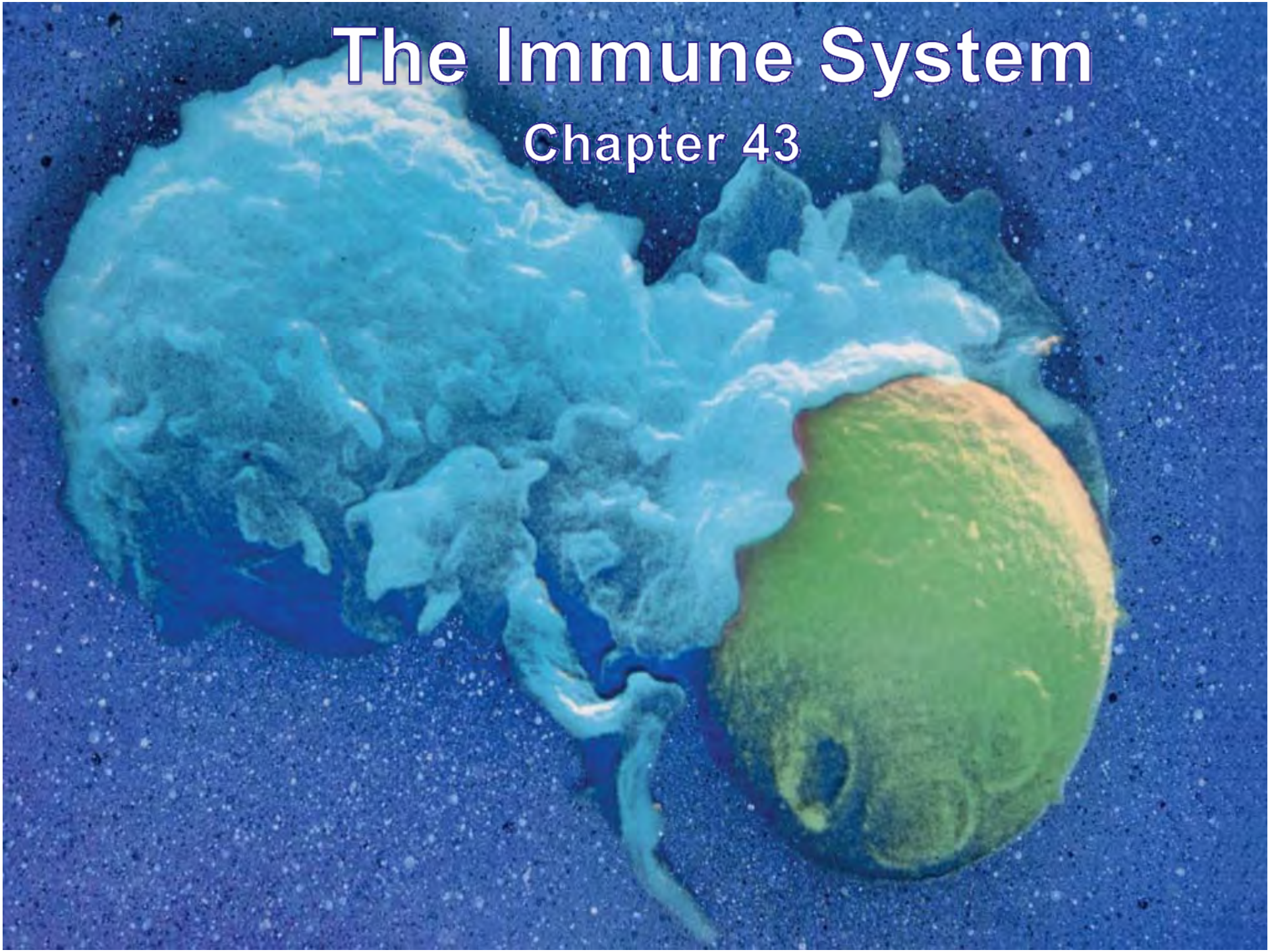
The Immune System

Chapter 43



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Immune System

A collection of biological structures (cells, tissues, organs) and processes within an organism that help protects against disease by removing pathogens and abnormal cells

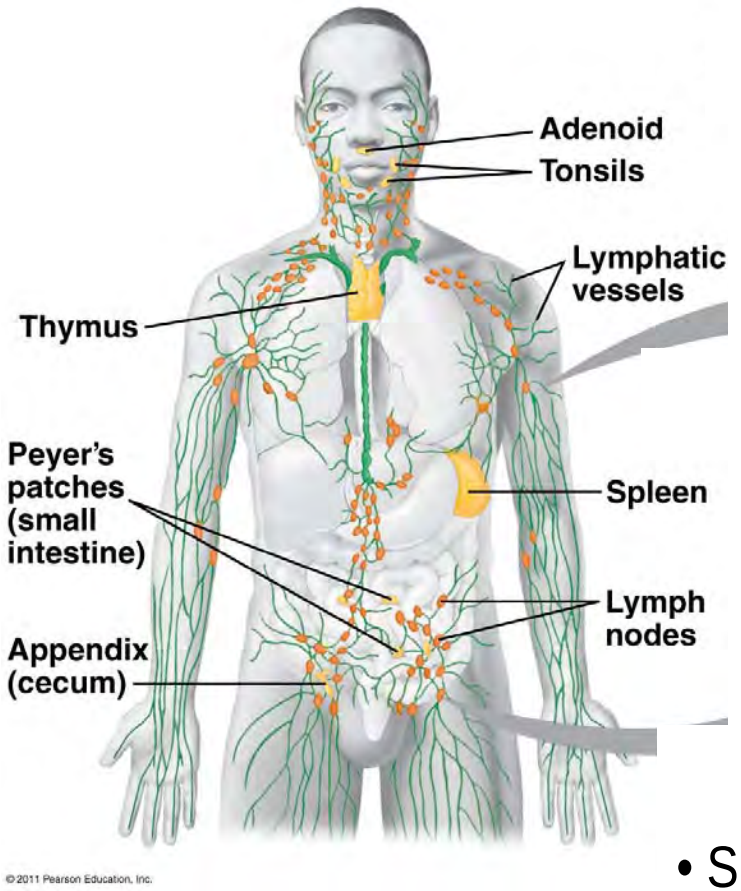
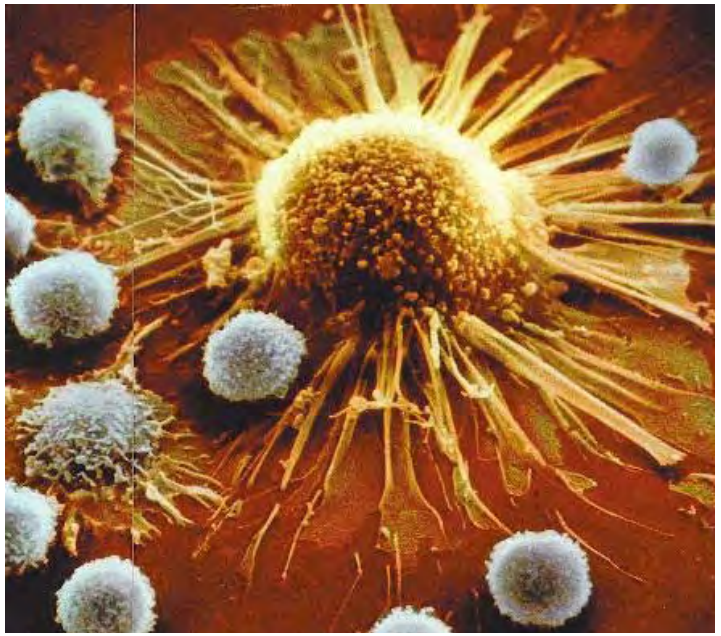


Figure 43.7 (Campbell 9th ed)



