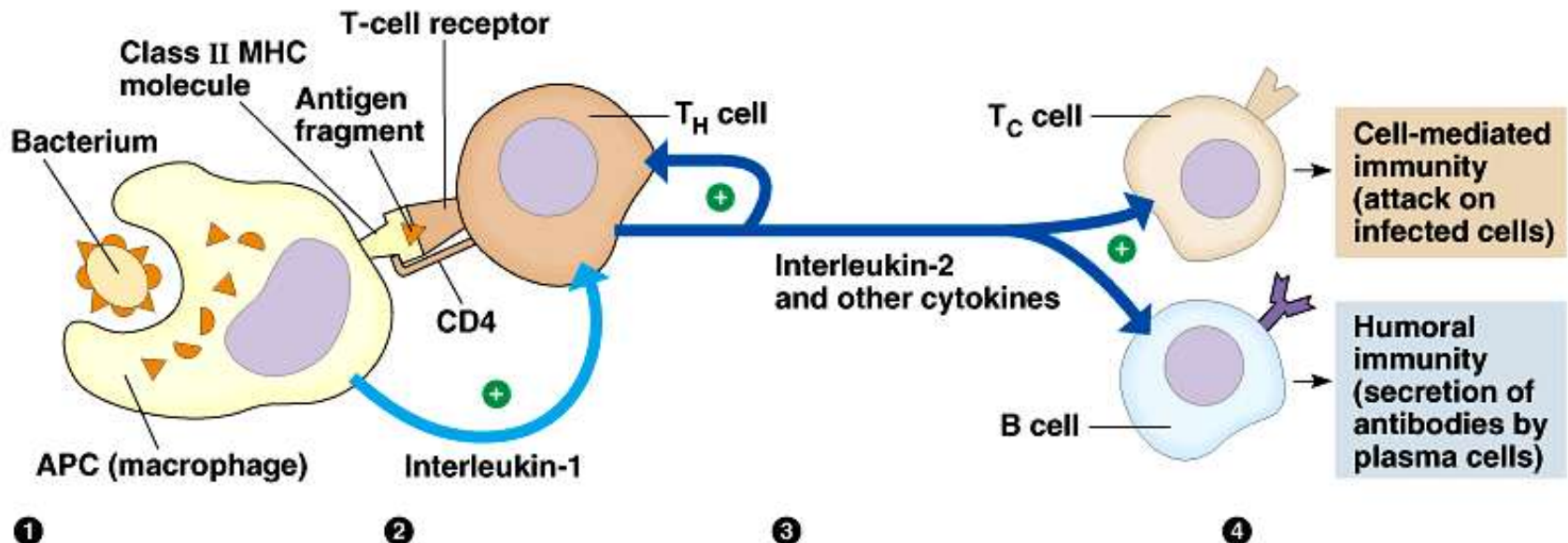
Types of immune responses

- Humoral immunity
- B cell activation
- Production of antibodies
- Defend against bacteria, toxins, and viruses free in the lymph and blood plasma
- Cell-mediated immunity
- T cell activation
- Binds to and/or lyses cells
- Defend against cells infected with bacteria, viruses, fungi, protozoa, and parasites; nonself interaction



