Lymphocytes

Play major role in immunity

GENESIS

1.Lymphoblast:15-20 micrometer

Large nucleus with rarely more than 2 distinct nucleoli

Cytoplasm is blue as a narrow rim around the large nucleus

Prolymphocyte :

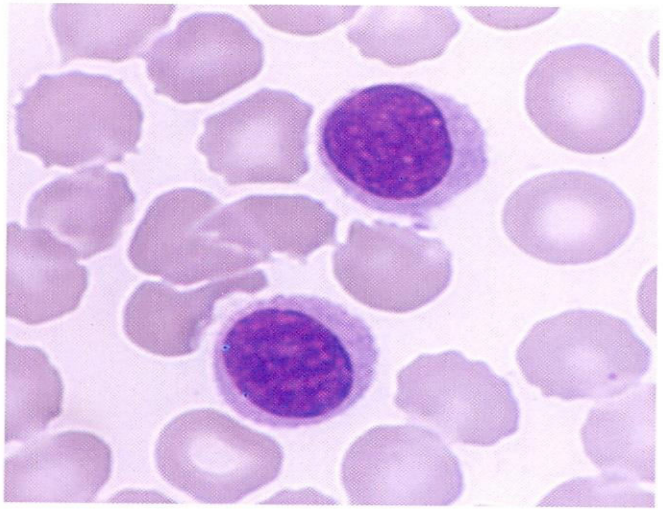
Prolymphocyte :

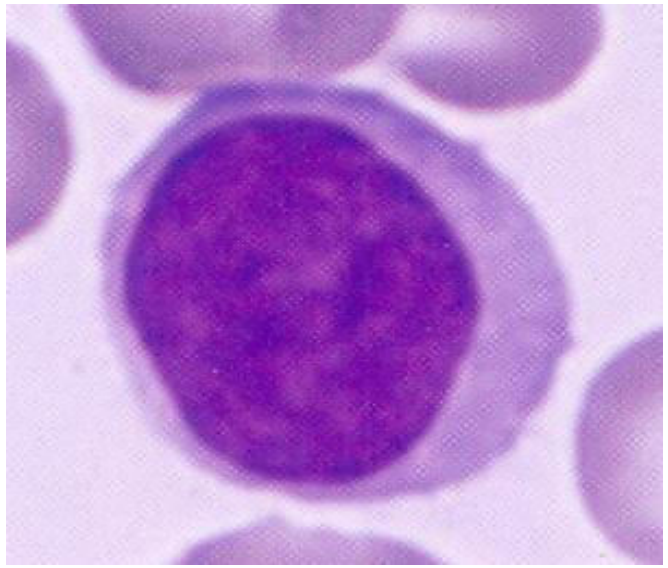
Cell and nucleus become smaller,

nucleoli distinct, cytoplasm less basophilic

Mature lymphocyte

- 9-14 micrometer
- Nucleus round but may be slightly indented or eccentric deep purplish blue and is composed of dense chromatin aggregates
- Cytoplasm is light blue present as thin rim around the nucleus or may be quite abundant depending on size
- Relative count 30%





LYMPHOCYTES

T lymphocytes---cause direct destruction of virus invaded cells and mutant cells through non phagocytic means → Cell mediated immunity

B lymphocytes---secrete antibodies that indirectly lead to the destruction of foreign material → Humoral immunity

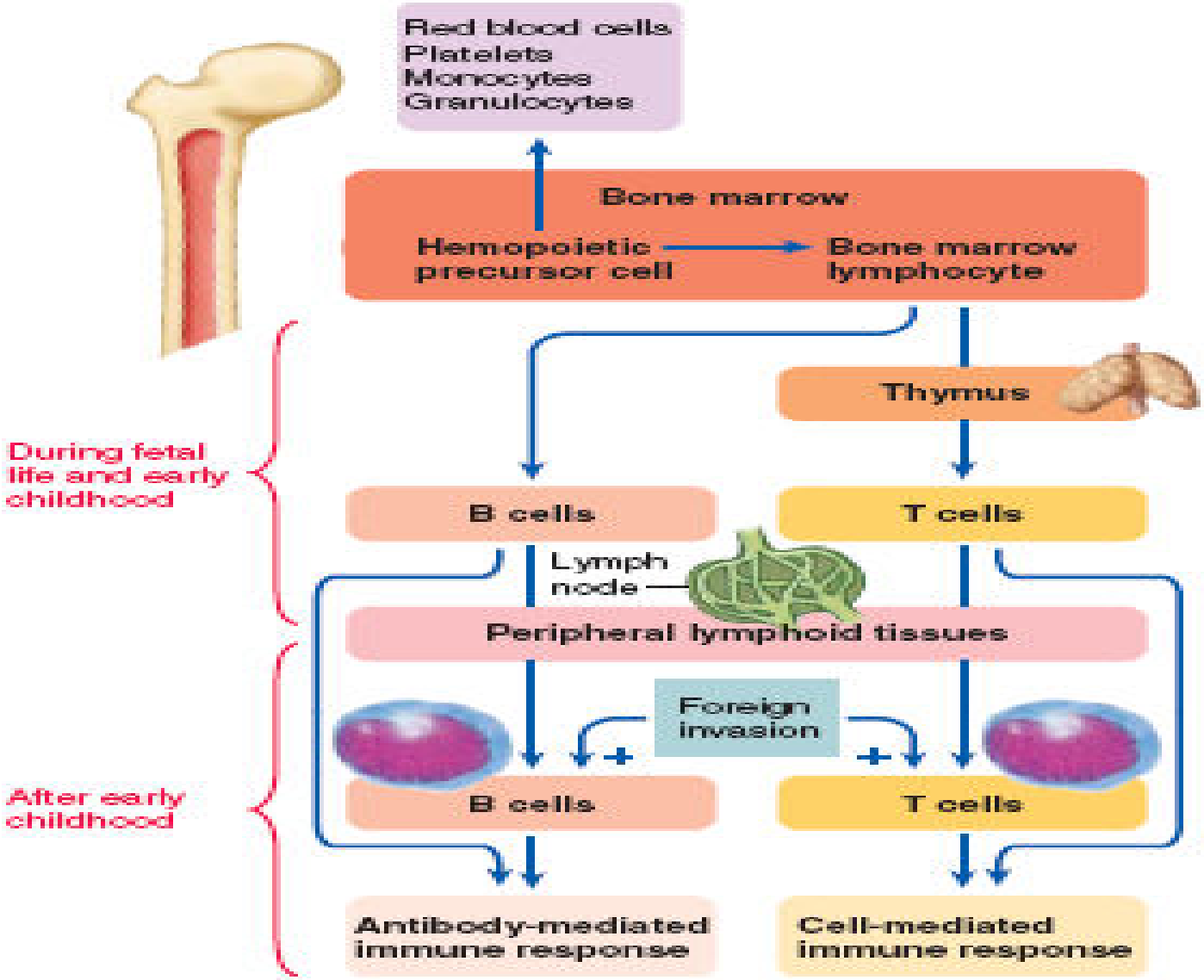
Thymus Gland preprocesses T lymphocytes

- Preprocessing occurs shortly before birth and for a few months after birth.
- T cells after origination from bone marrow migrate to thymus where they divide rapidly and develop extreme diversity.
- Thymus makes certain that T cell leaving it will not react with proteins or antigens present in the body's own tissues.
- After preprocessing migrate to lymphoid tissues

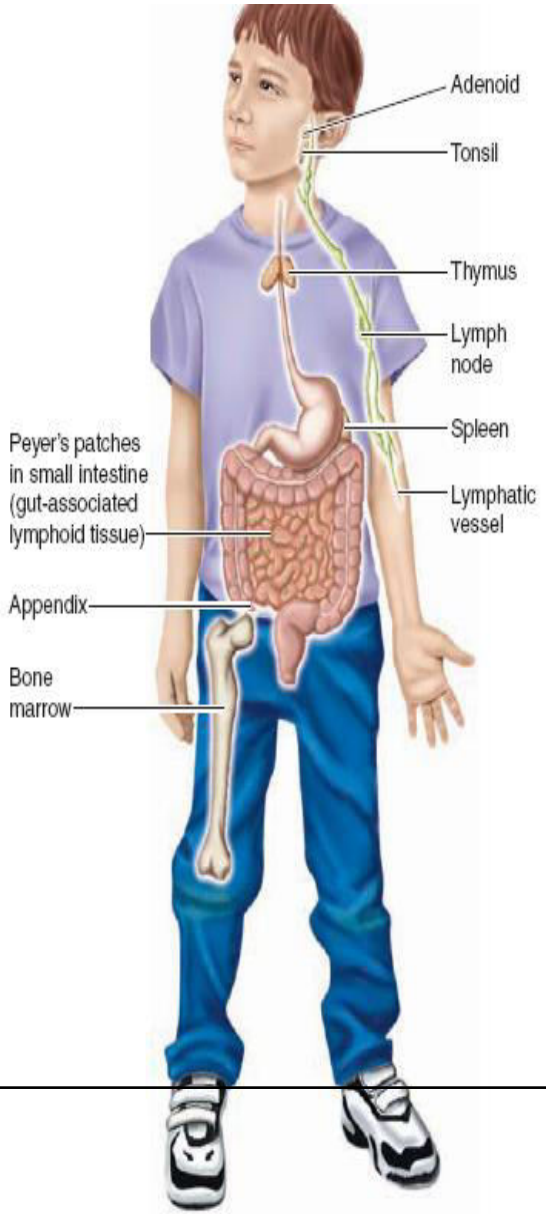
Bone marrow and liver preprocesses B lymphocytes

- Liver---in mid-fetal life
- Bone marrow---late fetal and after birth
- B cells secrete antibodies and have greater diversity
- After preprocessing migrate to lymphoid tissues where they lodge near but slightly removed from T lymphocytes
- Def of Abs

Origin of T and B Lymphocytes



Lymphoid Tissue



- Bone marrow
- Thymus
- Tonsils and Adenoids
- Spleen
- Lymph node
- Gut associated lymphoid tissue(GALT) e.g. tonsils, appendix, payer's patches
- Lymphatic channels

