

# Immune System & Engineering

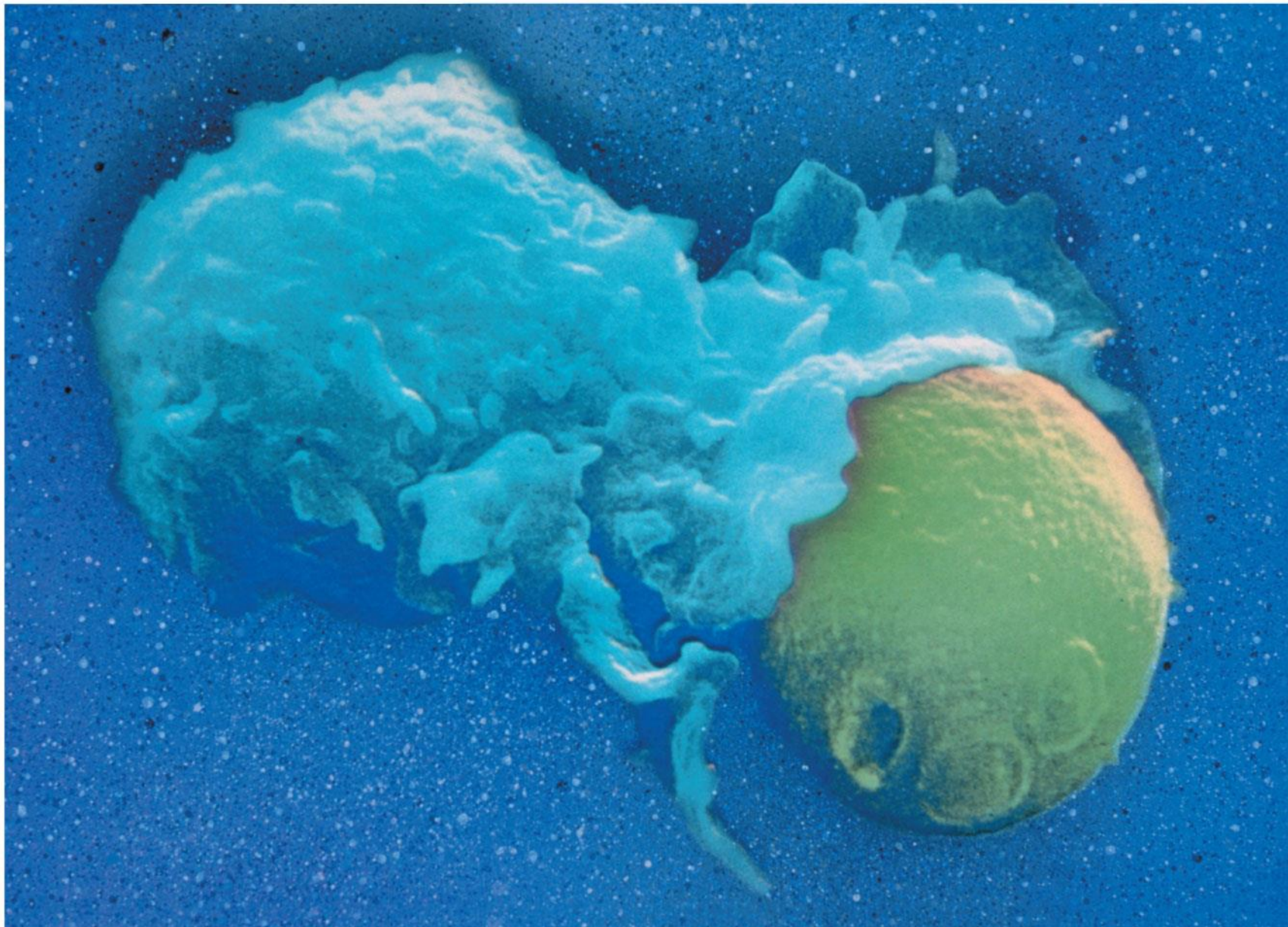
BME2105

# Immune Cells attacking Invaders



# Overview: Recognition and Response

- ▶ **Pathogens**, agents that cause disease, infect a wide range of animals, including humans
- ▶ The **immune system** recognizes foreign bodies and responds with the production of immune cells and proteins
- ▶ All animals have **innate immunity**, a defense active immediately upon infection
- ▶ Vertebrates also have **adaptive immunity**



# Immunity: Two Intrinsic Defense Systems

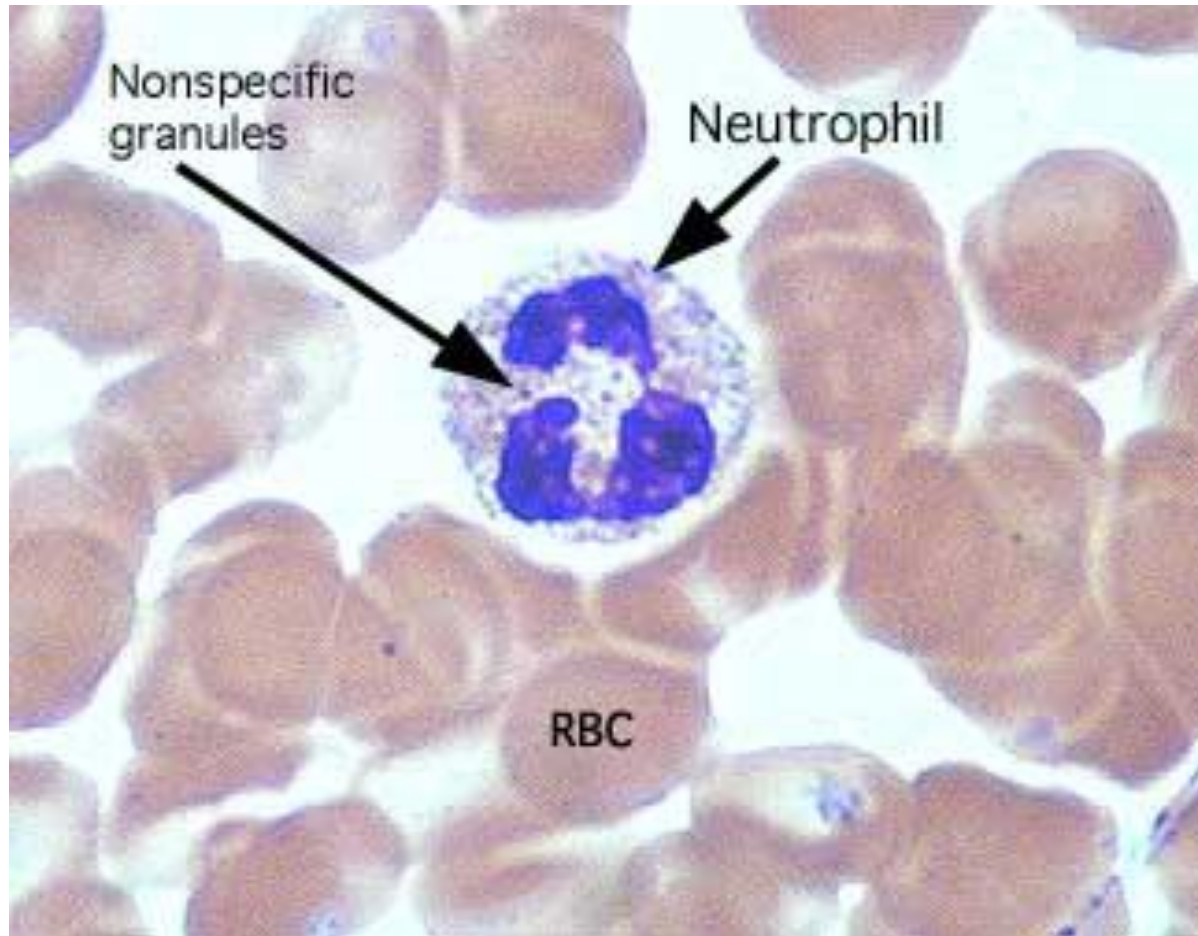
- ▶ **Innate (nonspecific)** system responds quickly and consists of:
  - **First line of defense** – intact **skin** and mucosae prevent entry of microorganisms
  - **Second line of defense** – **antimicrobial proteins**, **phagocytes**, and other cells
    - Inhibit spread of invaders throughout the body
    - Inflammation is its hallmark and most important mechanism

# Immunity: Two Intrinsic Defense Systems

- ▶ Adaptive (specific) defense system
  - Third line of defense – mounts attack against particular foreign substances
    - Takes longer to react than the innate system
    - Works in conjunction with the innate system