T-lymphocytes attack cancer cell

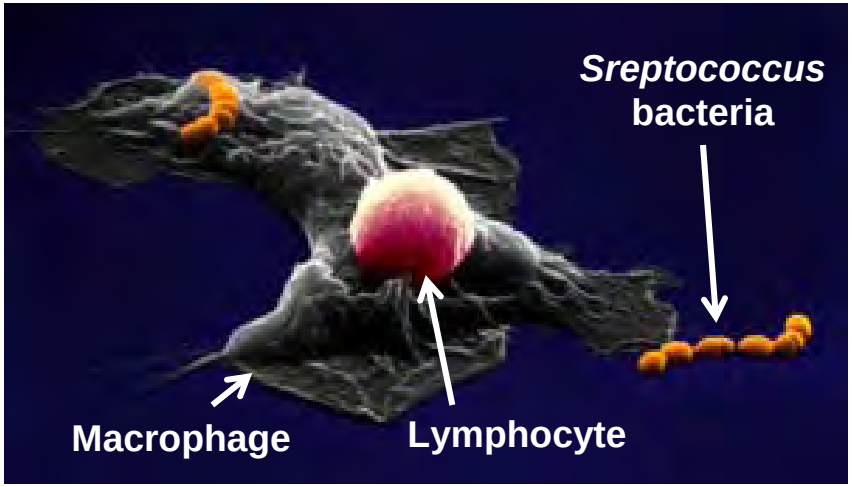
Lymphoid tissues and organs

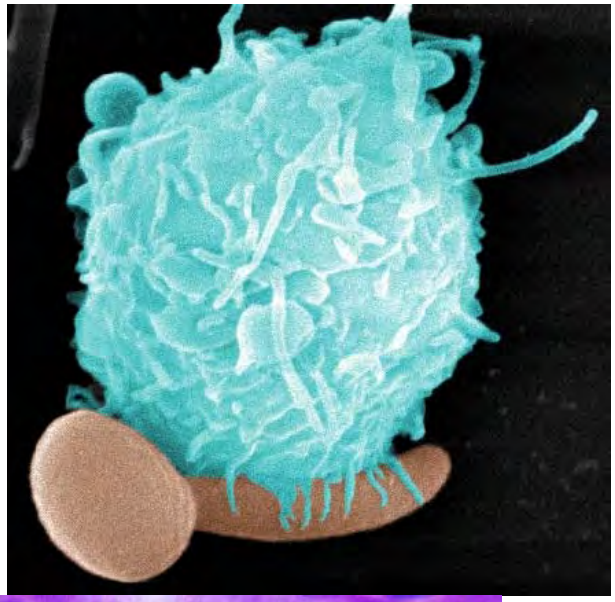
- Specialized connective tissues containing immune cells (e.g. lymphocytes, macrophages, etc…)
- Occur w/in other organ systems

3

Immune System

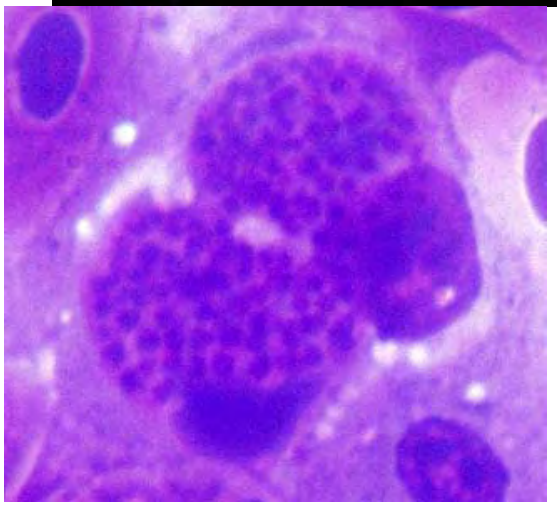
Pathogen = disease causing microorganisms, viruses and fungi





Macrophage

***Candida albicans* (a fungus)**



Liver smear of Macrophage with *Plasmodium* spp (phylum Apicomplexa) (a "protozoan")

The Immune System

Innate Immunity

- 1° defense
- Nonspecific
- Fast

- **External defenses**
  - try to prevent entry of pathogen
- **Internal defenses**
  - fight pathogen once inside

Plants

Invertebrates

Vertebrates

Acquired Immunity

- 2° defense
- Specific
- Slower

- **Cell-mediated response**
  - cytotoxic cells (lymphocytes)
- **Humoral response**
  - antibodies in body fluids

Jawed Vertebrates

Refer to Figure 43.2
(Campbell 9th ed)

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Innate Immunity

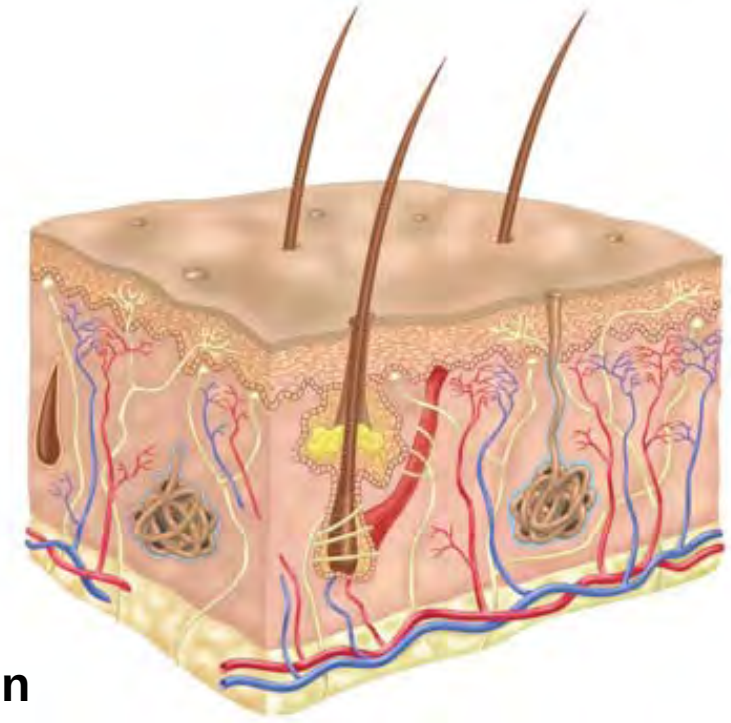
External Defenses

Skin, exoskeleton, egg shell, cuticle

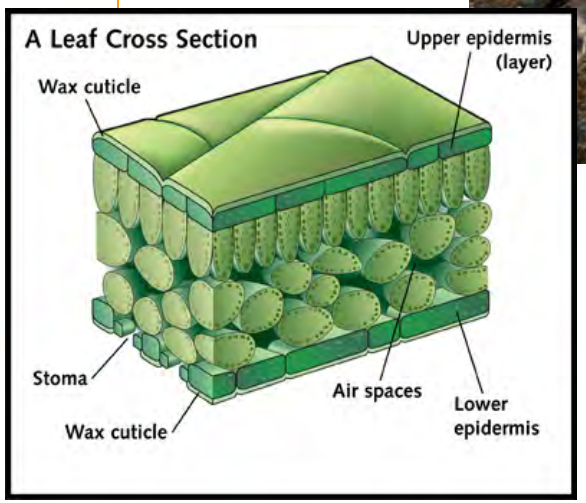
A physical barrier to prevent pathogens from entering body