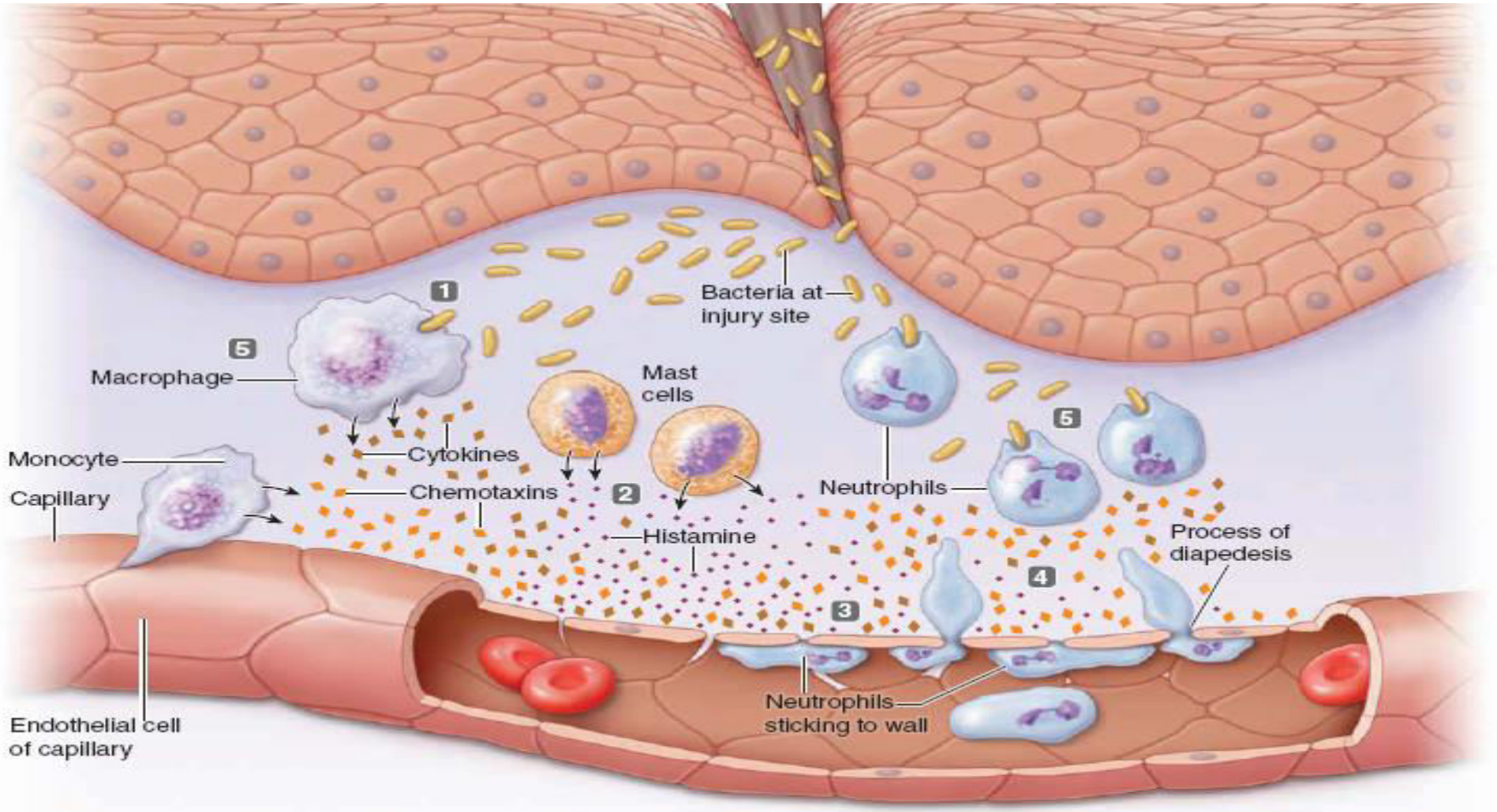
Blood– 2% of total body lymphocytes

Lymphocytosis

Increased number of lymphocytes in blood

Causes

- Infants and young children up to 4 years age
- Under nutrition, rickets, scurvy
- Lymphatic leukemia, whooping cough
- Influenza ,tuberculosis, typhoid, mumps, measles, chicken pox



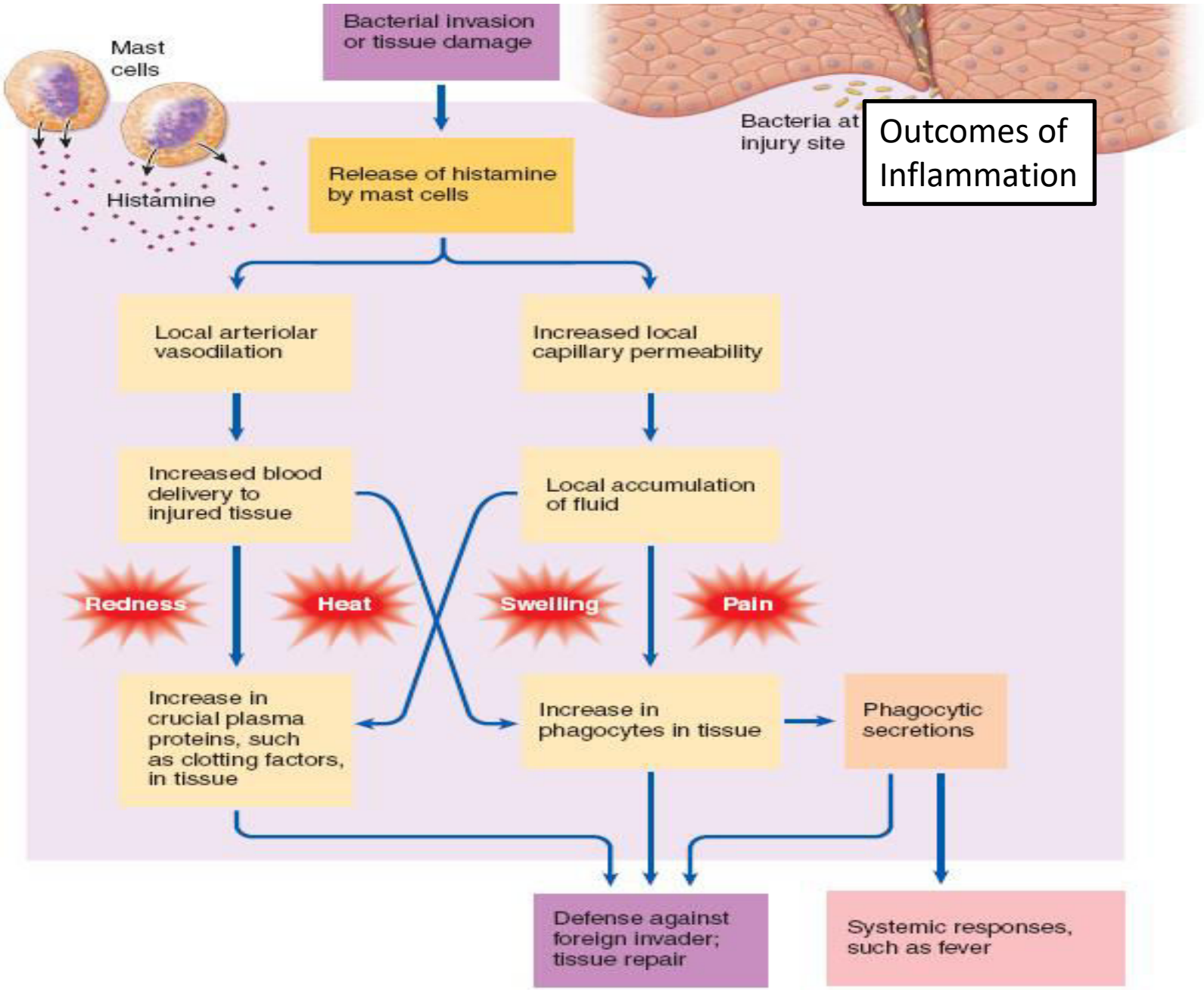
1 A break in the skin introduces bacteria, which reproduce at the wound site. Activated resident macrophages engulf the pathogens and secrete cytokines and chemotaxins.

2 Activated mast cells release histamine.

3 Histamine and cytokines dilate local blood vessels and widen the capillary pores. The cytokines also make the blood vessel wall sticky, causing neutrophils and monocytes to attach.

4 Chemotaxins attract neutrophils and monocytes, which squeeze out between cells of the blood vessel wall, a process called diapedesis, and migrate to the infection site.

5 Monocytes enlarge into macrophages. Newly arriving macrophages and neutrophils engulf the pathogens and destroy them.



IMMUNITY

The capability to resist almost all type of organisms or toxins that tend to damage tissues or organs.

Immune responses may be either

- Innate or non-specific results from general processes
- Acquired or adaptive or specific does not develop until after the body is first exposed by bacterium, virus or toxin and often requires weeks or months to develop

Innate Immunity

- Phagocytosis
- Inflammation
- Acid secretions of stomach and digestive enzymes
- Skin
- Chemical compounds attached to foreign organisms and toxins e .g. lysozymes, basic polypeptides, complement system, natural killer cells, interferons

Acquired Immunity

Is caused by immune system that form antibodies and/ or activated lymphocytes that attack and destroy the specific invading organism or toxin

- Passive immunity--- produced by already made antibodies or activated T cells from horse or human serum
- Active immunity--- a person itself produces an immune reaction in response to the entry of antigens into the body

Active Immunity

- **Humoral Immunity**

  B lymphocytes produce gamma globulins called immnoglobulins or antibodies
- **Cell mediated Immunity**

  T lymphocytes become activated

Both forms of active immunity are initiated

by ANTIGENS

ANTIGENS

- Antigen means antibody generation
- An antigen is a foreign molecule that triggers a specific immune response against itself, such as generation of antibodies that leads to its destruction when it gains entry into the body.
- Proteins highly antigenic –size and structural complexity, large polysaccharides, lipids

Clones of Lymphocytes

- All the different lymphocytes capable of forming one specifity of antibodies or T lymphocytes are called a clone of lymphocytes
- On surface of B cells membrane highly specific 100,000 Abs and on surface of T cells membrane highly specific “surface receptor proteins” or “T cell markers”are present
- When exposed T and B cells activated

Role of Macrophages in activation process

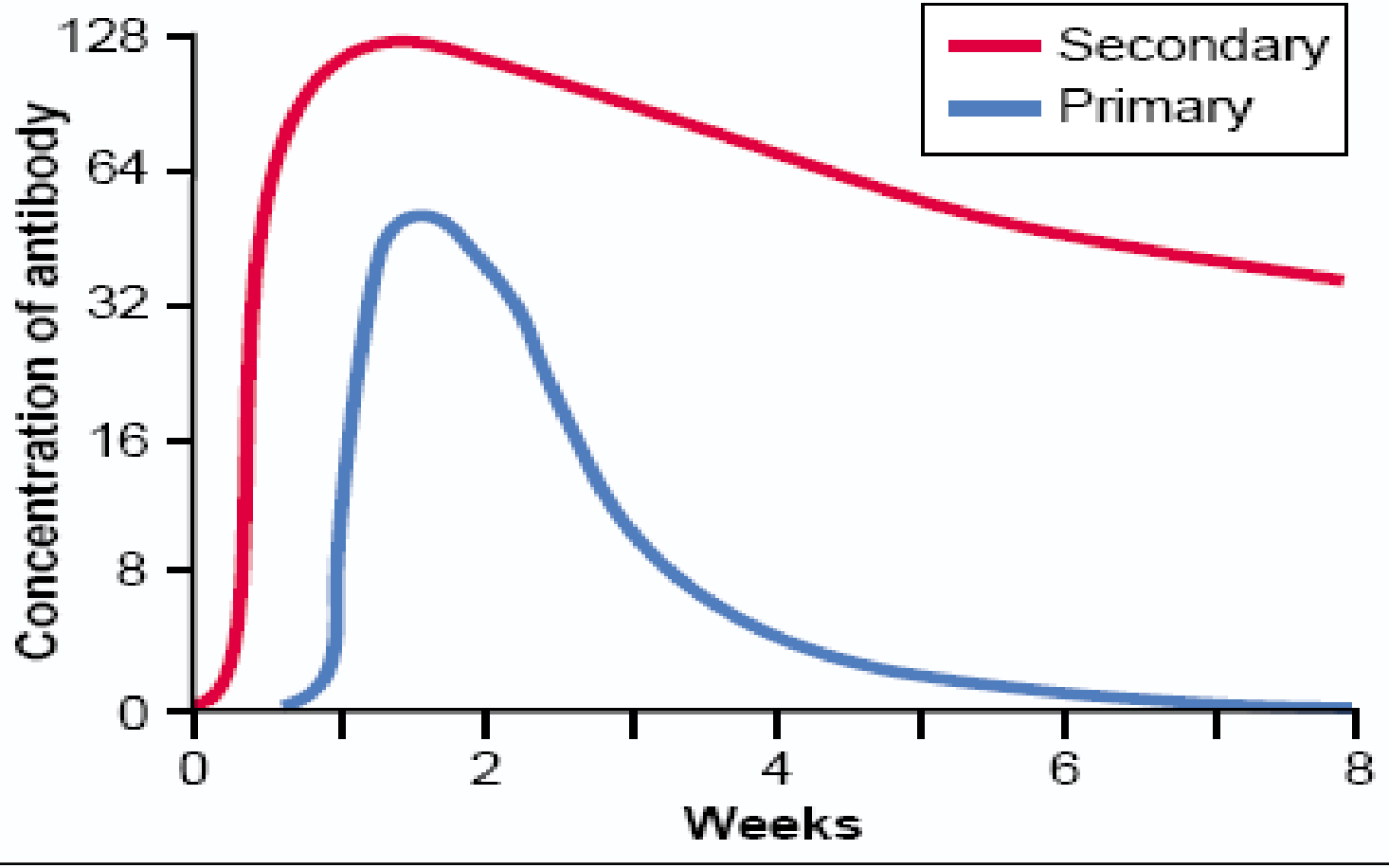
- Macrophages present in tissues, phagocytose and partially digest Ag and pass antigenic products by cell to cell contact directly to lymphocytes, leading to activation of specified lymphocytic clones
- They also secrete Interleukin-1 which promotes still further growth and reproduction of specific lymphocytes