# neutrophil

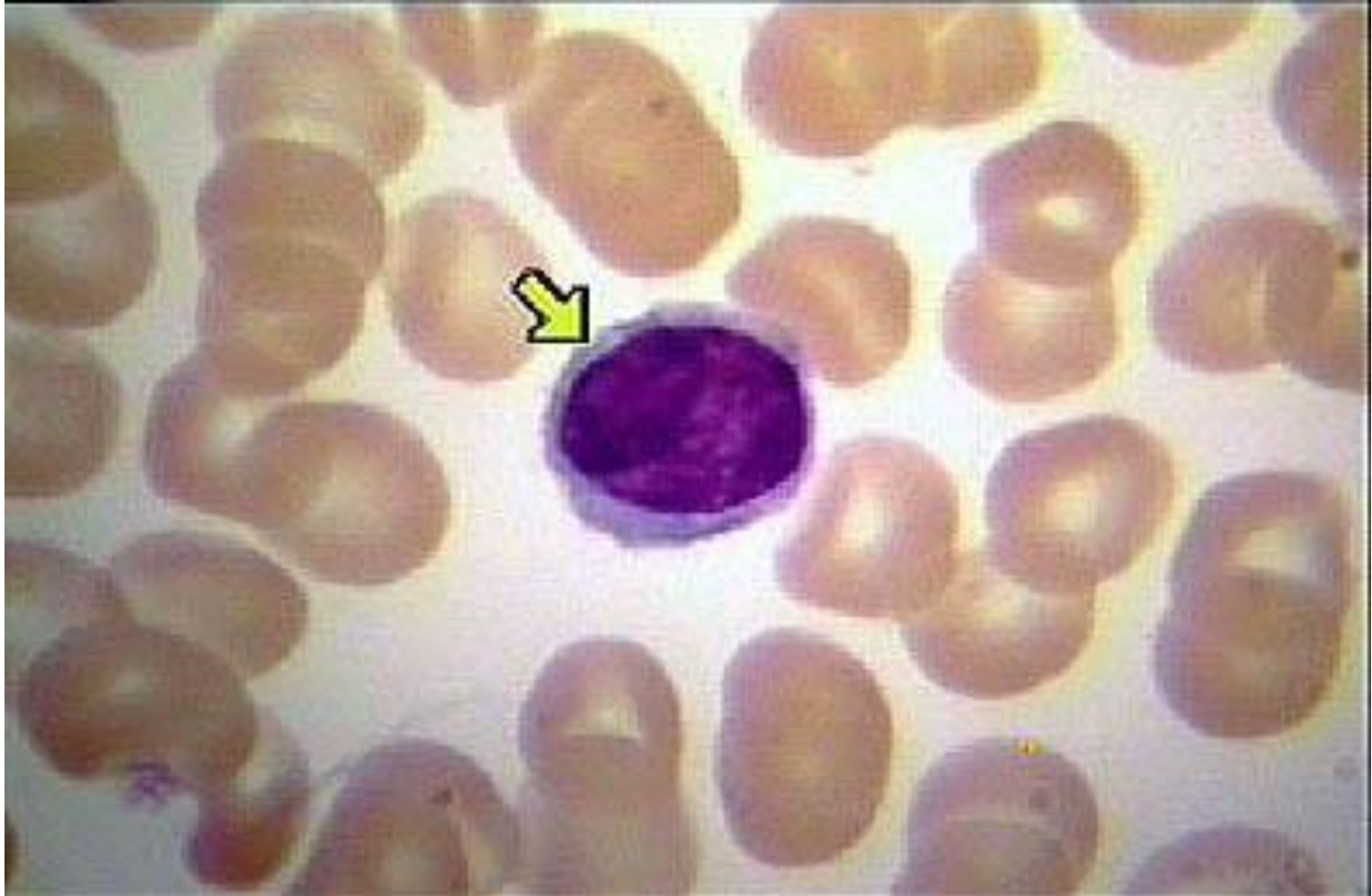


# NEUTROPHIL

- ▶ multi-lobed nucleus.
- ▶ 50–70% of circulating WBC (higher numbers suggestive of bacterial infection).
- ▶ Phagocytosis and killing of ingested microorganisms.
- ▶ The phagosome fuses with granules to destroy internalized bacteria, oxygen dependent respiratory burst.
- ▶ DO NOT function as APCs.
- ▶ Neutrophils are the 1st cells to arrive. A number of substances produced during an inflammatory response recruit neutrophils to a site of inflammation.



# lymphocyte

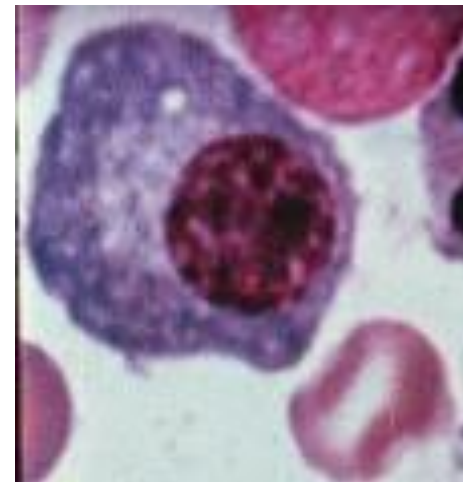
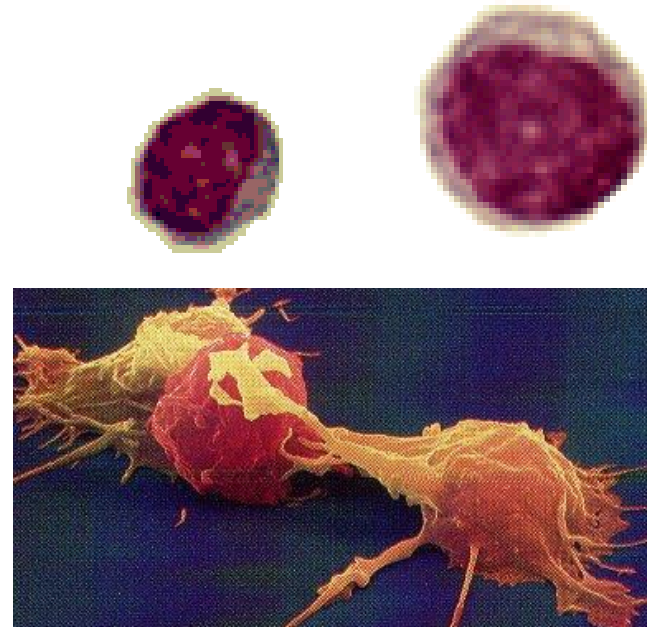


# LYMPHOCYTES

- ▶ responsible for the specific immune response.  
Represent 20–40% of circulating WBC in blood  
extravasate and enter the tissues – return 99% of cells in lymph
- ▶ small 6µm, contain a single nucleus, little visible cytoplasm around their nucleus.
- ▶ T lymphocytes and B lymphocytes and natural killer cells.
- ▶ T and B lymphocytes are small, motile, nonphagocytic cells which cannot be distinguished from each other morphologically.
- ▶ Once stimulated with antigen enlarges 15µm into a blast cell. Lymphoblasts further differentiate into effector cells or memory cells. [Plasma cells, T-helper cells, T-cytotoxic cells].
- ▶ The memory cells are long-lived cells that reside in the G<sub>0</sub> phase of the cell cycle until activated by a secondary encounter with antigen.
- ▶ Different lineages or different maturational stages of lymphocytes can be distinguished by their expression of membrane CD molecules (Cluster of Differentiation (CD))