Shed cicada nymph exoskeleton

Tarantula molting exoskeleton



Skin



Innate Immunity

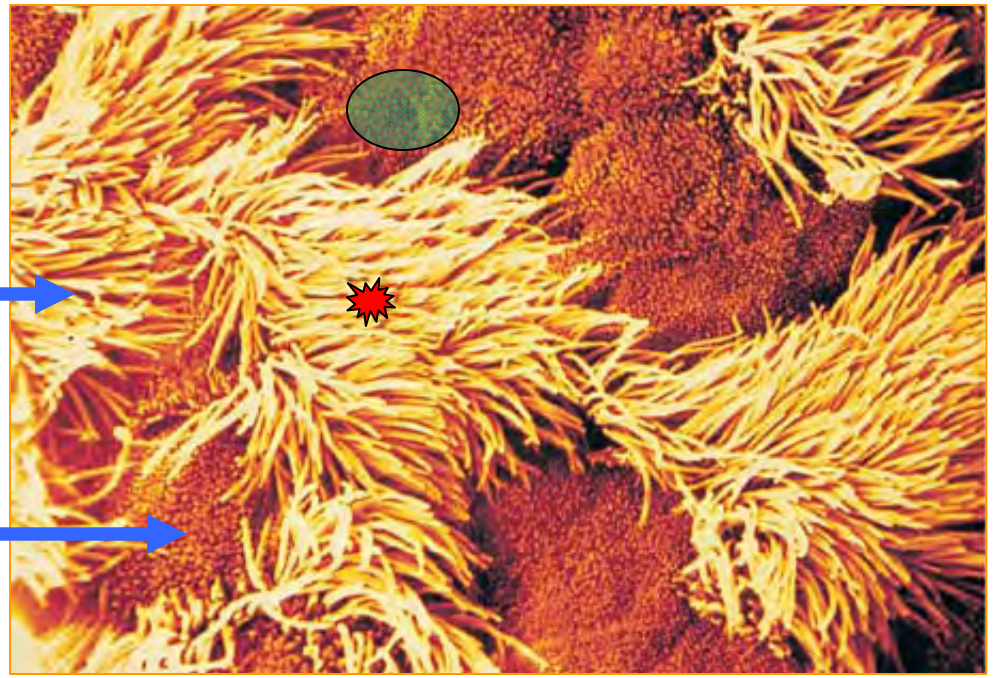
External Defenses

- Skin and exoskeleton, eggshell, cuticle
- Ciliated epithelia
- Secretions
  - work with cilia to stop/ slow movement of unwanted particles and expel them from the body

Nose & trachea

Ciliated cells

Mucus cell



Innate Immunity

External Defenses

- Skin, exoskeleton, etc…
- Ciliated epithelia
- Secretions
  - antibacterial

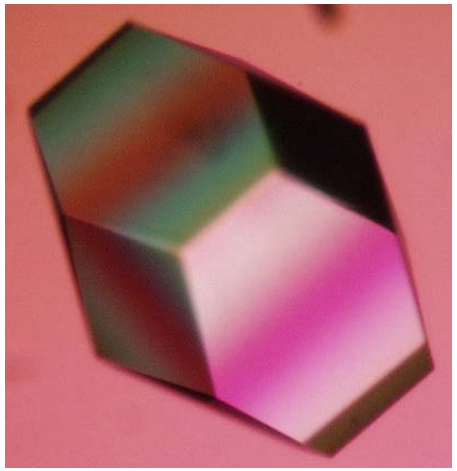
Tears

Breast milk

Saliva

Many secretions are antibacterial due to an enzyme called lysoZYme

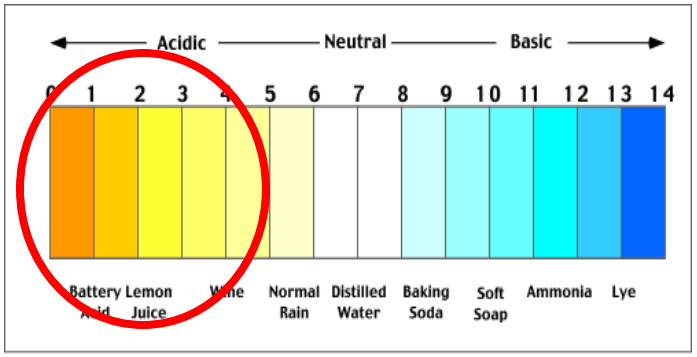
(NOT lysoSOme, which is an organelle)



Innate Immunity

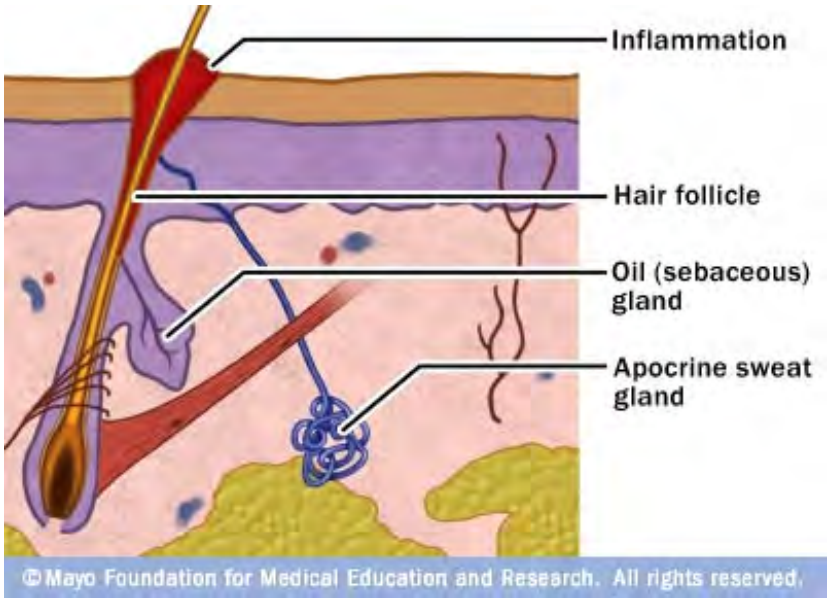
External Defenses

- Skin, exoskeleton, eggshell, cuticle
- Ciliated epithelia
- Secretions
  - antibacterial

