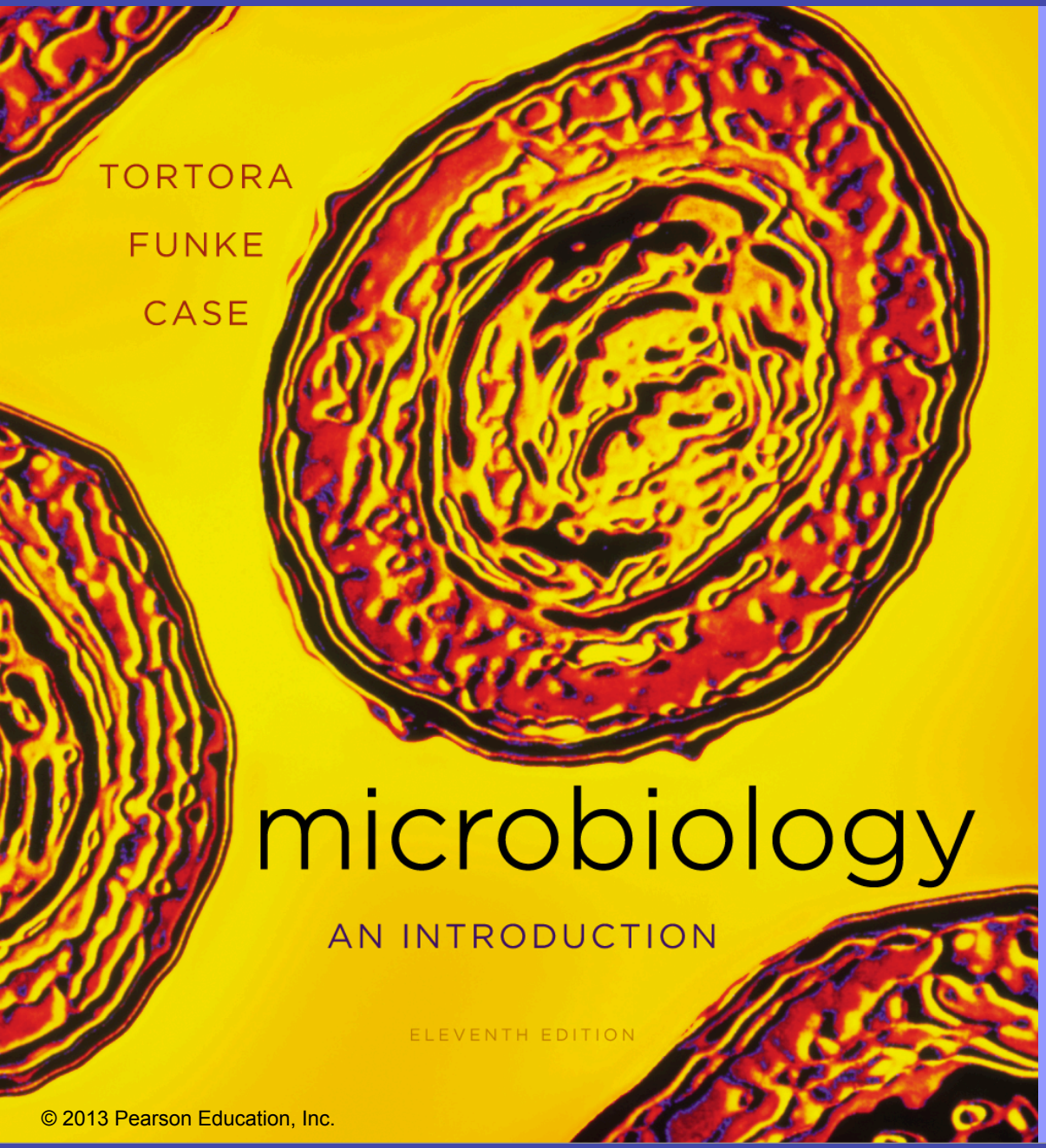
Module 11

Adaptive Immunity



Chapter 17

Adaptive Immunity

Lectures prepared by Helmut Kae

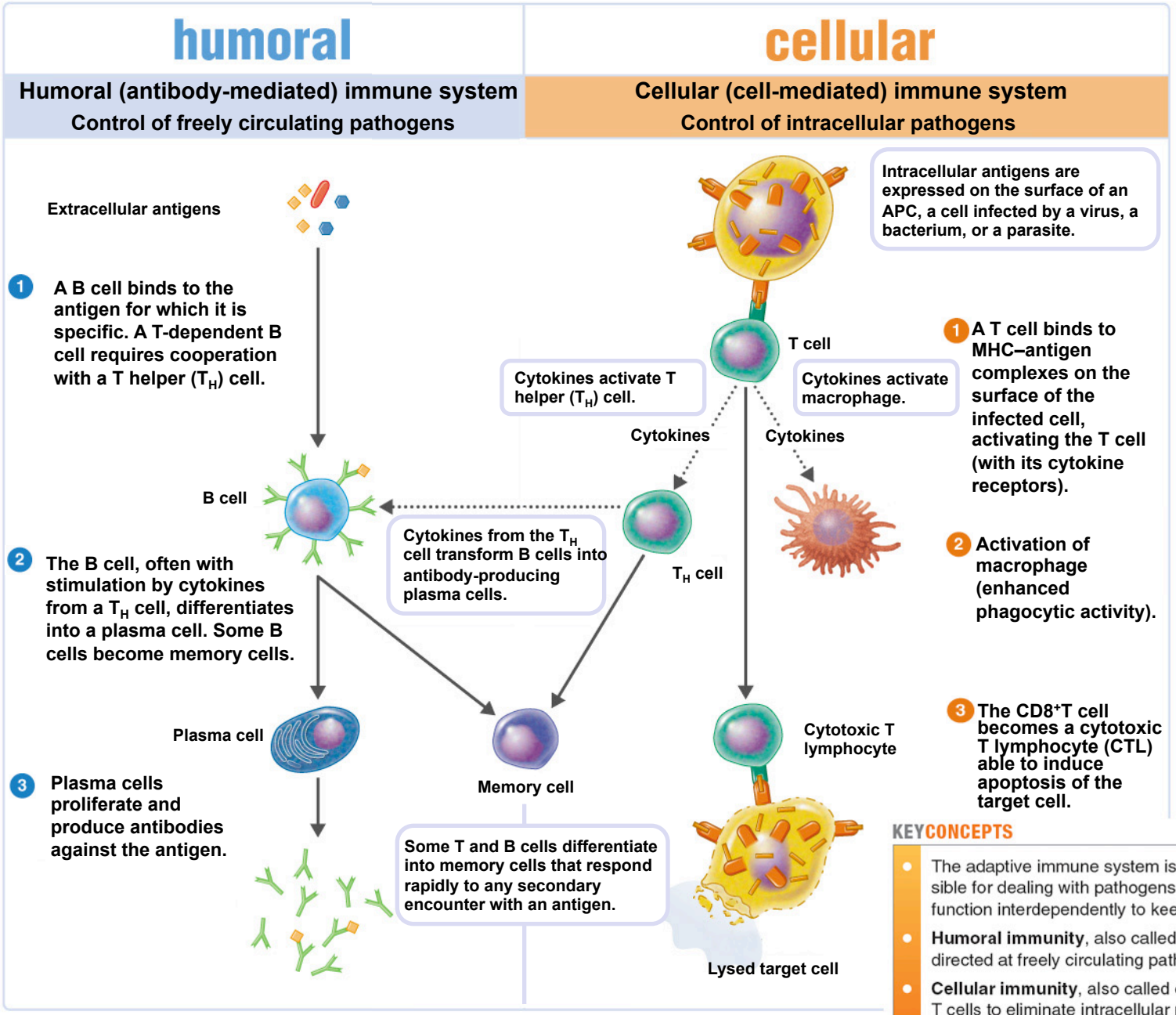
The Immune System

- **Innate immunity**: defenses against any pathogen
  - Reacts the same way every time
- **Adaptive immunity**: induced and adapts to a specific microbe or foreign substance
  - Has memory component, major difference from innate immunity

Dual Nature of Adaptive Immunity

- Two components to adaptive immunity
- **Humoral immunity**: immunity mediated by antibodies
  - Aka antibody-mediated immunity
  - Control of freely circulating pathogens
  - Via **B cells**
- **Cellular immunity**: immunity mediated by cells
  - Aka cell-mediated immunity
  - Control of intracellular pathogens
  - Via **T cells**

Figure 17.20 The dual nature of the adaptive immune system.