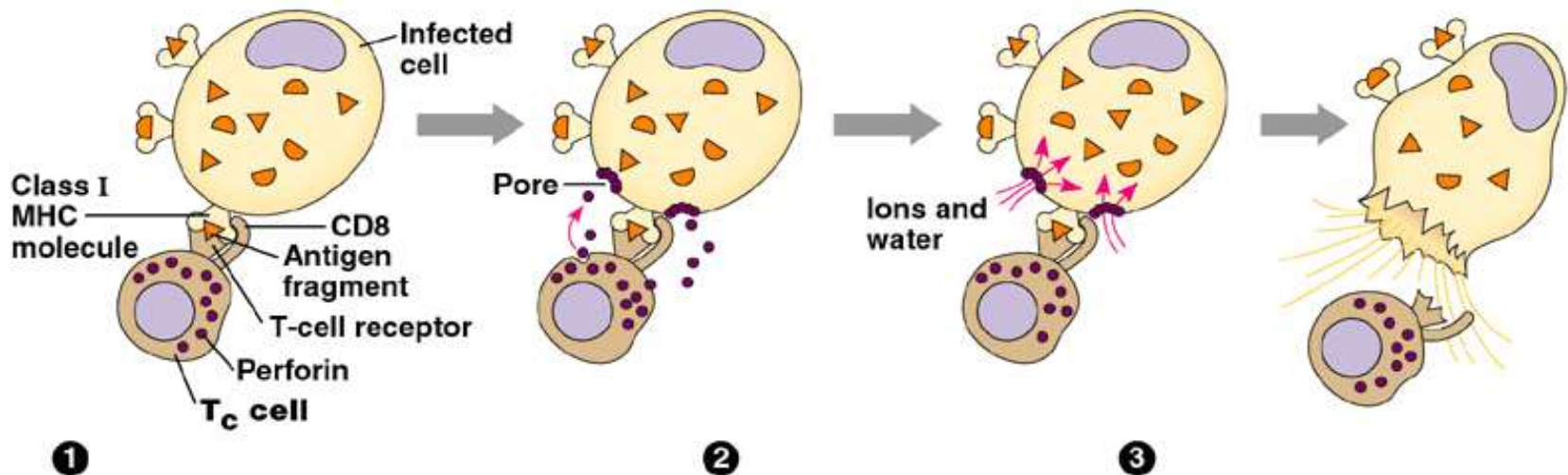
Helper T lymphocytes

- Function in both humoral & cell-mediated immunity
- Stimulated by antigen presenting cells (APCs)
- T cell surface protein CD4 enhances activation
- Cytokines secreted (stimulate other lymphocytes):
 - a) interleukin-2 (IL-2): activates B cells and cytotoxic T cells
 - b) interleukin-1 (IL-1): activates helper T cell to produce IL-2



Cell-mediated: cytotoxic T cells

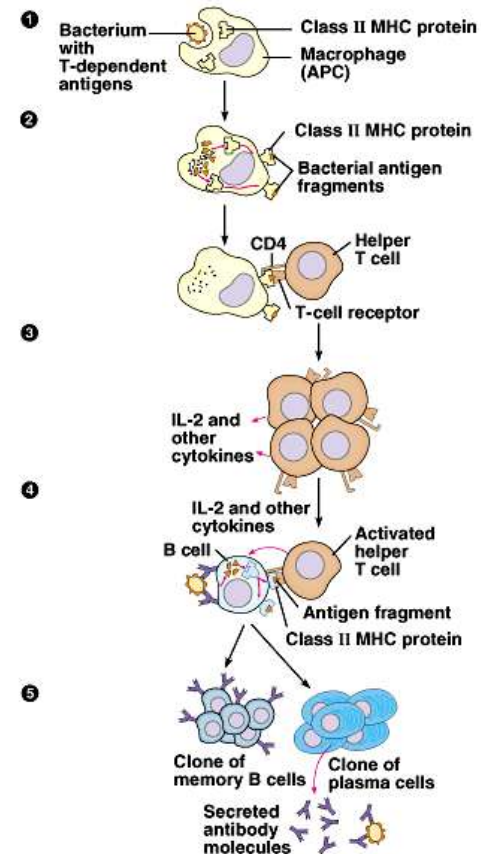
- Destroy cells infected by intracellular pathogens and cancer cells
- Class I MHC molecules (nucleated body cells) expose foreign proteins
- Activity enhanced by CD8 surface protein present on most cytotoxic T cells (similar to CD4 and class II MHC)
- T_c cell releases perforin, a protein that forms pores in the target cell membrane; cell lysis and pathogen exposure to circulating antibodies



(a)

