



Antigens antibodies and Immune response

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The Immune Response

Immunity: “Free from burden”. The ability of an organism to recognize and defend itself against *specific* pathogens or antigens.

Immune Response: Third line of defense. Involves the production of antibodies and generation of specialized lymphocytes against specific antigens.

Antigen: Molecules from a pathogen or foreign organism that provoke a specific immune response.

The Immune System is the Third Line of Defense Against Infection

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



Innate or Genetic Immunity:

Immunity an organism is born with.

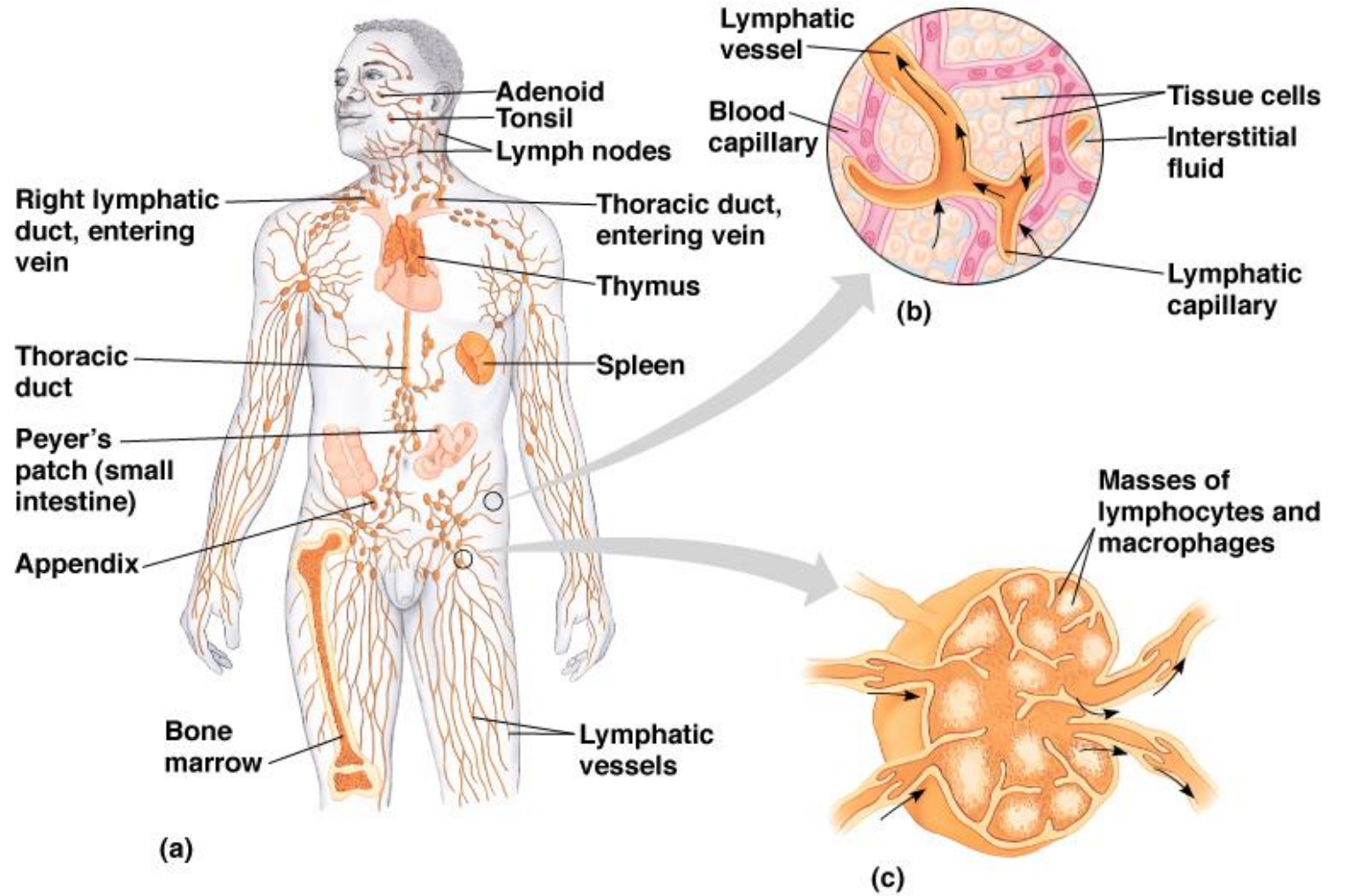
- Genetically determined.
- May be due to lack of receptors or other molecules required for infection.
 - Innate human immunity to canine distemper.
 - Immunity of mice to poliovirus.

Acquired Immunity:

Immunity that an organism *develops* during lifetime.

- Not genetically determined.
- May be acquired naturally or artificially.
 - Development of immunity to measles in response to infection or vaccination.

Components of Human Immune System



Types of Acquired Immunity

I. Naturally Acquired Immunity: Obtained in the course of daily life.

A. Naturally Acquired Active Immunity:

- *Antigens* or pathogens enter body naturally.
- Body generates an immune response to antigens.
- Immunity may be lifelong (chickenpox or mumps) or temporary (influenza or intestinal infections).

B. Naturally Acquired Passive Immunity:

- *Antibodies* pass from mother to fetus via placenta or breast feeding (colostrum).
- No immune response to antigens.
- Immunity is usually short-lived (weeks to months).
- Protection until child's immune system develops.

Types of Acquired Immunity (Continued)



II. Artificially Acquired Immunity: Obtained by receiving a vaccine or immune serum.

1. Artificially Acquired Active Immunity:

- *Antigens* are introduced in vaccines (immunization).
- Body generates an immune response to antigens.
- Immunity can be lifelong (oral polio vaccine) or temporary (tetanus toxoid).

2. Artificially Acquired Passive Immunity:

- Preformed *antibodies* (antiserum) are introduced into body by injection.
 - Snake antivenom injection from horses or rabbits.
- Immunity is short lived (half life three weeks).
- Host immune system does not respond to antigens.

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- **Serum:** Fluid that remains after blood has clotted and cells have been removed.
 - **Antiserum:** Serum containing antibodies to a specific antigen(s). Obtained from injecting an animal (horse, rabbit, goat) with antigen (snake venom, botulism or diphtheria toxin).
 - **Serology:** The study of reactions between antibodies and antigens.
 - **Gamma Globulins:** Fraction of serum that contains most of the antibodies.
 - **Serum Sickness:** Disease caused by multiple injections of antiserum. Immune response to foreign proteins. May cause fever, kidney problems, and joint pain. Rare today.