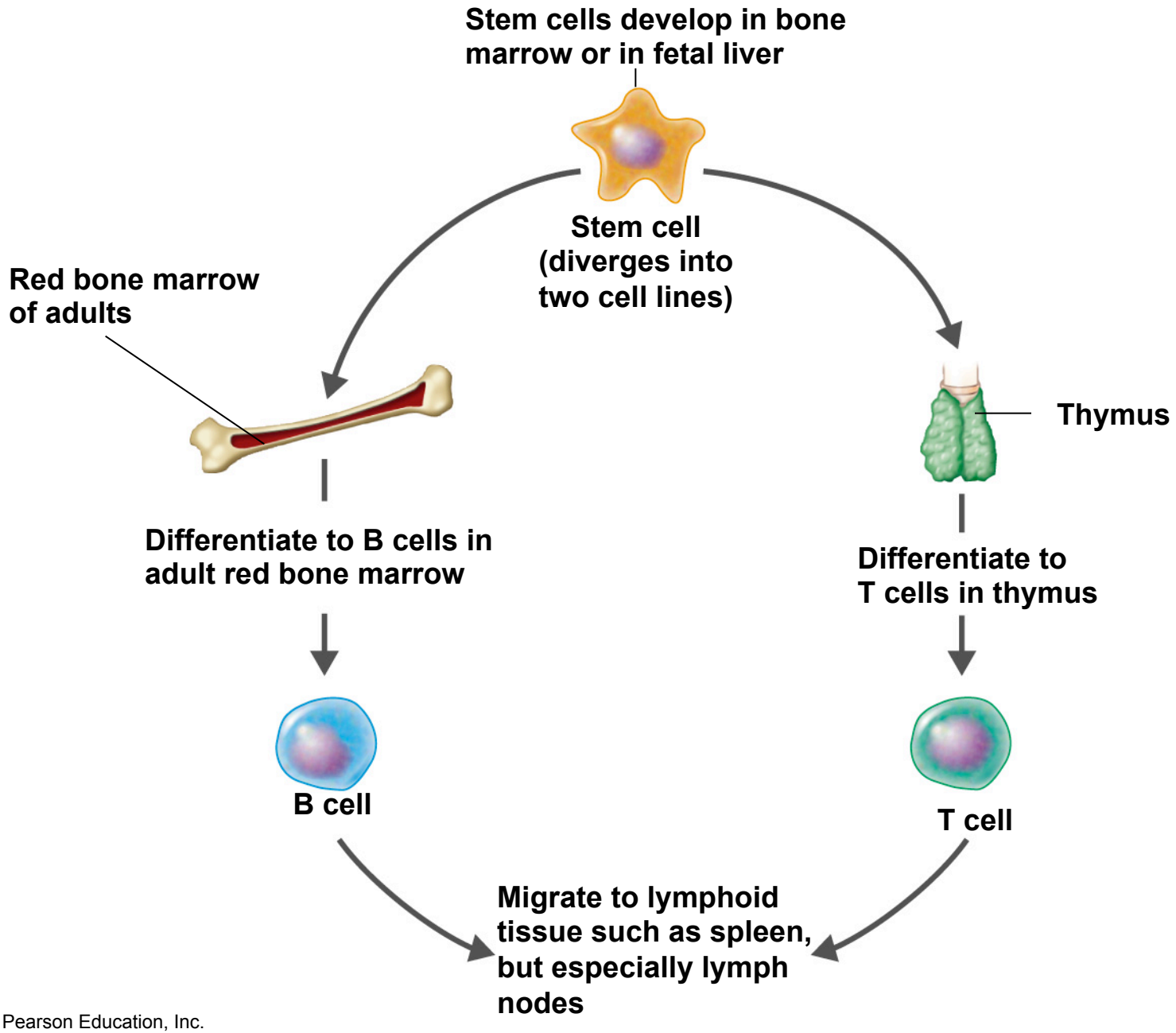
KEY CONCEPTS

- The adaptive immune system is divided into two parts, each responsible for dealing with pathogens in different ways. These two systems function interdependently to keep the body free of pathogens.
- **Humoral immunity**, also called antibody-mediated immunity, is directed at freely circulating pathogens and depends on B cells.
- **Cellular immunity**, also called cell-mediated immunity, depends on T cells to eliminate intracellular pathogens, reject foreign tissue recognized as nonself, and destroy tumor cells.

Dual Nature of Adaptive Immunity

- T and B cells develop from stem cells in red bone marrow

Figure 17.8 Differentiation of T cells and B cells.



Humoral Immunity

- Immunity mediated by antibodies
  - Aka antibody-mediated immunity
  - Control of freely circulating pathogens
  - Via **B cells**

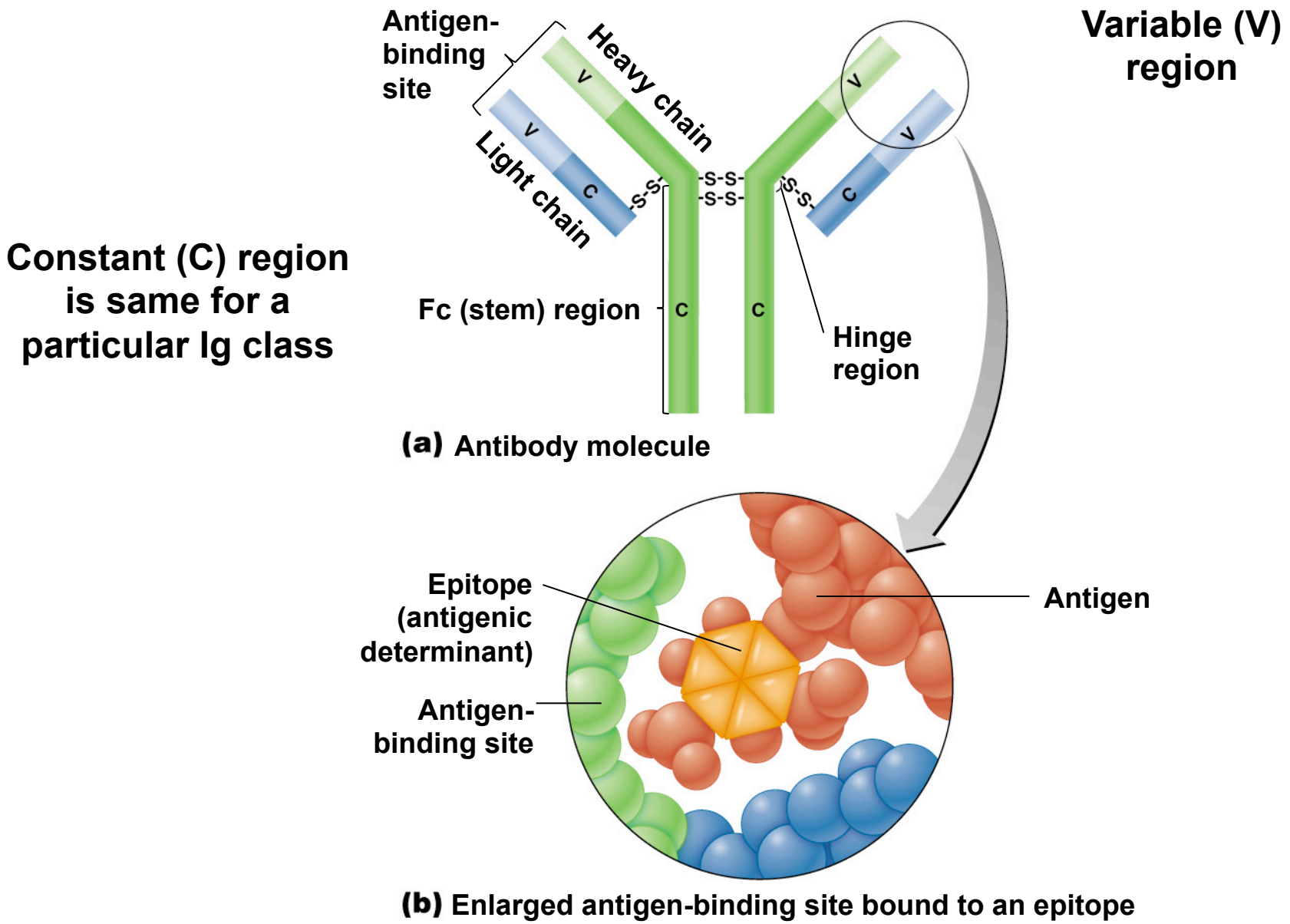
Antigens and Antibodies

- **Antigen (Ag)**: a substance that stimulates the immune system
  - Often external structures of pathogens
  - Or pollen, egg whites, cells & tissues
- Antigens in body are recognized by antibodies