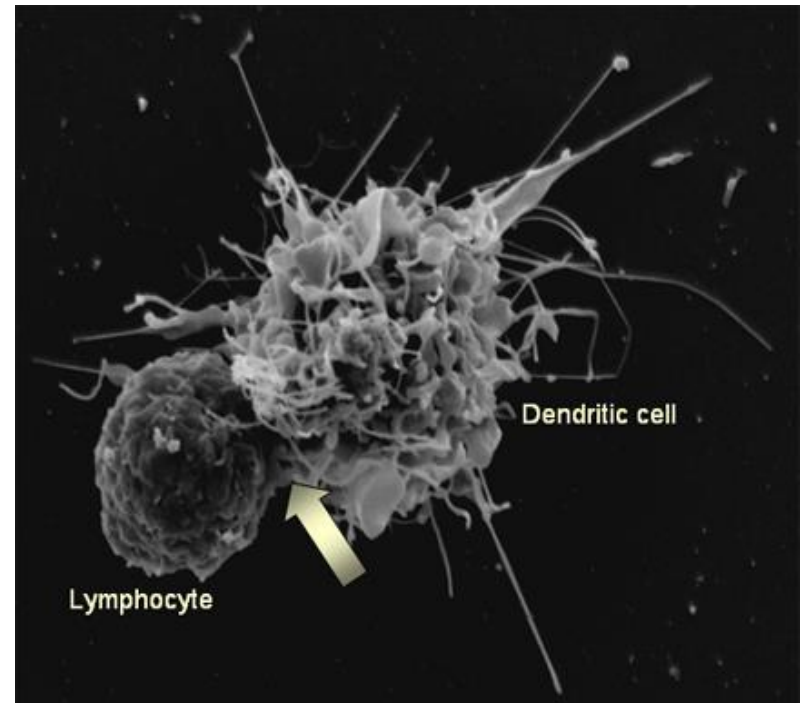
# T and B Lymphocytes

- ▶ T cells respond to antigens. Some of them (CD4+) secrete lymphokines which act on other cells involved in the immune response. Others (CD8+, cytotoxic) are able to cause lysis of infected cells.
- ▶ The major function of B lymphocytes is the production of antibodies in response to foreign proteins of bacteria, viruses, and tumor cells.
- ▶ Antibodies are specialized proteins that specifically recognize and bind to one particular protein that specifically recognize and bind to one particular protein.
- ▶ Antibody production and binding to a foreign substance or antigen, often is critical as a means of signaling other cells to engulf, kill or remove that substance from the body.



# Dendritic Cells

- ▶ originate in the bone marrow
- ▶ function as antigen presenting cells (APC).
- ▶ found in the structural compartment of the lymphoid organs
- ▶ found in the bloodstream and other tissues of the body
- ▶ capture antigen or bring it to the lymphoid organs where an immune response is initiated.



**Pathogens**  
(such as bacteria,  
fungi, and viruses)

```
graph TD; Pathogens([Pathogens  
(such as bacteria,  
fungi, and viruses)]) --> Barrier[Barrier defenses:  
Skin  
Mucous membranes  
Secretions]; Pathogens --> Internal[Internal defenses:  
Phagocytic cells  
Natural killer cells  
Antimicrobial proteins  
Inflammatory response]; Pathogens --> Humoral[Humoral response:  
Antibodies defend against  
infection in body fluids.]; Pathogens --> CellMediated[Cell-mediated response:  
Cytotoxic cells defend  
against infection in body cells.];
```

**INNATE IMMUNITY**  
(all animals)

- Recognition of traits shared by broad ranges of pathogens, using a small set of receptors
- Rapid response

**Barrier defenses:**  
Skin  
Mucous membranes  
Secretions

**Internal defenses:**  
Phagocytic cells  
Natural killer cells  
Antimicrobial proteins  
Inflammatory response

**ADAPTIVE IMMUNITY**  
(vertebrates only)

- Recognition of traits specific to particular pathogens, using a vast array of receptors
- Slower response

**Humoral response:**  
Antibodies defend against infection in body fluids.

**Cell-mediated response:**  
Cytotoxic cells defend against infection in body cells.

# Adaptive immunity defends against infection of body fluids and body cells

- Acquired immunity has two branches: the humoral immune response and the cell-mediated immune response
- In the **humoral immune response** antibodies help neutralize or eliminate toxins and pathogens in the blood and lymph
- In the **cell-mediated immune response** specialized T cells destroy affected host cells

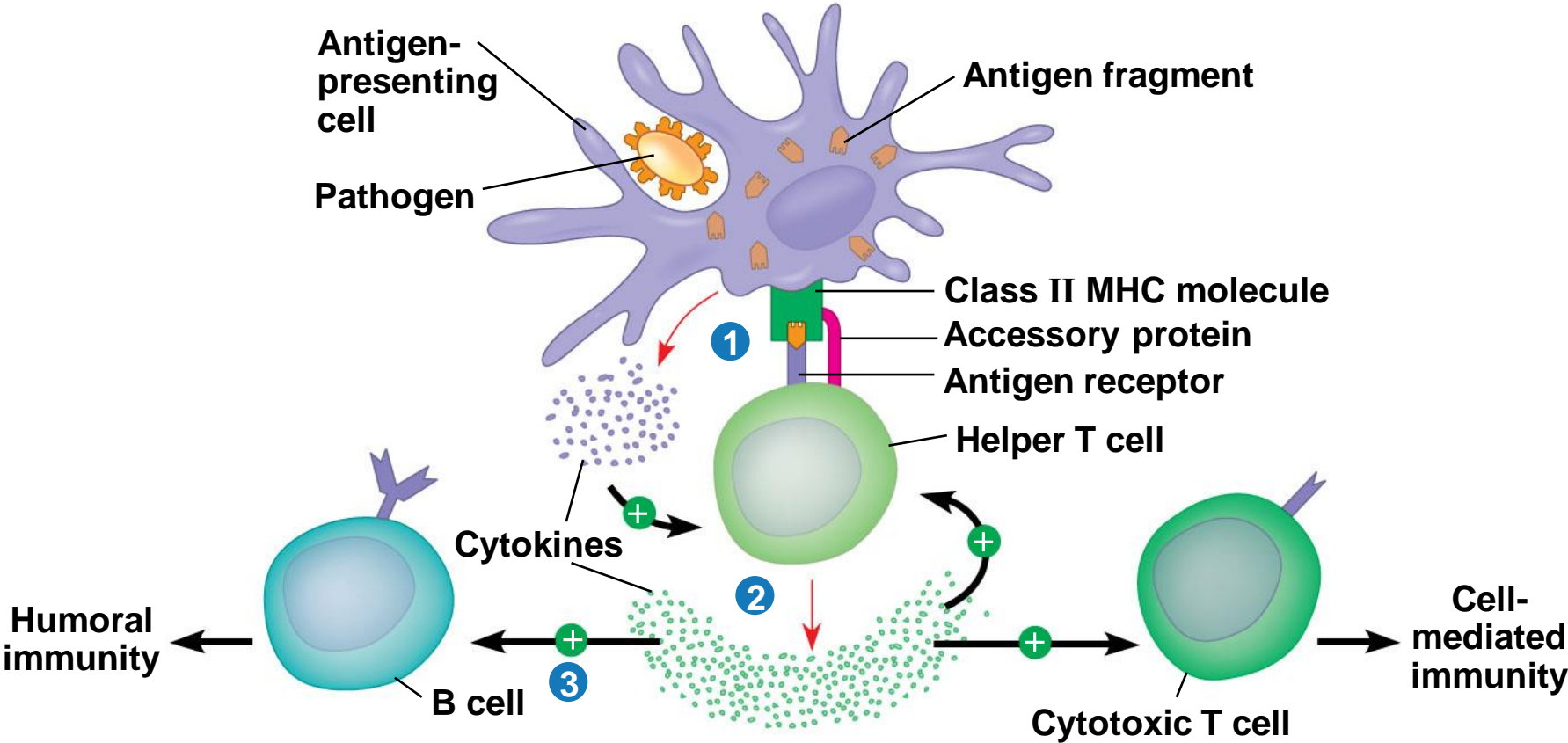


# Helper T Cells: A Response to Nearly All Antigens

- ▶ A type of T cell called a **helper T cell** triggers both the humoral and cell-mediated immune responses
- ▶ Signals from helper T cells initiate production of antibodies that neutralize pathogens and activate T cells that kill infected cells
- ▶ **Antigen-presenting cells** have class I and class II MHC molecules on their surfaces

- ▶ Class II MHC molecules are the basis upon which antigen-presenting cells are recognized
- ▶ Antigen receptors on the surface of helper T cells bind to the antigen and the class II MHC molecule; then signals are exchanged between the two cells
- ▶ The helper T cell is activated, proliferates, and forms a clone of helper T cells, which then activate the appropriate B cells