Formation of Antibodies

- Stored lymphocytes → Appearance of lymphoblast → Plasmablast → Plasma cells----

  Produce 2000 molecules of Abs / second → secreted into lymph → enter general circulation → after several days or weeks plasma cell dies.
- Some lymphocytes form new lymphocytes-- Memory cells

Primary and Secondary Response



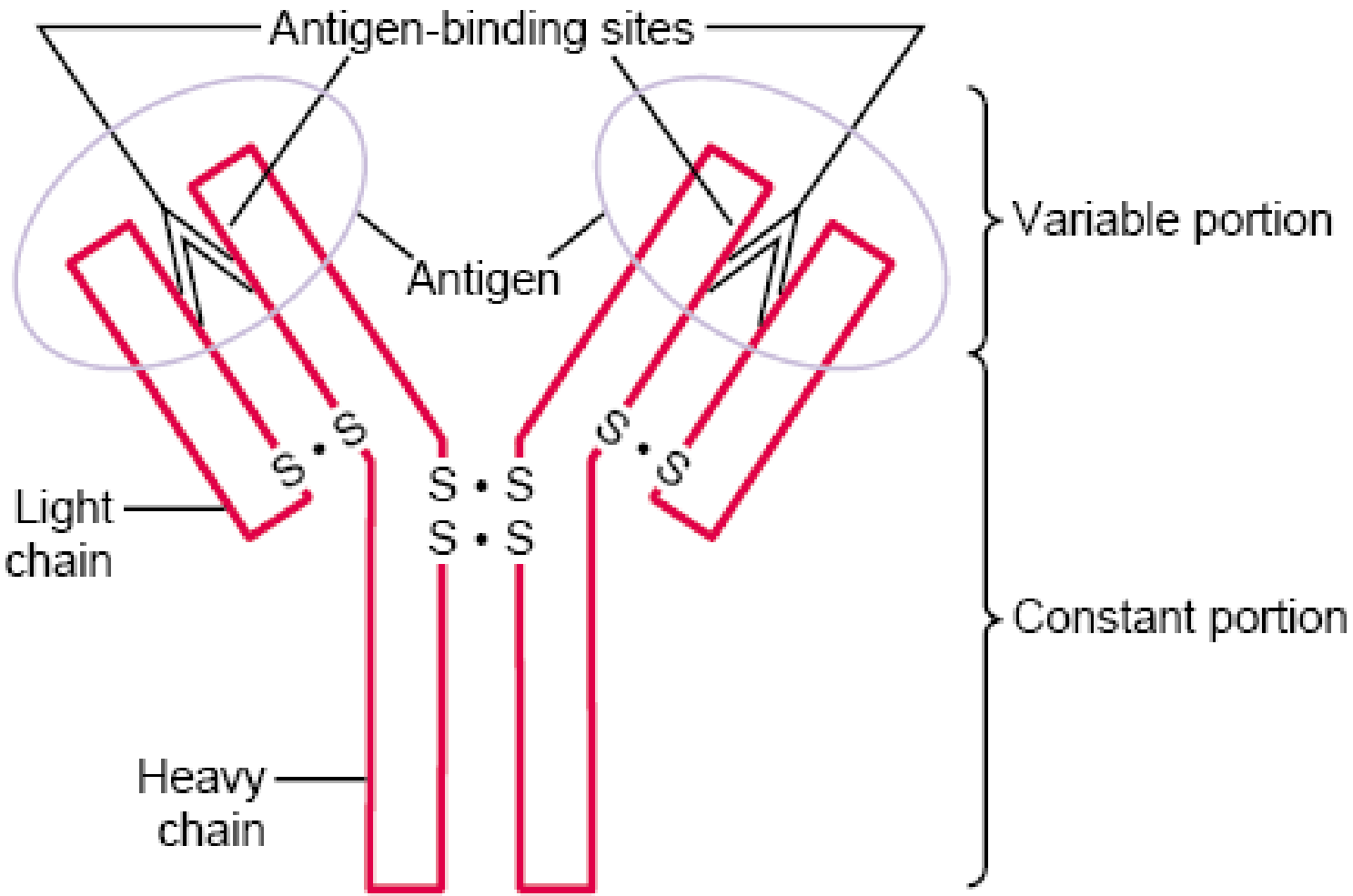
Immunization

- By injecting dead organisms– typhoid fever, whooping cough, diphtheria
- By treating toxins– tetanus, botulism
- By injecting live attenuated organisms– poliomyelitis, yellow fever, measles, small pox and many other viral infections

Classes of Antibodies

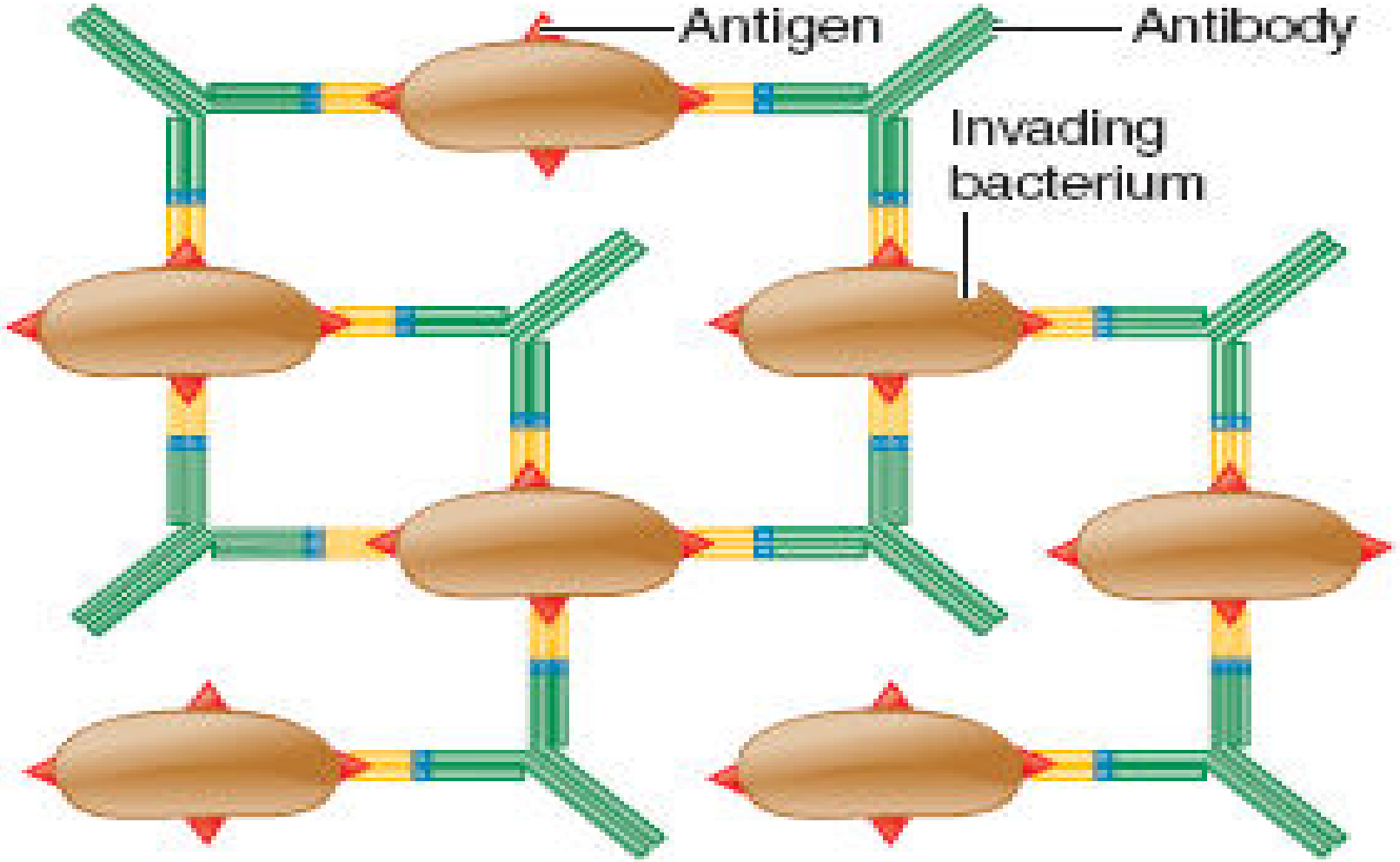
1. Immunoglobulin G (IgG)---makes up75% of the serum Abs, Abs of secondary response, give immunity to infants
2. Immunoglobulin A (IgA)---external secretions of body such as saliva, tears, breast milk, bronchial and intestinal mucus
3. Immunoglobulin E(IgE)---allergic responses
4. Immunoglobulin M (IgM)--- primary immune response, Abs that react with blood group antigens
5. Immunoglobulin D (IgD)---present on surface of B lymphocytes along with IgM , role not clear

Structure of a typical IgG

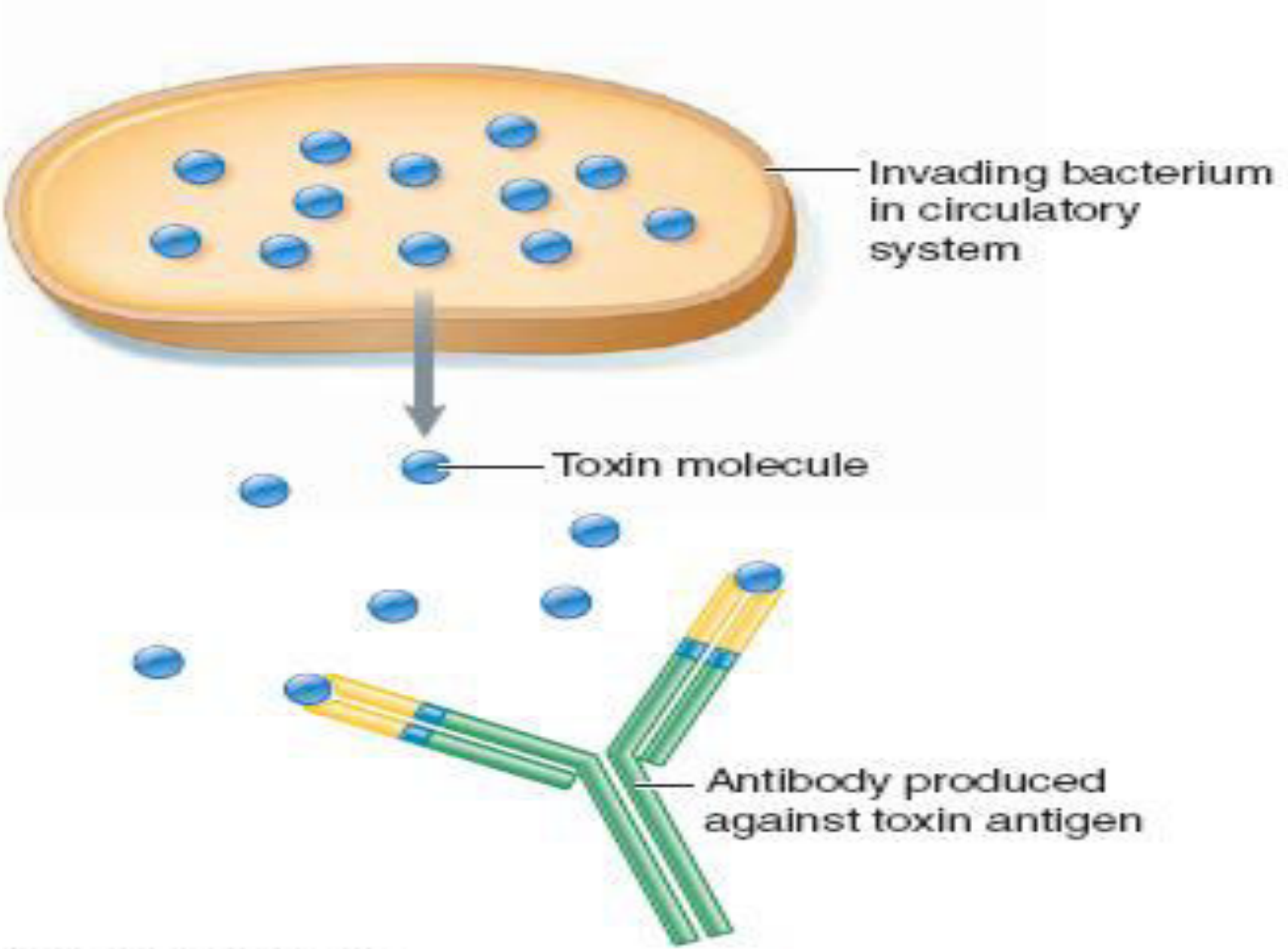


Mechanism of action of Abs

- By direct attack on invader
  - Agglutination
  - Precipitation
  - Neutralization
  - Lysis
- By complement system