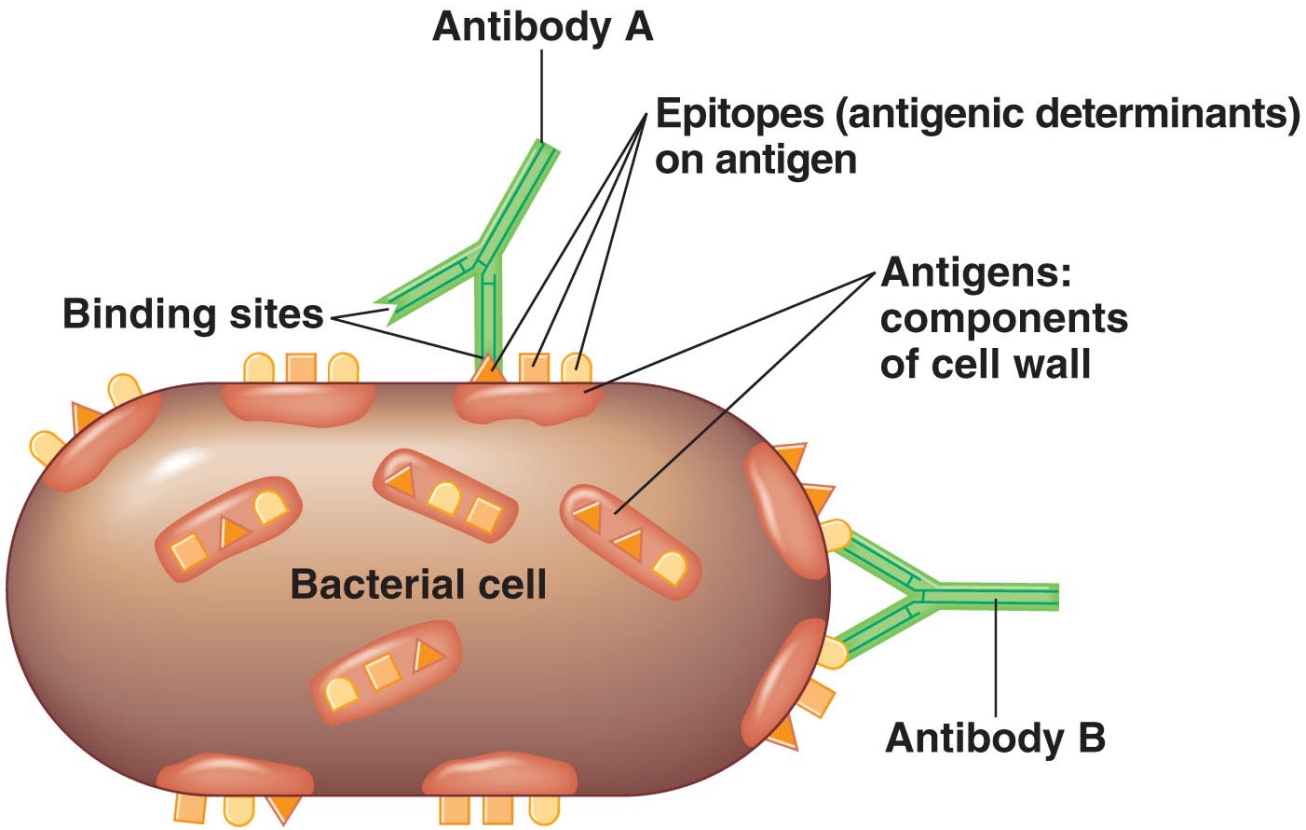
The Nature of Antibodies

- Antibodies are aka **immunoglobulins (Ig)**
- Antibodies are made in response to an antigen
  - Recognize and bind to a specific antigen
- Antibodies are “Y-shaped” proteins

Figure 17.3ab The structure of a typical antibody molecule.



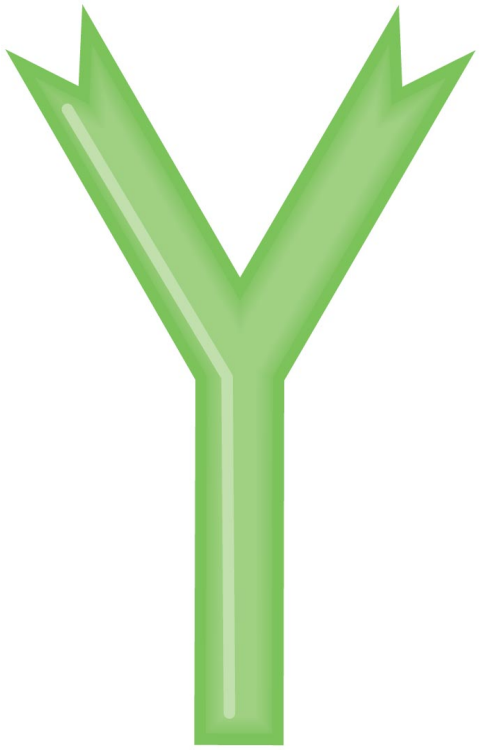
Antibody Binding



- Function of antibodies varies on class of Ig molecule
- 5 Ig classes

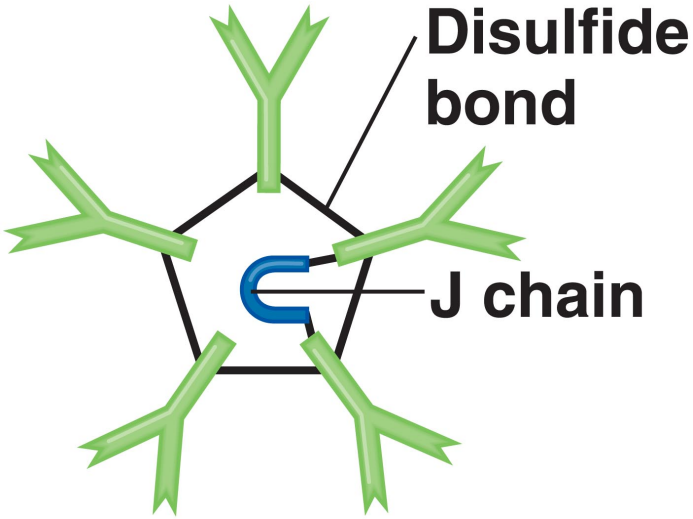
Immunoglobulin Classes

- **IgG**: monomer
- Most abundant, 80%
- Roams, protects body fluids, blood and lymph
- Protect against bacteria, viruses, toxins in blood, enhance phagocytosis
- Protect fetus and newborn
- Long lived
  - Half-life = 23 days



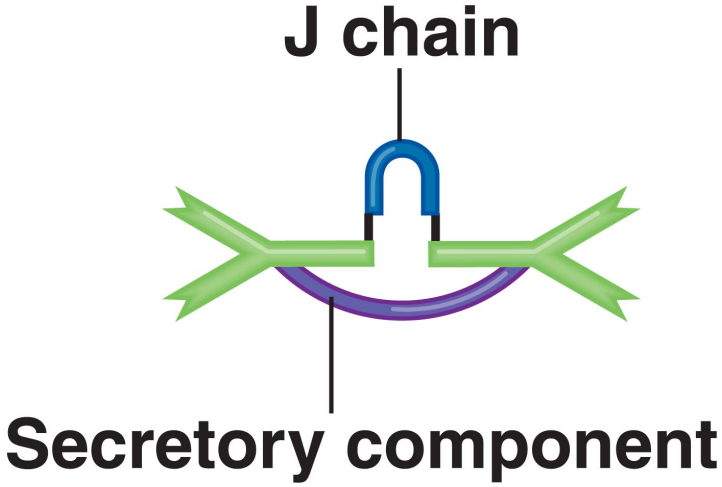
Immunoglobulin Classes

- **IgM**: pentamer (5)
- Stays in bloodstream
- First antibody produced in response to infection, short-lived
  - Used in diagnosing pathogen in early stages of infection
  - Half-life = 5 days
- Effective in agglutinating antigens, enhances phagocytosis against bacteria



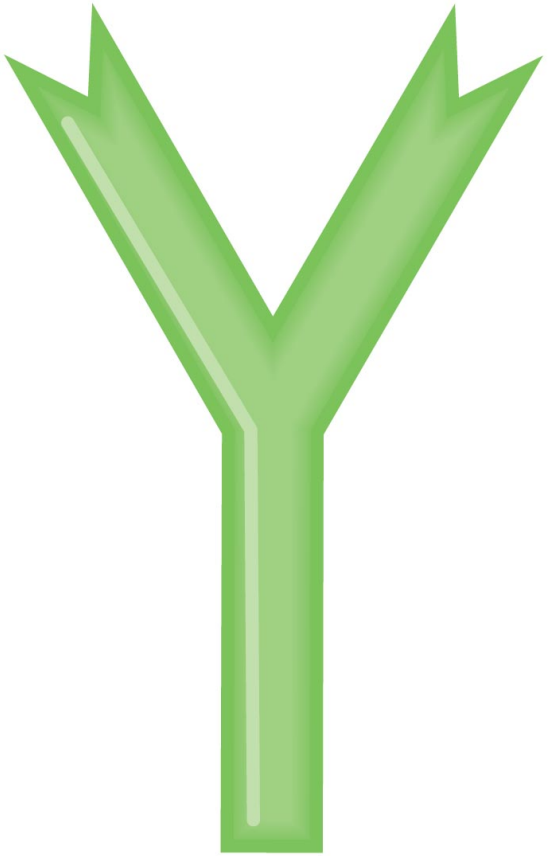
Immunoglobulin Classes

- **IgA**: monomers or dimers
- 10-15%
- Most common in mucous membranes and body secretions
- Prevent adherence of microbes to mucosal surfaces
- Short-lived
  - Half-life = 6 days