Duality of Immune System

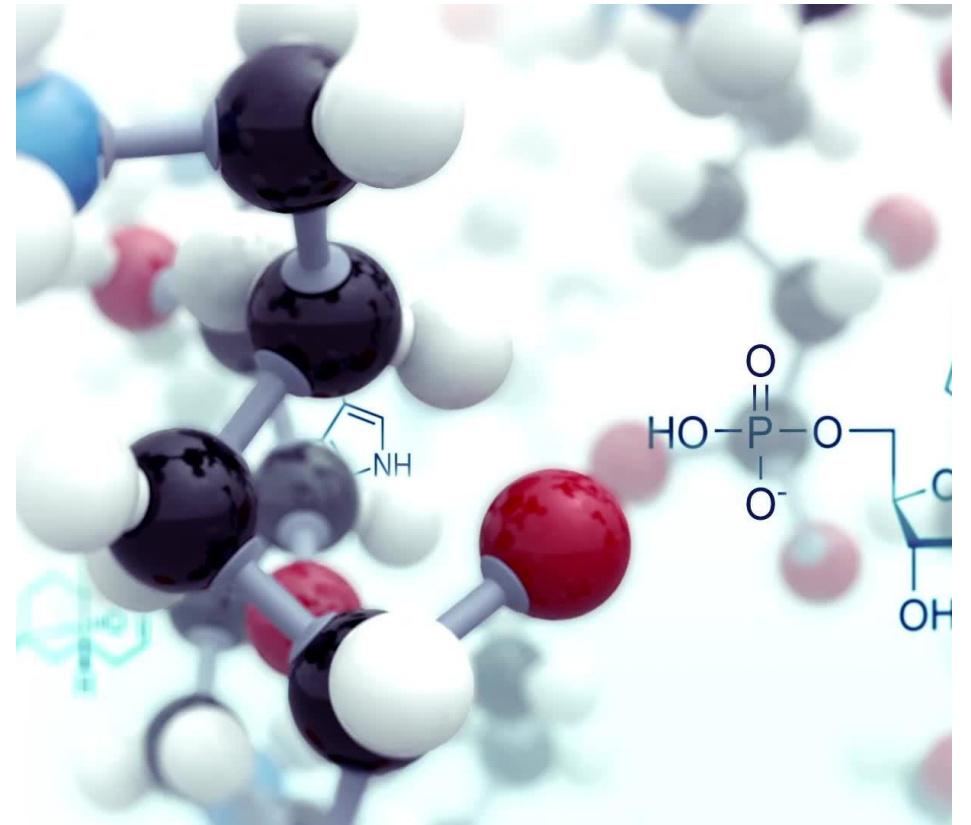
- **Humoral (Antibody-Mediated) Immunity**
 - Involves production of antibodies against foreign antigens.
 - Antibodies are produced by a subset of lymphocytes called B cells.
 - B cells that are stimulated will actively secrete antibodies and are called *plasma cells*.
 - Antibodies are found in extracellular 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.

Antigens

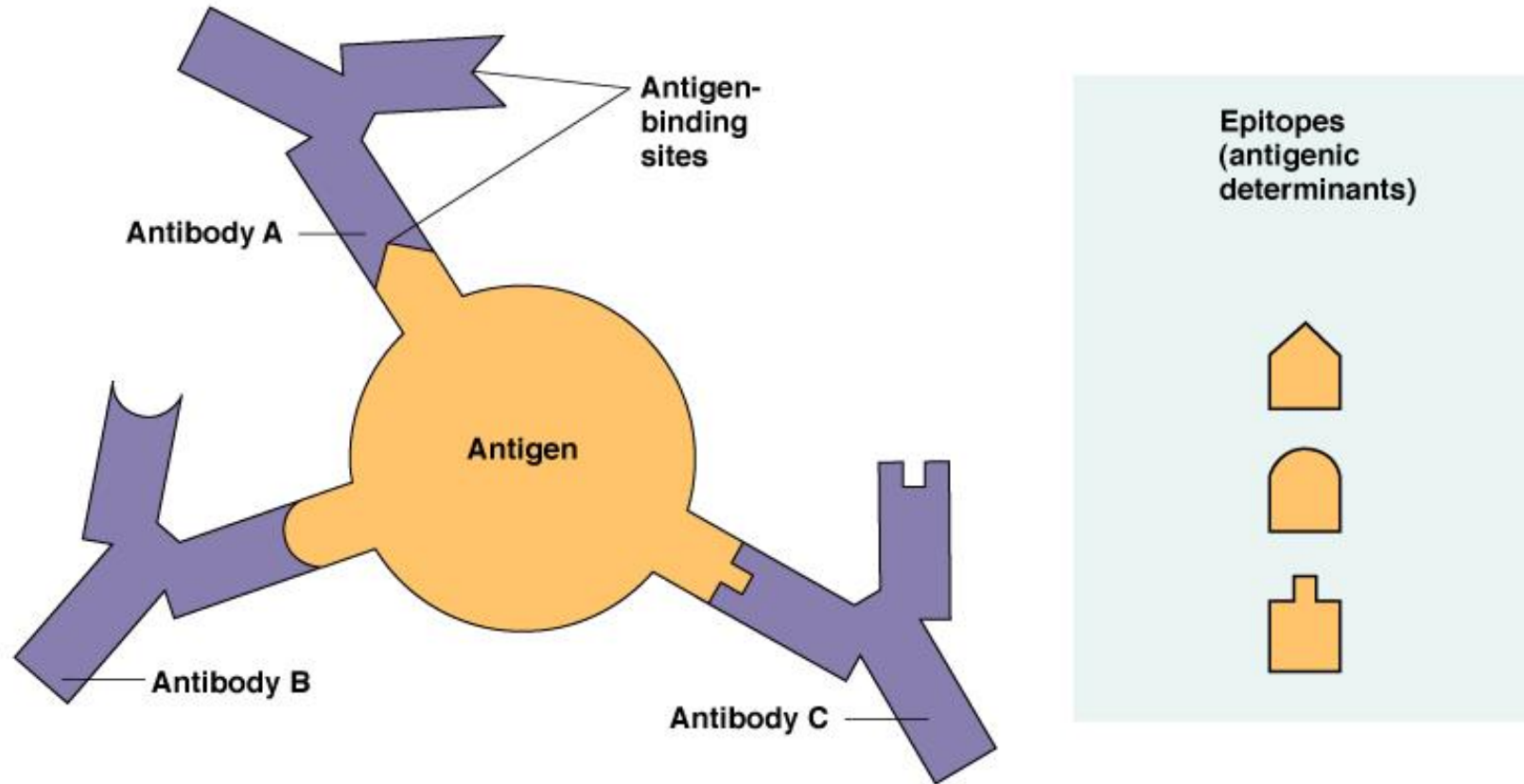
- Most are proteins or large polysaccharides from a foreign organism.
 - Microbes: Capsules, cell walls, toxins, viral capsids, flagella, etc.
 - Nonmicrobes: Pollen, egg white, red blood cell surface molecules, serum proteins, and surface molecules from transplanted tissue.
- Lipids and nucleic acids 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.

Antigens

- **Epitope:**
- Small part of an antigen that interacts with an antibody.
- Any given antigen may have several epitopes.
- Each epitope is recognized by a different antibody.