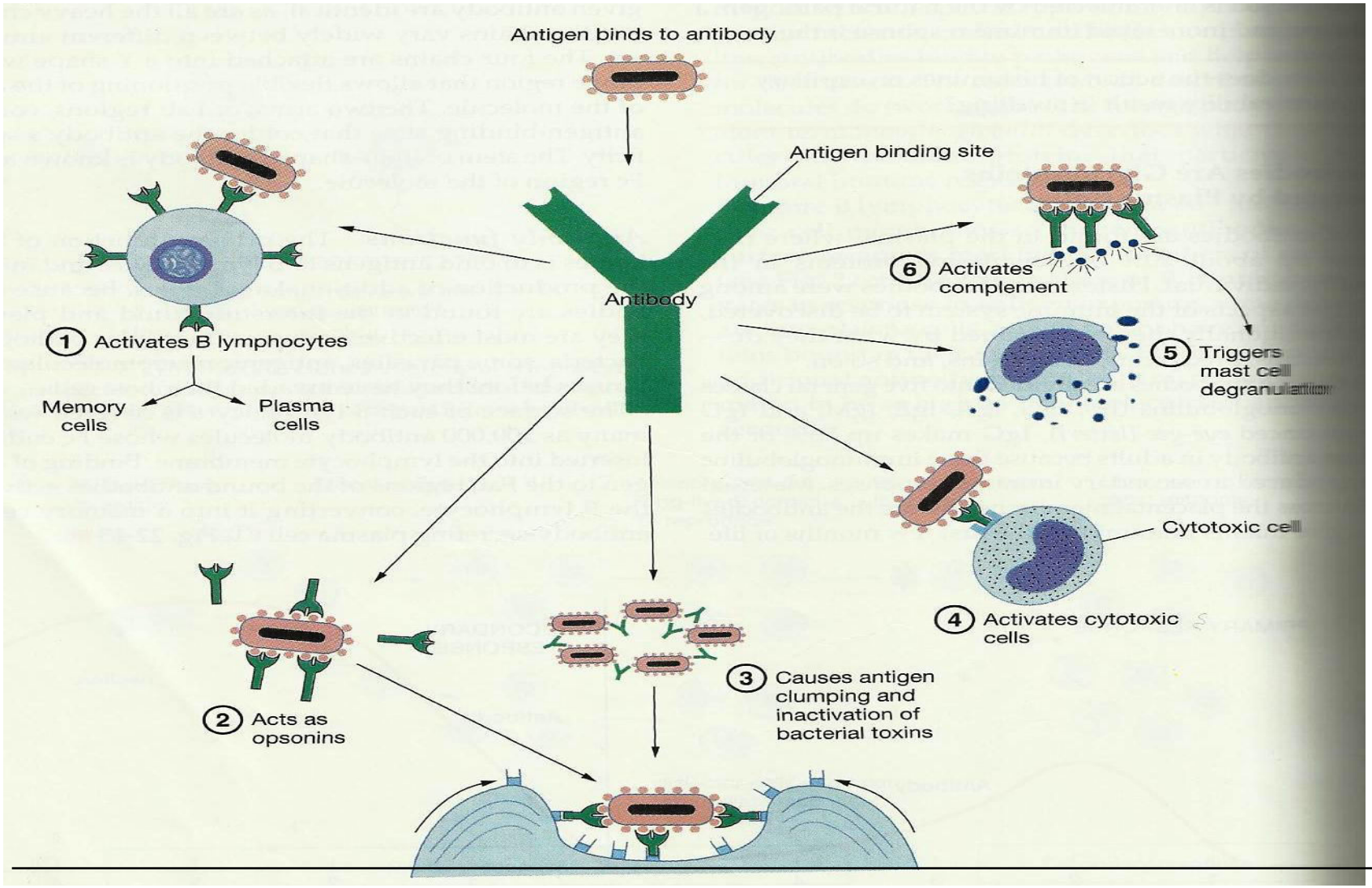


(b) **Agglutination** (clumping of antigenic cells) and **precipitation** (if soluble antigen–antibody complex is too large to stay in solution)



(a) Neutralization

Functions of Antibodies

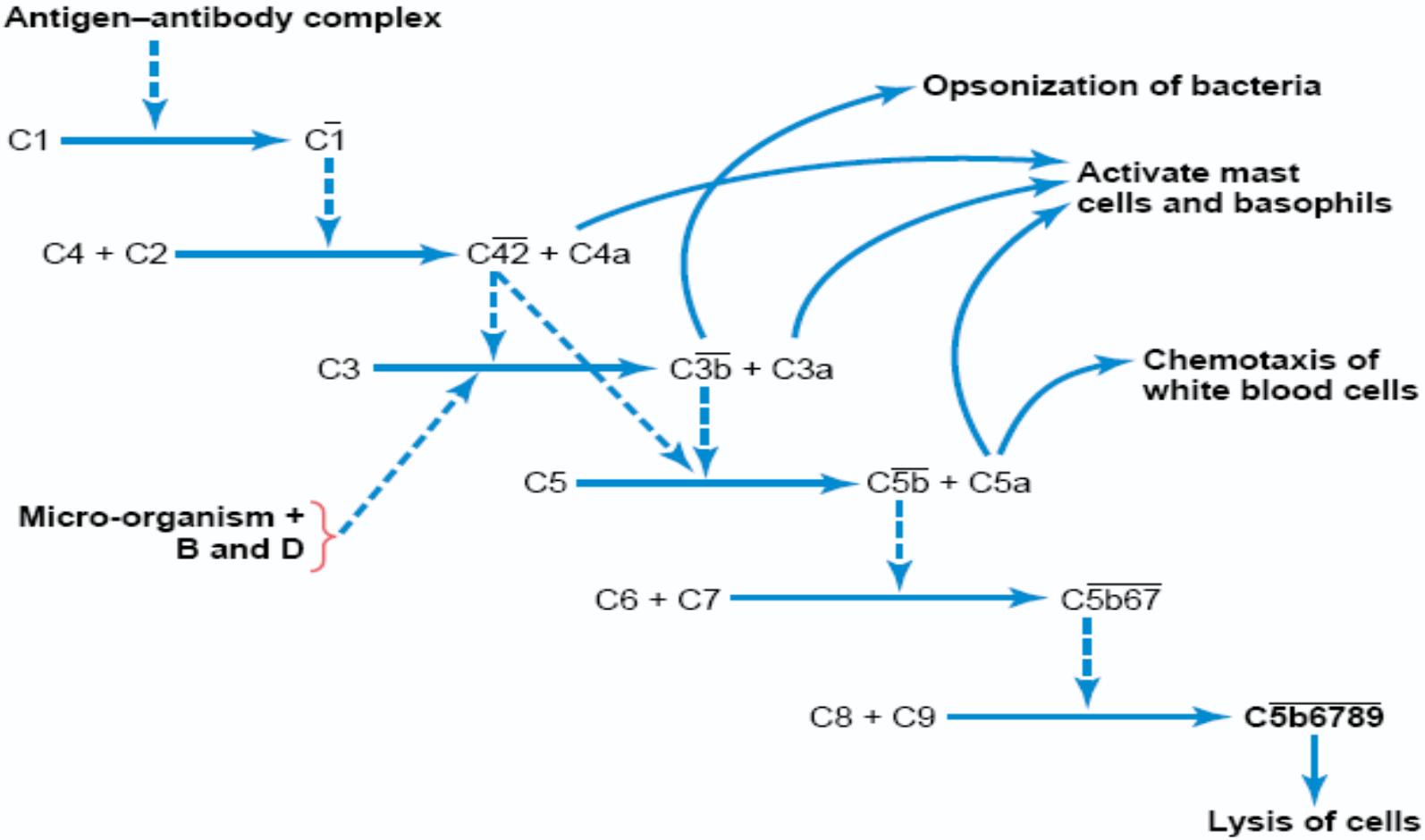


Complement System

- System of about 25-30 proteins

- Present normally among the plasma proteins in blood as well as among the proteins that leak out of the capillaries into the tissue spaces

