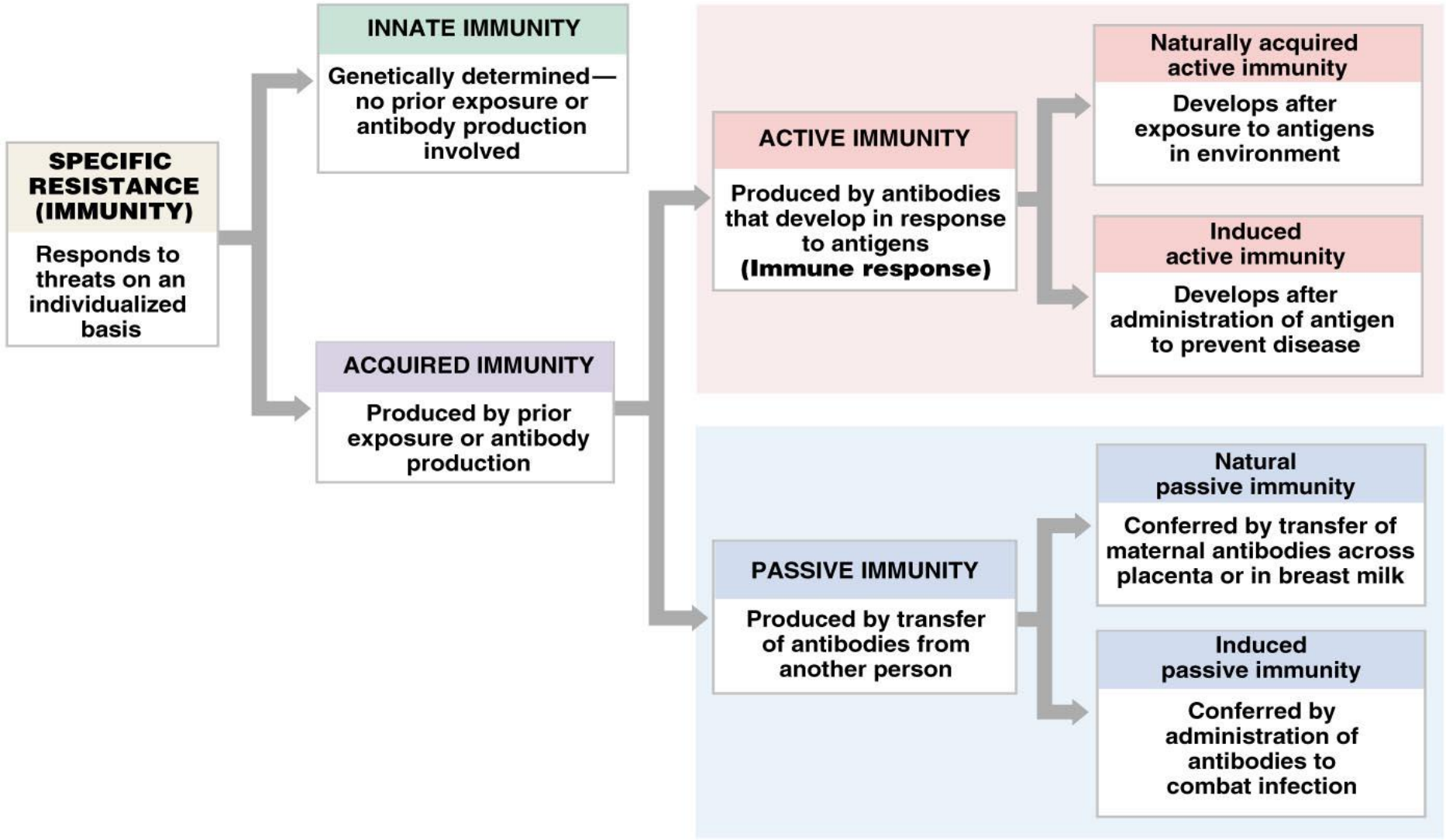
Blood and Immune system

Acquired Immunity

Immunity

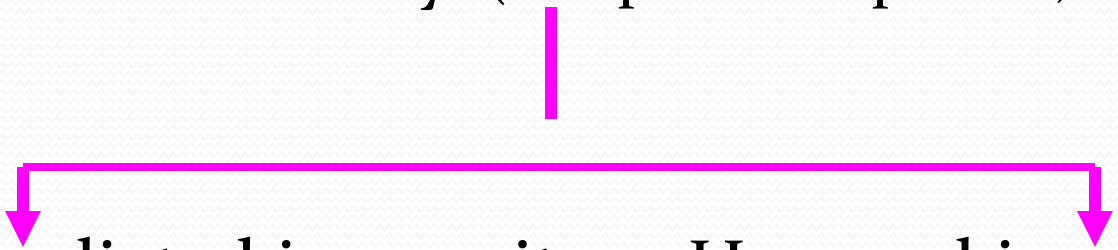


Acquired (Adaptive) Immunity

Defensive mechanisms include :

1) Innate immunity (Natural or Non specific)

2) Acquired immunity (Adaptive or Specific)



Cell-mediated immunity Humoral immunity

Active Immunity

I. Humoral (Antibody-Mediated) Immunity

- **Involves production of antibodies against foreign antigens.**
- **Antibodies are produced by a subset of lymphocytes called B cells.**
- **B cells that are stimulated will actively secrete antibodies and are called *plasma cells*.**
- **Antibodies are found in extracellular fluids (blood plasma, lymph, mucus, etc.) and the surface of B cells.**
- **Defense against bacteria, bacterial toxins, and viruses that circulate freely in body fluids, *before* they enter cells.**
- **Also cause certain reactions against transplanted tissue.**

II. Cell Mediated Immunity

Involves specialized set of lymphocytes called T cells that recognize foreign antigens on the surface of cells, organisms, or tissues:

- Helper T cells
- Cytotoxic T cells
- Memory T Cells
- T Suppressor (Ts) Cells

T cells regulate proliferation and activity of other cells of the immune system: B cells, macrophages, neutrophils, etc.

Defense against:

- Bacteria and viruses that are inside host cells and are inaccessible to antibodies.
- Fungi, protozoa, and helminths
- Cancer cells
- Transplanted tissue

Antigens

- Most are proteins or large polysaccharides from a foreign organism.
  - Microbes: Capsules, cell walls, toxins, viral capsids, flagella, etc.
  - Nonmicrobes: Pollen, egg white , red blood cell surface molecules, serum proteins, and surface molecules from transplanted tissue.
- Lipids and nucleic acids are only antigenic when combined with proteins or polysaccharides.
- Molecular weight of 10,000 or higher.
  - Hapten: Small foreign molecule that is not antigenic. Must be coupled to a carrier molecule to be antigenic. Once antibodies are formed they will recognize hapten.