Epitopes: Antigen Regions that Interact with Antibodies



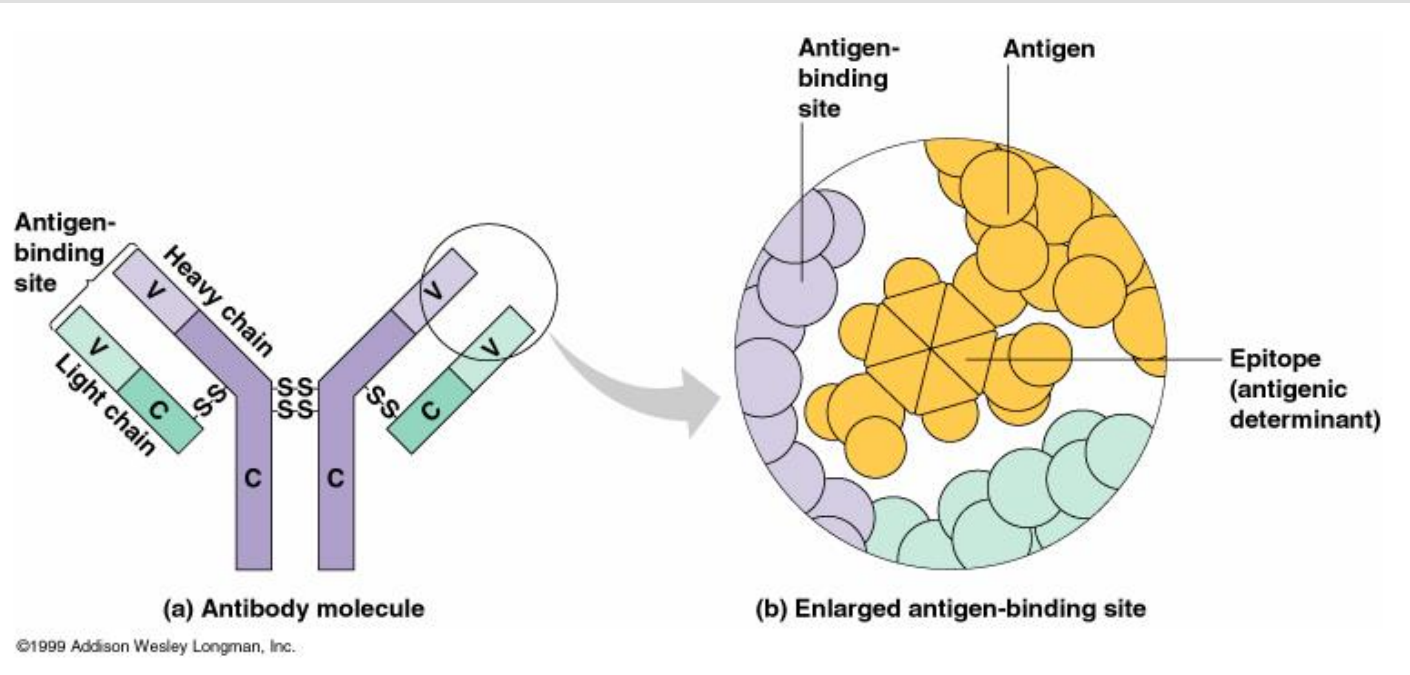
Antibodies

- Proteins that recognize and bind to a particular antigen with very high *specificity*.
- Made in response to exposure to the antigen.
- One virus or microbe may have several *antigenic determinant sites*, to which different antibodies may bind.
- Each antibody has at least two identical sites that bind antigen: *Antigen binding sites*.
- Valence of an antibody: Number of antigen binding sites. Most are bivalent.
- Belong to a group of serum proteins called immunoglobulins (Igs).

Antibody Structure

- **Monomer:** A flexible Y-shaped molecule with four protein chains:
 - 2 identical *light* chains
 - 2 identical *heavy* chains
- **Variable Regions:** Two sections at the end of Y's arms. Contain the antigen binding sites (Fab). Identical on the same antibody, but vary from one antibody to another.
- **Constant Regions:** Stem of monomer and lower parts of Y arms.
- **Fc region:** Stem of monomer only. Important because they can bind to complement or cells.

Antibody Structure



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

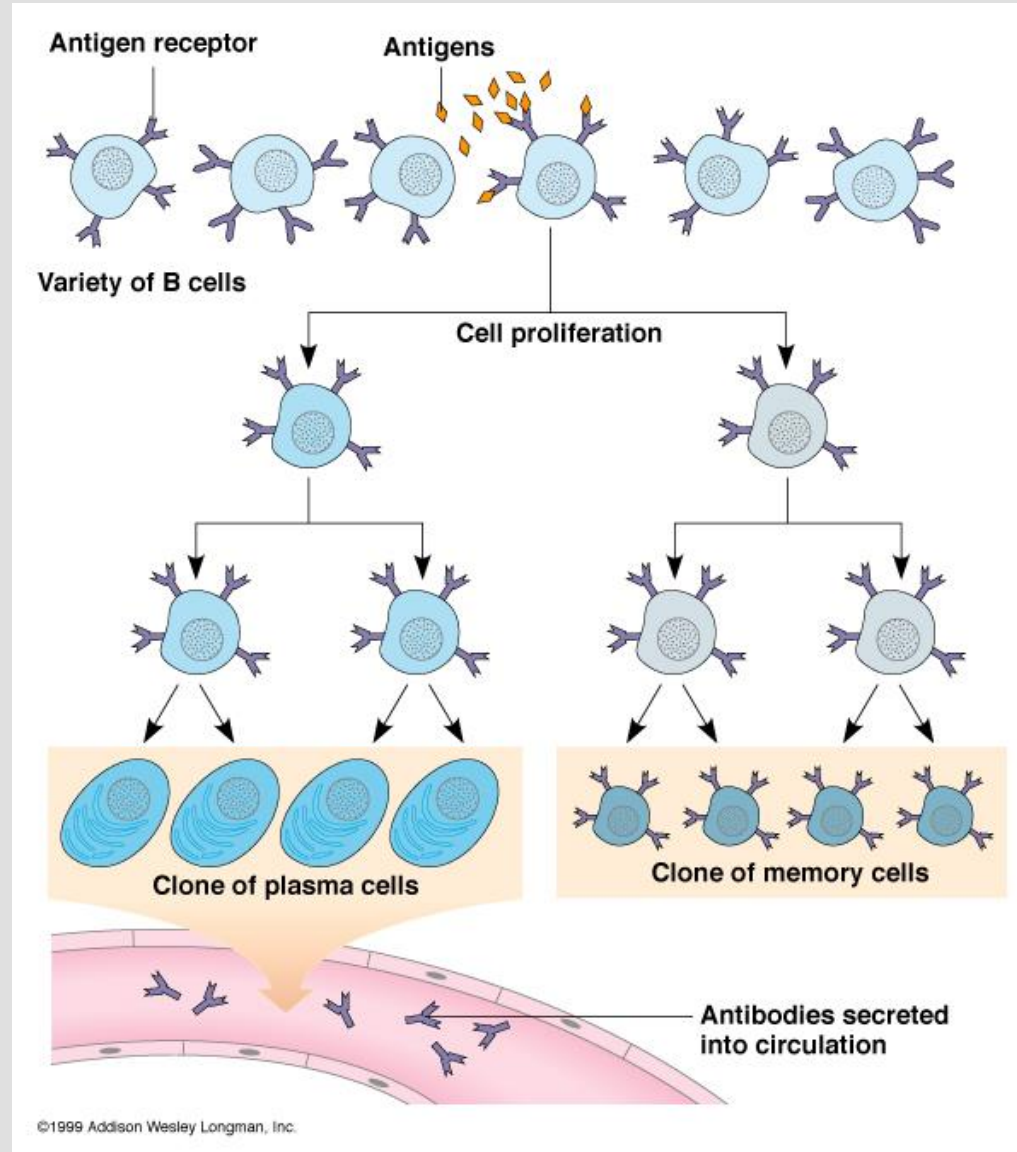
- **V. IgE**
- Structure: Monomer
- Percentage serum antibodies: 0.002%
- Location: Bound to mast cells and basophils throughout body. Blood.
- Half-life in serum: 2 days
- Complement Fixation: No
- Placental Transfer: No
- Known Functions: Allergic reactions. Possibly lysis of worms.