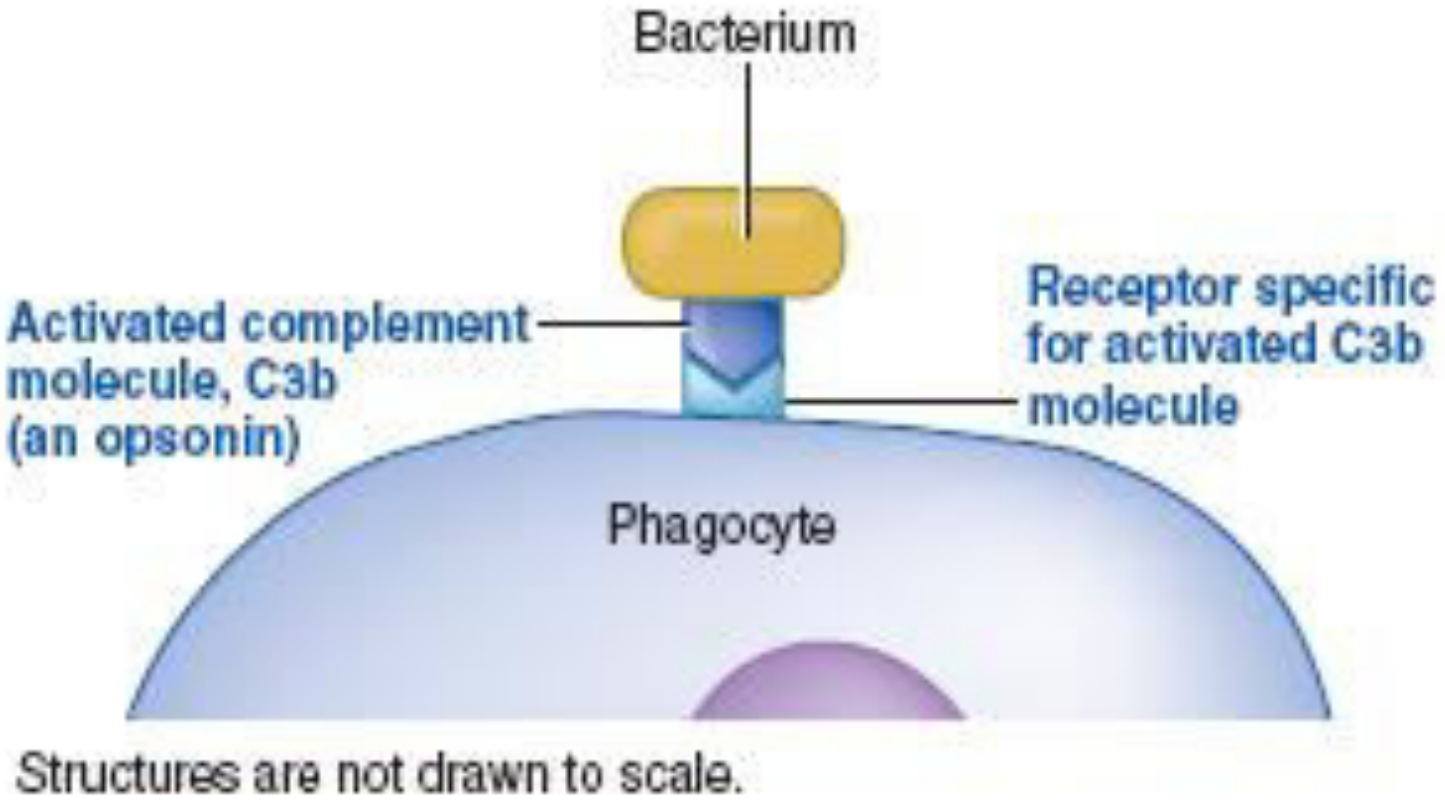
Complement System



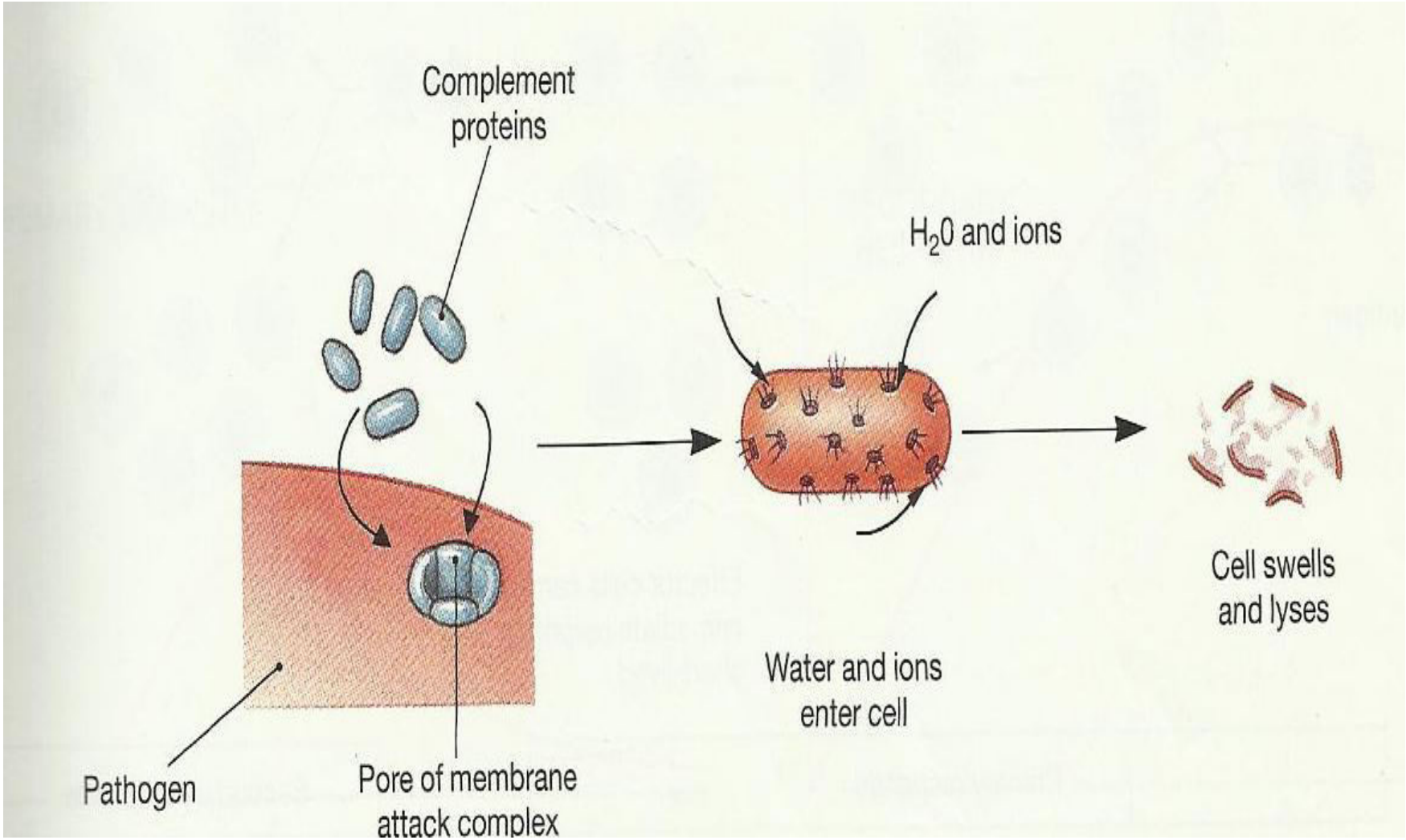
Important Effects of Complement System

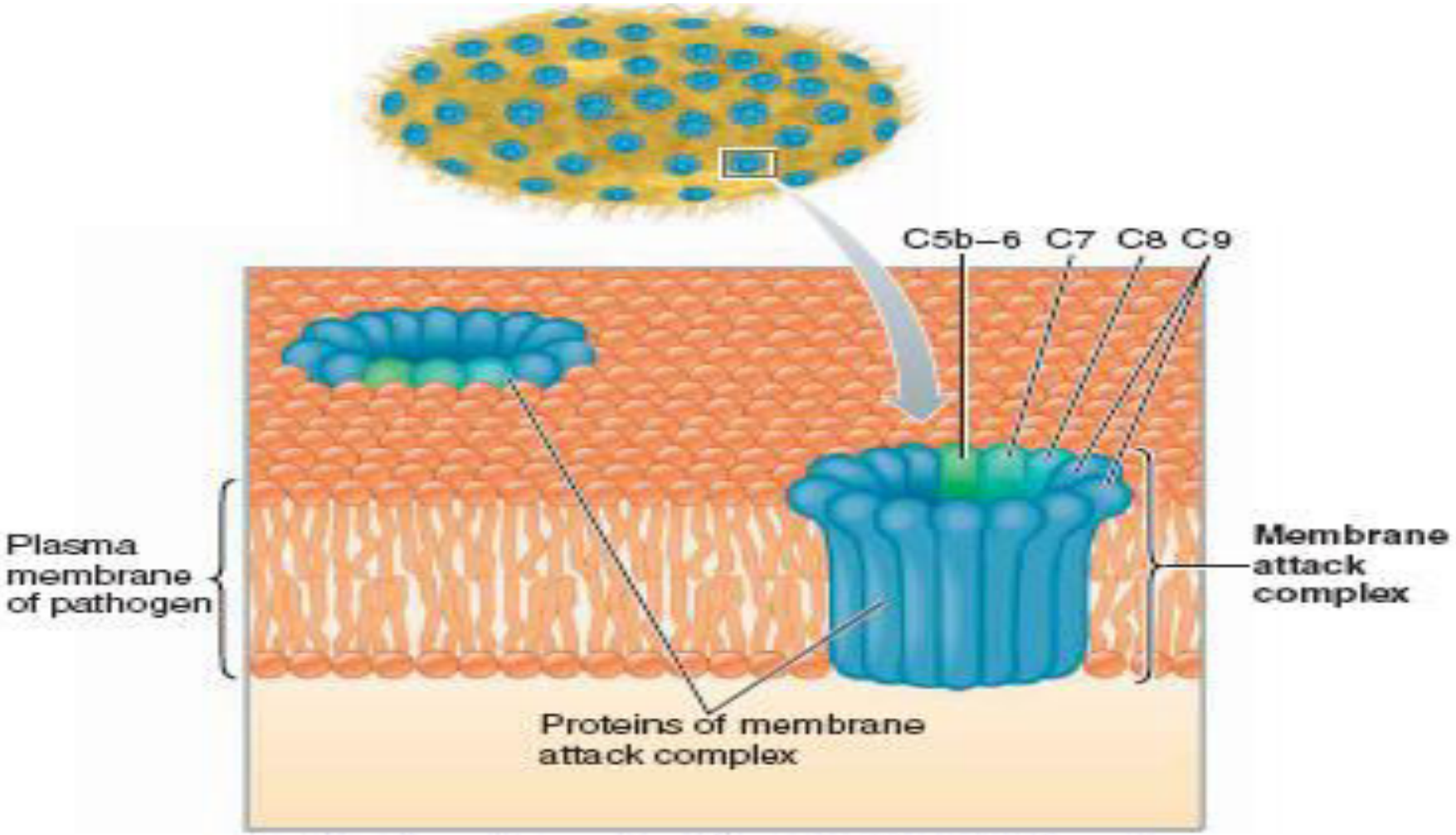
- Opsonization and phagocytosis
- Lysis
- Neutralization
- Agglutination of viruses
- Chemotaxis
- Activation of mast cells and basophils
- Inflammatory effects

Opsonization



Membrane attack complex or Lytic complex





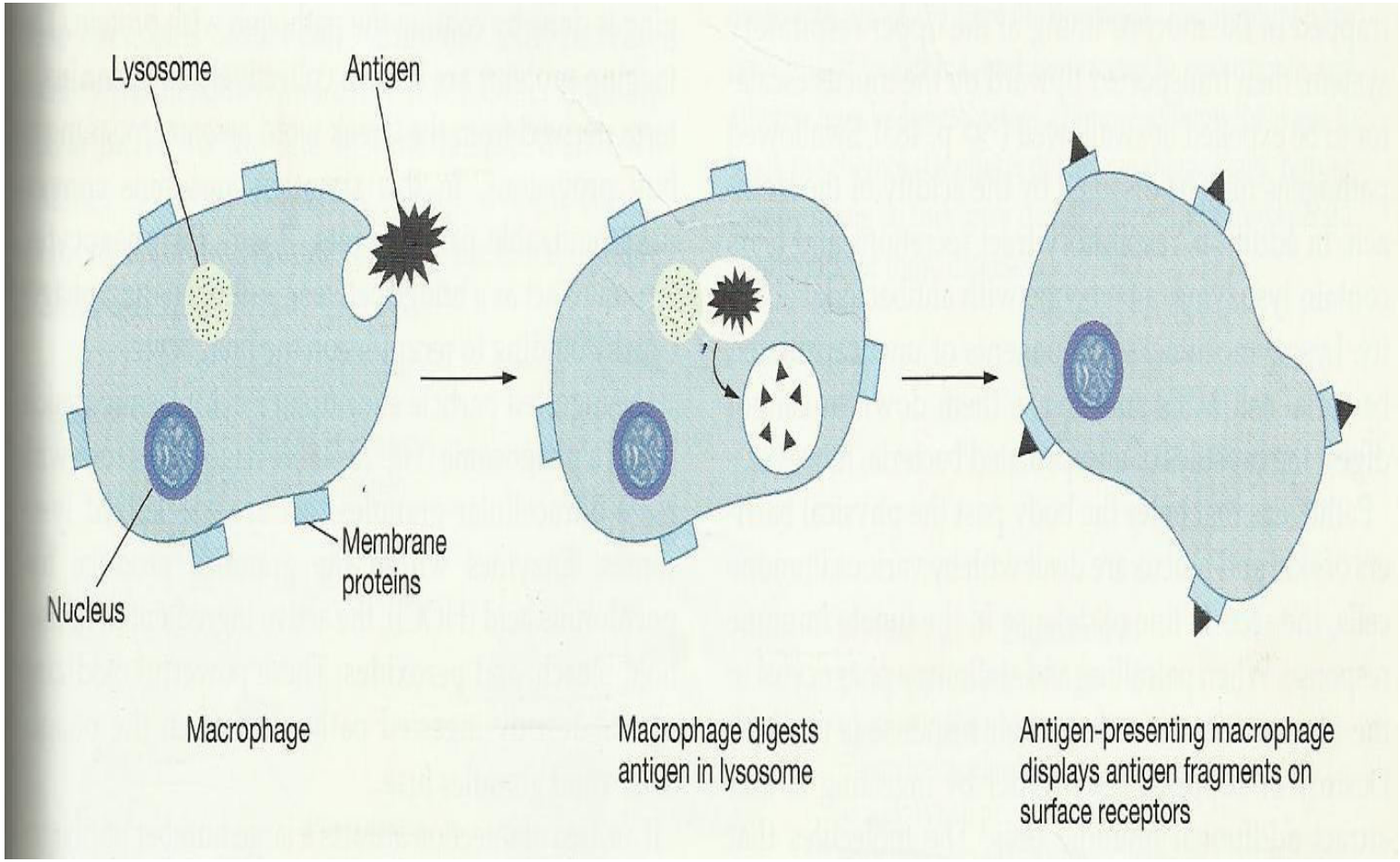
Activated complement proteins C5, C6, C7, C8, and a number of C9s aggregate to form a porelike channel in the plasma membrane of the target cell. The resulting leakage leads to destruction of the cell.