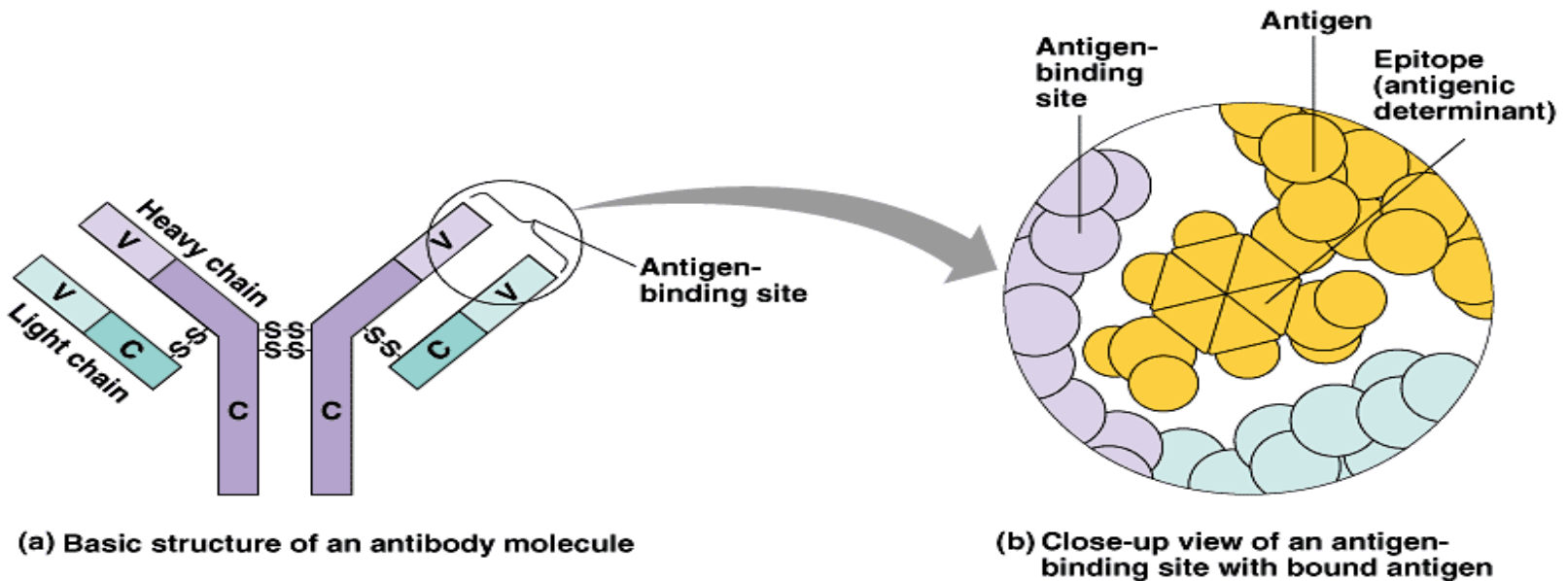
Humoral response: B cells

- Stimulated by T-dependent antigens (help from TH cells)
- Macrophage (APCs) with class II MHC proteins
- Helper T cell (CD4 protein)
- Activated T cell secretes IL-2 (cytokines) that activate B cell
- B cell differentiates into memory and plasma cells (antibodies)



Antibody Structure & Function

- Epitope: region on antigen surface recognized by antibodies
- 2 heavy chains and 2 light chains joined by disulfide bridges
- Antigen-binding site (variable region)

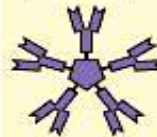


5 classes of Immunoglobulins

- **IgM**: 1st to circulate; indicates infection; too large to cross placenta
- **IgG**: most abundant; crosses walls of blood vessels and placenta; protects against bacteria, viruses, & toxins; activates complement
- **IgA**: produced by cells in mucous membranes; prevent attachment of viruses/bacteria to epithelial surfaces; also found in saliva, tears, and perspiration
- **IgD**: do not activate complement and cannot cross placenta; found on surfaces of B cells; probably help differentiation of B cells into plasma and memory cells
- **IgE**: very large; small quantity; releases histamines-allergic reaction

Table 43.1 The Five Classes of Immunoglobulins

IgM
(pentamer)



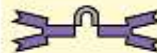
IgMs are the first circulating antibodies to appear in response to an initial exposure to an antigen; their concentration in the blood then declines rapidly. Thus the presence of IgM usually indicates a current infection. IgM consists of five Y-shaped monomers arranged in a pentagonal structure. The numerous antigen-binding sites make it very effective in agglutinating antigens and in reactions involving complement. IgM is too large to cross the placenta and does not confer maternal immunity.

IgG
(monomer)



IgG is the most abundant of the circulating antibodies. It readily crosses the walls of blood vessels and enters tissue fluids. IgG also crosses the placenta and confers passive immunity on the fetus. IgG protects against bacteria, viruses, and toxins in the blood and lymph, and triggers action of the complement system.