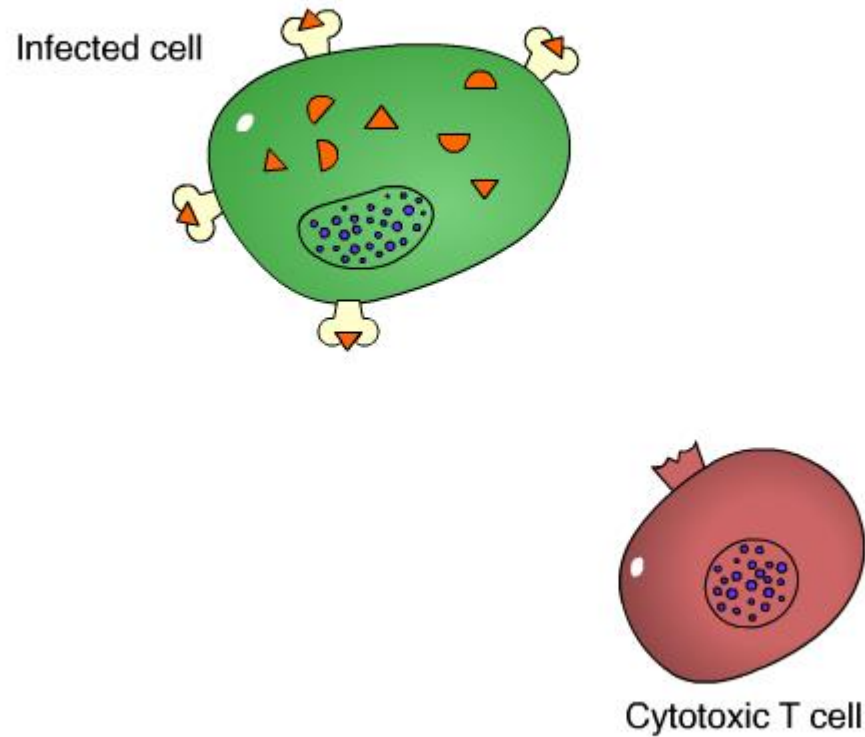
Figure 43.16



# Cytotoxic T Cells: A Response to Infected Cells

- ▶ **Cytotoxic T cells** are the effector cells in the cell-mediated immune response
- ▶ Cytotoxic T cells recognize fragments of foreign proteins produced by infected cells and possess an accessory protein that binds to class I MHC molecules
- ▶ The activated cytotoxic T cell secretes proteins that disrupt the membranes of target cells and trigger apoptosis

## Cell-mediated Immunity



Animation: Cytotoxic T Cells  
Right-click slide / select "Play"

Figure 43.17-1

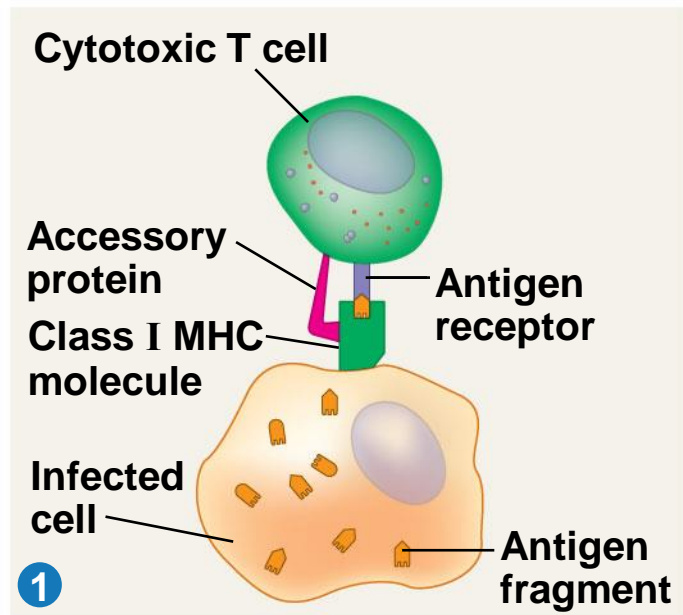




Figure 43.17-2

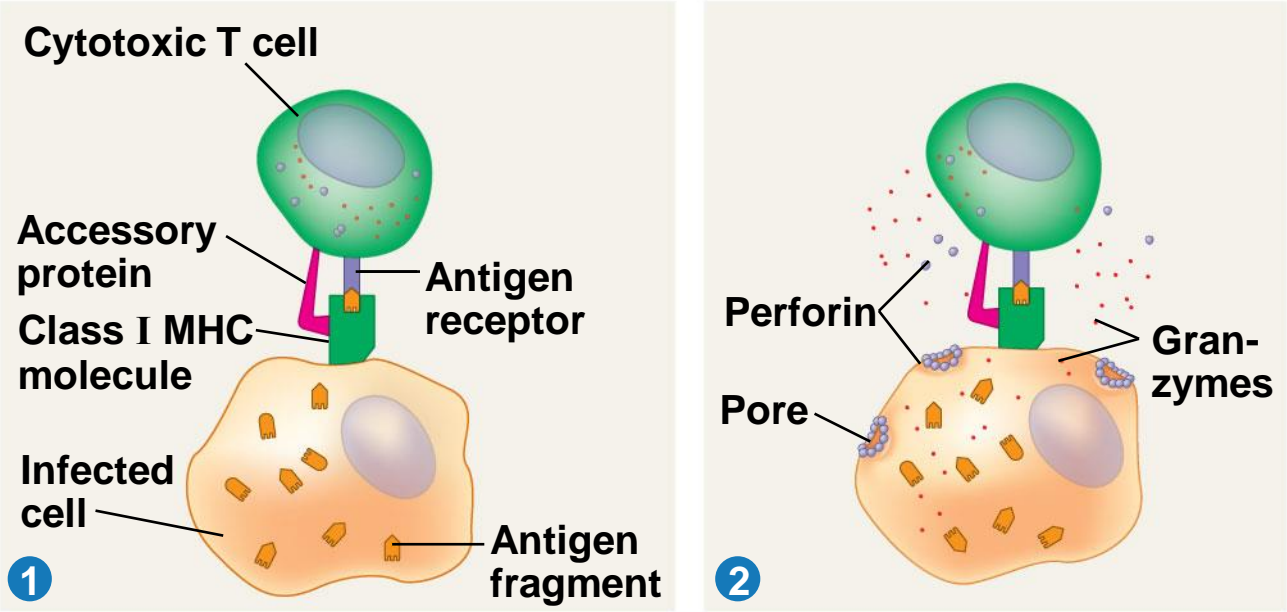
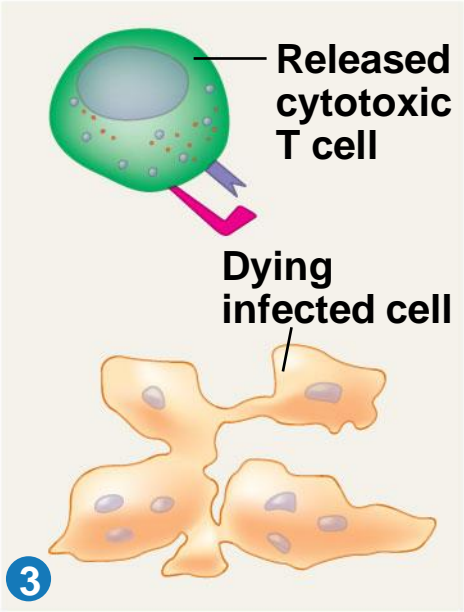
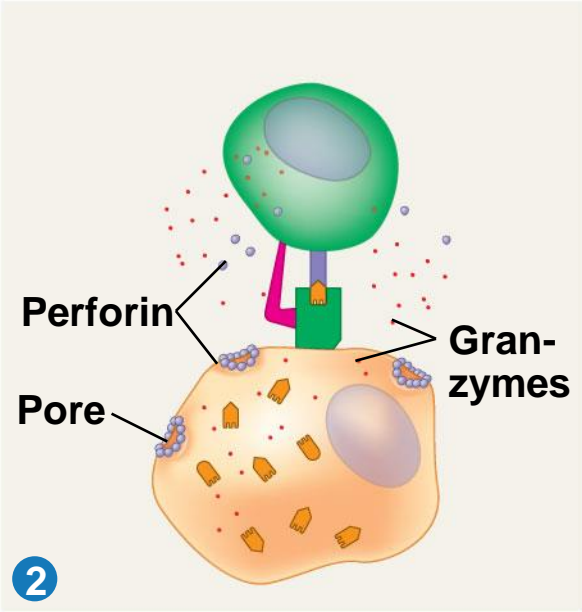
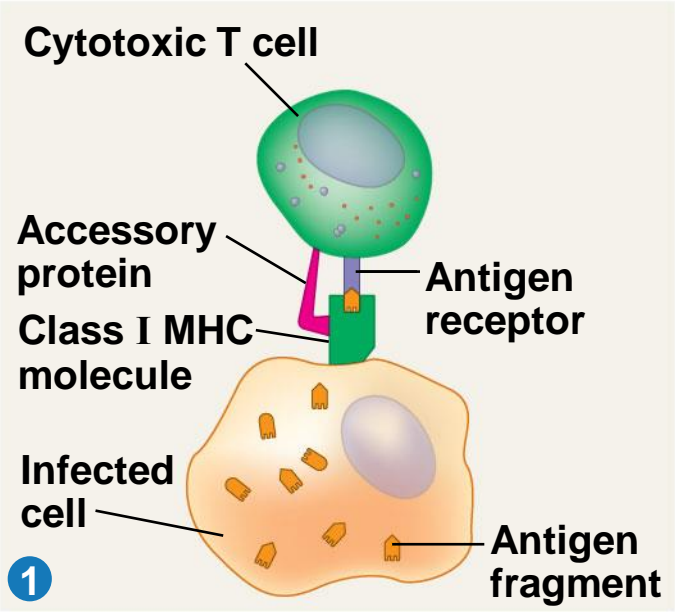