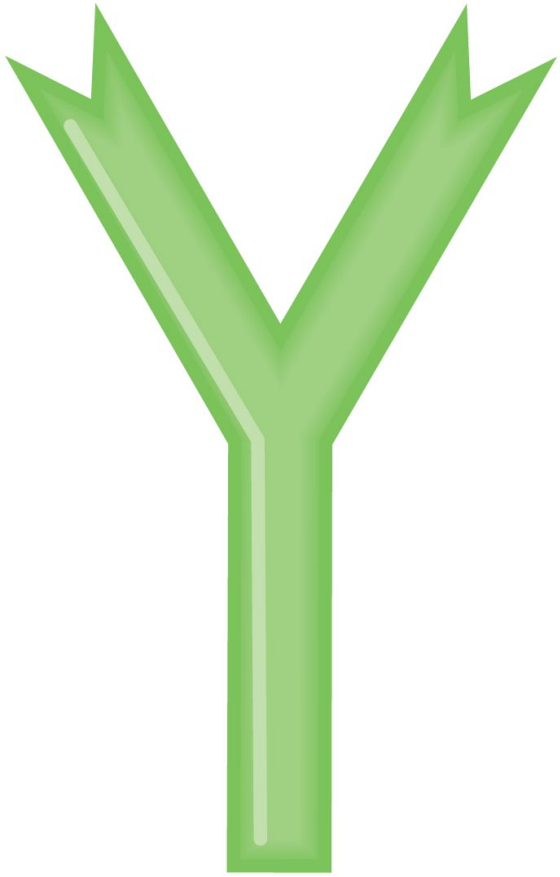
Immunoglobulin Classes

- **IgD**: monomer
- 0.2% of serum antibodies
- In blood, in lymph, and on B cells
- On B cells, initiate immune response
- Half-life = 3 days



Immunoglobulin Classes

- **IgE**: monomer
- 0.002%
- Bind to mast cells, basophils
- Involved in allergic reactions
  - Stimulates histamine release
- Attracts phagocytes, causes hay fever
- Binds to parasitic worms – recruit eosinophils
- Half-life = 2 days



B cells and humoral immunity

- Protection mediated by antibodies
- Produced by activating lymphocytes, B cells
- Activation of naïve B cells starts with exposure to “free” or “extracellular” antigens

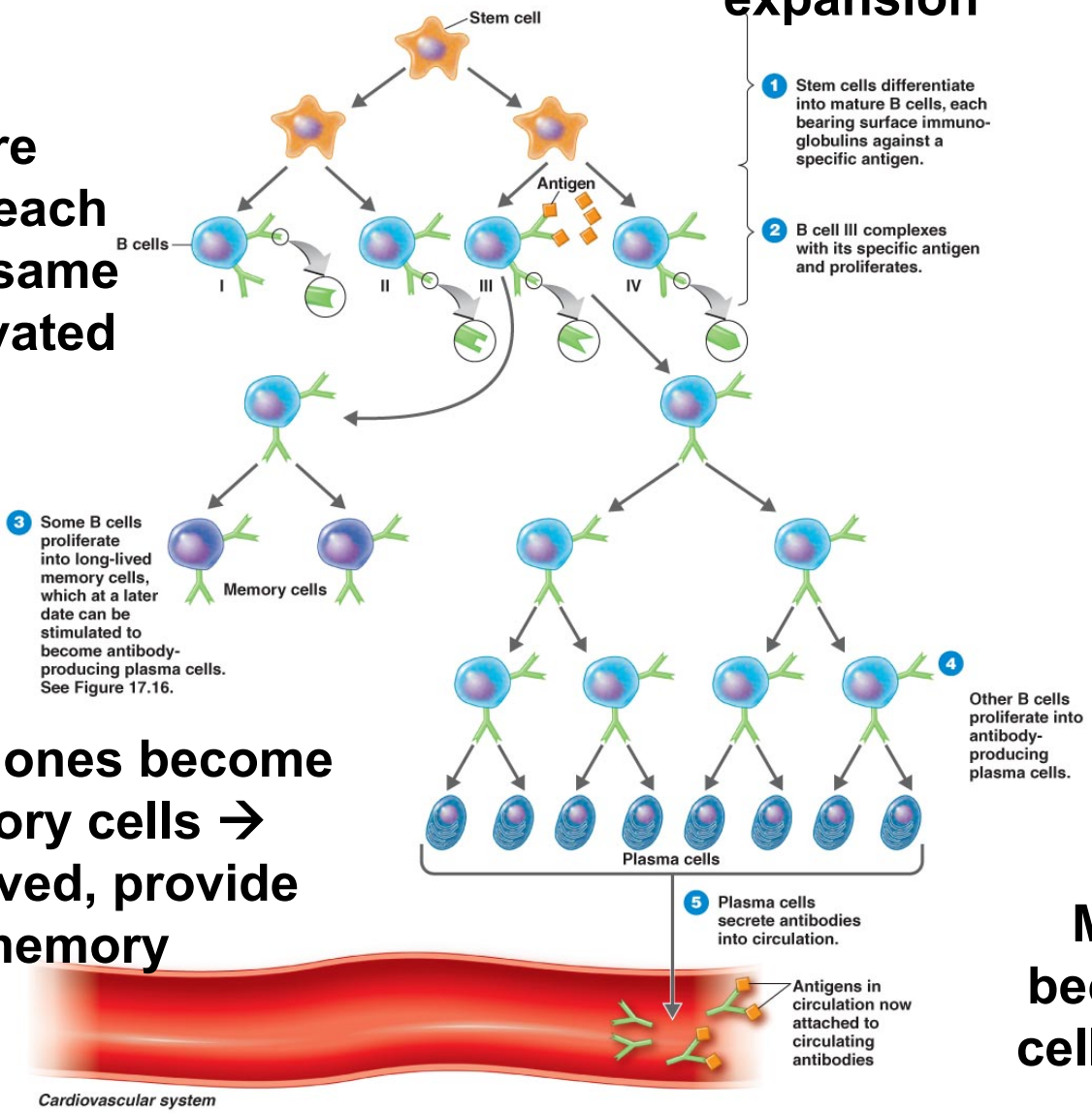
Activation of B Cells

- Naïve B cells carry **B cell receptors (BCR)** on cell surface
  - "Antibodies bound to cell membrane"
  - 100,000+ BCRs, all bind to same antigen
  - Each B cell binds to unique antigen
- Binding of antigen activates naïve B cell

Activation of B Cells

Activated B cell undergoes clonal expansion

Clones are identical to each other, carry same BCR as activated B cell



Some clones become memory cells → long-lived, provide memory

Most clones become plasma cells → antibody producers

Activation of B Cells

- **Major histocompatibility complex (MHC)** expressed on mammalian cells
- **T-dependent antigens**
  - Ag presented with MHC to T_H cell
  - T_H cell produces cytokines that activate the B cell
- **T-independent antigens**
  - Stimulate the B cell to make Abs without help of T_H cell

Figure 17.6 T-independent antigens.