(b) Formation of membrane attack complex

Role of Macrophages in activation process

- Macrophages present in tissues, phagocytose and partially digest Ag and pass antigenic products by cell to cell contact directly to lymphocytes, leading to activation of specified lymphocytic clones
- They also secrete Interleukin-1 which promotes still further growth and reproduction of specific lymphocytes

Antigen presenting Cell

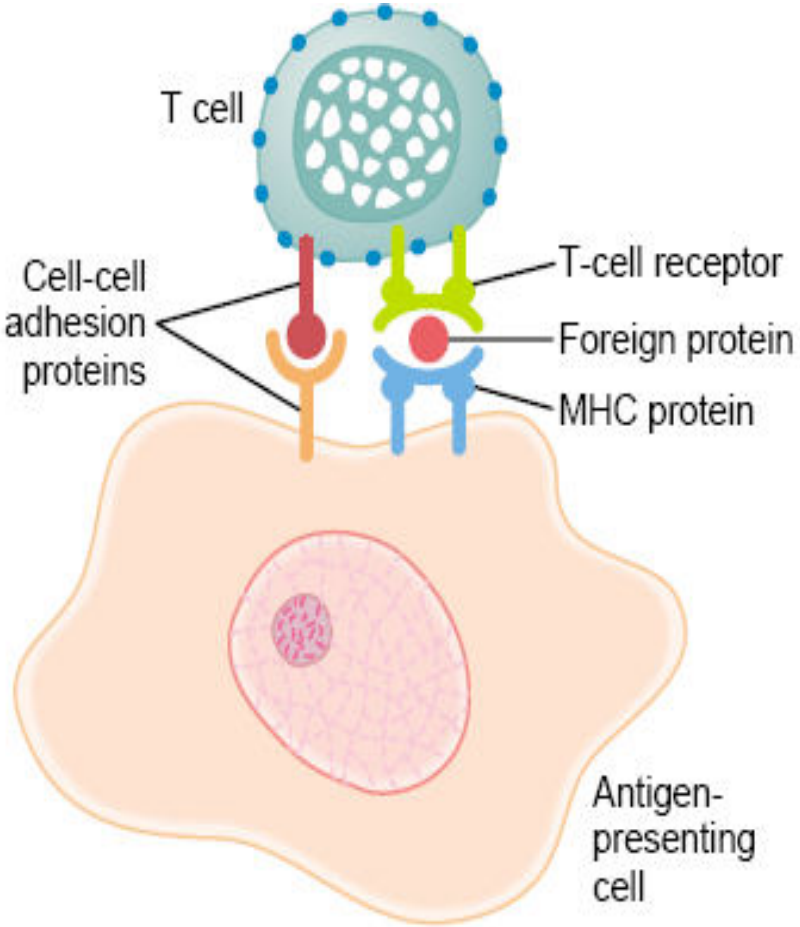


Antigen Presenting Cell(APC)

- Macrophages
- B lymphocytes
- Dendritic cells in spleen and lymph nodes
- Langerhan's cells in skin

MHC I proteins present antigen to cytotoxic T cells

MHC II proteins present antigen to helper T cells



David Scharf/Peter Arnold, Inc.

FIGURE 12-18 Dendritic cell.

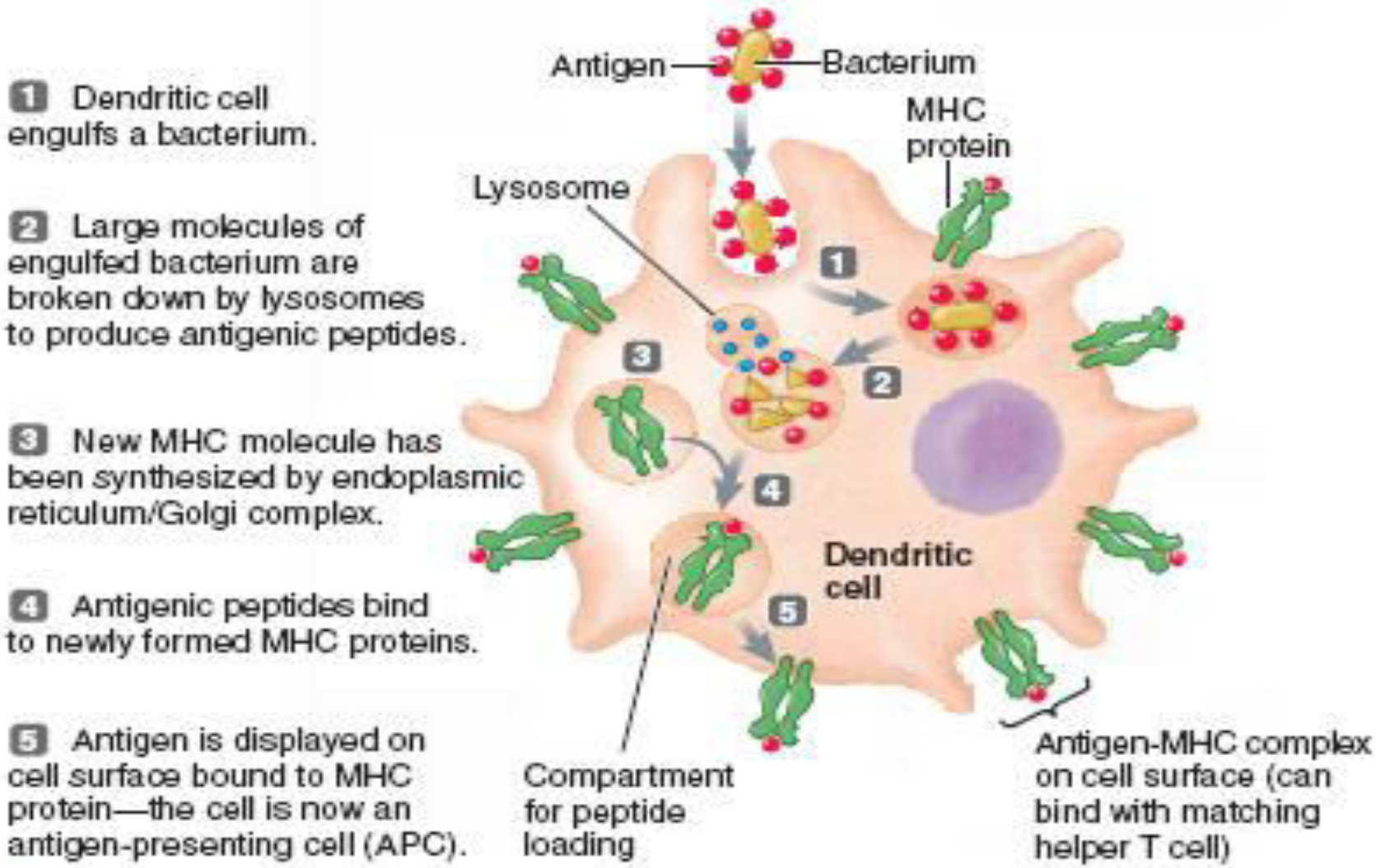
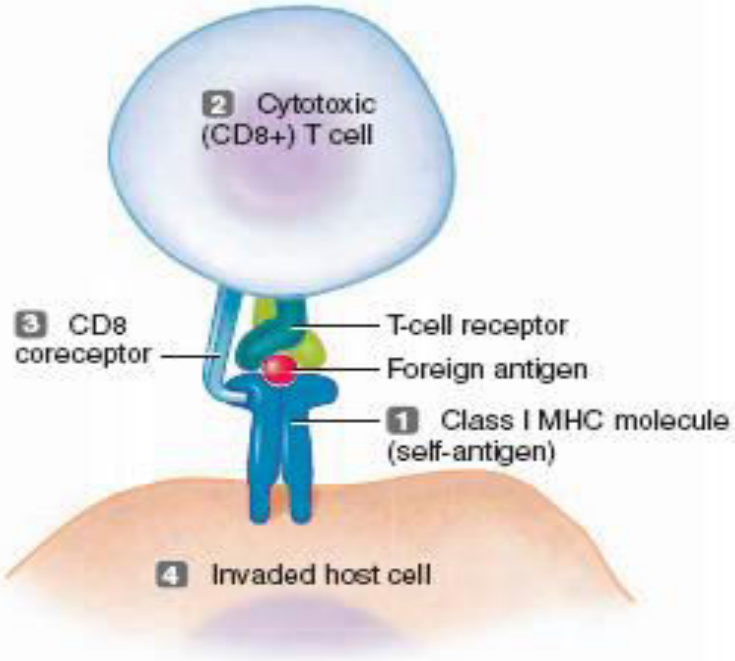


FIGURE 12-19 Generation of an antigen-presenting cell when a dendritic cell engulfs a bacterium.



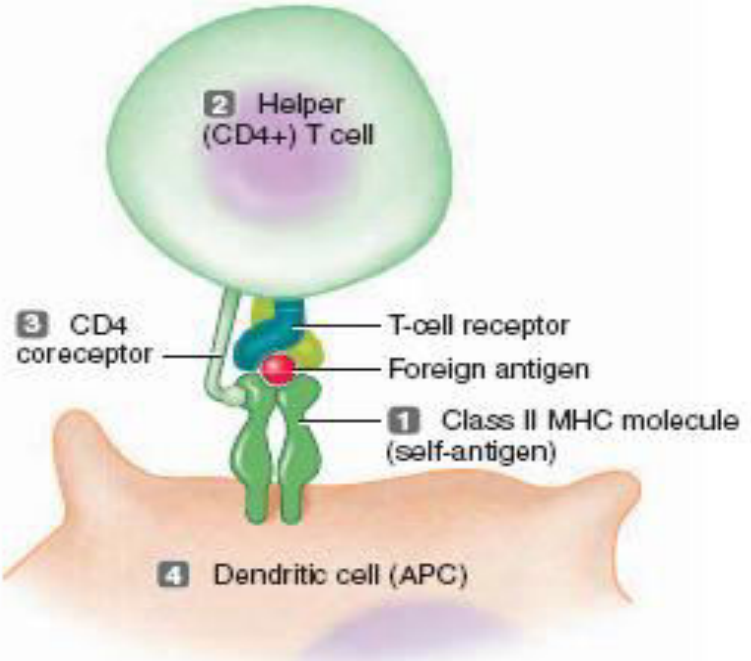
1 Class I MHC molecules are found on surface of all cells.

2 They are recognized only by cytotoxic (CD8+) T cells.

3 CD8 coreceptor links the two cells together.

4 Linked in this way, cytotoxic T cells can destroy body cells if invaded by foreign (viral) antigen.

(a) Class I MHC self-antigens



1 Class II MHC molecules are found on the surface of immune cells with which helper T cells interact: dendritic cells, macrophages, and B cells.

2 They are recognized only by helper (CD4+) T cells.

3 CD4 coreceptor links the two cells together.

4 To be activated, helper T cells must bind with a class II MHC-bearing APC (dendritic cell or macrophage). To activate B cells, helper T cell must bind with a class II MHC-bearing B cell with displayed foreign antigen.