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).
- Clonal Selection: 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



Humoral Immunity (Continued)

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.

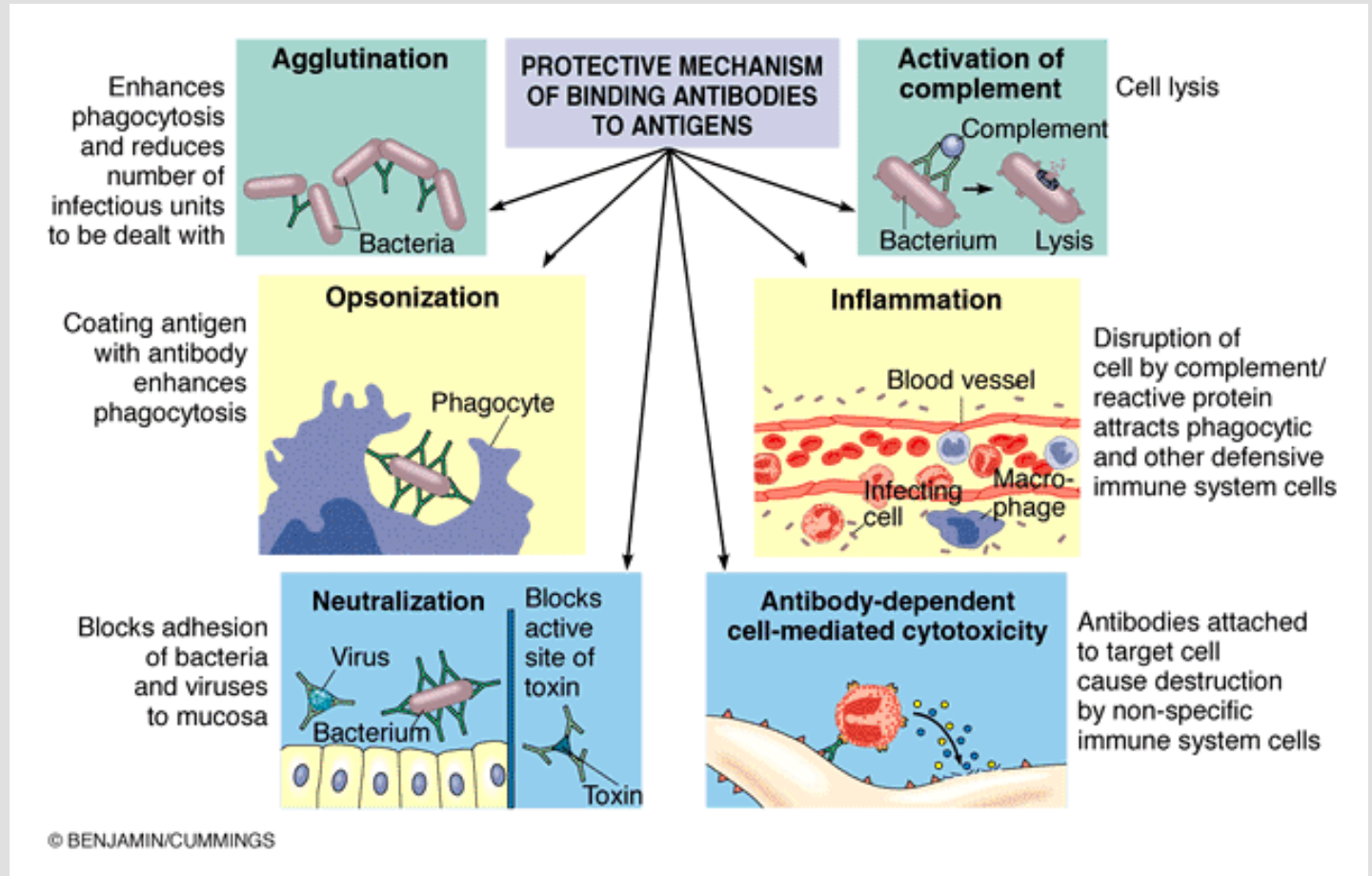
Humoral Immunity (Continued)

- **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 Antigen-Antibody Binding

- - Antigen-Antibody Complex: Formed when an antibody binds to an antigen it recognizes.
 - Affinity: A measure of binding strength.
 - 1. Agglutination: Antibodies cause antigens (microbes) to clump together.
 - IgM (decavalent) is more effective than IgG (bivalent).
 - Hemagglutination: Agglutination of red blood cells. Used to determine ABO blood types and to detect influenza and measles viruses.
 - 2. Opsonization: Antigen (microbe) is covered with antibodies that enhances its ingestion and lysis by phagocytic cells.