Antibodies

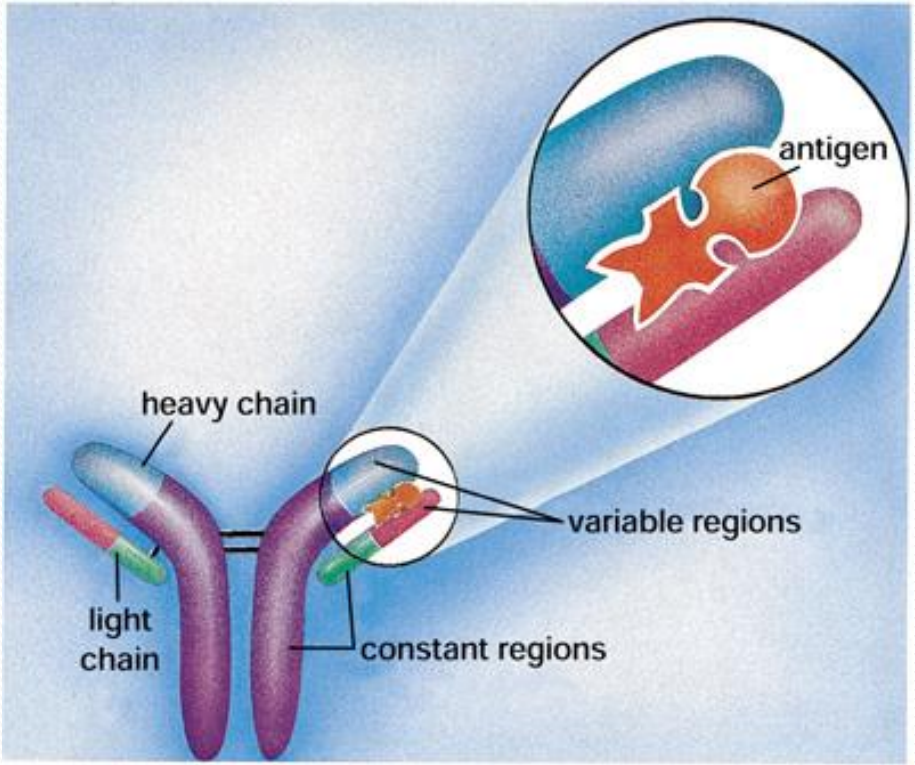
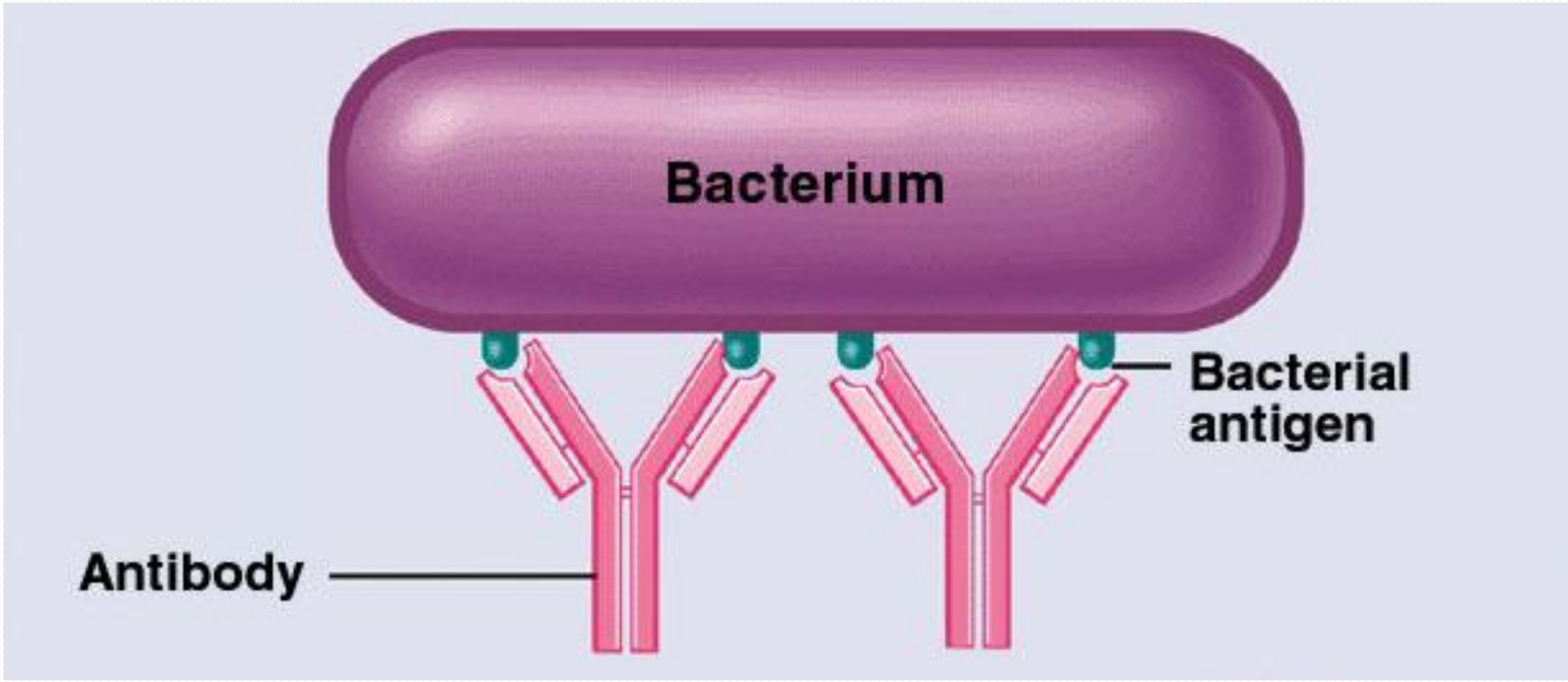


Figure 9.20. The structure of an antibody. Variations in the amino acid sequence produce the distinctive shape of the variable regions on different antibodies.

- Y-shaped *protein* molecule.
- Made up of *variable* and *constant* regions.
- Made up of ***Heavy*** and *Light* chains.
- Produced by B-Lymphocytes
- **Function:** Recognize antigens, bind to and deactivate them.
  - Note: Variable region recognizes the anitgens.

Deactivation of a bacterium by an antibody.

How an antibody operates/works?



Immunoglobulin Classes

I. IgG

- Structure: Monomer
- Percentage serum antibodies: 80%
- Location: Blood, lymph, intestine
- Half-life in serum: 23 days
- Complement Fixation: Yes
- Placental Transfer: Yes
- Known Functions: Enhances phagocytosis, neutralizes toxins and viruses, protects fetus and newborn.

Immunoglobulin Classes

II. IgM

- Structure: Pentamer
- Percentage serum antibodies: 5-10%
- Location: Blood, lymph, B cell surface (monomer)
- Half-life in serum: 5 days
- Complement Fixation: Yes
- Placental Transfer: No
- Known Functions: First antibodies produced during an infection. Effective against microbes and agglutinating antigens.

Immunoglobulin Classes

III. IgA

- **Structure: Dimer**
- **Percentage serum antibodies: 10-15%**
- **Location: Secretions (tears, saliva, intestine, milk), blood and lymph.**
- **Half-life in serum: 6 days**
- **Complement Fixation: No**
- **Placental Transfer: No**
- **Known Functions: Localized protection of *mucosal* surfaces. Provides immunity to infant digestive tract.**

Immunoglobulin Classes

IV. IgD

- **Structure: Monomer**
- **Percentage serum antibodies: 0.2%**
- **Location: B-cell surface, blood, and lymph**
- **Half-life in serum: 3 days**
- **Complement Fixation: No**
- **Placental Transfer: No**
- **Known Functions: In serum function is unknown. On B cell surface, initiate immune response.**