(b) Class II MHC self-antigens

Types of T Cells

- Helper T cells
- Cytotoxic T cells– attack and destroy invading agent or antigen
- Suppressor T Cells– Inhibit or terminate activities of killer cells, plasma cells or T helper cells when their activities are no more needed

Lymphokines secreted by Helper T cells

- Helper T cells serve as the major regulator of virtually all immune functions, secrete lymphokines e.g. Inerleukin-2,3,4,5,6
- Granulocyte-monocyte CSF
- Gamma interferon

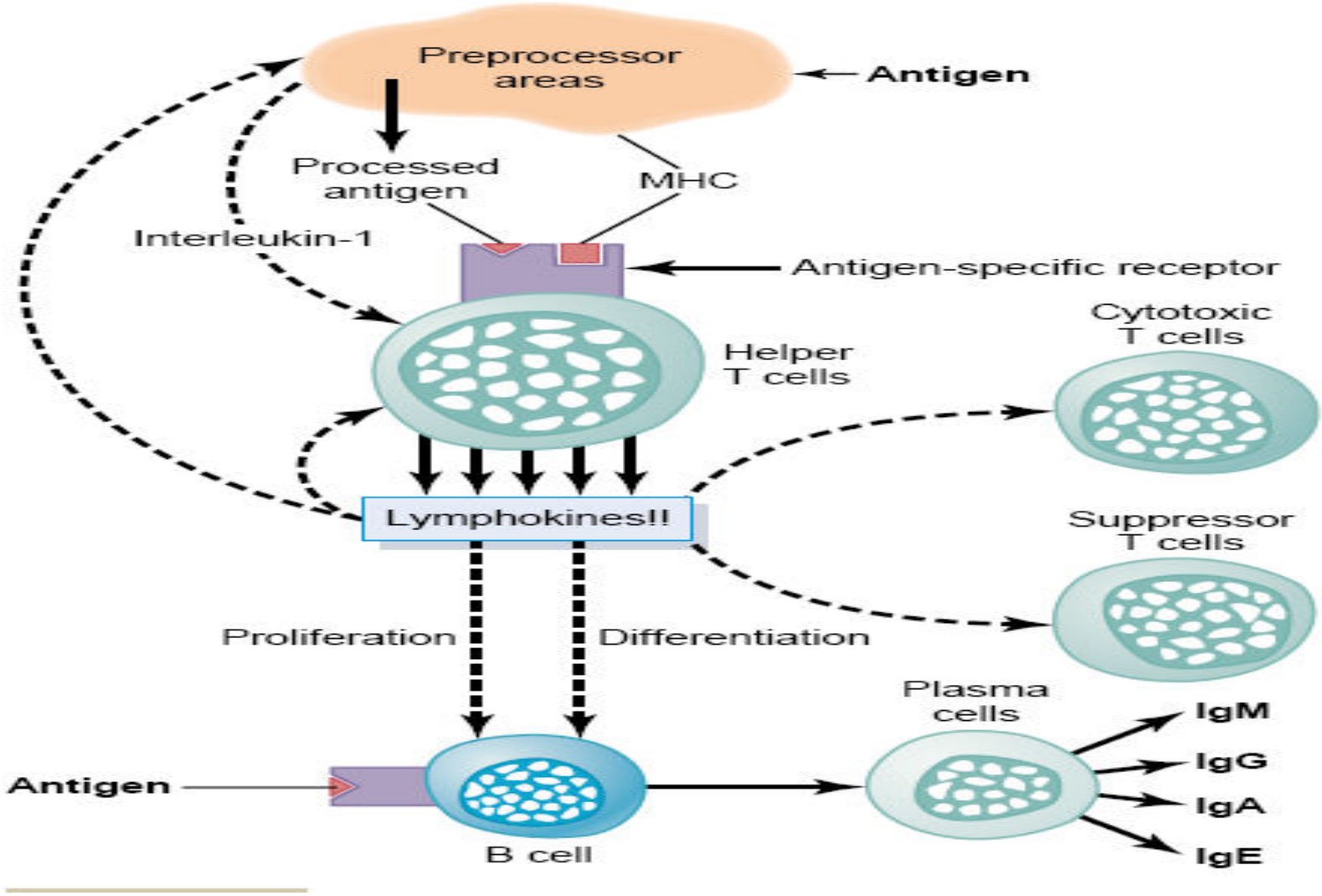
Regulatory Functions

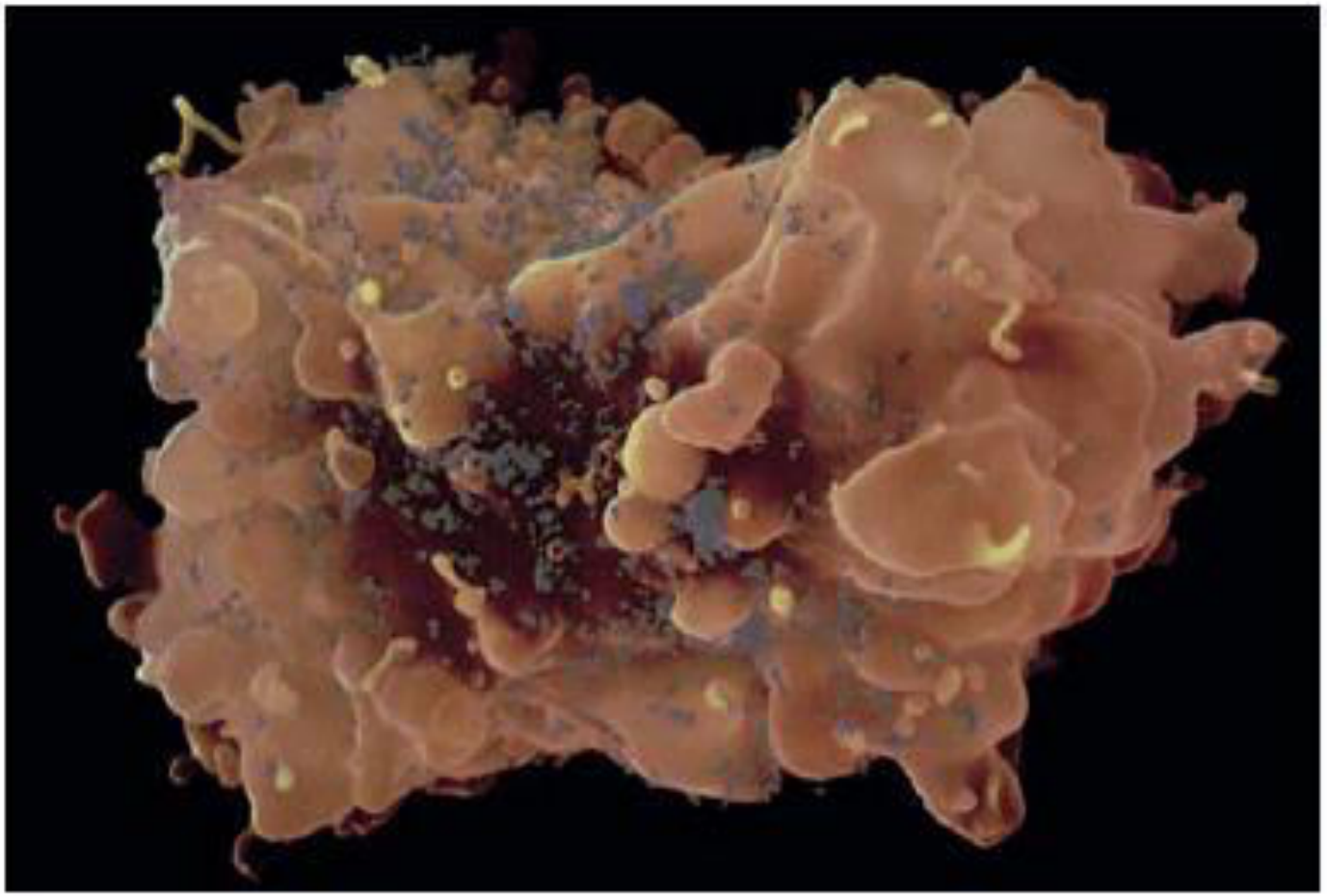
1. Stimulation of growth and proliferation of Cytotoxic and suppressor T cells: Interleukin--2
2. Stimulation of B cell growth and differentiation to form plasma cells and antibodies:IL-4,5,6
3. Activation of macrophage system
4. Feedback stimulatory effect on helper T cells themselves: IL 2

Role of T cells in activation of B cells

- Usually both the cells are activated simultaneously
- Helper T cells secrete lymphokines that activate specific B lymphocytes. Without its aid quantity of Abs formed is slight