Figure 43.17-3



# B Cells and Antibodies: A Response to Extracellular Pathogens

- ▶ The humoral response is characterized by secretion of antibodies by B cells

# *Activation of B Cells*

- ▶ Activation of the humoral immune response involves B cells and helper T cells as well as proteins on the surface of pathogens
- ▶ In response to cytokines from helper T cells and an antigen, a B cell proliferates and differentiates into memory B cells and antibody-secreting effector cells called **plasma cells**

Figure 43.18-1

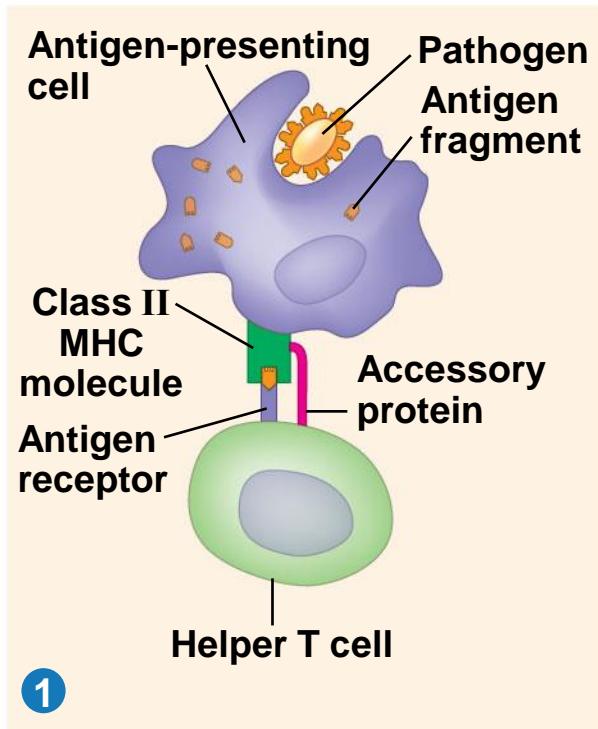


Figure 43.18-2

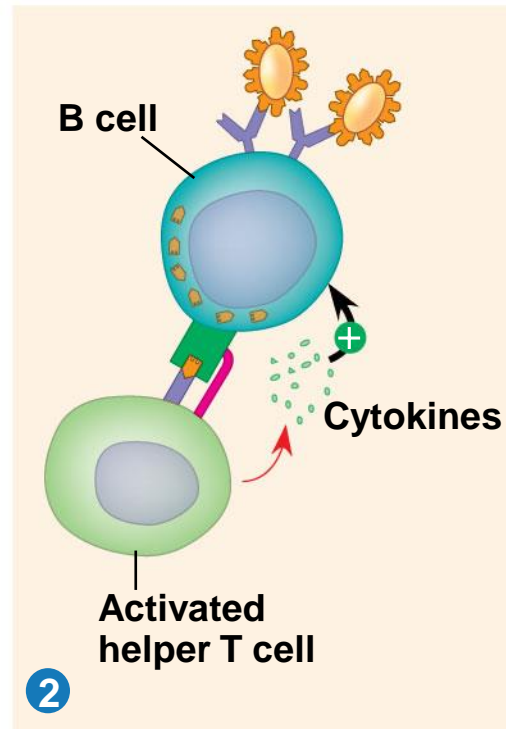
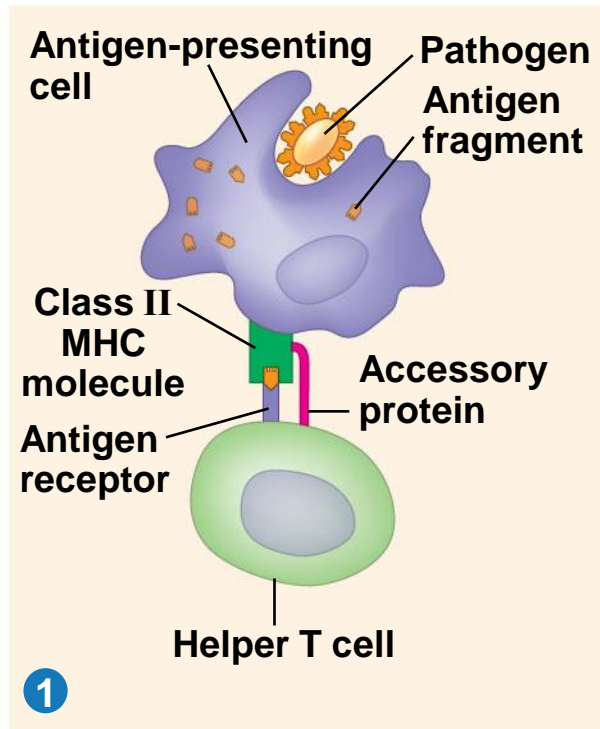
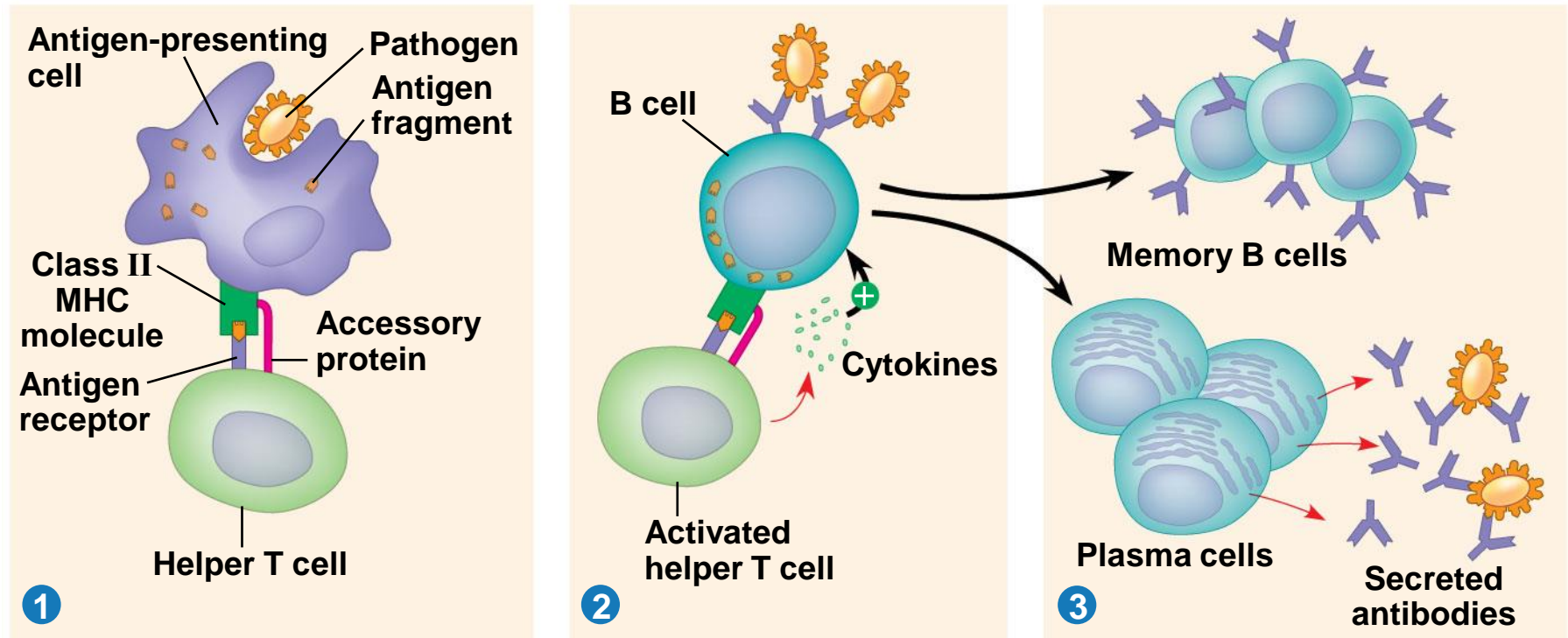