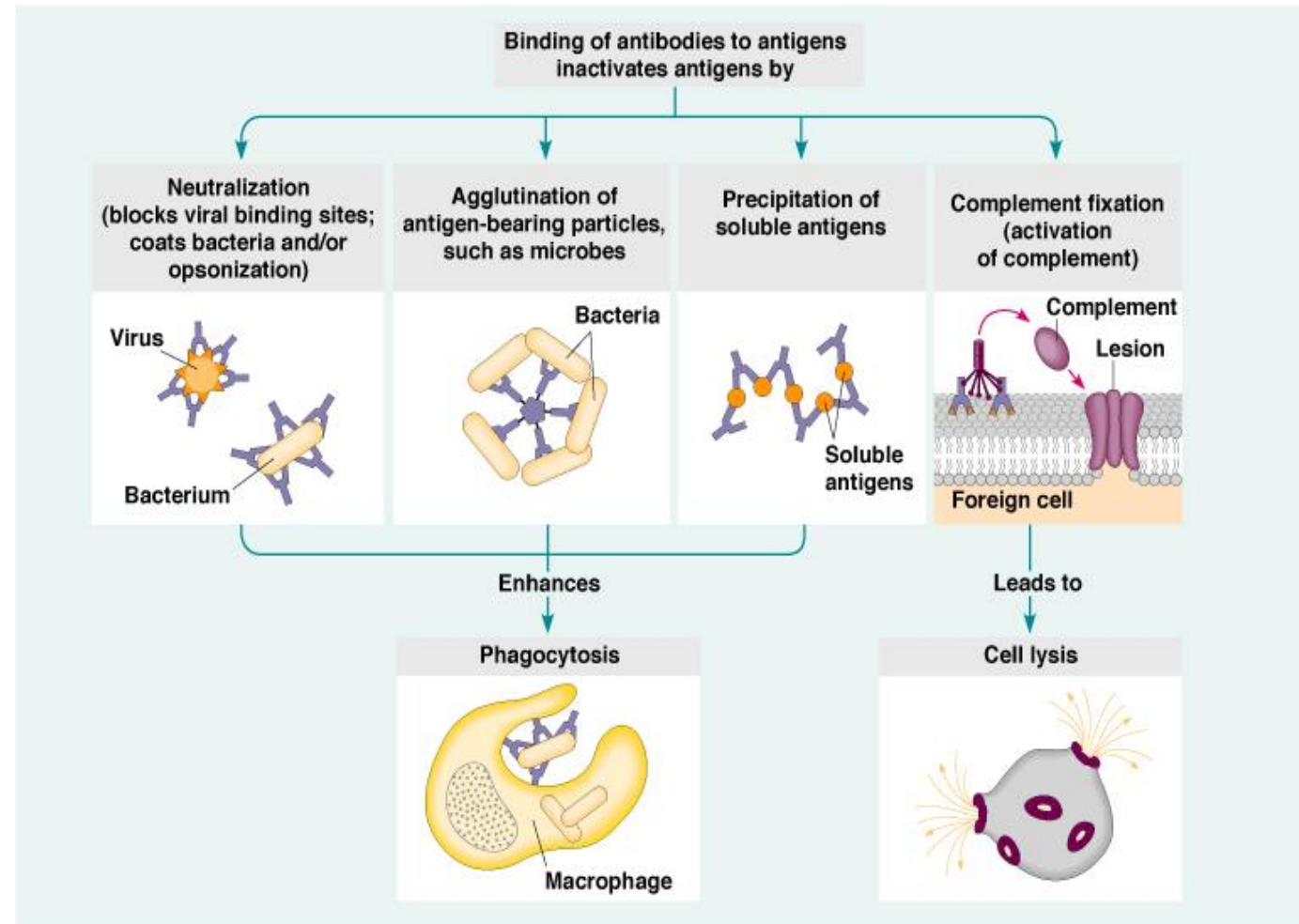
Consequences of Antibody Binding



Humoral Immunity (Continued)

3. Neutralization: IgG inactivates viruses by binding to their surface and neutralize toxins by blocking their active sites.
4. Antibody-dependent cell-mediated cytotoxicity: Used to destroy large organisms (e.g.: worms). Target organism is coated with antibodies and bombarded with chemicals from nonspecific immune cells.
5. Complement Activation: Both IgG and IgM trigger the complement system which results in cell lysis and inflammation.

Consequences of Antibody Binding



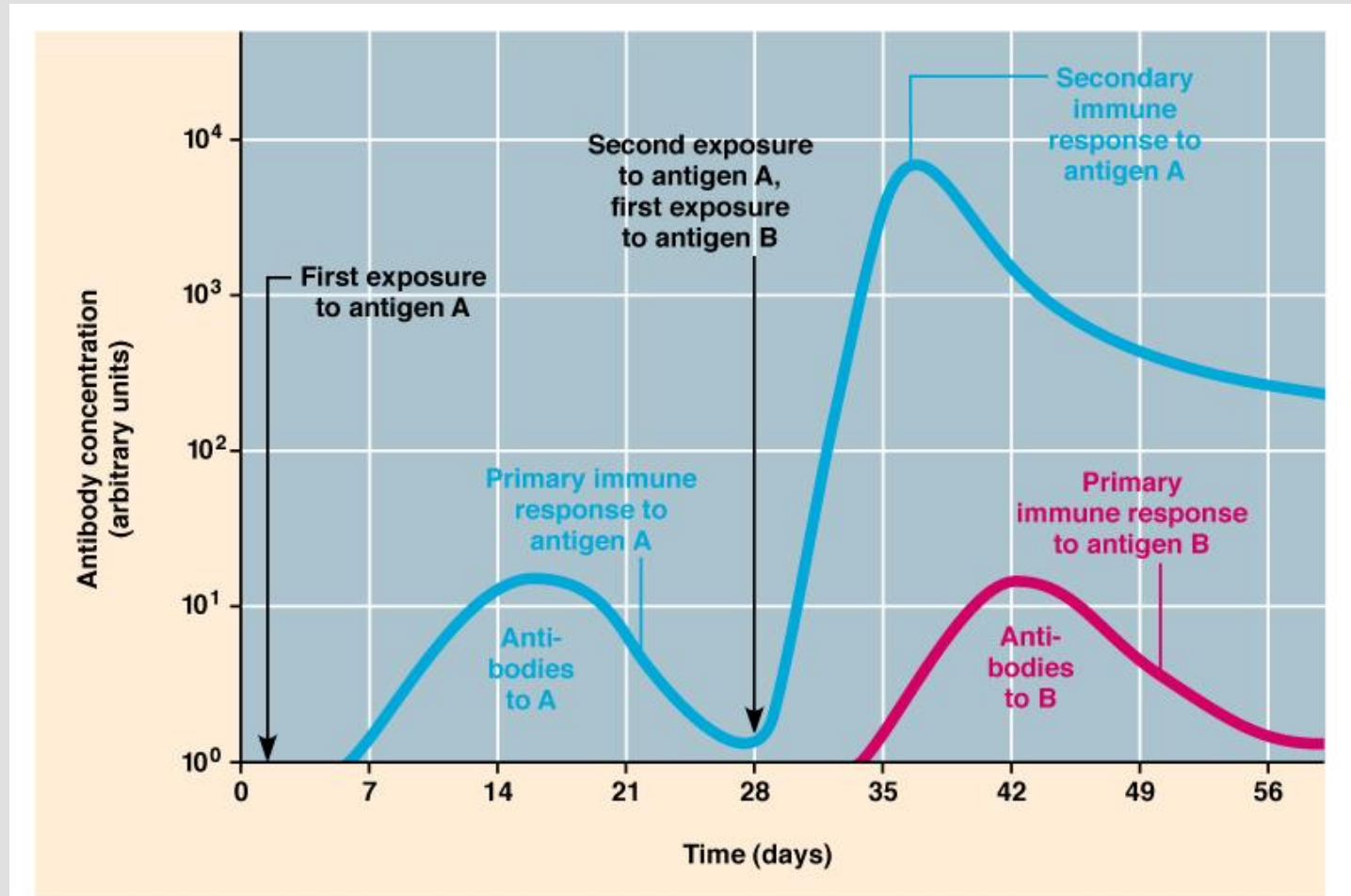
Immunologic al Memory

- - 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.