Immunoglobulin Classes

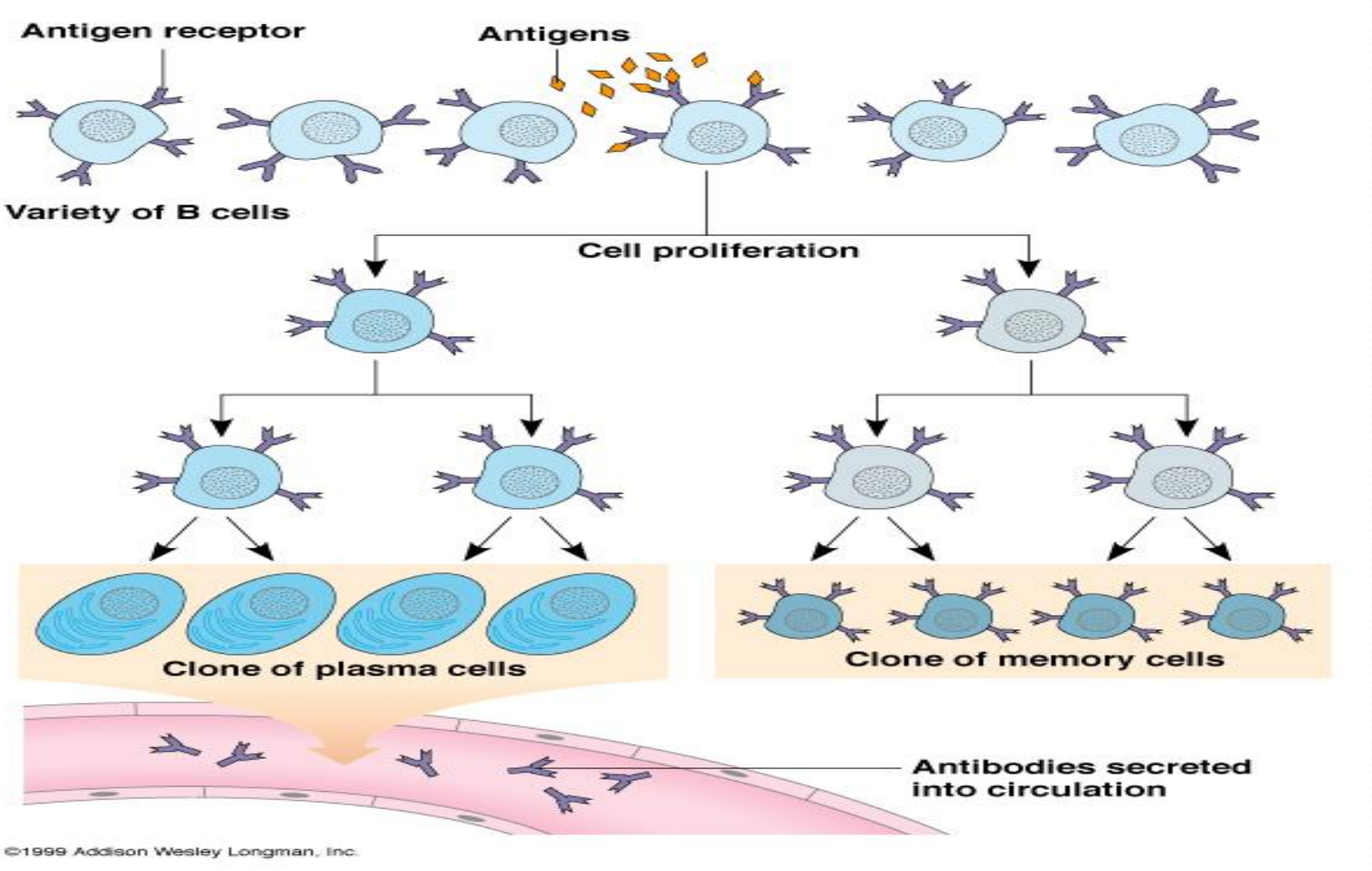
V. IgE

- Structure: Monomer
- Percentage serum antibodies: 0.002%
- Location: Bound to mast cells and basophils throughout body. Blood.
- Half-life in serum: 2 days
- Complement Fixation: No
- Placental Transfer: No
- Known Functions: Allergic reactions. Possibly lysis of worms.

How Do B Cells Produce Antibodies?

- **B cells develop from stem cells in the bone marrow of adults (liver of fetuses).**
- **After maturation B cells migrate to lymphoid organs (lymph node or spleen).**
- **<u>Clonal Selection</u>: When a B cell encounters an antigen it recognizes, it is stimulated and divides into many clones called plasma cells, which actively secrete antibodies.**
- **Each B cell produces antibodies that will recognize only one antigenic determinant.**

Clonal Selection of B Cells is Caused by Antigenic Stimulation



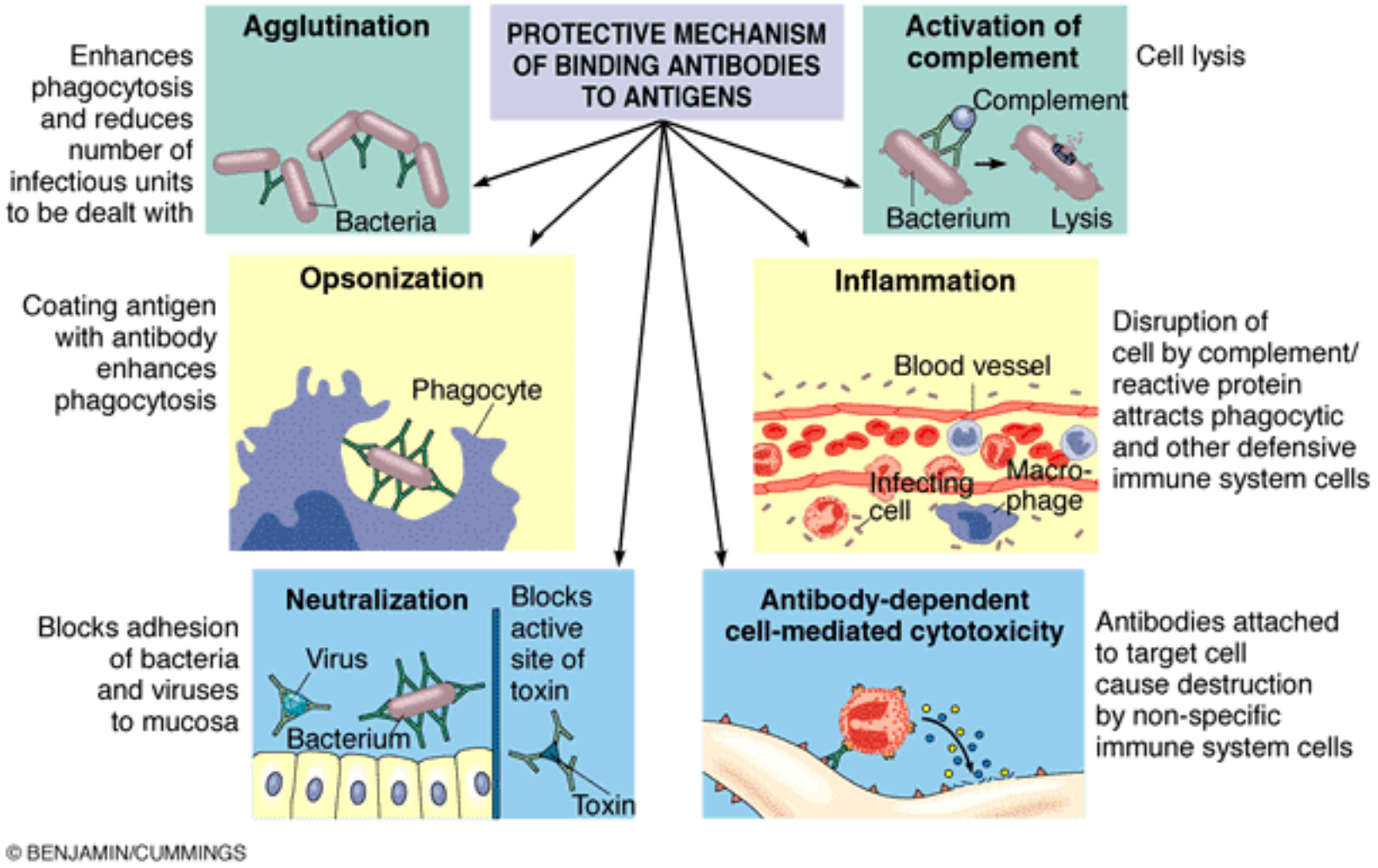
Apoptosis

- **Programmed cell death (“Falling away”).**
- **Human body makes 100 million lymphocytes every day. If an equivalent number doesn’t die, will develop leukemia.**
- **B cells that do not encounter stimulating antigen will self-destruct and send signals to phagocytes to dispose of their remains.**
- **Many virus infected cells will undergo apoptosis, to help prevent spread of the infection.**

Clonal Selection

- **Clonal Selection: B cells (and T cells) that encounter stimulating antigen will proliferate into a large group of cells.**
- **Why don't we produce antibodies against our own antigens? We have developed *tolerance* to them.**
- **Clonal Deletion: B and T cells that react against *self* antigens appear to be destroyed during fetal development. Process is poorly understood.**

Consequences of Antibody Binding



Immunological Memory

Antibody Titer: The amount of antibody in the serum.