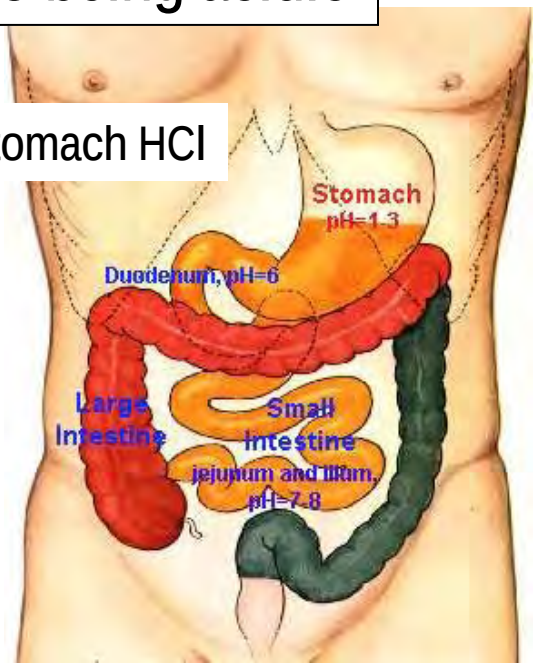


Other secretions are antibacterial due to being acidic

Sweat & oil (sebaceous) gland secretions



stomach HCl



Innate Immunity

Internal Defenses

Phagocytosis | **Antimicrobial peptides** | **Inflammation** | **NK Cells**

Only in vertebrates

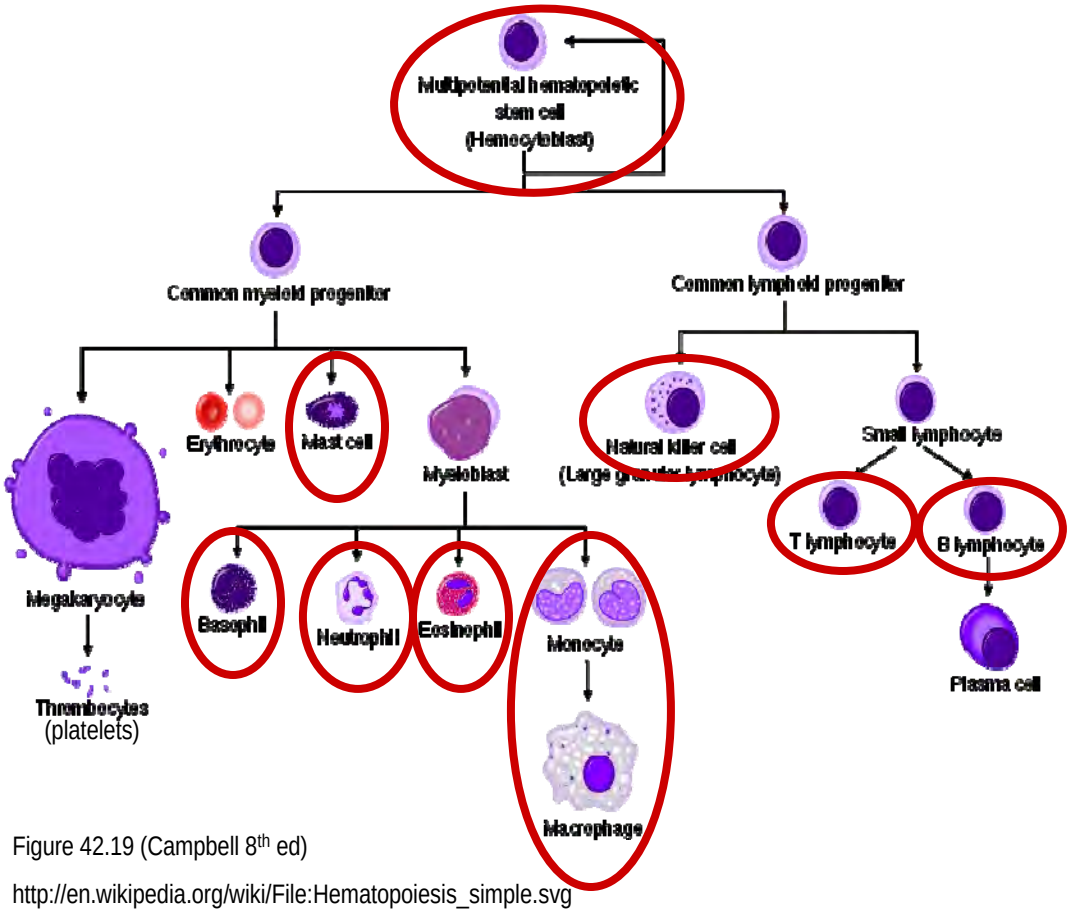


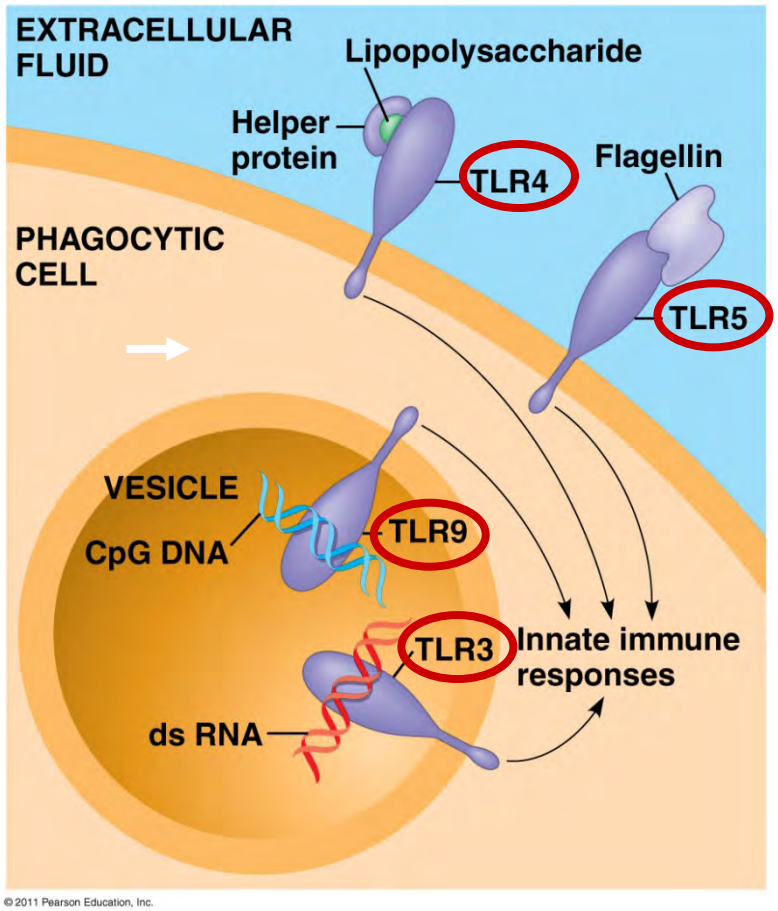
Figure 42.19 (Campbell 8th ed)

http://en.wikipedia.org/wiki/File:Hematopoiesis_simple.svg

- White blood cell (WBC) (aka leucocyte) = 5-7 types of cells of immune system
- All but 2 types are involved in the internal innate immune response
- Two types are involved in acquired immunity (B and T lymphocytes)
- 1 type of stem cell is capable of giving rise to all blood cell types (WBCs, RBCs, platelets)

Innate Immunity

Internal Defenses



(TLR = "toll-like receptor")

Figure 43.6 (Campbell 9th ed)

Initiation of Internal Defenses

- WBCs have special receptors (TLRs) that bind to certain molecules on a pathogen's surfaces;
- Binding to a pathogen initiates internal innate defenses (phagocytosis, inflamation etc...)
- Some receptors are within the WBC outer membrane, others are in vesicle membranes;
- Different kinds of WBCs have different TLRs
- Each TLR type can identify a broad group of pathogens (e.g. bacteria, gram+ bacteria, fungi, DNA viruses…);
  - Bind to molecules on pathogen surface that are common to all members of the broad group;
  - Do not recognize specific pathogens (i.e. bacteria in general but not *E. coli*)

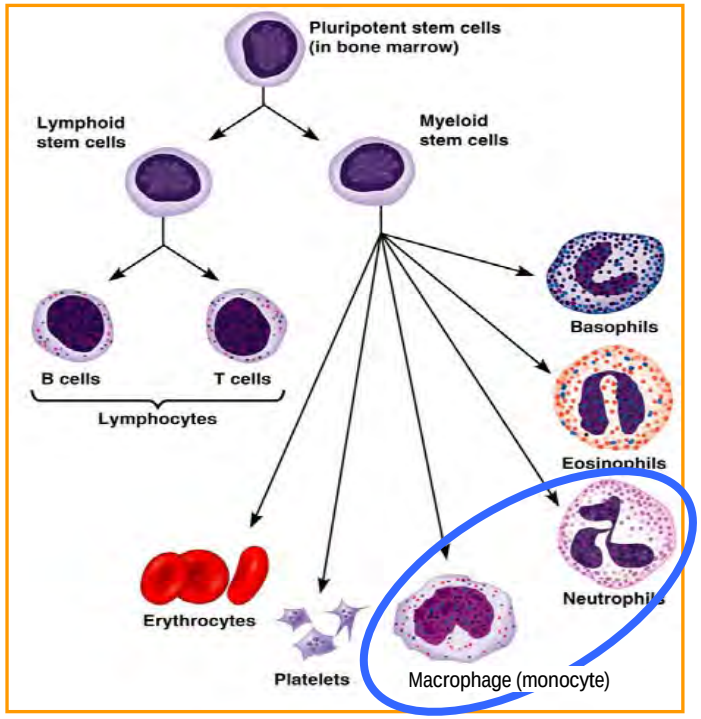
Innate Immunity

Internal Defenses

Phagocytosis

Primarily by 2 types of WBCs: (1) neutrophils; (2) macrophages

- Pathogen brought into internal vacuole
- Vacuoles w/ pathogens bind to lysosomes containing toxins (e.g. Nitrous oxide gas or lysozyme (an enzyme))