Antibody Response After Exposure to Antigen



T Cells and Cell Mediated Immunity

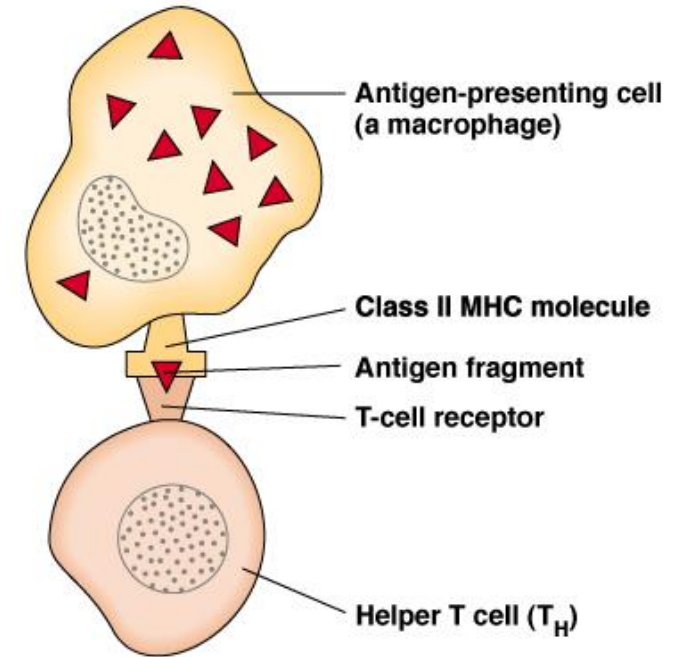
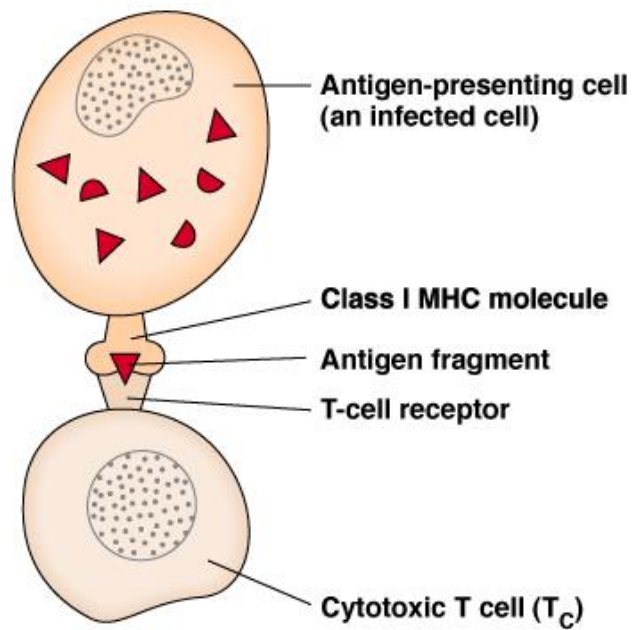
- - Antigens that stimulate this response are mainly *intracellular*.
 - Requires constant presence of antigen to remain effective.
 - Unlike humoral immunity, cell mediated immunity is not transferred to the fetus.
 - Cytokines: Chemical messengers of immune cells.
 - Over 100 have been identified.
 - Stimulate and/or regulate immune responses.
 - Interleukins: Communication between WBCs.
 - Interferons: Protect against viral infections.
 - Chemokines: Attract WBCs to infected areas.

T Cells and Cell Mediated Immunity

Cellular Components of Immunity:

- T cells are key cellular component of immunity.
- T cells have an antigen receptor that recognizes and reacts to a specific antigen (T cell receptor).
- T cell receptor only recognize antigens combined with major histocompatibility (MHC) proteins on the surface of cells.
 - MHC Class I: Found on all cells.
 - MHC Class II: Found on phagocytes.
- Clonal selection increases number of T cells.

T Cells Only Recognize Antigen Associated with MHC Molecules on Cell Surfaces



(a)

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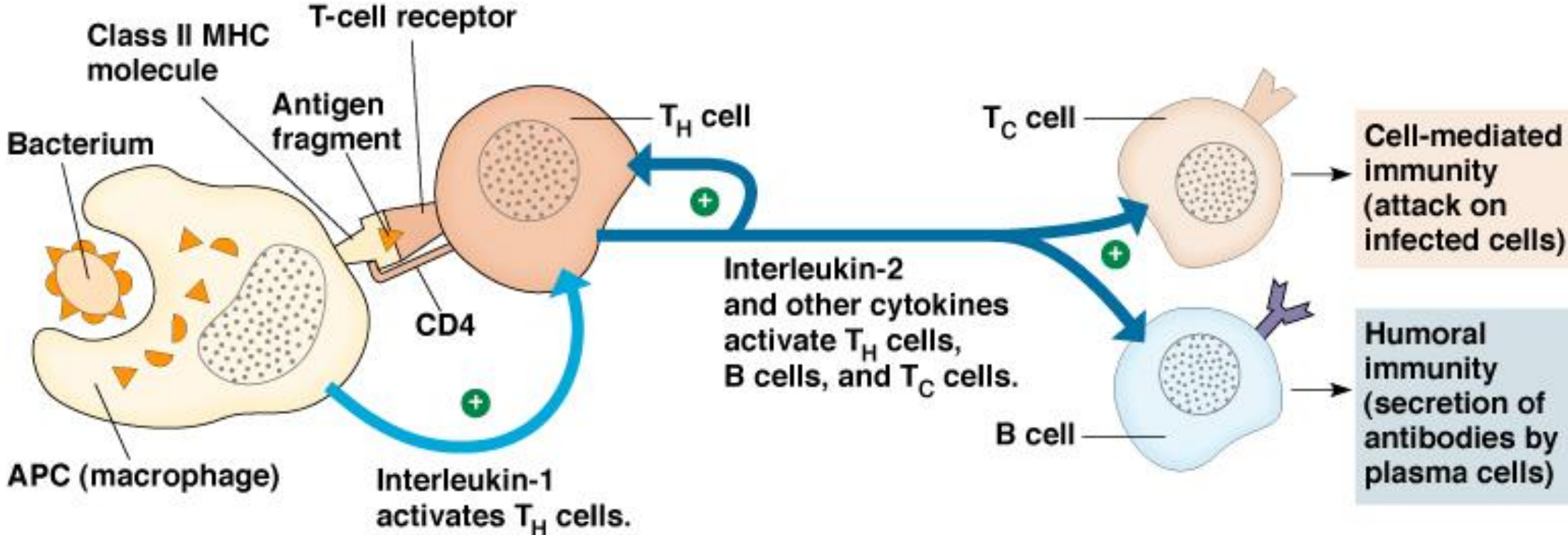
(b)

T Cells and Cell Mediated Immunity

Types of T cells

1. T Helper (T_H) Cells: Central role in immune response.
 - Most are $CD4^+$
 - Recognize antigen on the surface of antigen presenting cells (e.g.: macrophage).
 - Activate macrophages
 - Induce formation of cytotoxic T cells
 - Stimulate B cells to produce antibodies.