Pattern of Antibody Levels During Infection

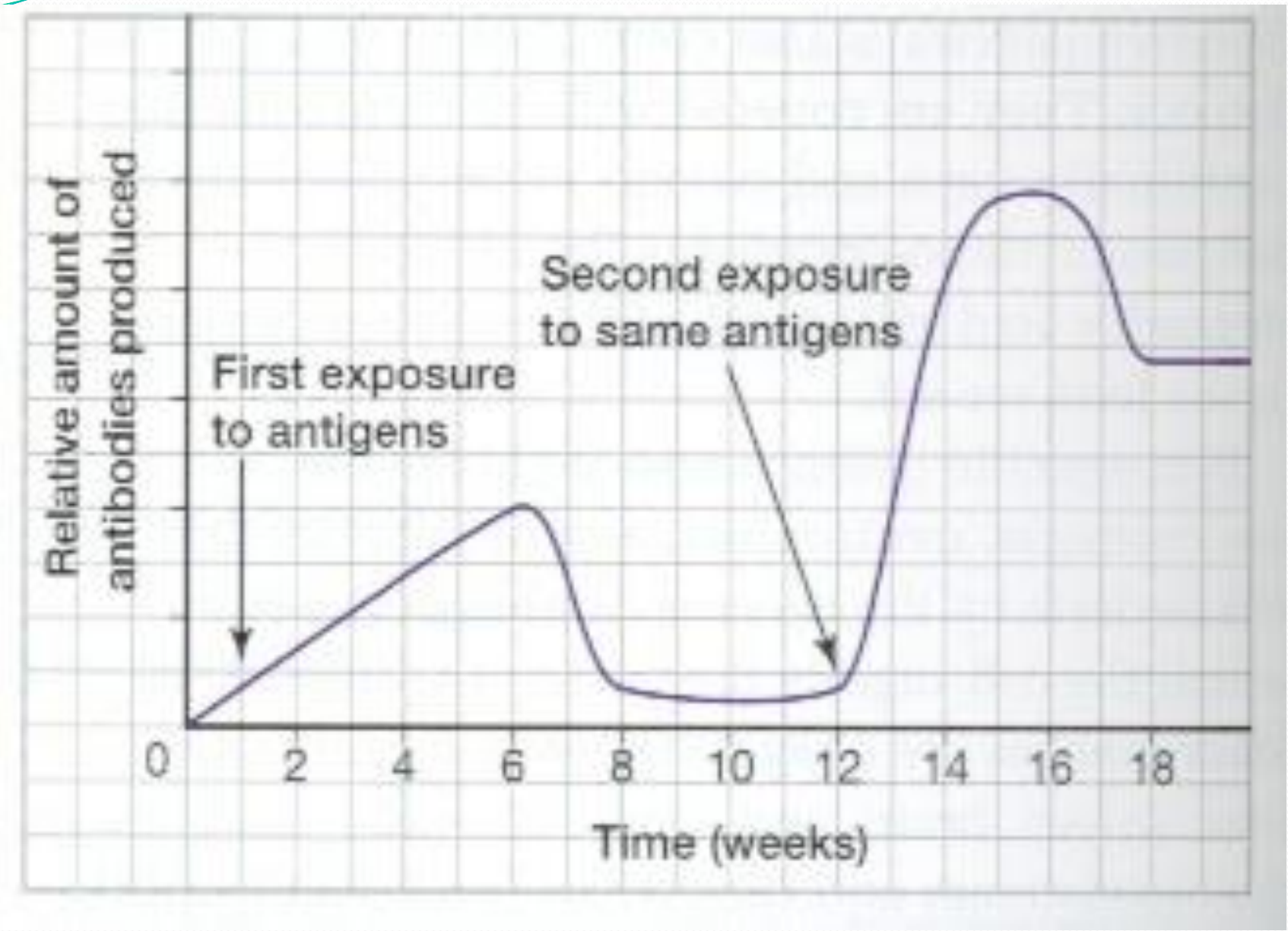
Primary Response:

- **After *initial* exposure to antigen, no antibodies are found in serum for several days.**
- **A gradual increase in titer, first of IgM and then of IgG is observed.**
- **Most B cells become plasma cells, but some B cells become long living *memory cells*.**
- **Gradual decline of antibodies follows.**

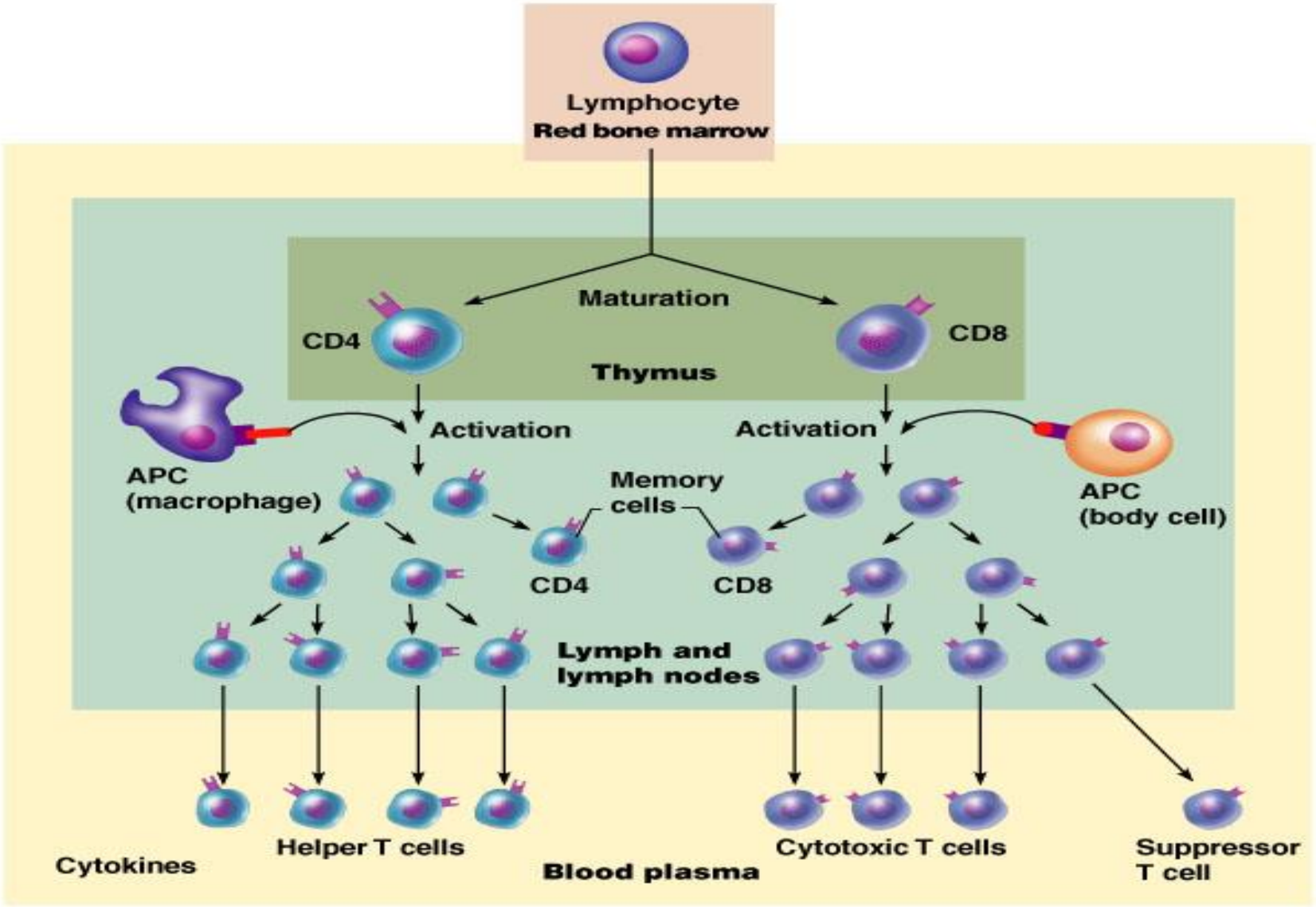
Immunological Memory (Continued)