Monocytes are a precursor to macrophages

Figure 42.19 (Campbell 9th ed)

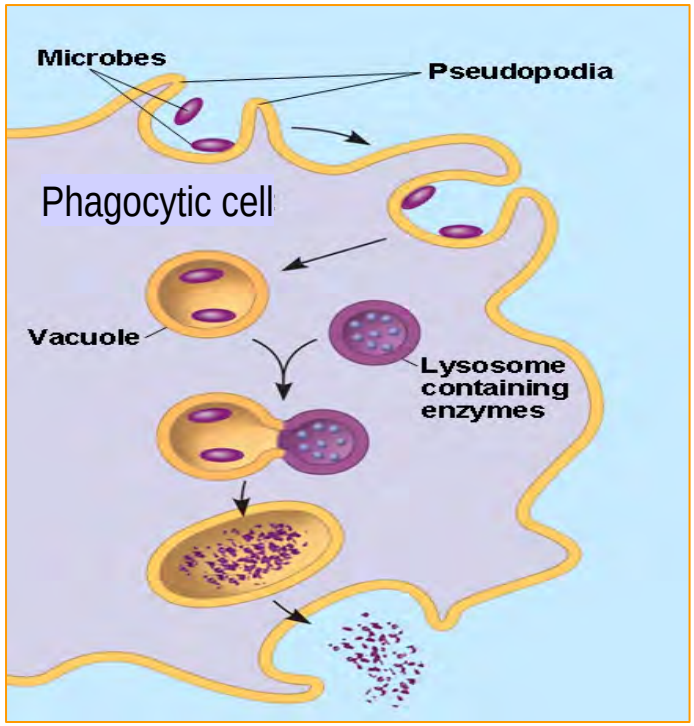
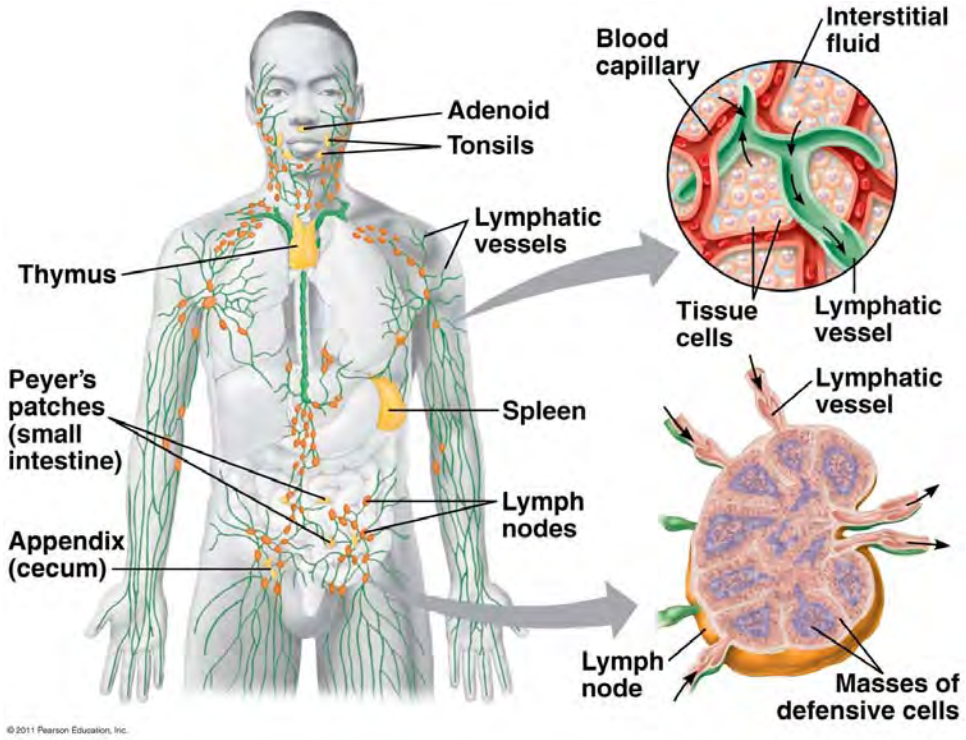


Figure 43.3 (Campbell 9th ed)

Innate Immunity

Internal Defenses

Phagocytosis



Neutrophils & Macrophages either:

1. roam through the vascular & lymphatic systems or;
2. wait in various tissues and organs (esp lymphatic tissues)

Figure 43.7 (Campbell 9th ed)

Innate Immunity

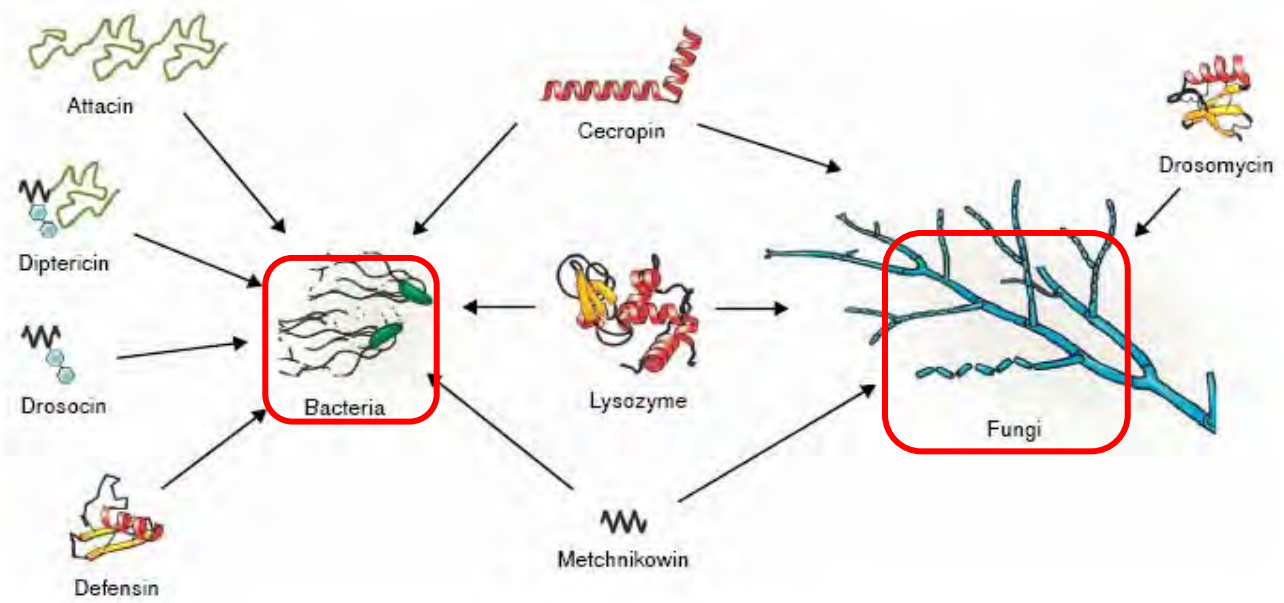
Internal Defenses

Phagocytosis

Antimicrobial peptides

- Proteins (not cells!) that attack microbes or impede their reproduction
- Usually recognize broad groups of pathogens (e.g. gram + or – bacteria, fungi)
- May already be in the tissue or produced upon recognition of a pathogen

  (Produced by macrophages, epithelial cells, or infected cells)