Central Role of Helper T Cells

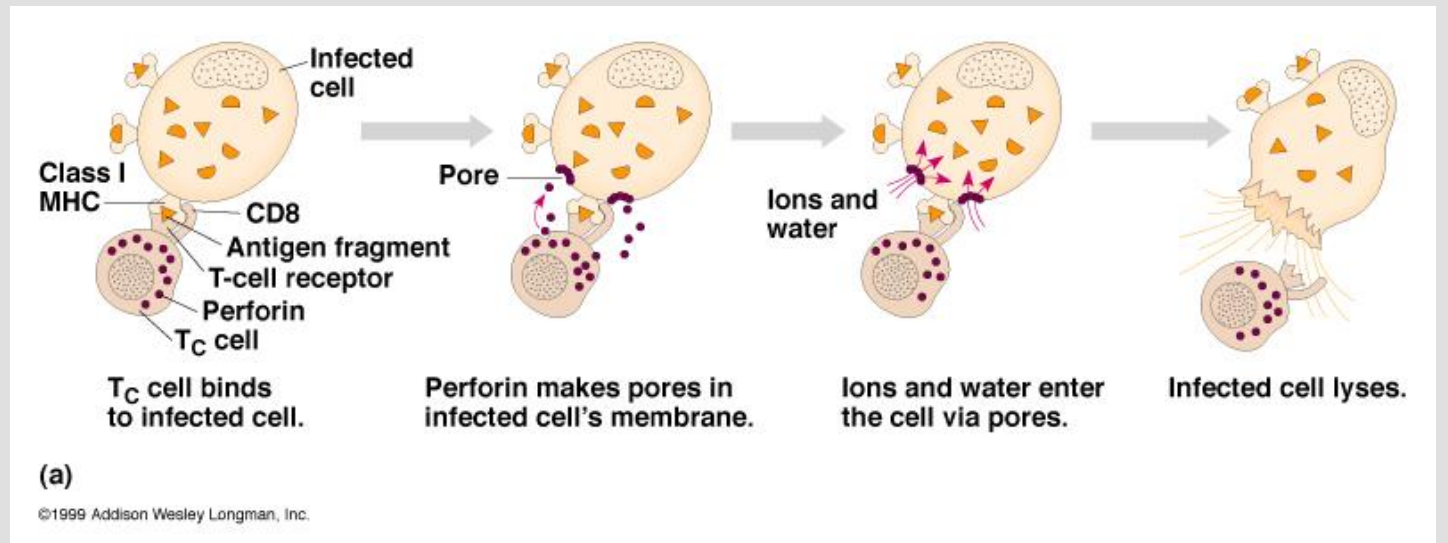


Types of T cells (Continued)

2. Cytotoxic T (Tc) Cells: Destroy target cells.

- Most are CD4 negative (CD4⁻).
- Recognize antigens on the surface of all cells:
 - Kill host cells that are infected with viruses or bacteria.
 - Recognize and kill cancer cells.
 - Recognize and destroy transplanted tissue.
- Release protein called *perforin* which forms a pore in target cell, causing lysis of infected cells.
- Undergo apoptosis when stimulating antigen is gone.

Cytotoxic T Cells Lyse Infected Cells



Types of T cells (Continued)

- 3. Delayed Hypersensitivity T (T_D) Cells:** Mostly T helper and a few cytotoxic T cells that are involved in some allergic reactions (poison ivy) and rejection of transplanted tissue.
- 4. T Suppressor (T_s) Cells:** May shut down immune response.

Nonspecific Cellular Components

- 1. Activated Macrophages: Stimulated phagocytes.**
 - Stimulated by ingestion of antigen
 - Larger and more effective phagocytes.
 - Enhanced ability to eliminate intracellular bacteria, virus-infected and cancerous cells.
- 2. Natural Killer (NK) Cells:**
 - Lymphocytes that destroy virus infected and tumor cells.
 - Not specific. Don't require antigen stimulation.
 - Not phagocytic, but must contact cell in order to lyse it.

Relationship Between Cell- Mediated and Humoral Immunity

1. Antibody Production

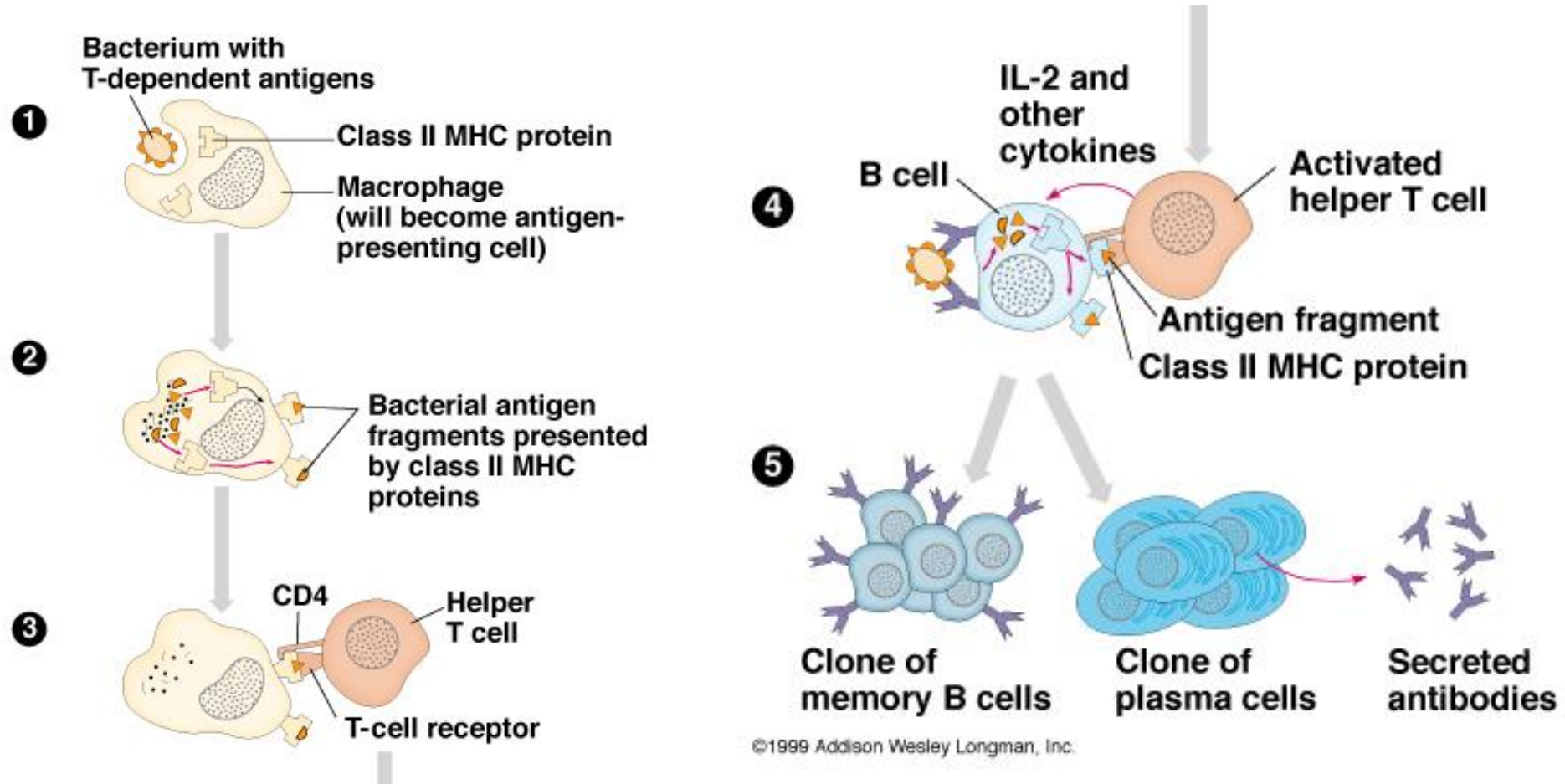
T-Dependent Antigens:

- Antibody production requires assistance from T helper cells.
- A macrophage cells ingest antigen and presents it to T_H cell.
- T_H cell stimulates B cells specific for antigen to become plasma cells.
- Antigens are mainly proteins on viruses, bacteria, foreign red blood cells, and haptten-carrier molecules.

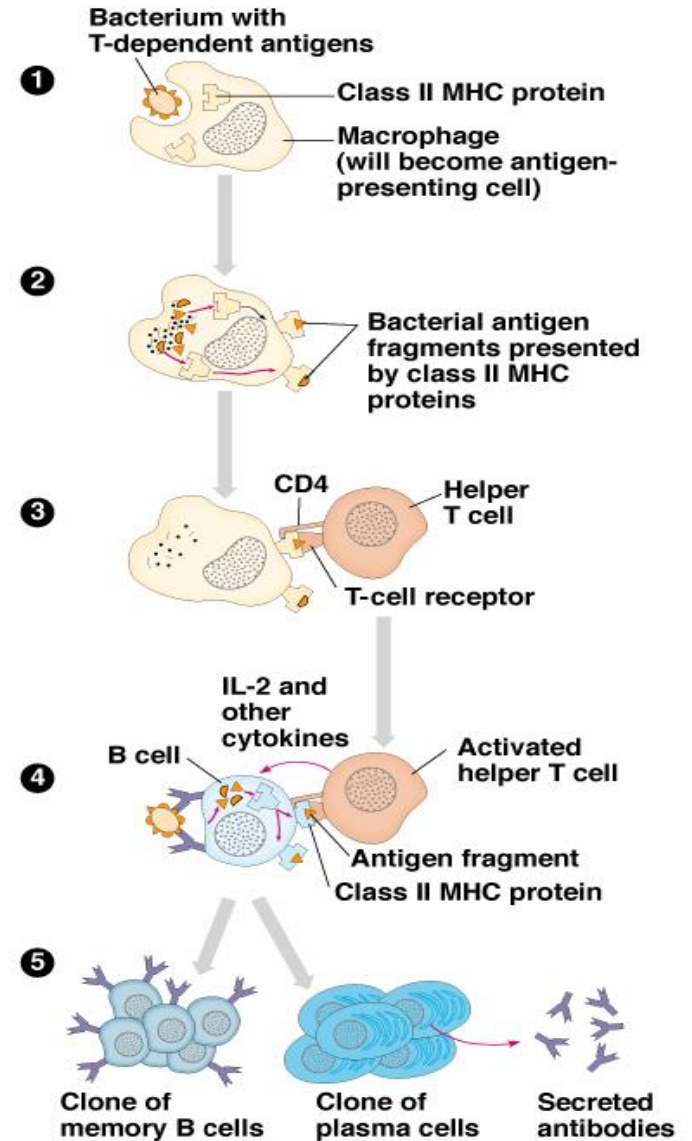
T-Independent Antigens:

- Antibody production does not require assistance from T cells.
- Antigens are mainly polysaccharides or lipopolysaccharides with repeating subunits (bacterial capsules).
- Weaker immune response than for T-dependent antigens.

Humoral Response to T Dependent Antigens



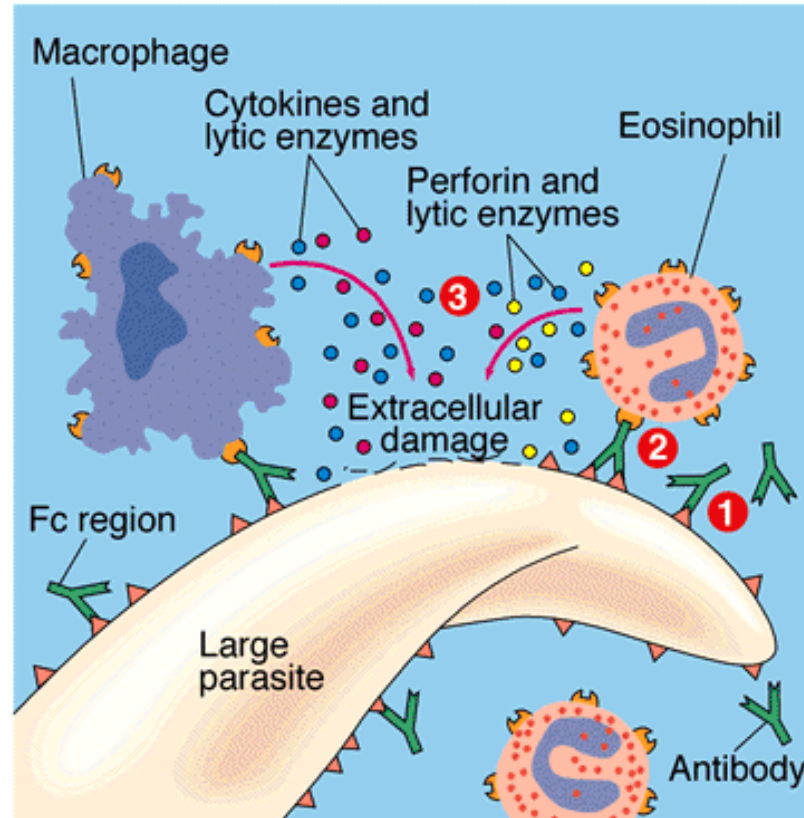
Humoral Response to T Dependent Antigens



Relationship Between Cell- Mediated and Humoral Immunity

2. Antibody Dependent Cell Mediated Cytotoxicity
 - Target cell is covered with antibodies, leaving Fc portion sticking outwards.
 - Natural killer and other nonspecific cells that have receptors for Fc region are stimulated to kill targeted cells.
 - Target organism is lysed by substances secreted by attacking cells.
 - Used to destroy large organisms that cannot be phagocytosed.

Destruction of Large Parasites by ADCC



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Overview of the Immune Response