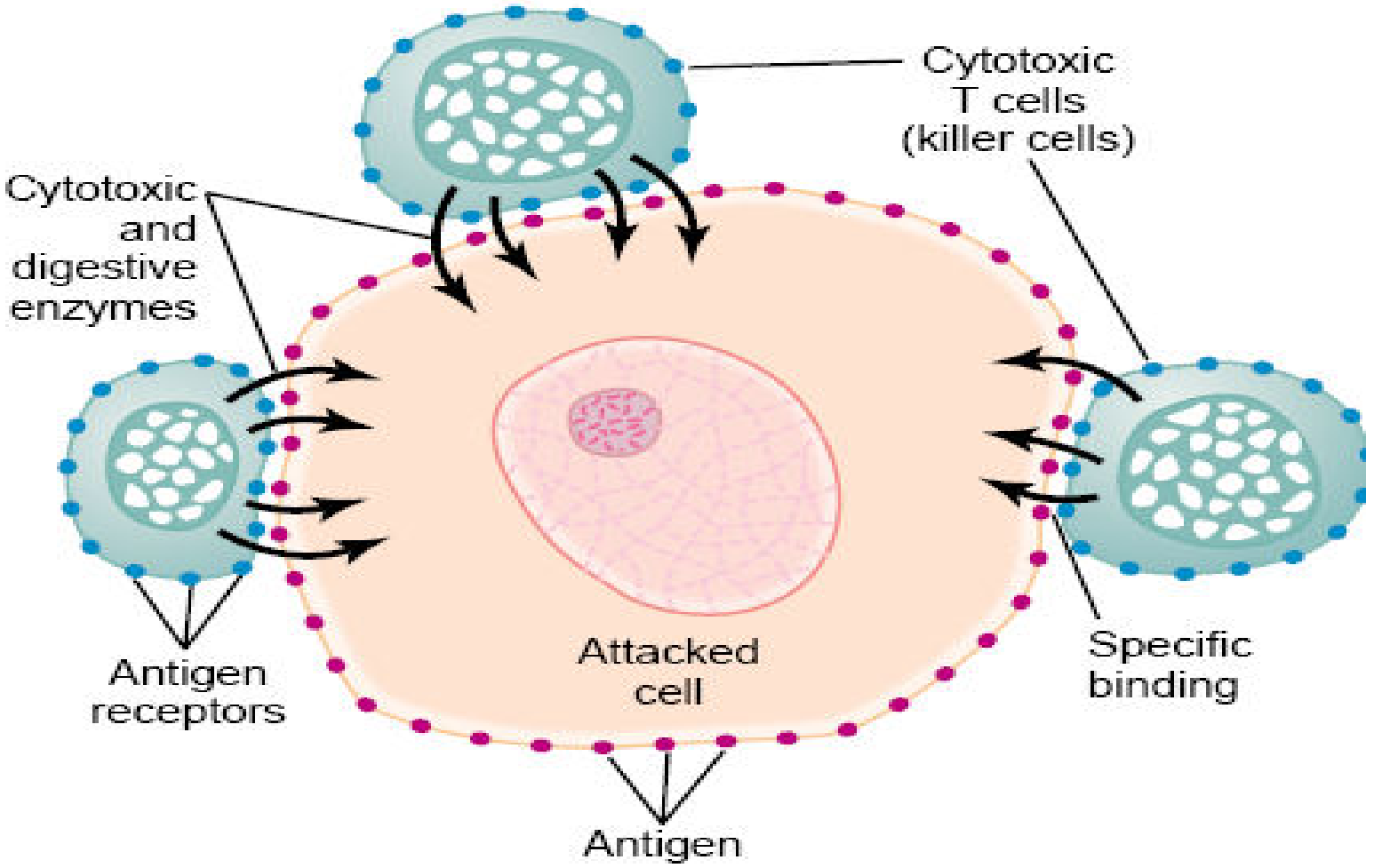
Pivotal role of Helper T Cell



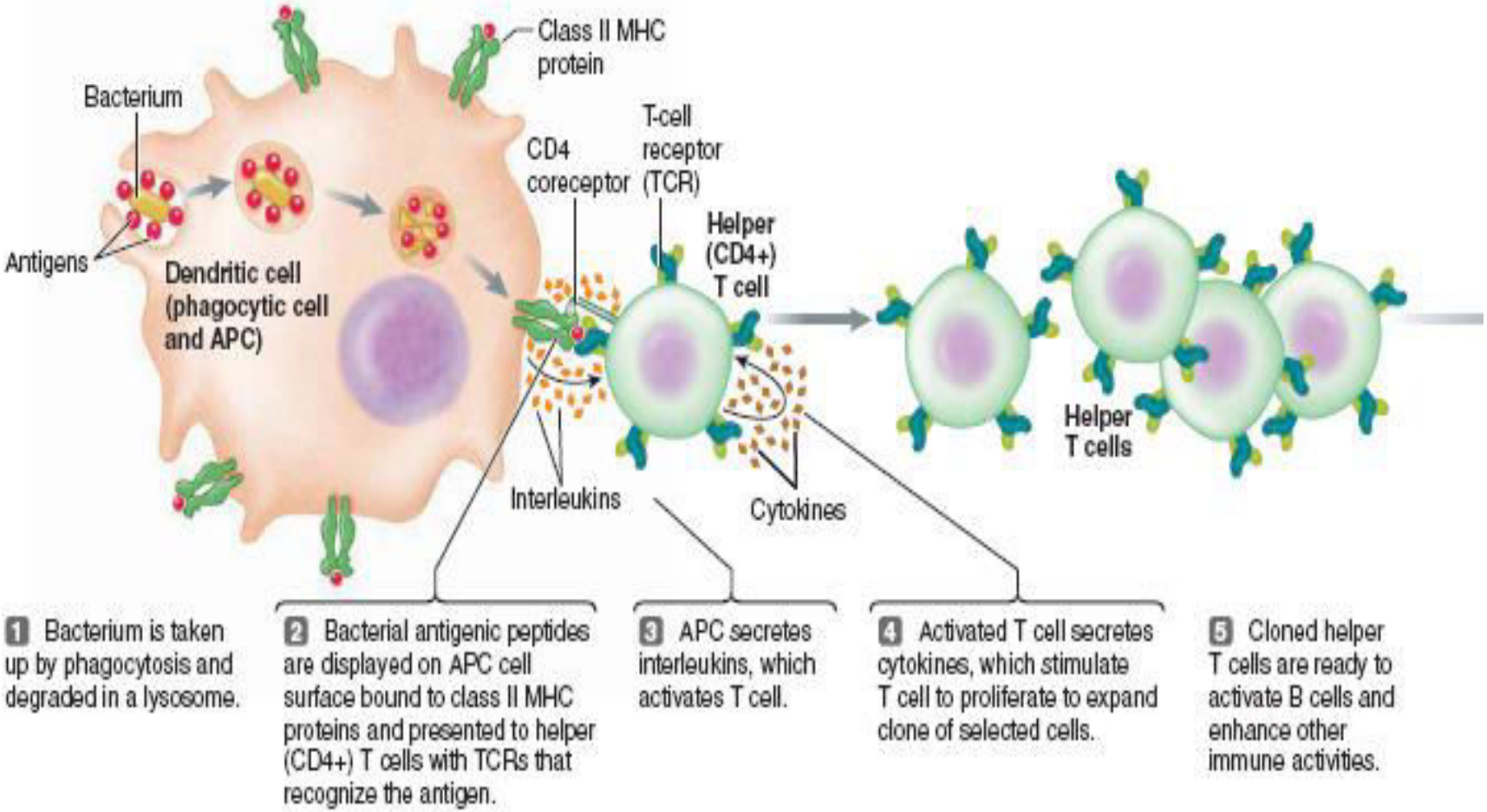


● **FIGURE 12-17 AIDS virus.** Human immunodeficiency virus (HIV) (in gray), the AIDS-causing virus, on a helper T lymphocyte, HIV's primary target.

Destruction by Cytotoxic T cell

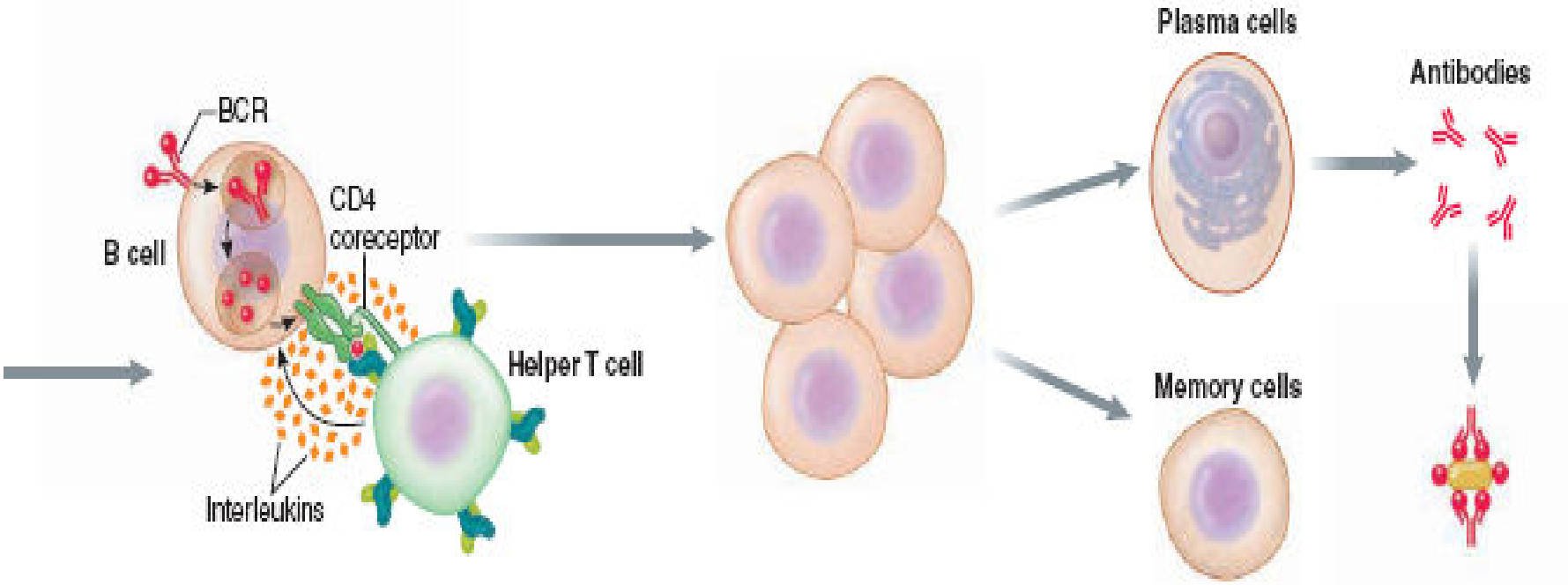


Activation of helper T cells by antigen presentation



● **FIGURE 12-21 Interactions among large phagocytic cells (APCs), helper T cells, and B cells responsive to T-dependent antigen.**

Activation of B cells responsive to T-dependent antigen



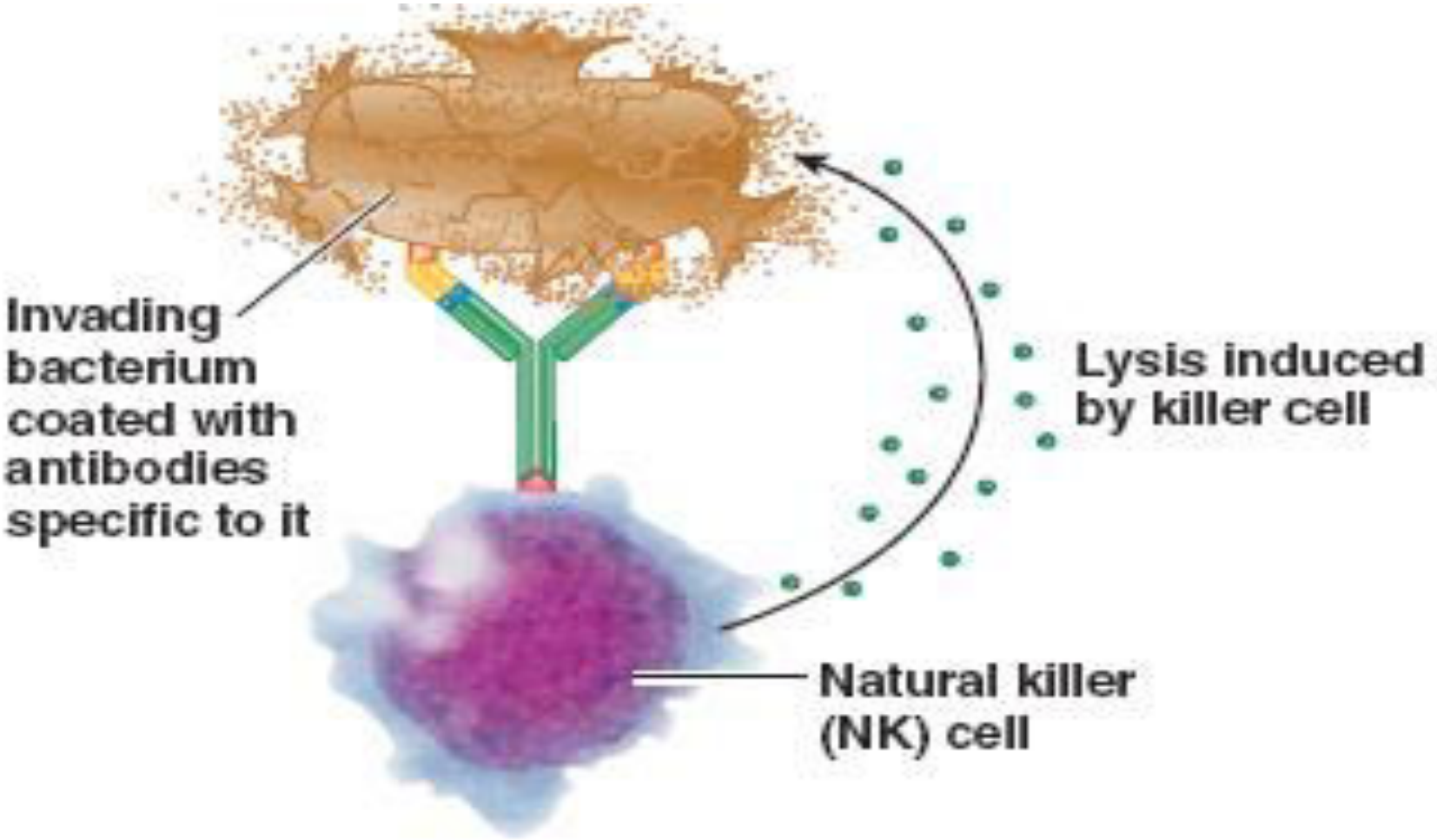
6 BCR binds to antigen. Antigen is internalized by receptor-mediated endocytosis and its macromolecules degraded. Antigenic peptides produced are displayed on cell surface bound to class II MHC proteins.

7 TCR of a helper T cell recognizes specific antigen on B cell, and CD4 coreceptor links the two cells together.

8 Helper T cell secretes interleukins, which stimulate B cell proliferation to produce clone of selected cells.

9 Some cloned B cells differentiate into plasma cells, which secrete antibodies specific for the antigen, while a few differentiate into memory B cells.

10 Antibodies bind with antigen, targeting antigenic invader for destruction by the innate immune system.



(e) Stimulation of natural killer (NK) cells: antibody-dependent cellular cytotoxicity

Structures are not drawn to scale.

Autoimmune Diseases

Immune Tolerance and role of suppressor T cells

- Rheumatic Fever
- Glomerulonephritis
- Myasthenia gravis
- Rheumatoid arthritis
- Lupus erythematosis

Allergy and Hypersensitivity

Is an inflammatory immune response to a non-pathogenic antigen--- allergen

Delayed hypersensitivity reaction –mediated by activated T cells e.g ivy toxin

Immediate hypersensitivity reaction—mediated by Abs

Excess IgE(Reagin Abs) antibodies allergy

- Anaphylaxis
- Urticaria
- Hay fever
- Asthma