Figure 43.18-3

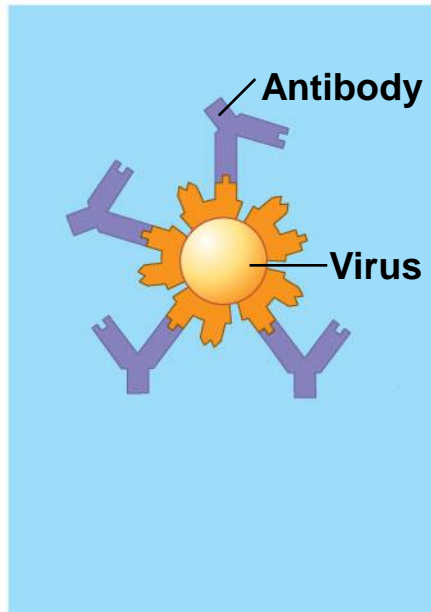


# *Antibody Function*

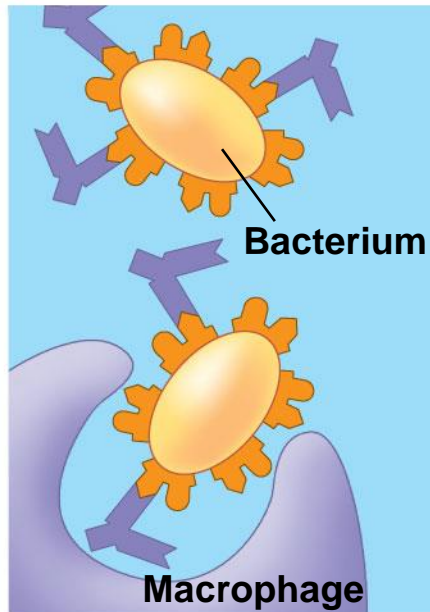
- ▶ Antibodies do not kill pathogens; instead they mark pathogens for destruction
- ▶ In neutralization, antibodies bind to viral surface proteins preventing infection of a host cell
- ▶ Antibodies may also bind to toxins in body fluids and prevent them from entering body cells

- ▶ In opsonization, antibodies bind to antigens on bacteria creating a target for macrophages or neutrophils, triggering phagocytosis
- ▶ Antigen–antibody complexes may bind to a complement protein—which triggers a cascade of complement protein activation
- ▶ Ultimately a membrane attack complex forms a pore in the membrane of the foreign cell, leading to its lysis

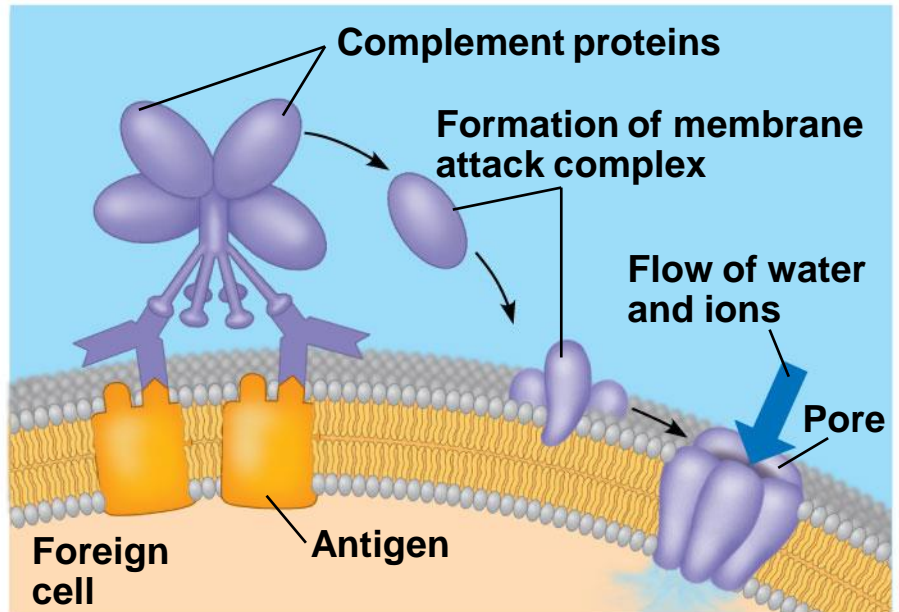
### Neutralization



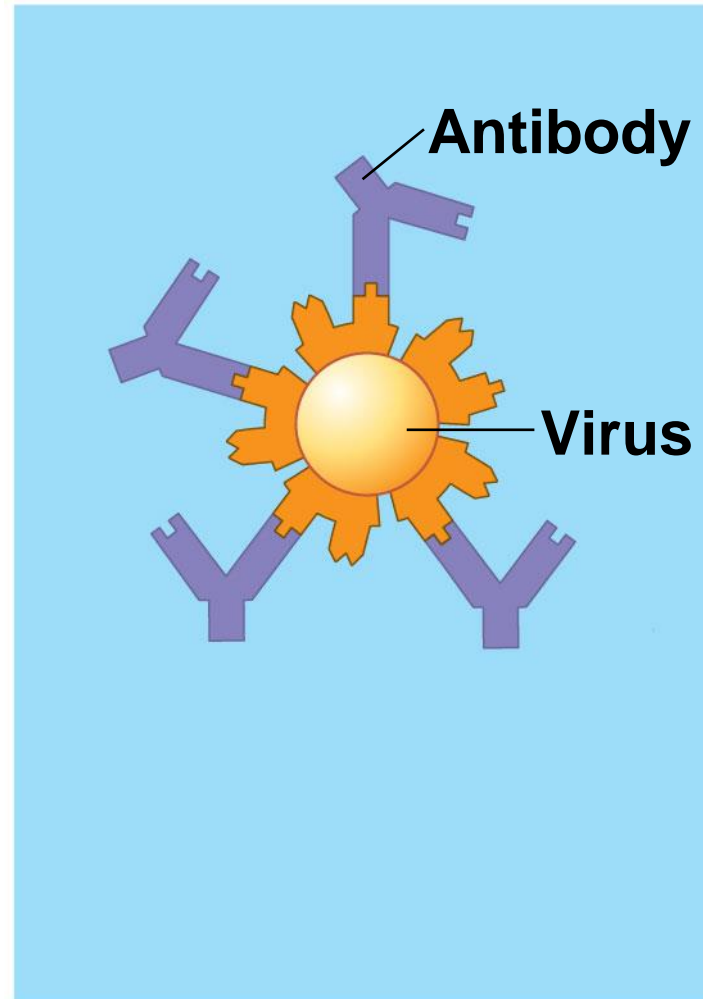
### Opsonization



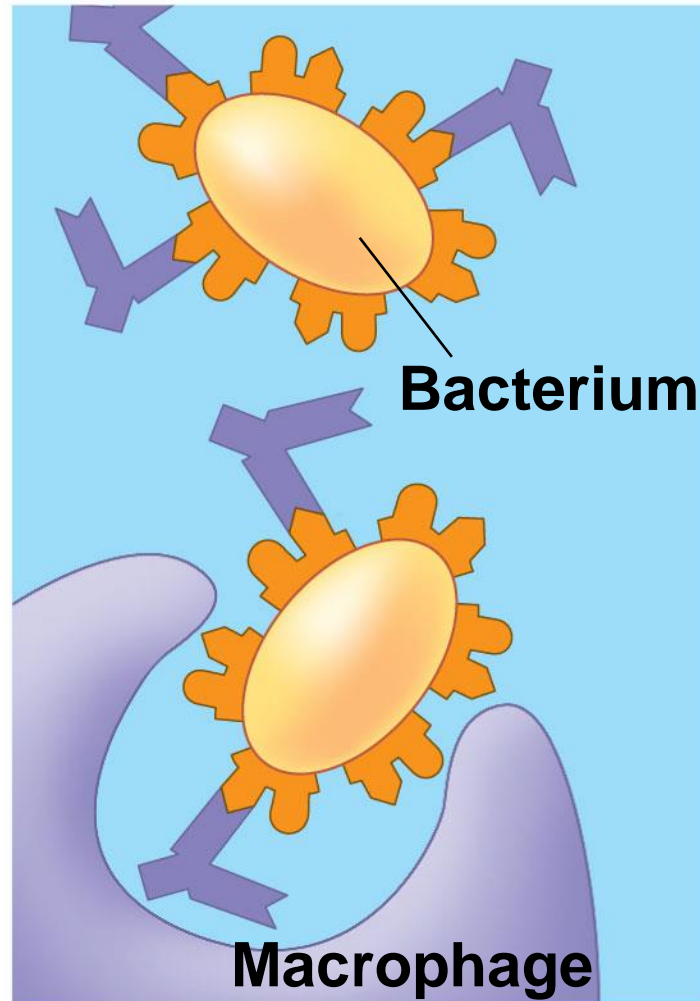
### Activation of complement system and pore formation