Secondary Response:

- **Subsequent exposure to the same antigen displays a faster and more intense antibody response.**
- **Increased antibody response is due to the existence of memory cells, which rapidly produce plasma cells upon antigen stimulation.**

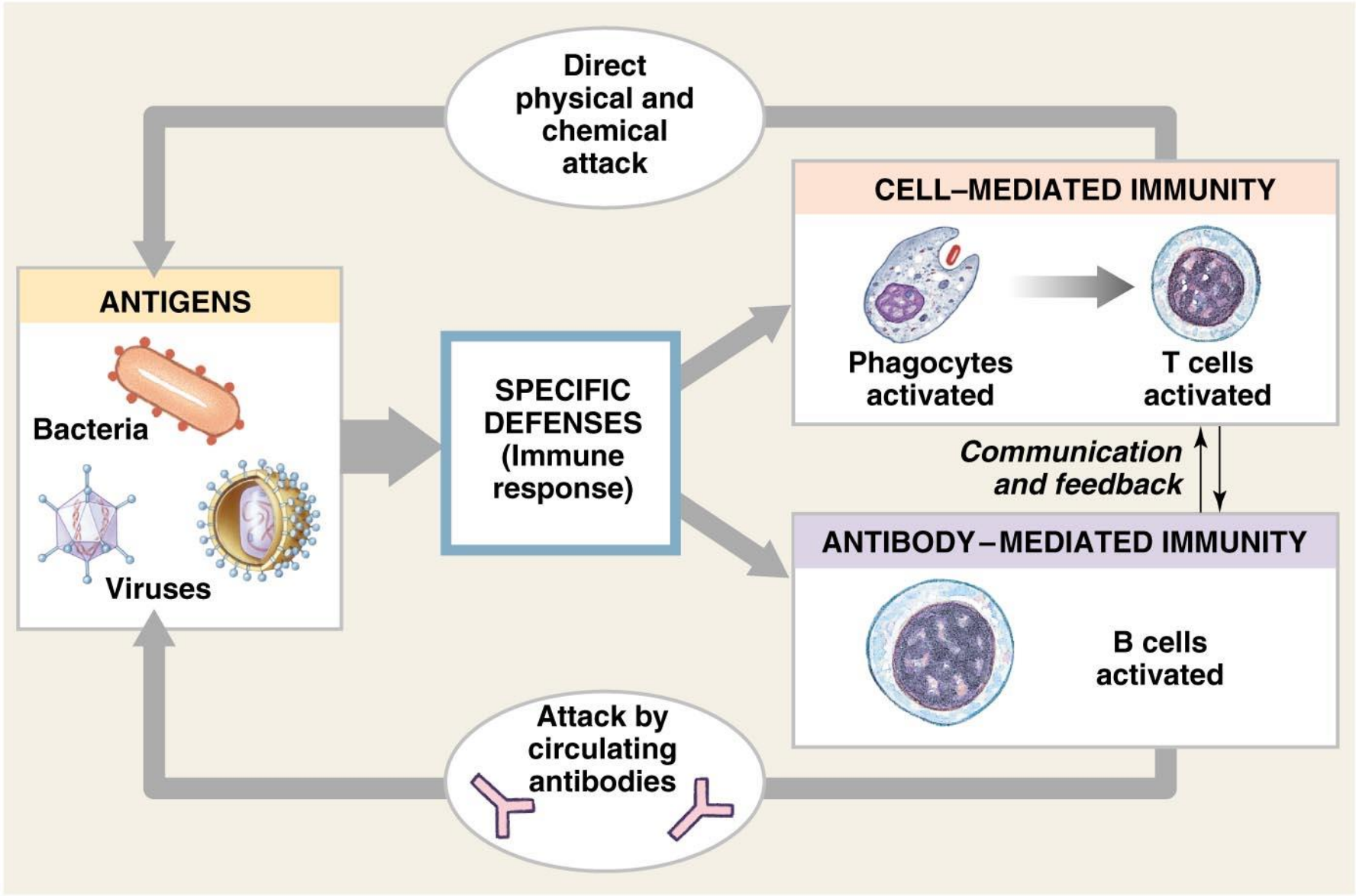

Relative amount of antibodies produced
First exposure to antigens
Second exposure to same antigens
0
2
4
6
8
10
12
14
16
18
Time (weeks)

T lymphocytes



Overview of the immune response

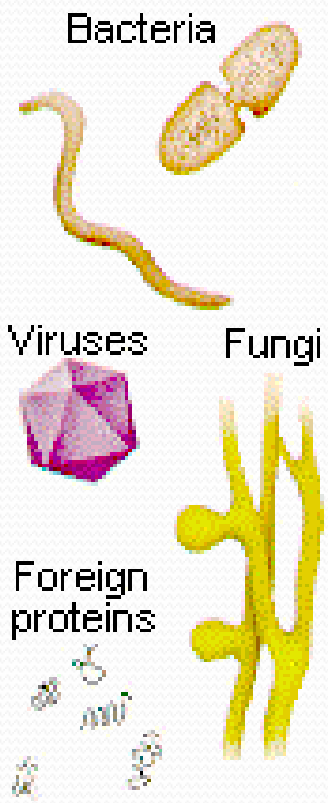
- The purpose of the immune response is to inactivate or destroy pathogens, abnormal cells & foreign molecules (such as toxins)
- In order for the response to occur, lymphocytes must be "activated" by the process of *antigen recognition*
- T cells are usually activated first, & then B cells. T cells mainly rely on activation by phagocytic cells collectively known as "*antigen presenting cells (APC's)*" (ie. Macrophages, dendritic cells)
- Once activated, T cells both attack the invader, & stimulate the activation of B cells
- Activated B cells mature into "plasma cells" which produce specific antibodies designed to destroy the particular antigen.



Cell Mediated (a.k.a. Cellular) Immunity

- In order for T cells to respond, they must first be activated by exposure to an antigen, which is bound to membrane receptors of phagocytic antigen presenting cells (APC's) ("*antigen recognition*")
- These membrane receptors on cells are called "MHC proteins" (major histocompatibility complex proteins), & are genetically determined (i.e. differ among individuals)
- Antigens bound to MHC proteins "tell" the T lymphocyte what the specific foreign invader is (i.e. a specific bacteria) so that the lymphocytes can mount a cellular defense