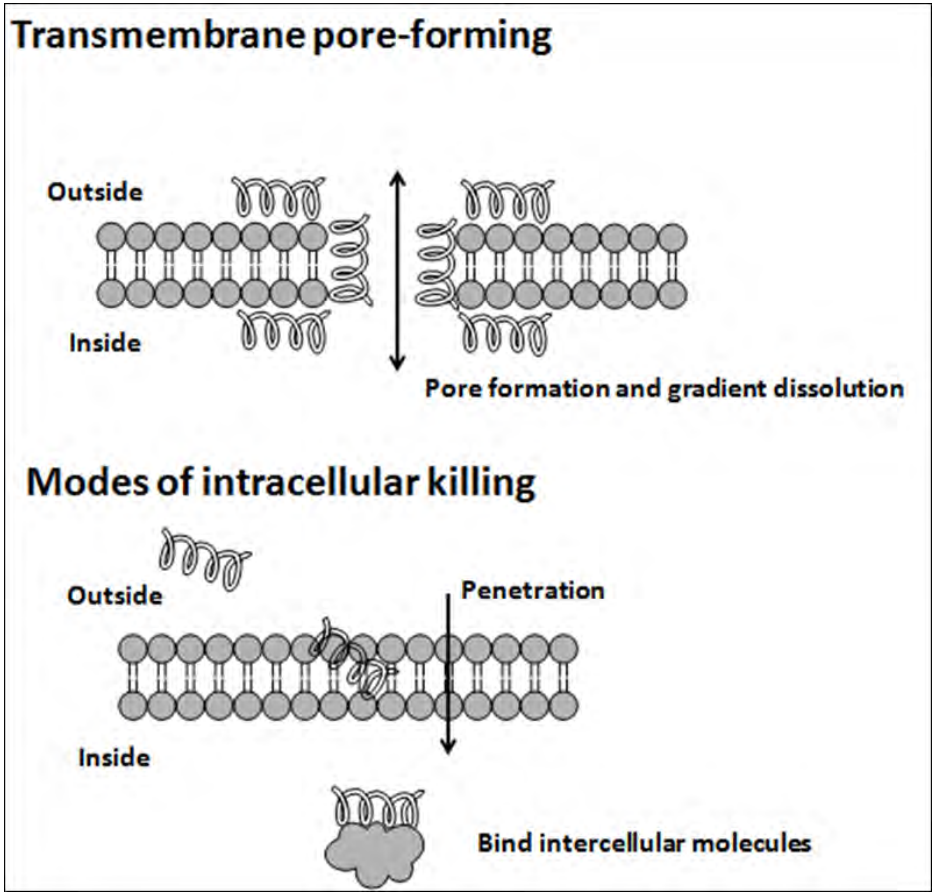
Innate Immunity

Internal Defenses

Phagocytosis | **Antimicrobial peptides**

- Kill cells in a variety of ways
  - Integrate w/
    - membranes
      - causing a hole and/or
      - altering membrane function
    - intracellular molecules
      - altering their function

- Huge area of disease research as many mechanisms and thus potential uses are unknown…



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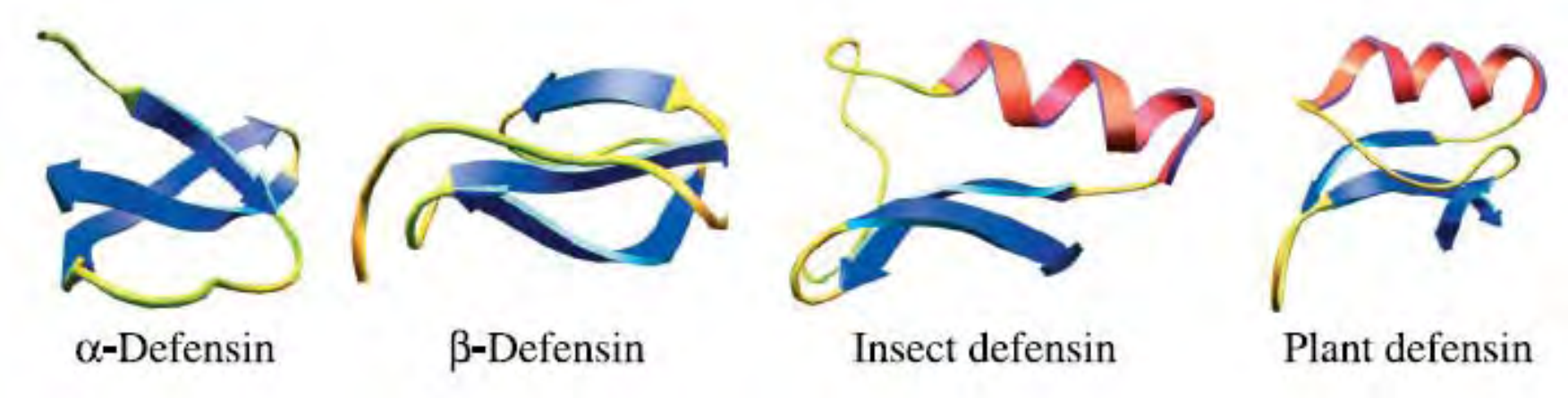
Innate Immunity

Internal Defenses

Phagocytosis

Antimicrobial peptides

- Some are present in a variety of organisms



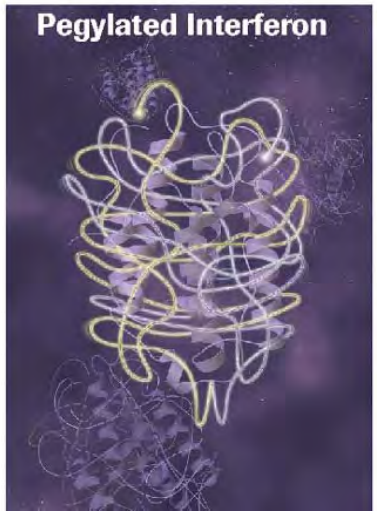
Innate Immunity

Internal Defenses

Phagocytosis

Antimicrobial peptides

- Others are only present in vertebrates
  - e.g. interferon
    - Induces cells to produce antiviral substances
    - Some interferons are manufactured by drug companies to combat specific diseases