## Neutralization

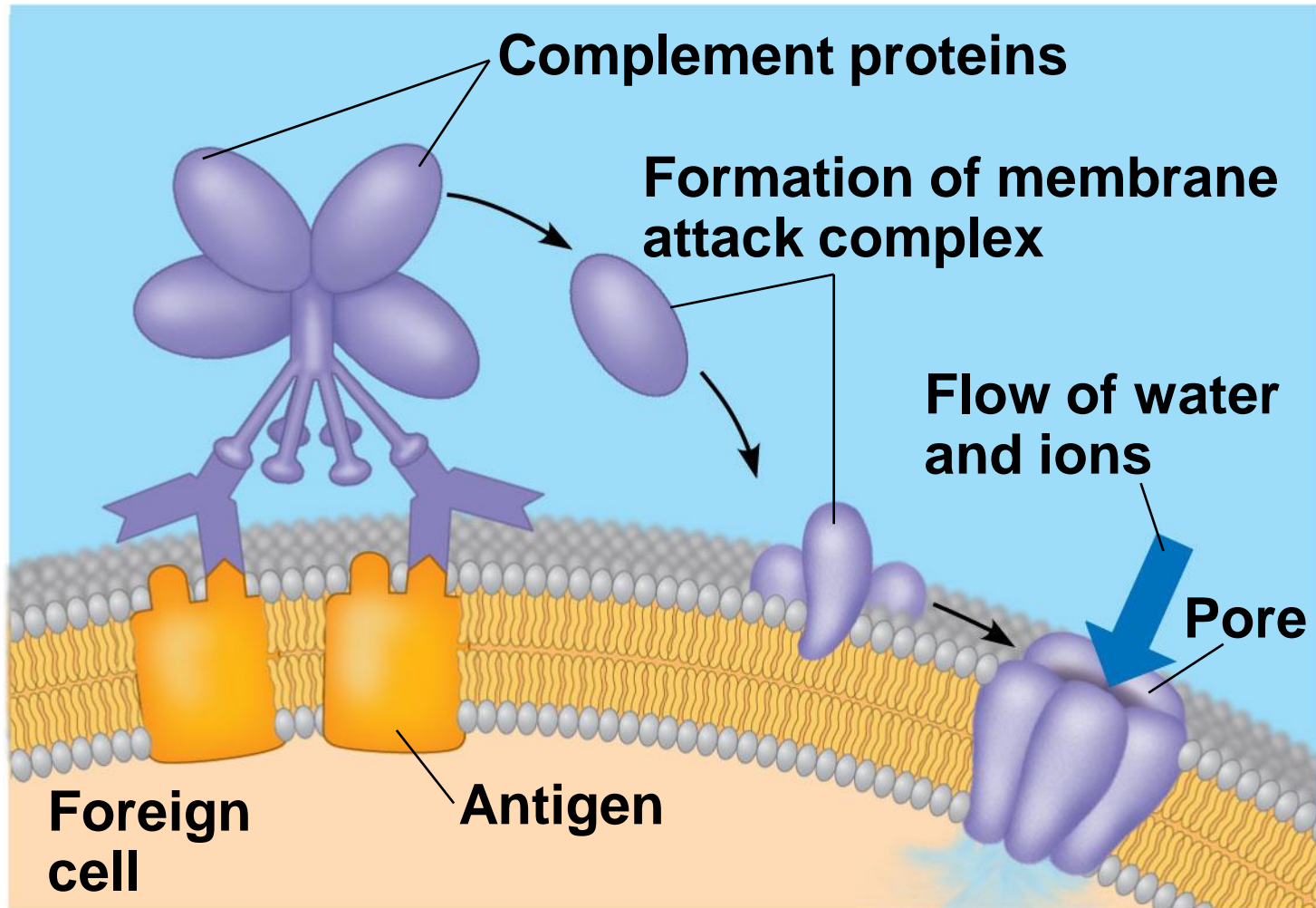


## Opsonization





## Activation of complement system and pore formation



# Summary of the Humoral and Cell-Mediated Immune Responses

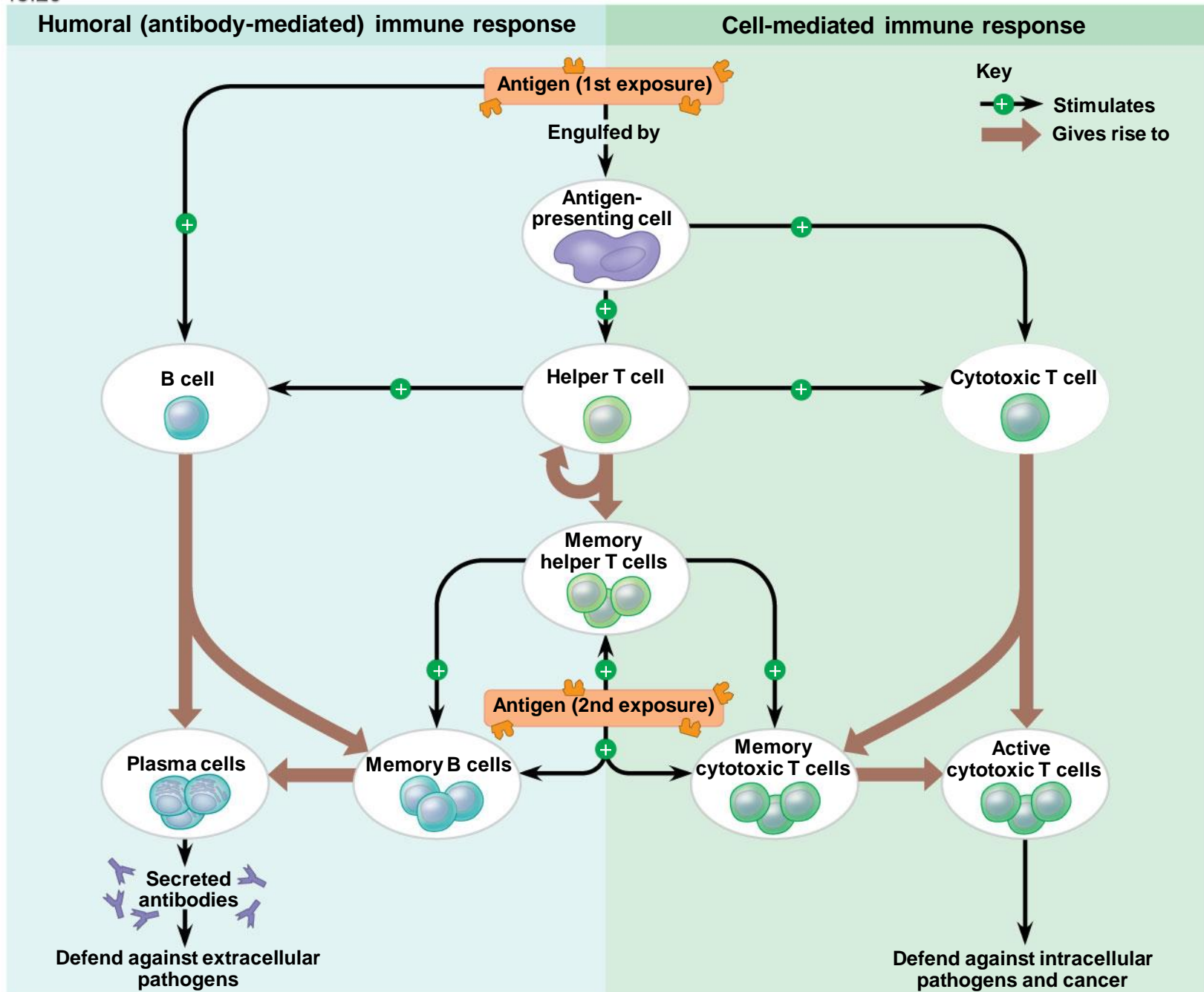
- ▶ Both the humoral and cell-mediated responses can include primary and secondary immune response
- ▶ Memory cells enable the secondary response

# Active and Passive Immunization

- ▶ **Active immunity** develops naturally when memory cells form clones in response to an infection
- ▶ It can also develop following **immunization**, also called **vaccination**
- ▶ In immunization, a nonpathogenic form of a microbe or part of a microbe elicits an immune response to an immunological memory

- ▶ **Passive immunity** provides immediate, short-term protection
- ▶ It is conferred naturally when IgG crosses the placenta from mother to fetus or when IgA passes from mother to infant in breast milk
- ▶ It can be conferred artificially by injecting antibodies into a nonimmune person