IgA
(dimer)



IgA is produced by cells in mucous membranes. The main function of IgA is to prevent the attachment of viruses and bacteria to epithelial surfaces. IgA is also found in many body secretions, such as saliva, perspiration, and tears. Its presence in the first milk produced helps protect the infant from gastrointestinal infections.

IgD
(monomer)



IgD antibodies do not activate the complement system and cannot cross the placenta. They are mostly found on the surfaces of B cells, probably functioning as antigen receptors that help initiate the differentiation of B cells into plasma cells and memory B cells.

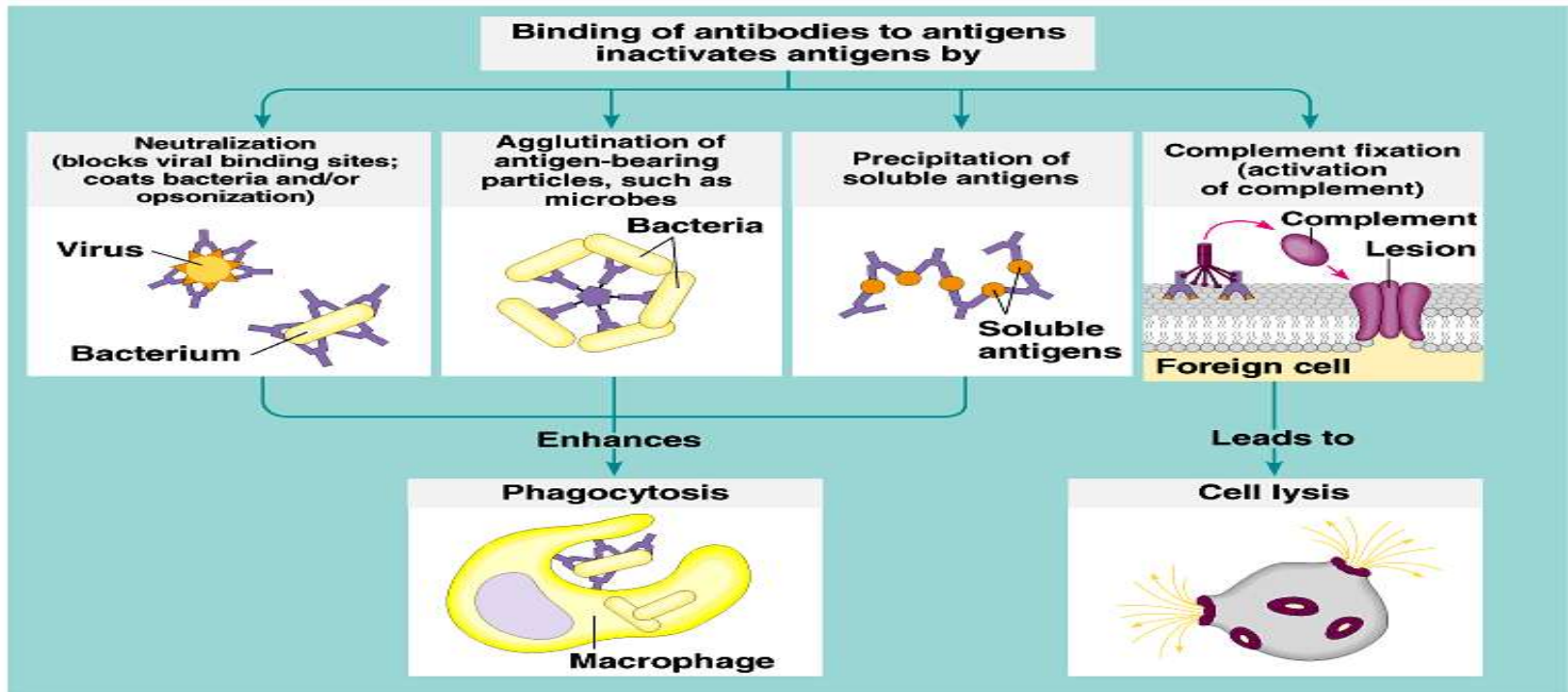
IgE
(monomer)



IgE molecules are slightly larger than IgG and represent only a small fraction of the antibodies in the blood. The tails attach to mast cells and basophils and, when triggered by an antigen, cause the cells to release histamine and other chemicals that cause an allergic reaction.