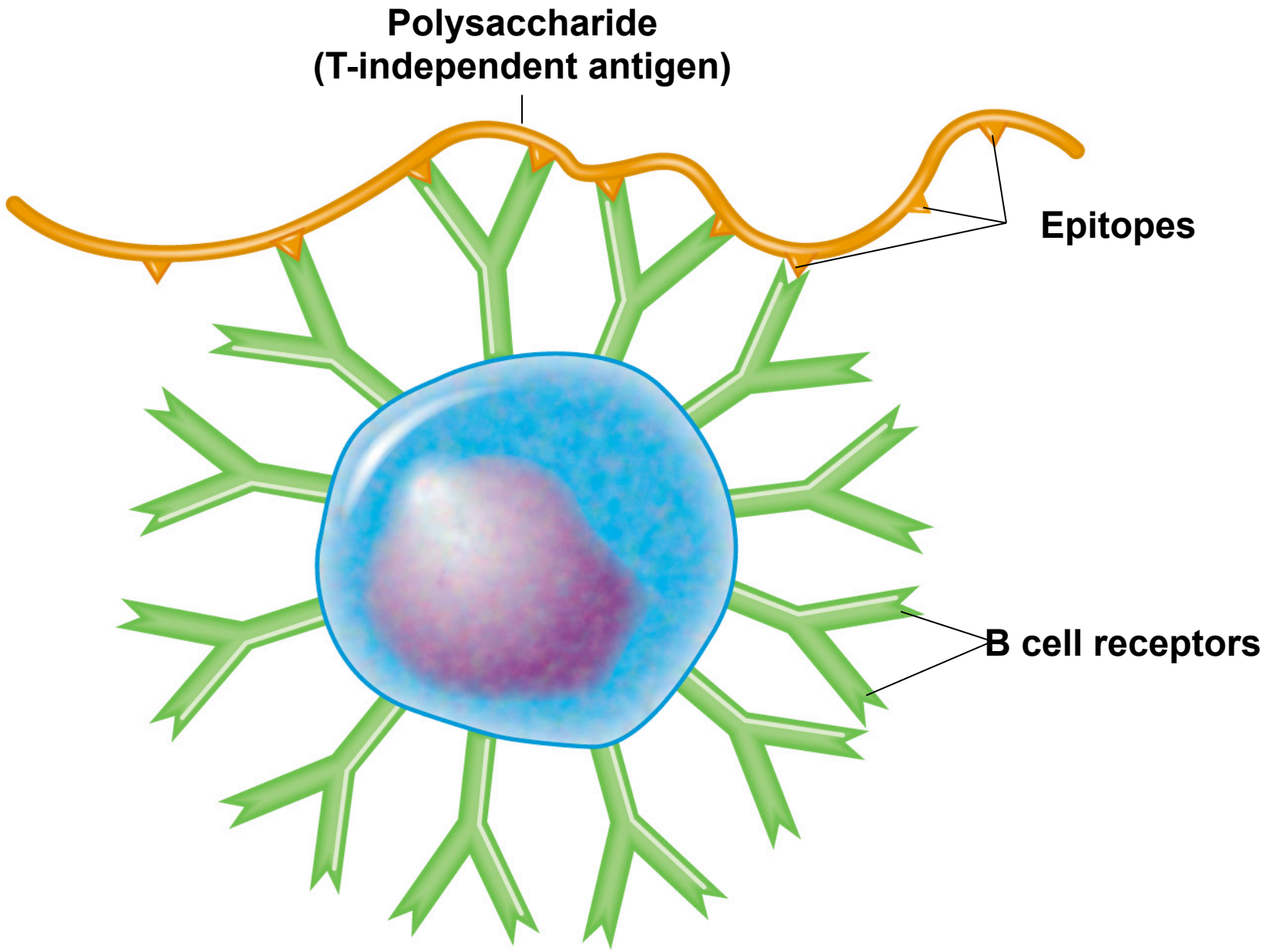
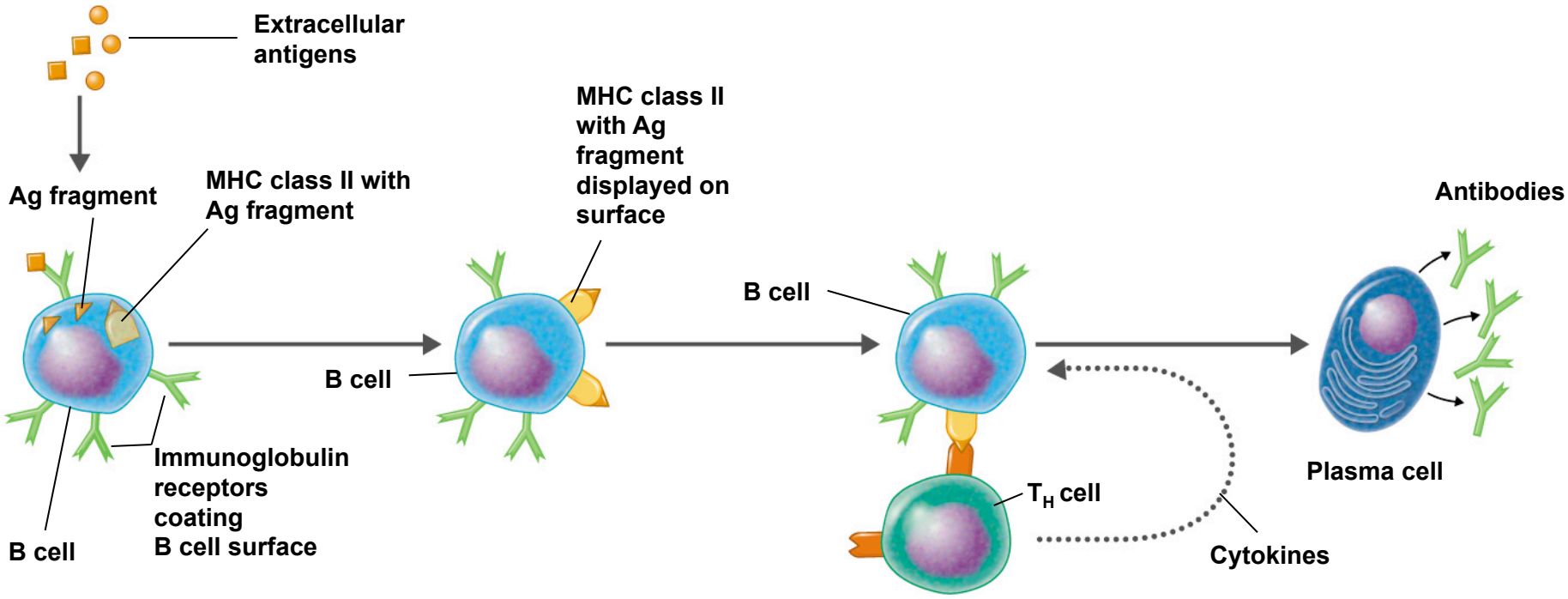


Figure 17.4 Activation of B cells to produce antibodies.



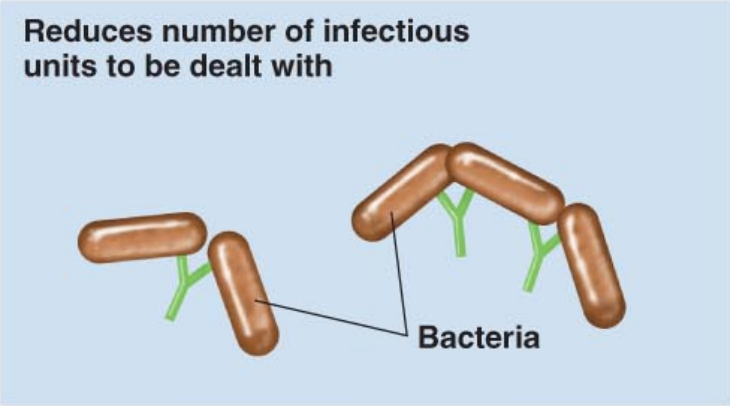
1. Immunoglobulin receptors on B cell surface recognize and attach to antigen, which is then internalized and processed. Within the B cell a fragment of the antigen combines with MHC class II.
2. MHC class II–antigen-fragment complex is displayed on B cell surface.
3. Receptor on the T helper cell (T_H) recognizes complex of MHC class II and antigen fragment and is activated—producing cytokines, which activate the B cell. The T_H cell has been previously activated by an antigen displayed on a dendritic cell (see Figure 17.10).
4. B cell is activated by cytokines and begins clonal expansion. Some of the progeny become antibody-producing plasma cells.

Antigen–Antibody Binding

- Antibody-antigen binding results in a number of responses

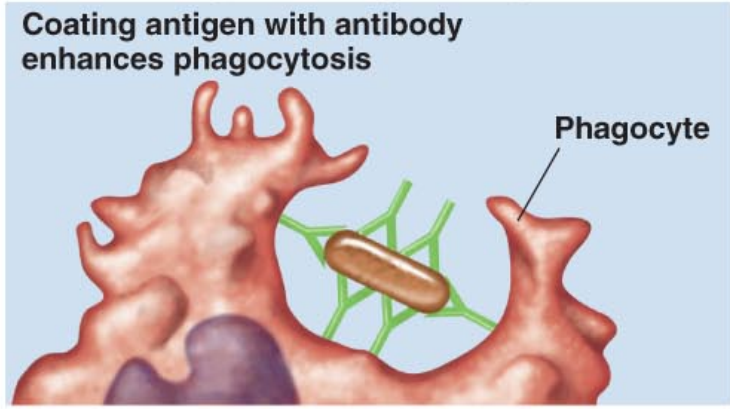
- Agglutination
- Opsonization
- Activation of complement
- Antibody-dependent cell-mediated cytotoxicity
- Neutralization

The Results of Antibody Binding



Agglutination

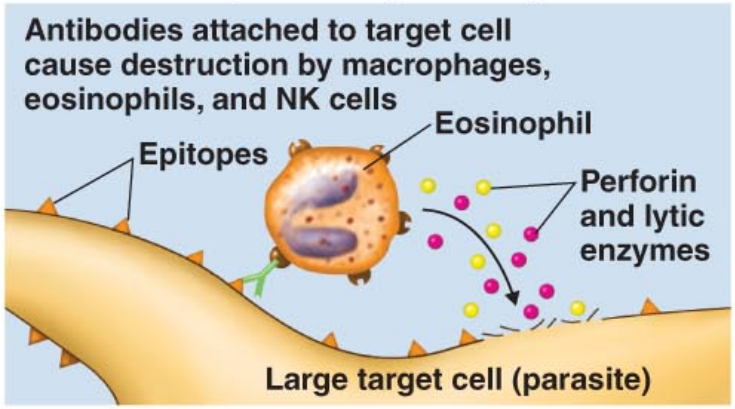
- Reduces number of particles to clean-up
- Enhances phagocytosis