Figure 43.20



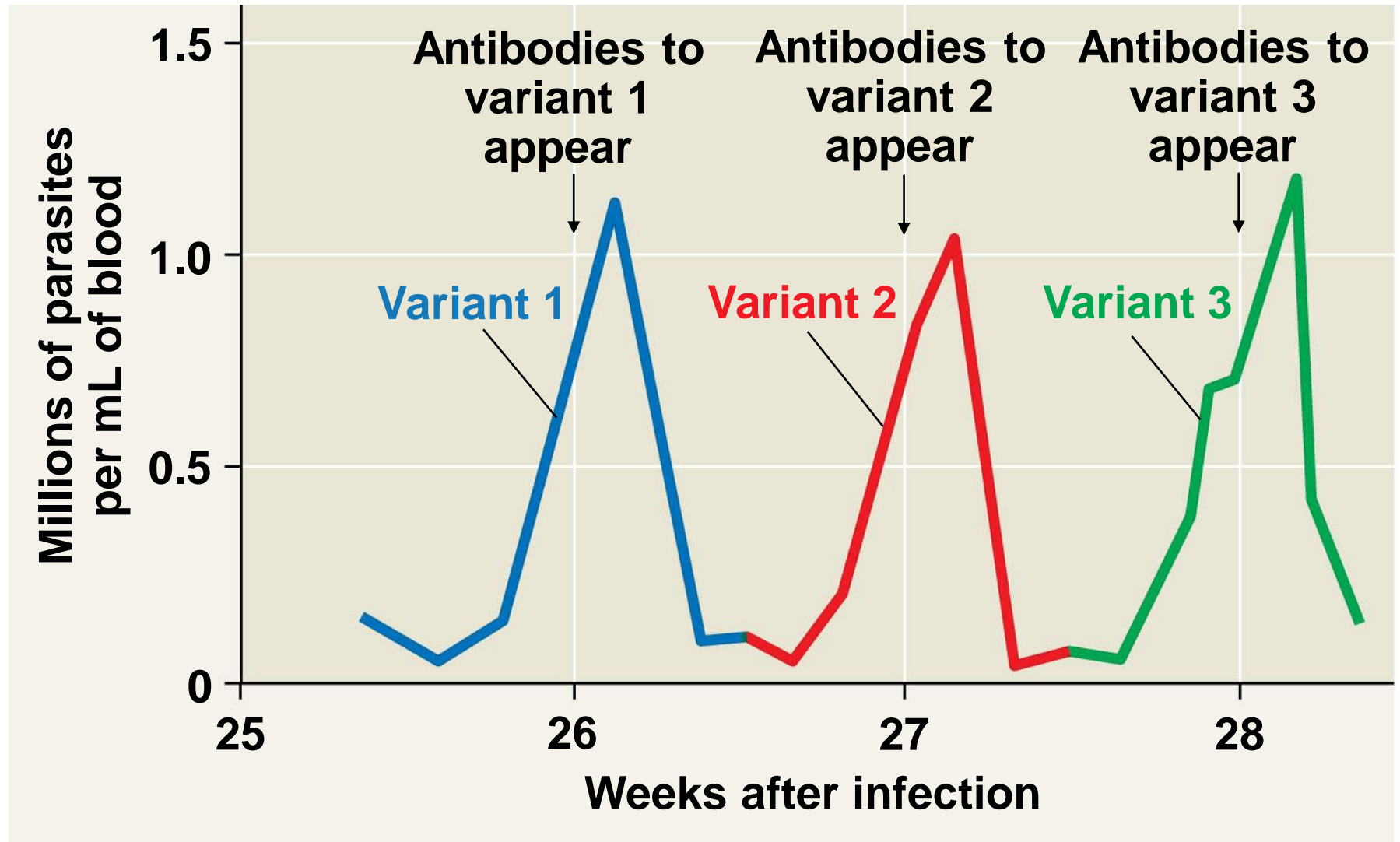
# Antibodies as Tools

- ▶ Antibody specificity and antigen–antibody binding have been harnessed in research, diagnosis, and therapy
- ▶ Polyclonal antibodies, produced following exposure to a microbial antigen, are products of many different clones of plasma cells, each specific for a different epitope
- ▶ **Monoclonal antibodies** are prepared from a single clone of B cells grown in culture

# *Antigenic Variation*

- ▶ Through antigenic variation, some pathogens are able to change epitope expression and prevent recognition
- ▶ The human influenza virus mutates rapidly, and new flu vaccines must be made each year
- ▶ Human viruses occasionally exchange genes with the viruses of domesticated animals
- ▶ This poses a danger as human immune systems are unable to recognize the new viral strain

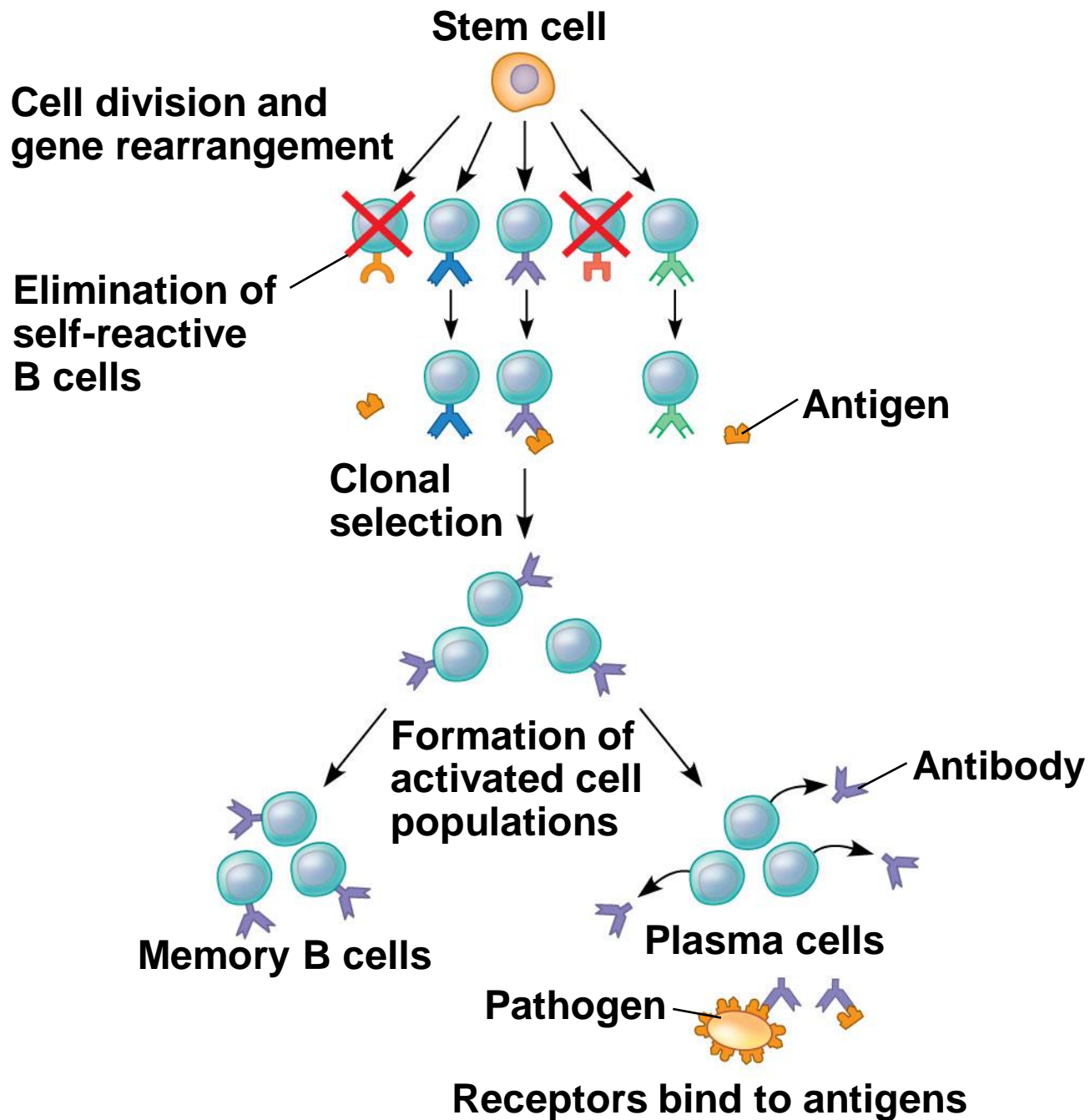
Figure 43.24





# Cancer and Immunity

- ▶ The frequency of certain cancers increases when adaptive immunity is impaired
- ▶ 20% of all human cancers involve viruses
- ▶ The immune system can act as a defense against viruses that cause cancer and cancer cells that harbor viruses
- ▶ In 2006, a vaccine was released that acts against human papillomavirus (HPV), a virus associated with cervical cancer



# Engineering the Immune System