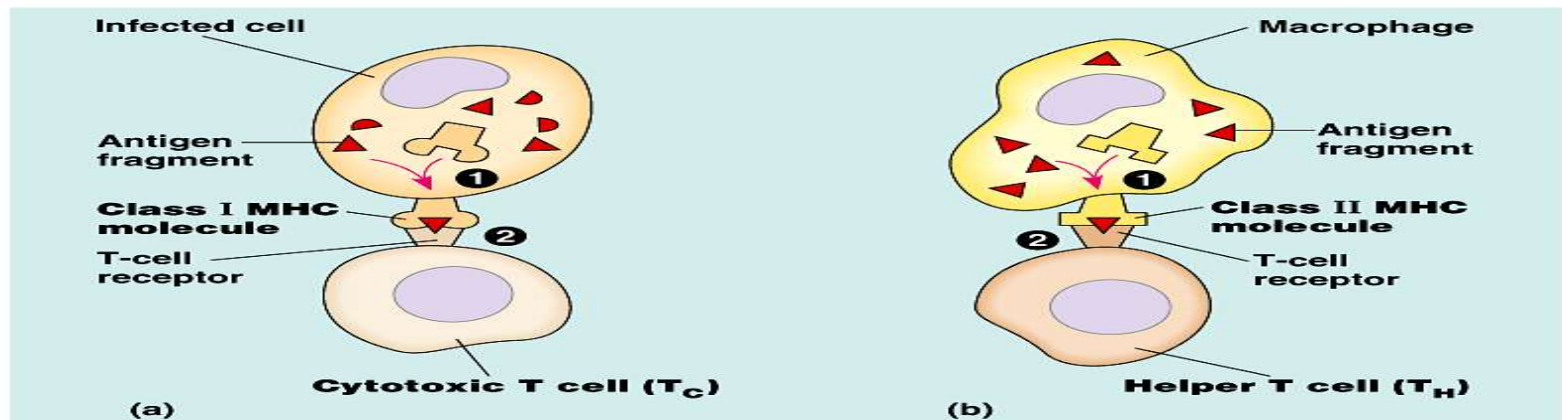
Antibody-mediated Antigen Disposal

- Neutralization (opsonization): antibody binds to and blocks antigen activity
- Agglutination: antigen clumping
- Precipitation: cross-linking of soluble antigens
- Complement fixation: activation of 20 serum proteins, through cascading action, lyse viruses and pathogenic cells



Self/Nonself Recognition

- Self-tolerance: capacity to distinguish self from non-self
- Autoimmune diseases: failure of self-tolerance; multiple sclerosis, lupus, rheumatoid arthritis, insulin-dependent diabetes mellitus
- Major Histocompatibility Complex (MHC): body cell surface antigens coded by a family of genes
- Class I MHC molecules: found on all nucleated cells
- Class II MHC molecules: found on macrophages, B cells, and activated T cells
- Antigen presentation: process by which an MHC molecule “presents” an intracellular protein to an antigen receptor on a nearby T cell
- Cytotoxic T cells (T_C): bind to protein fragments displayed on class I MHC molecules
- Helper T cells (T_H): bind to proteins displayed by class II MHC molecules



Immunity in Health & Disease

- Active immunity/natural: conferred immunity by recovering from disease
- Active immunity/artificial: immunization and vaccination; produces a primary response
- Passive immunity: transfer of immunity from one individual to another
 - natural: mother to fetus; breast milk
 - artificial: rabies antibodies
- ABO blood groups (antigen presence)
- Rh factor (blood cell antigen); Rh-mother vs. an Rh+ fetus (inherited from father)



Abnormal immune function

- Allergies (anaphylactic shock): hypersensitive responses to environmental antigens (allergens); causes dilation and blood vessel permeability (antihistamines); epinephrine
- Autoimmune disease: multiple sclerosis, lupus, rheumatoid arthritis, insulin-dependent diabetes mellitus
- Immunodeficiency disease: SCIDS (bubble-boy); A.I.D.S.