Opsonization

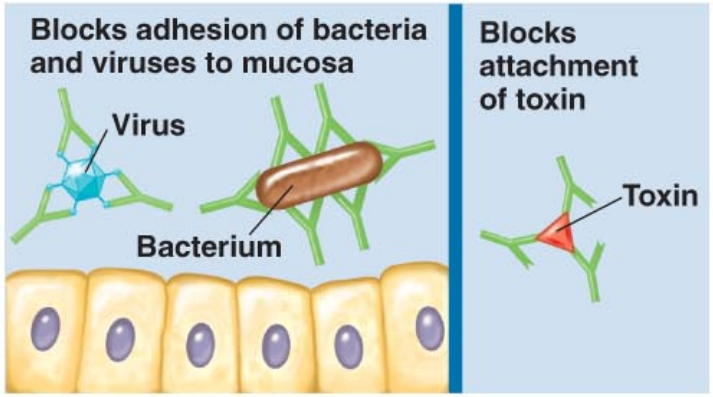
- Enhancement of phagocytosis

The Results of Antibody Binding



Antibody-dependent cell-mediated cytotoxicity

- Destruction by cells that remain *external* to target



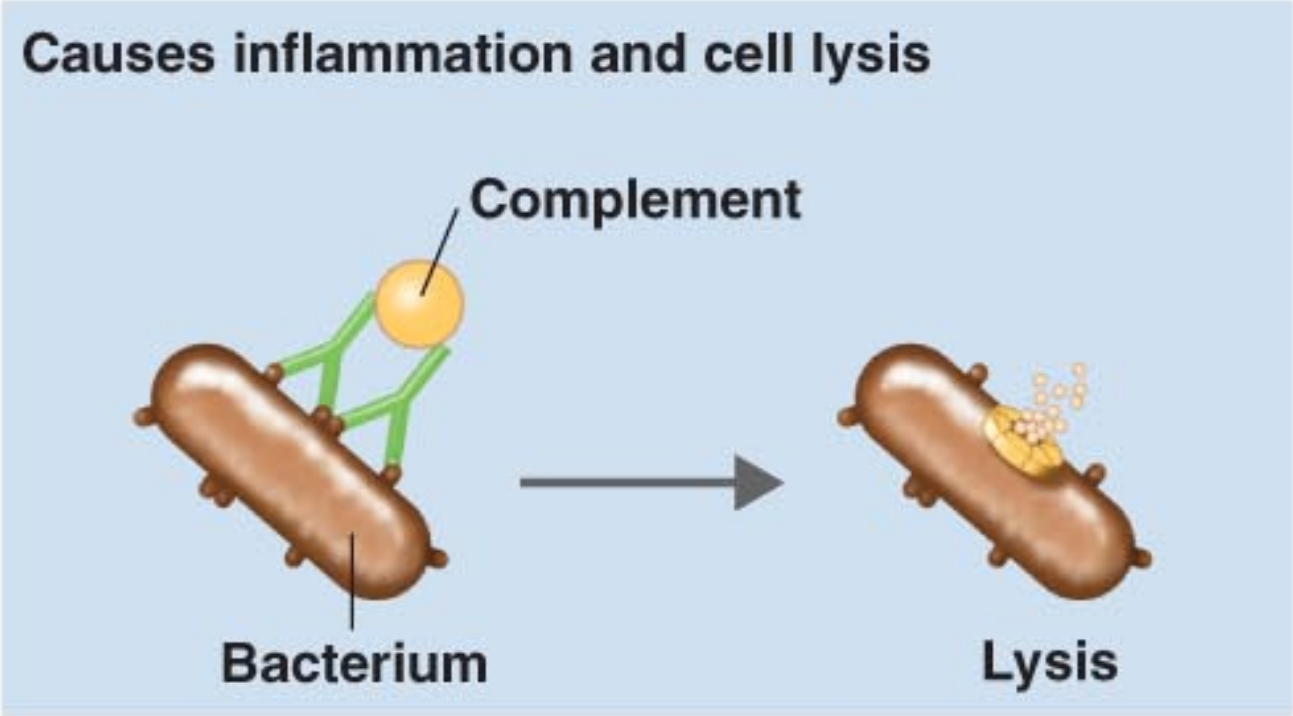
Neutralization

- Inactivation of viruses, toxins by blocking adherence

The Results of Antibody Binding

Activation of complement

- Causes inflammation, cell lysis



Cellular Immunity

- Immunity mediated by cells
  - Aka cell-mediated immunity
  - Control of intracellular pathogens
  - Via **T cells**

T Cells and Cellular Immunity

- Intracellular antigens (viruses, some bacteria) are not exposed to antibodies
  - Evade humoral defense mechanisms
- T cells help combat intracellular pathogens
  - Also recognize “non-self” cells – cancer, foreign cells
- T cells bind to specific to antigens via **T cell receptor (TCR)**

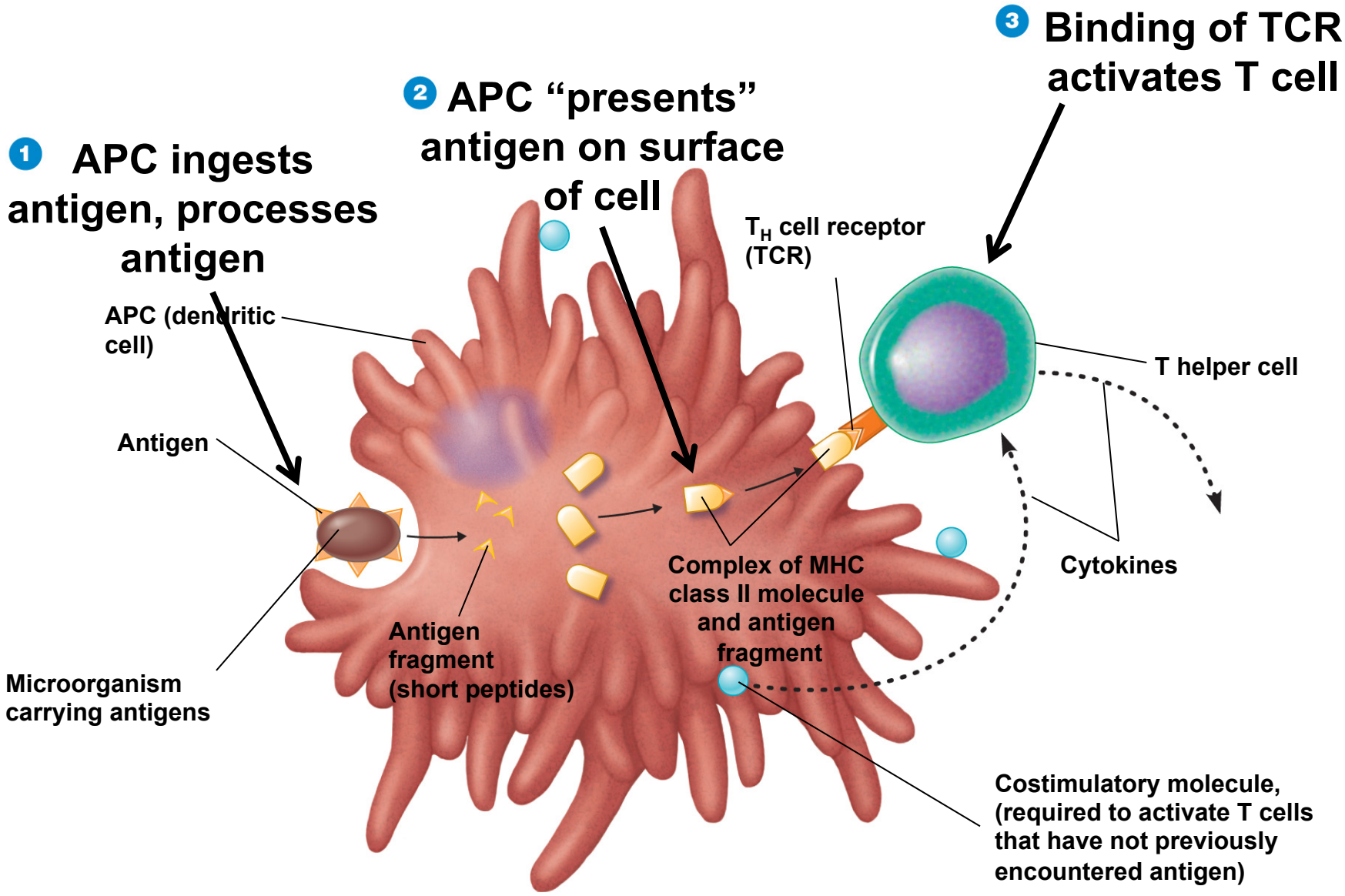
T Cells and Cellular Immunity

- T cells recognize antigens processed by **antigen-presenting cells (APC)**
  - Include macrophages, dendritic cells
- APC phagocytize antigen, process it, put it on surface via MHC molecule
  - "Present" antigen fragment to T cells
- Binding of TCR to antigen fragment activates T cells
  - Leads to clonal expansion → most become mature T cell, some become memory cells
- Response depends on type of T cell activated

T Helper Cells

- **$CD4^+$** or **T_H** cells
  - Activated T_H cells produce many kinds of **cytokines** – chemical signals that communicate with other cells