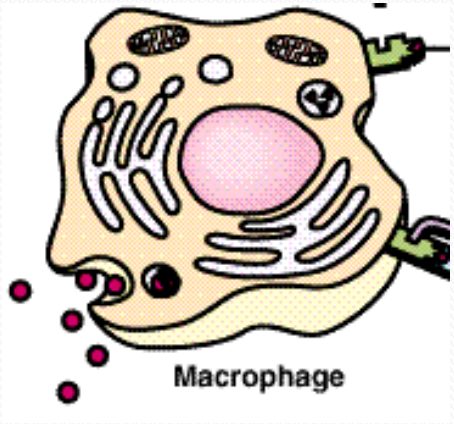
The Pathway of Specific Immune Response



Pathogens

Step 1

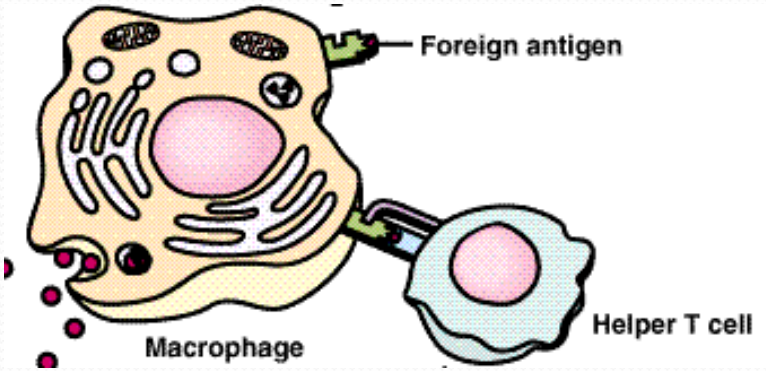
Pathogens eaten by Macrophage



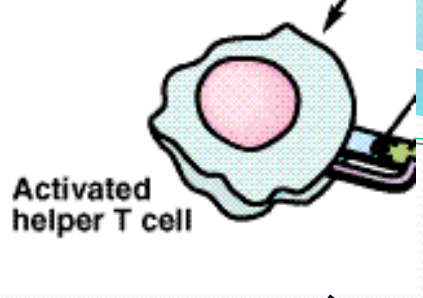
Step 2

Displays portion of Pathogen on surface

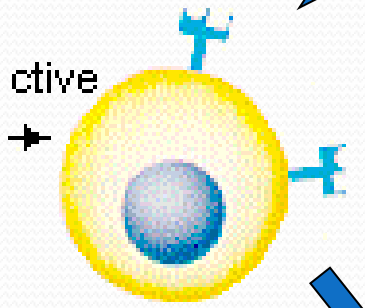
Step 3

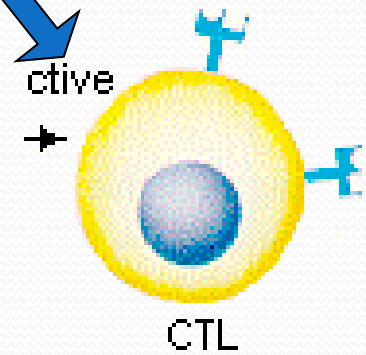


Helper-T cell recognizes Pathogen

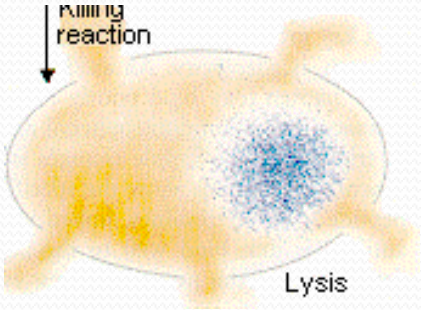


Activates Cytotoxic T- Cell



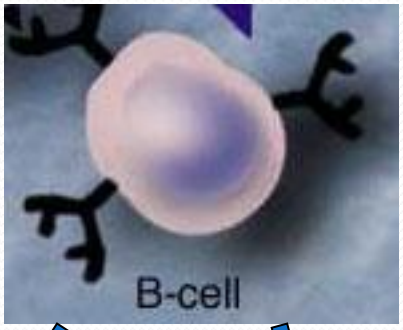


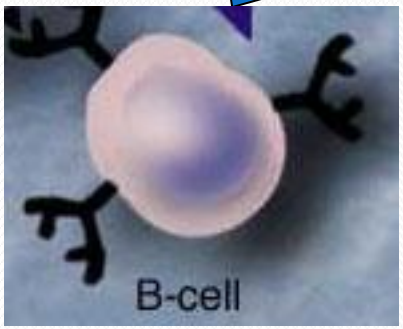
Memory T-Cell



Kills Infected Cells

Activates B- Cell

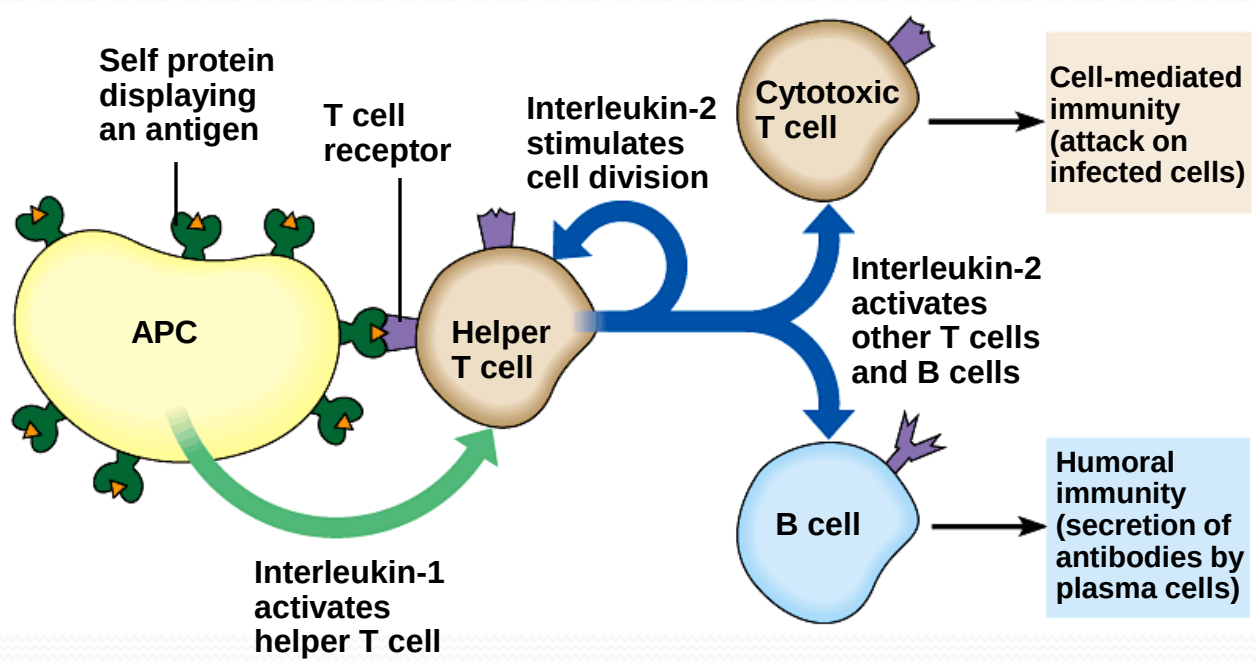




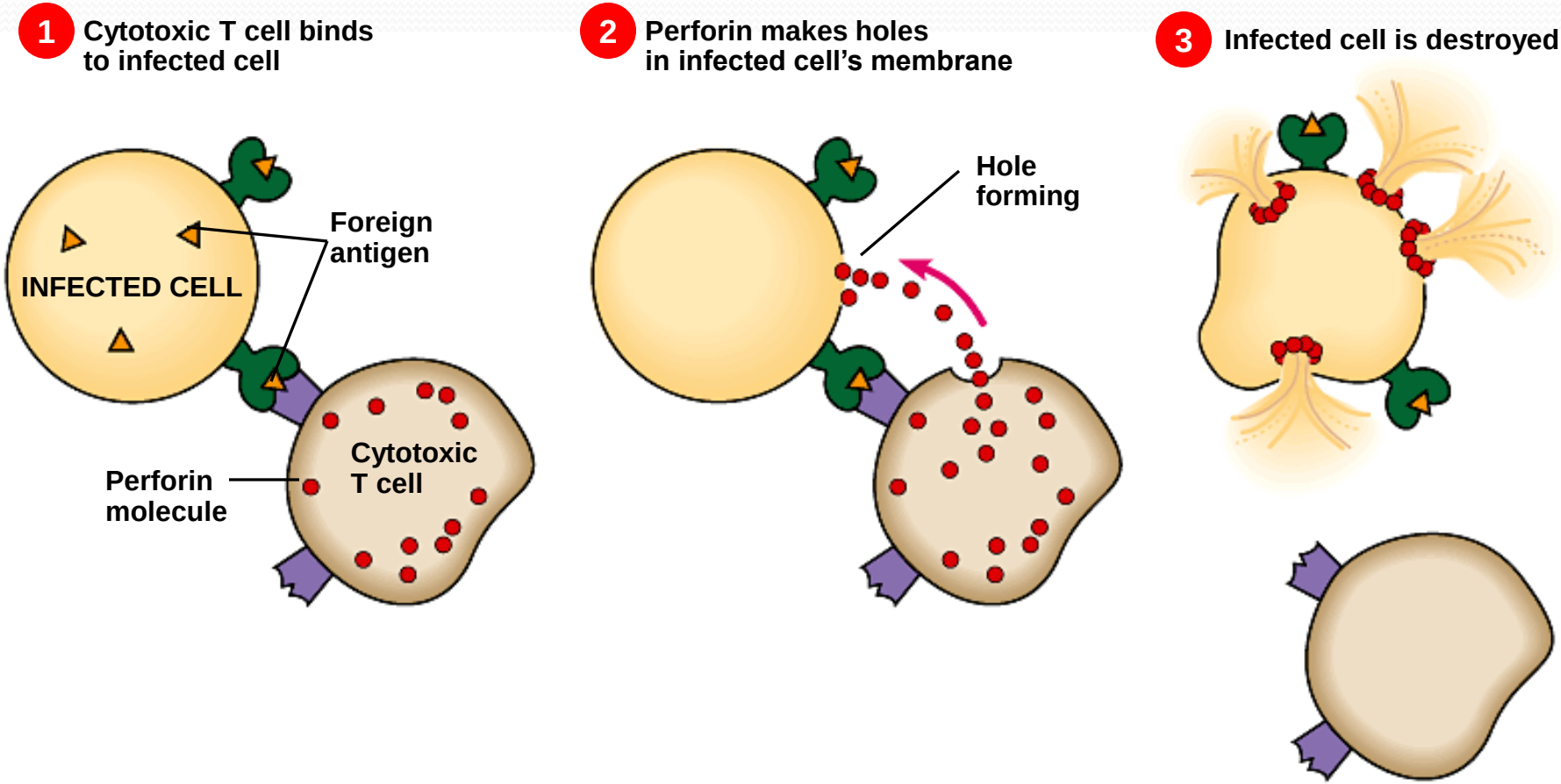
Memory B-Cell

Antibodies→

- Activation of helper T cell



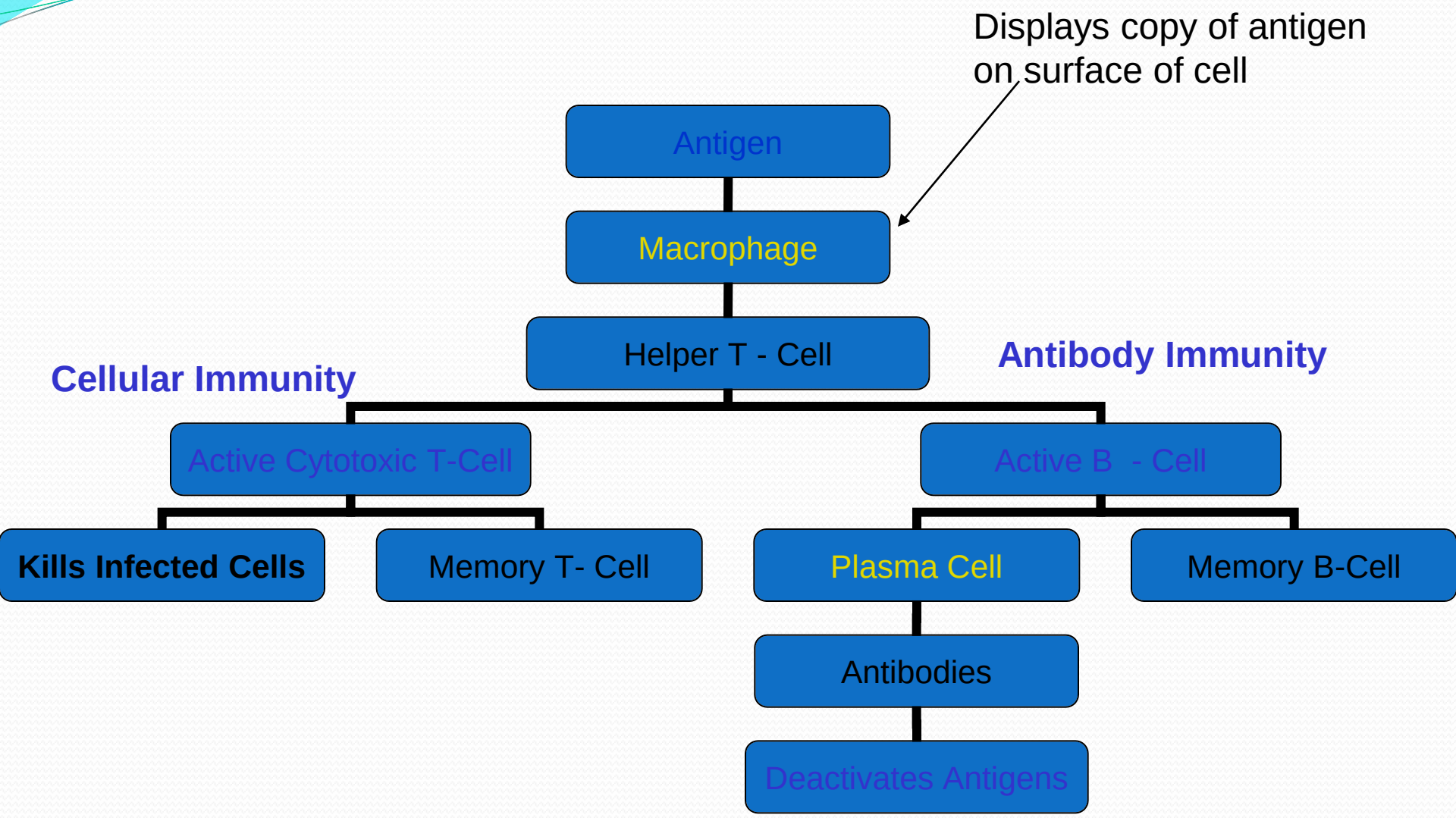
- Cytotoxic T cells bind to infected body cells and destroy them



Immune Response Explained

1. Antigen infects cells.
2. Macrophage ingests antigen and displays portion on its surface.
3. Helper T- Cell recognizes antigen on the surface of the macrophage and becomes active.
4. Active Helper T-Cell activates Cytotoxic T-Cells and B-Cells.
5. Cytotoxic T-Cells divide into Active Cytotoxic T-cells and Memory T – Cells.
6. Active Cytotoxic T-Cells kill infected cells.
7. At the same time, B-Cells divide into Plasma Cells and Memory B-Cells.
8. Plasma cells produce antibodies that deactivate pathogen.
9. Memory T and Memory B cells remain in the body to speed up the response if the same antigen reappears.
10. Supressor T-Cells stop the immune response when all antigens have been destroyed.

Immune Response Summary



Autoimmune Disease

- Autoimmune diseases are diseases where the immune system begins to attack itself.
  - Ex:
    - Rheumatoid Arthritis – crippling disease of the joints.
    - Lupus – disease of blood and organs.
    - Multiple Sclerosis – disease of nervous system
    - Myasthenia Gravis

- <u>Cause(s):</u> unknown
- <u>Cures/Treatments:</u> No known cures. Usually treated with drugs.