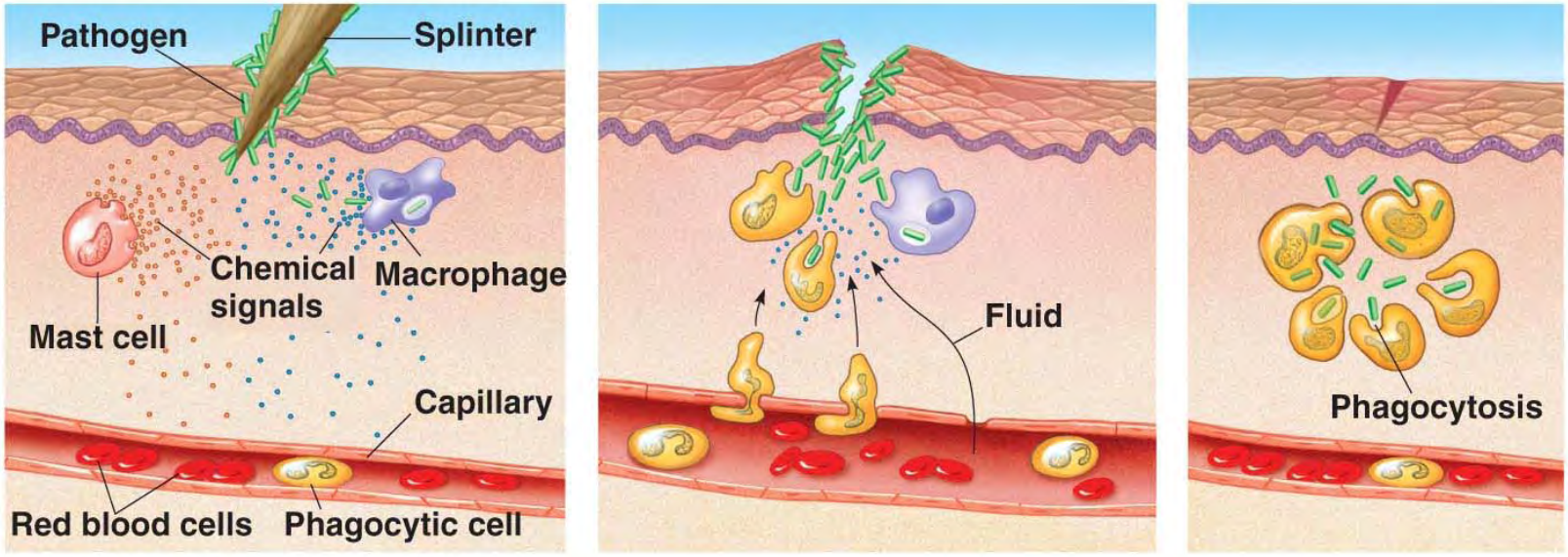


Used to treat:
- hepatitis B
- hepatitis C
- multiple sclerosis

Innate Immunity

Internal Defenses

Phagocytosis | **Antimicrobial peptides** | **Inflammation**



Upon introduction of a pathogen:

1. mast cells (a type of WBC) produce histamine;
   - Histamine increases blood vessel permeability allowing antimicrobial peptides to enter tissue
2. macrophages (another WBC) produce prostaglandins which attract other phagocytic WBCs

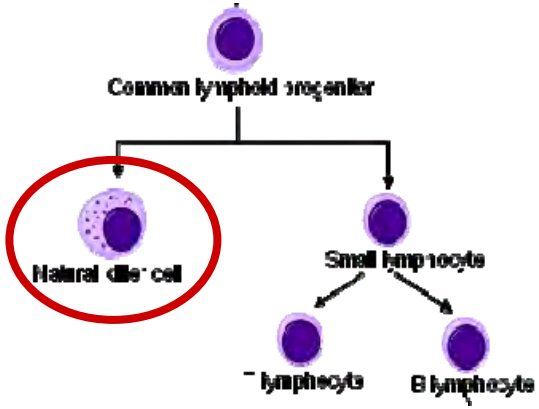
Figure 43.8 (Campbell 9th ed)

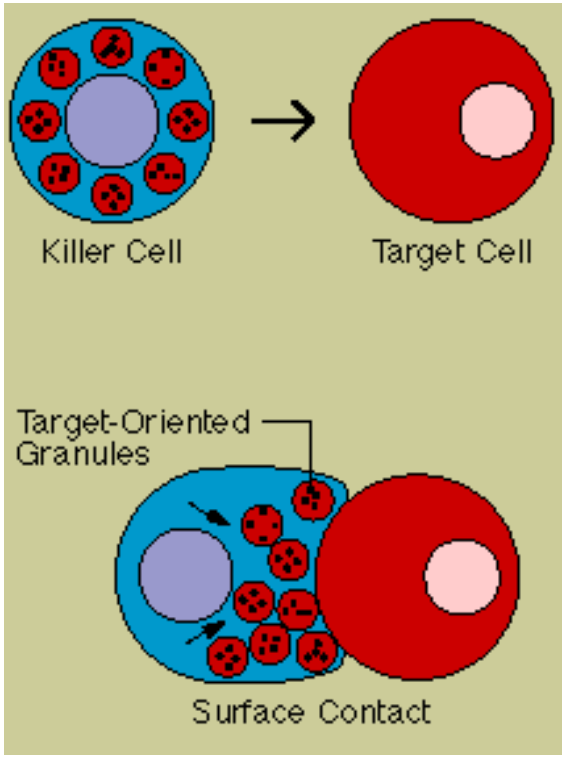
Innate Immunity

Internal Defenses

Phagocytosis | Antimicrobial peptides | Inflammation | Natural Killer (NK) Cells

- Are a type of lymphocyte produced by lymphoid stem cells (other lymphocyte types are involved in acquired immunity)
- Activated by chemicals from infected or cancerous body cells
- Release chemicals to kill damaged cell (<u>not</u> the pathogen itself)
  - Do <u>not</u> cause lysis (which would spread cell contents)
  - Do not phagocytize
    - Dead cells disposed of in urine and feces





The Immune System

Innate Immunity

- 1° defense
- Nonspecific
- Fast

- **Barrier defenses**
  e.g. skin, mucous
- **Internal defenses**
  e.g. inflammation, phagocytic cells

Plants

Invertebrates

Vertebrates

Acquired Immunity

- 2° defense
- Specific
- Slower

- **Cell-mediated response**
  - cytotoxic cells (lymphocytes)
- **Humoral response**
  - antibodies in body fluids

Jawed Vertebrates

Refer to Figure 43.2 (Campbell 9th ed)