Activation of T Helper Cells



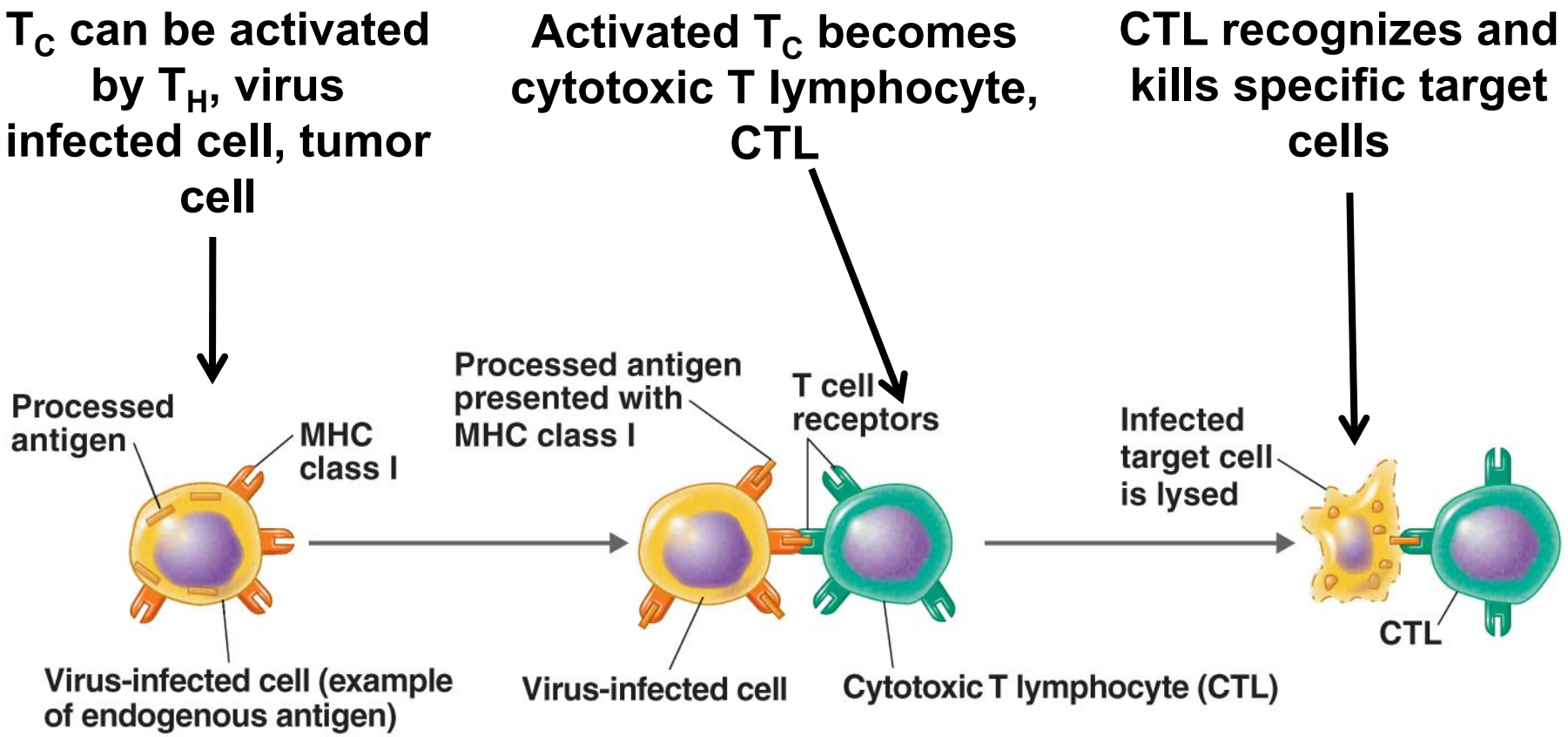
Activation of T Helper Cells

- Activated T_H coordinate adaptive immune response
- Release cytokines that recruit and activate immune cells
  - **T_H1** produce IFN-γ, which activates cells related to cell-mediated immunity, macrophages, and Abs
  - **T_H2** activate eosinophils and B cells to produce IgE
  - **T_H17** stimulate the innate immune system
  - **TF** stimulate B cells to produce plasma cells and are involved in class switching

T Cytotoxic Cells

- **$CD8^+$** or **T_C** cells
- Target cells are self-cells (host cells) carrying **processed internal antigens**
- Activated into **cytotoxic T lymphocytes (CTLs)**

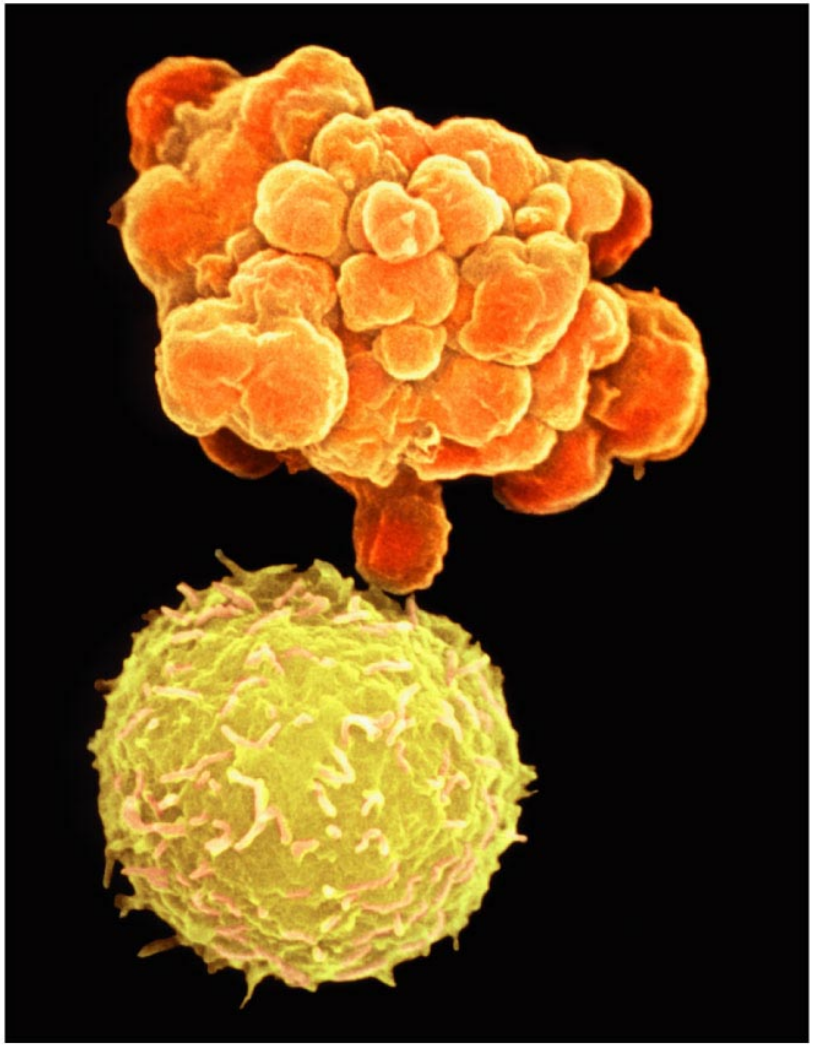
Activation of T Cytotoxic Cells



Activation of T Cytotoxic Cells

- Kill by inducing **apoptosis** → programmed cell death
- Cell shrinks, implodes
- Remains digested by macrophages