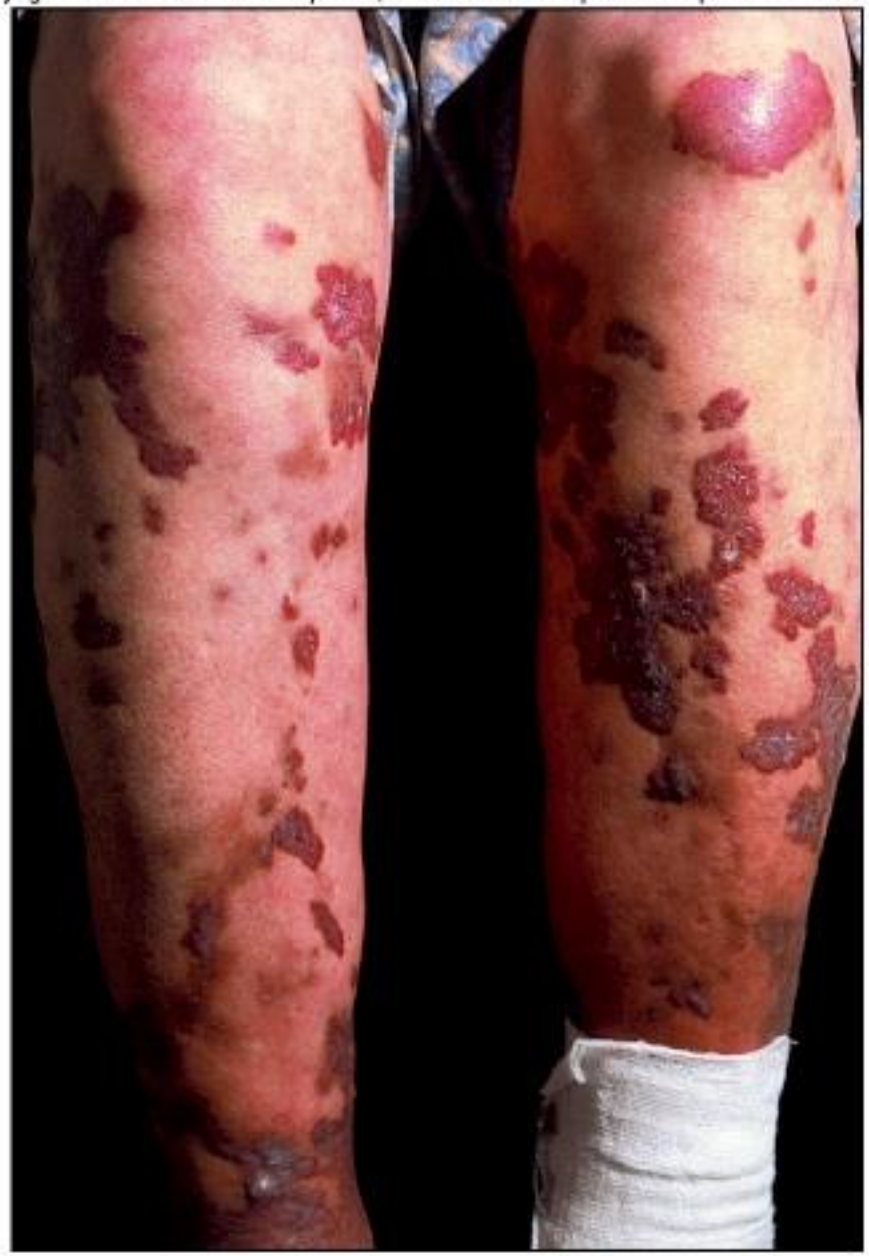
HIV/AIDS

Human immunodeficiency virus

Attacks helper T cells

Without production of IL-2, there is no second signal, and humoral and cell mediated immunity are shut off.
See increase in rare diseases:

TB, Kaposi sarcoma, etc.



Allergy

- An exaggerated response by the immune system to an allergen.

Allergies

Allergen: a normally harmless substance that causes an allergic reaction.

ex: dust, pollen, mould, food, insect stings

Types of Allergic reactions

There are two types of allergic reactions.

a. Immediate – occurs within seconds and normally lasts for about 30 mins.

b. Delayed – takes longer to react and can last for a much longer time.

- During an allergic reaction antibodies cause *histamines* to be released from certain cells.

What happens during an allergic reaction?

Histamines cause:

a. Swelling of tissues

b. Release of fluids (runny noses and eyes)

c. muscle spasms (some cases)

Anaphylaxis or anaphylactic shock:

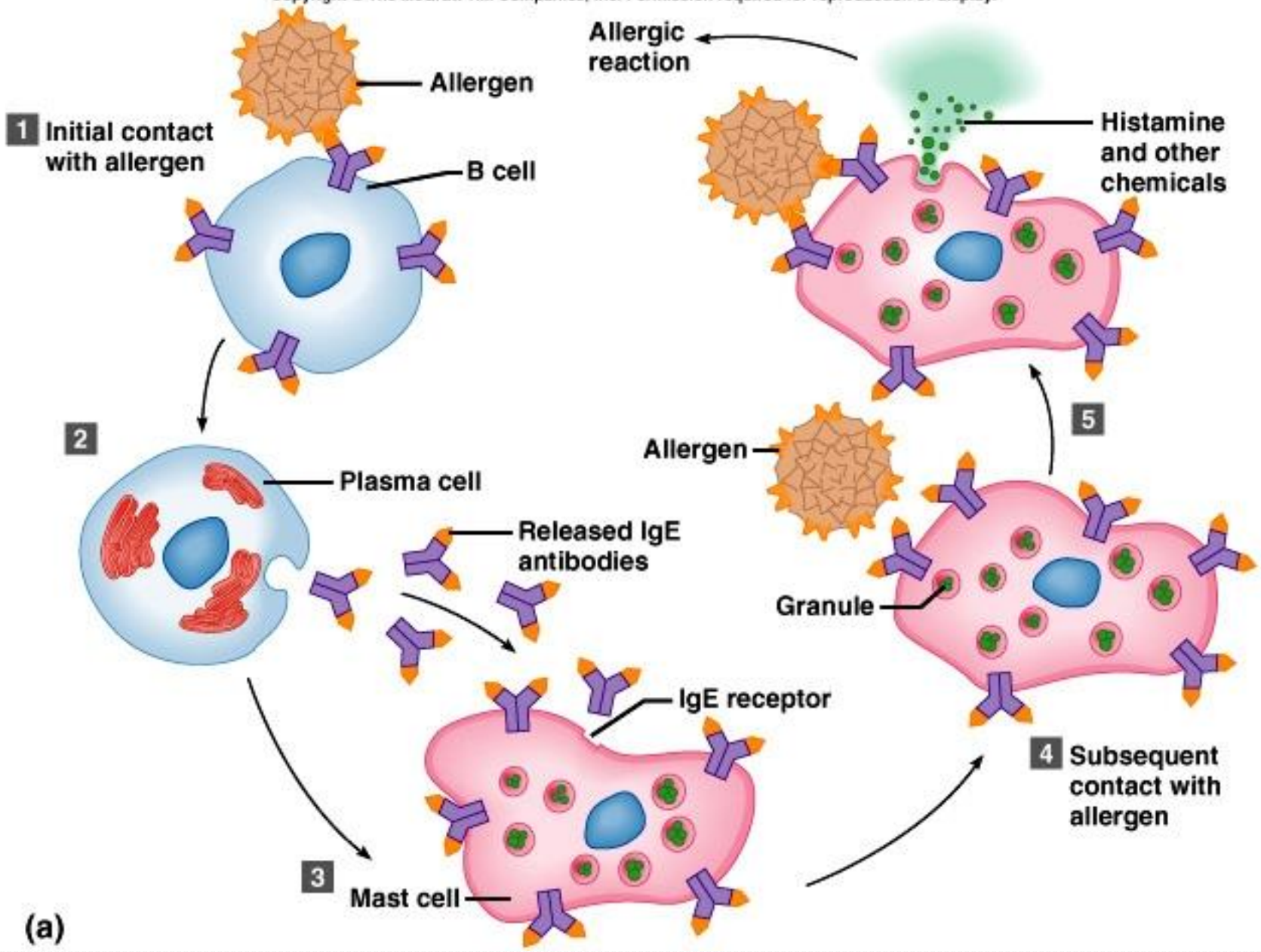
This is the sudden and severe allergic reaction to a substance that can cause death.

Treatments for Allergies

1. Avoidance of material – especially food.
2. Epinephrine –
3. Antihistamines

Immediate Type Hypersensitivity

- Exposure to certain antigens (allergens) results in the formation of IgE antibodies
- IgE antibodies bind to mast cells by the Fc end.
- When the antigen is encountered again, binding with the antibody causes mast cell to release histamine granules.



Delayed Hypersensitivity

A type of cell mediated immunity.

T cell – requires usual two signals

Second time antigen is encountered, T cell produces several cytokines that attract and activate macrophages, resulting in an inflammatory reaction.

Further reading:

- Review of Medical Physiology. By W.F. Ganong, Lange Medical Book. Prentice-Hall International.

- Textbook of Medical Physiology, Indu Khurana, Elsevier