Apoptosis

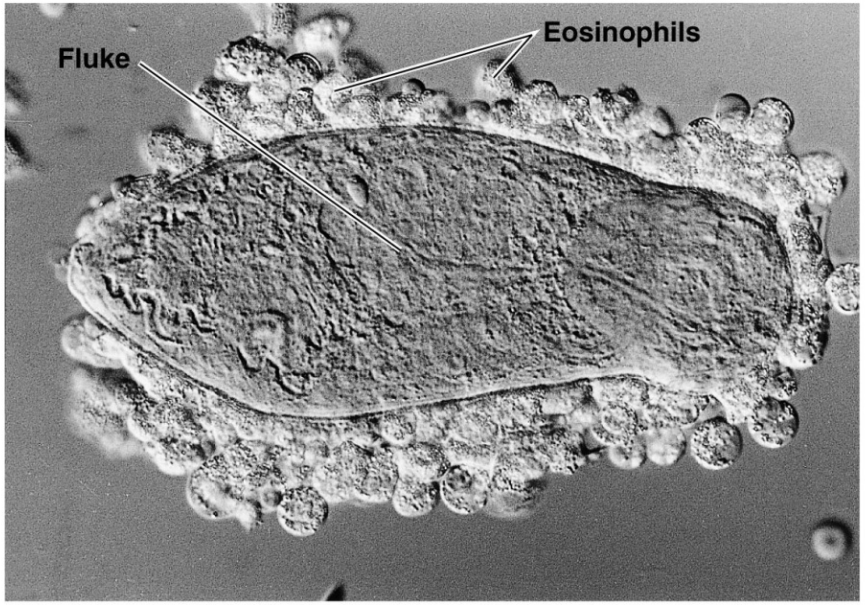


B cell undergoing apoptosis

Normal B cell

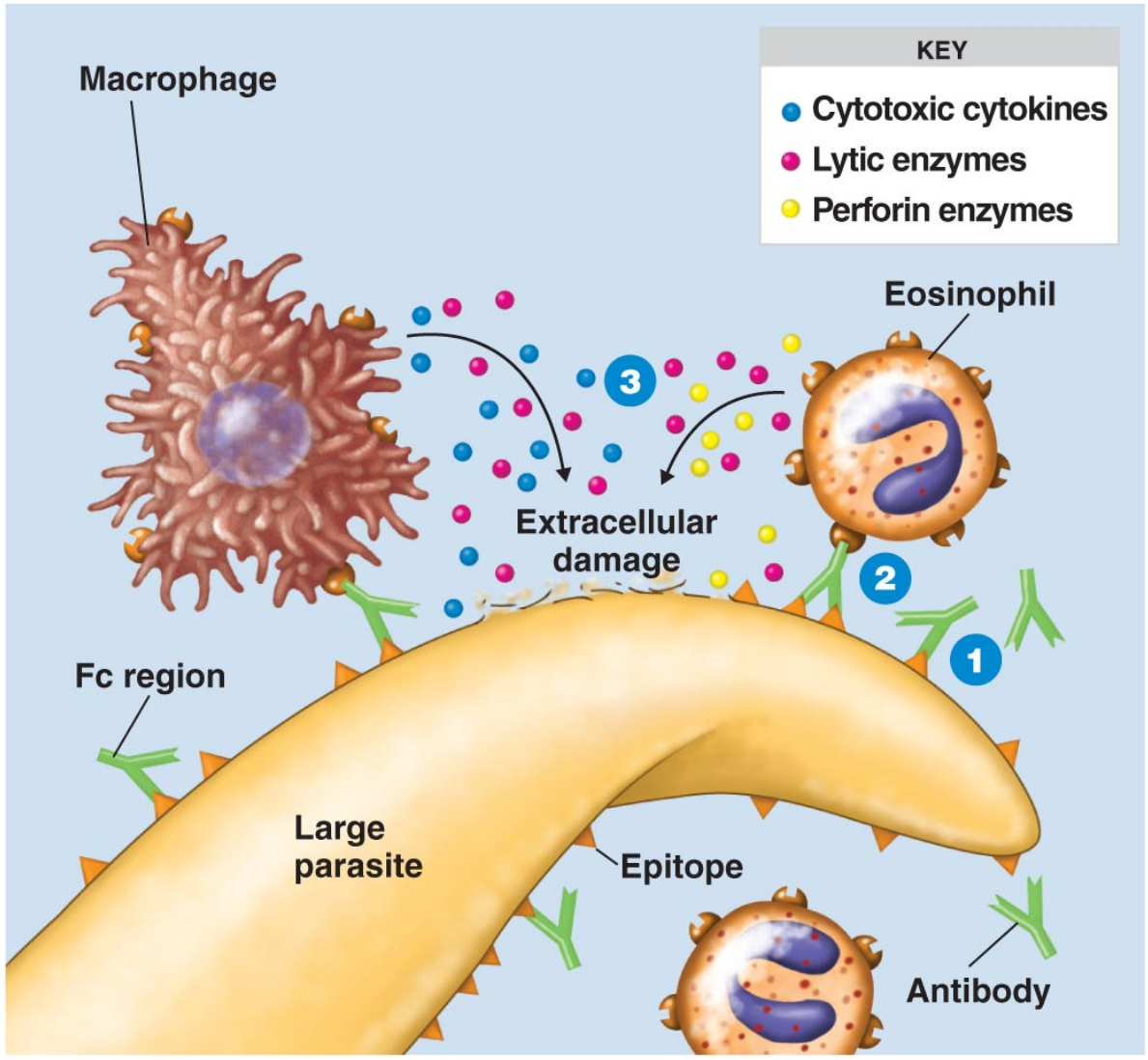
Extracellular Killing

- Eosinophils attack large parasites
  - Too large to phagocytize
  - Swarm around parasites
- NK cells can attack any "abnormal" cell
  - Tumor cells, viral infected cells
  - Non-specific
- Kill like CTLs, induce apoptosis



(b) Eosinophils adhering to the larval stage of a parasitic fluke.

Extracellular Killing



(a) Organisms, such as many parasites, that are too large for ingestion by phagocytic cells must be attacked externally.

Cytokines: Chemical Messengers

- Immune cells communicate with each other via cytokines
  - **Interleukins**: serve as communicators between WBC
  - **Chemokines**: induce migration of leukocytes
  - **Interferons**: protect against viral infection
  - **TNF-α**: important in inflammation, toxic to tumor cells
- Overproduction leads to **cytokine storm**

Immunological Memory

- **Antibody titer**: amount of antibody in serum
  - Indicator of intensity of humoral response
- Two responses:
  - **Primary response**
    - Slow, relatively weak
  - **Secondary response**
    - Fast, intense
    - Due to memory cells
- Response is similar for T cells

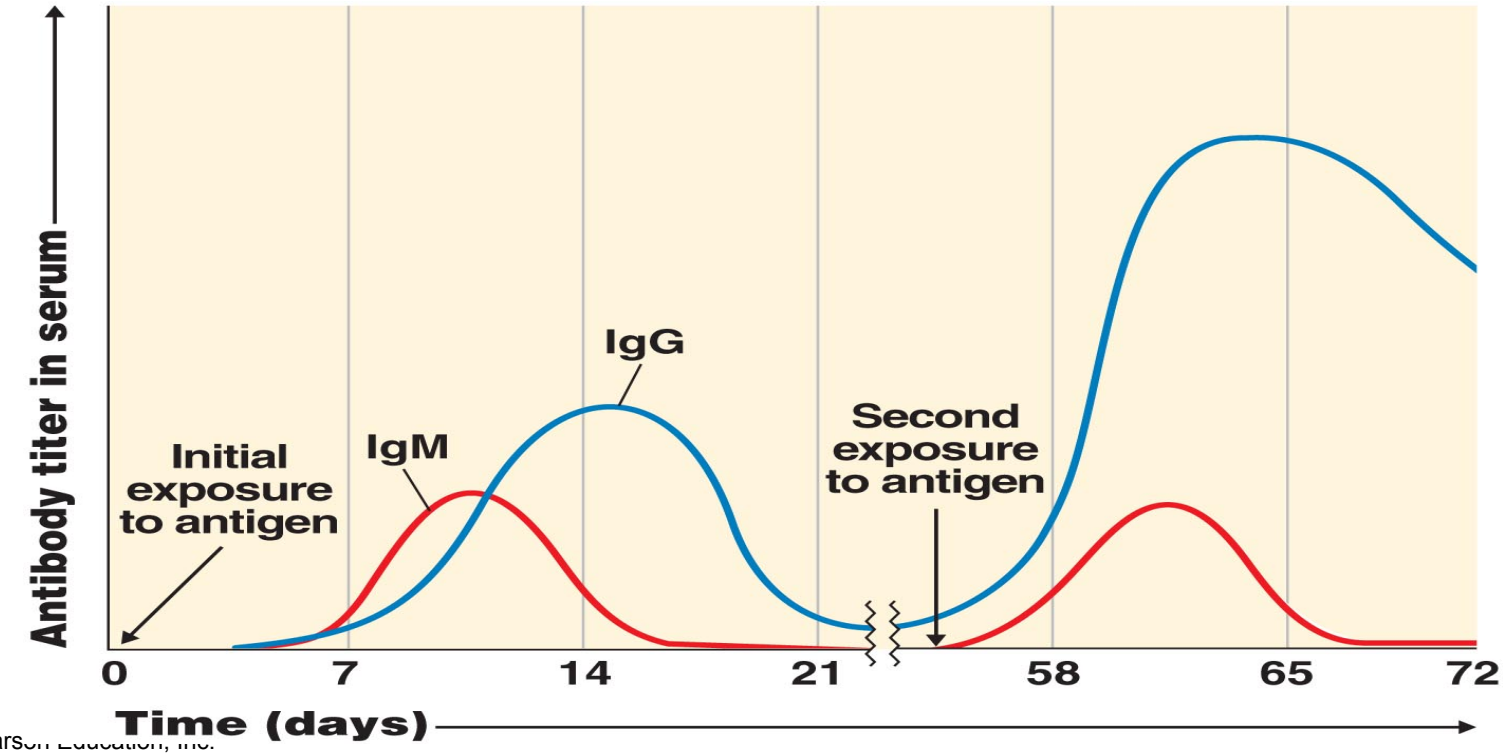
Immunological Memory

Primary response

- No antibodies for 4-7 days
- Slow rise in antibody titer
- Peaks in about 10-17 days

Secondary response aka “memory”

- Reached peak in 2-7 days
- Lasts many days
- Greater in magnitude



Types of Adaptive Immunity

- **Naturally acquired active immunity**
  - Resulting from infection
- **Naturally acquired passive immunity**
  - Transplacental or via colostrum
- **Artificially acquired active immunity**
  - Injection of Ag (vaccination)
- **Artificially acquired passive immunity**
  - Injection of Ab