Acquired Immunity

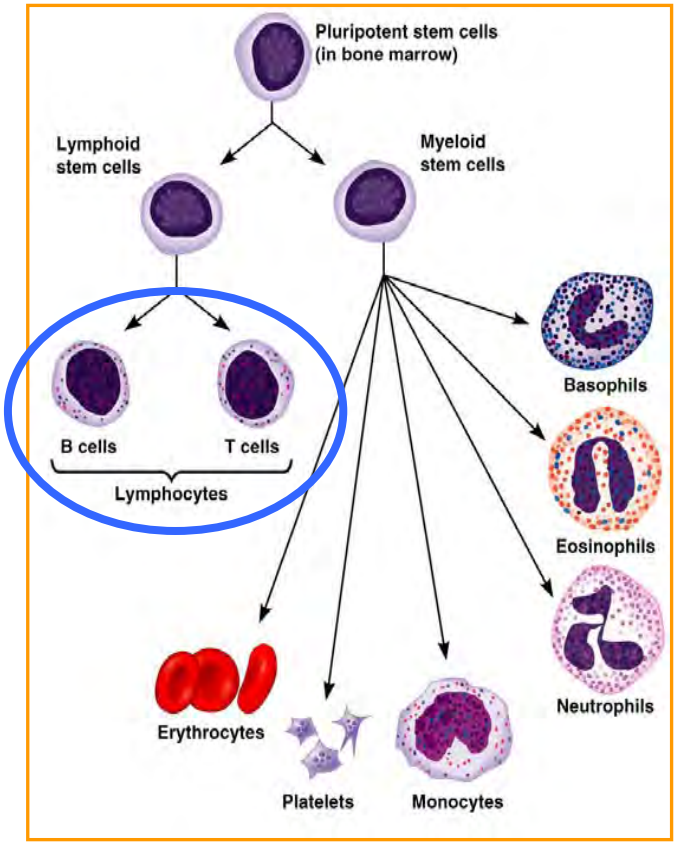
Lymphocytes

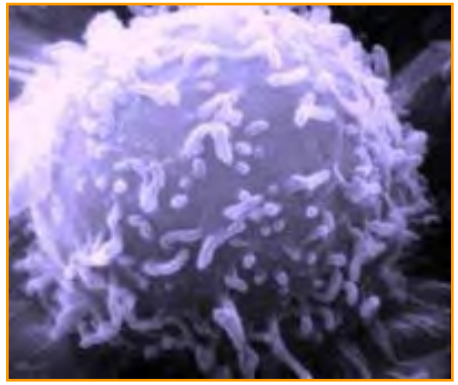
T- cells

Mature in thymus

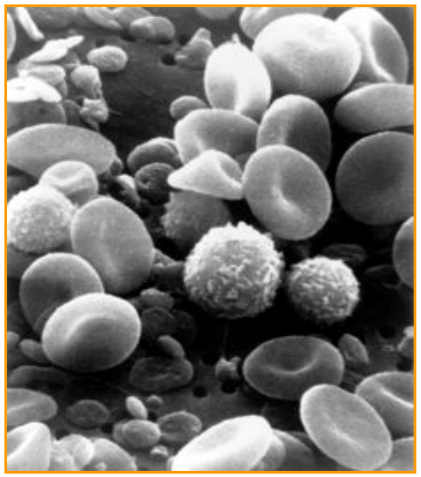
B- cells

Mature in bone marrow





Lymphocyte



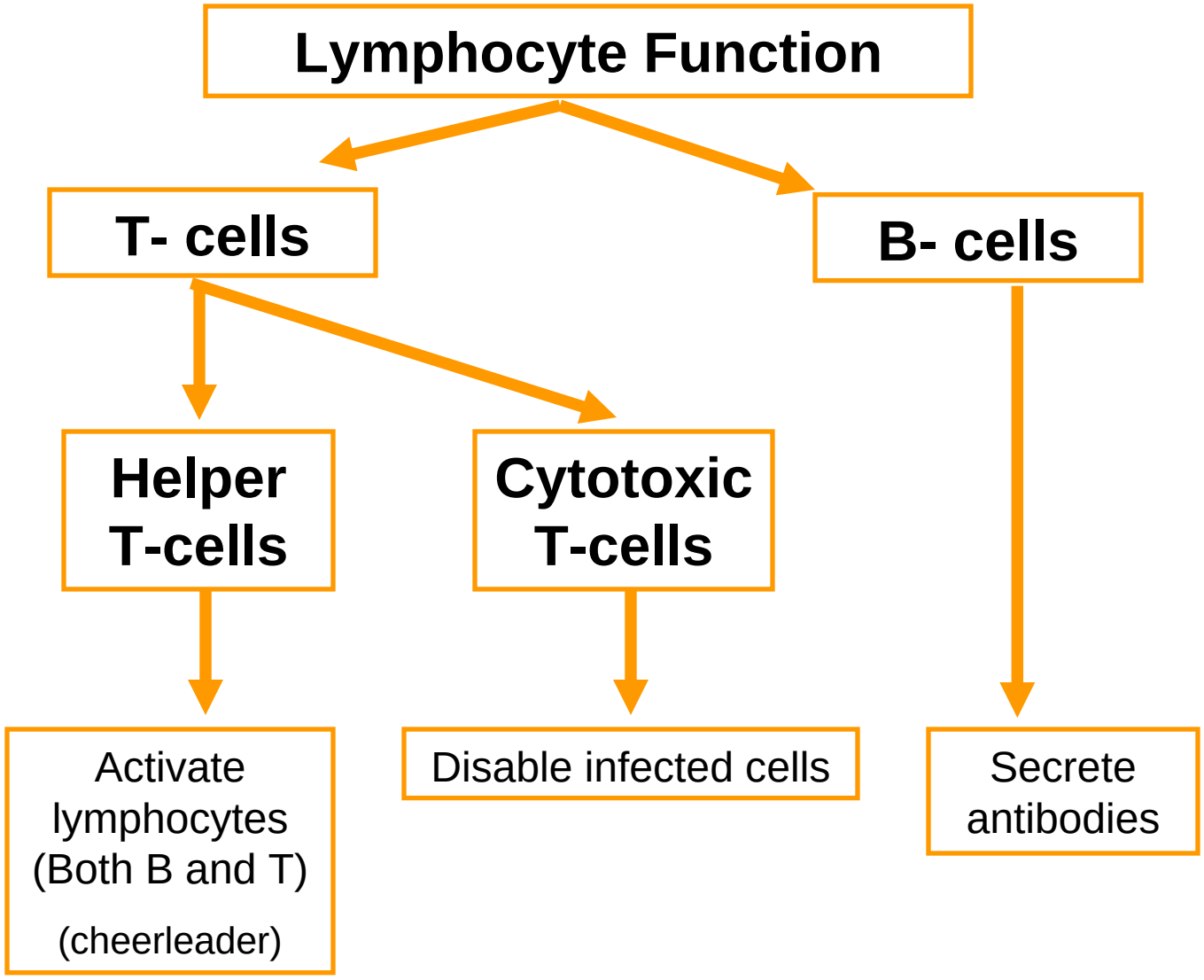
Both are activated by:

A. Chemicals secreted by macrophages

B. Binding to a foreign molecule (antigen)

- Antigen = any substance that elicits a response from a B- or T-cell

Acquired Immunity

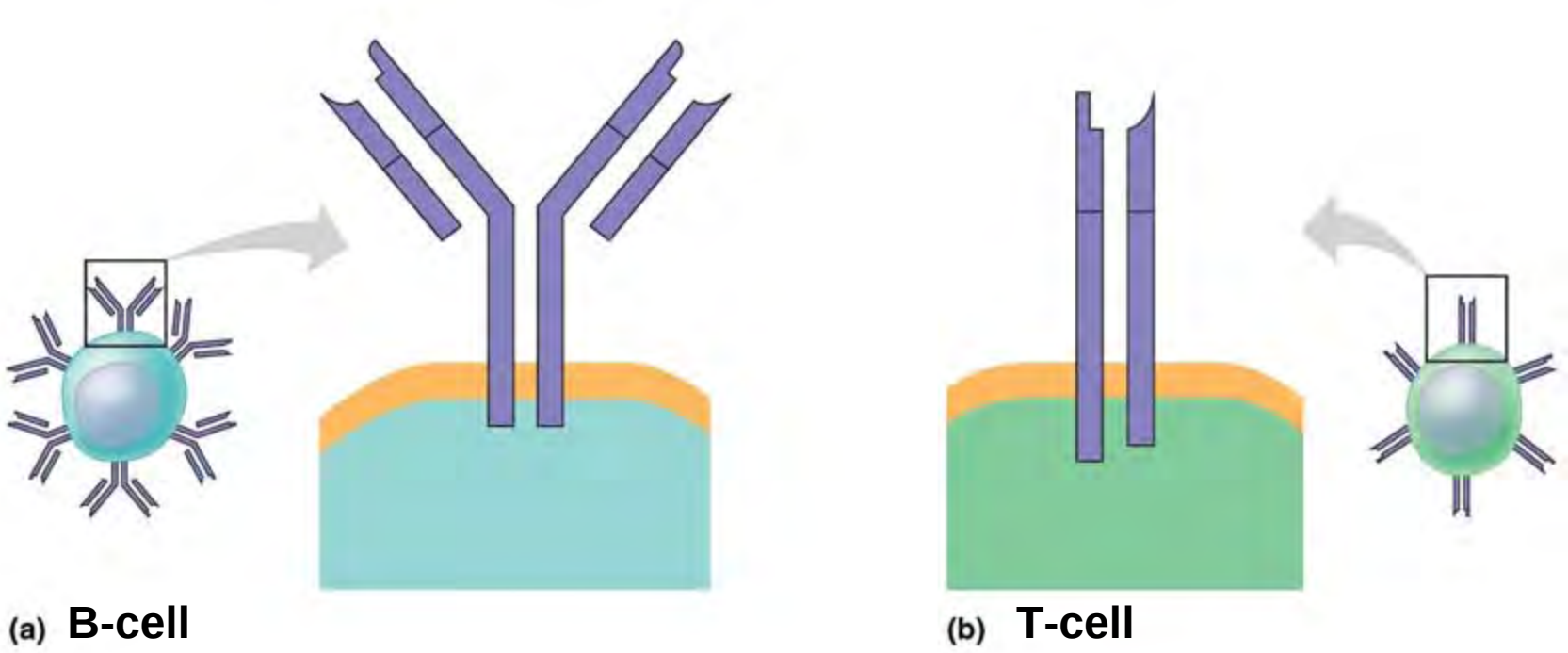


Are very specific: Different T- or B-cells for each different type of antigen

Antigen Receptors

Transmembrane protein that recognizes a specific antigen

vs. TLRs which are not specific

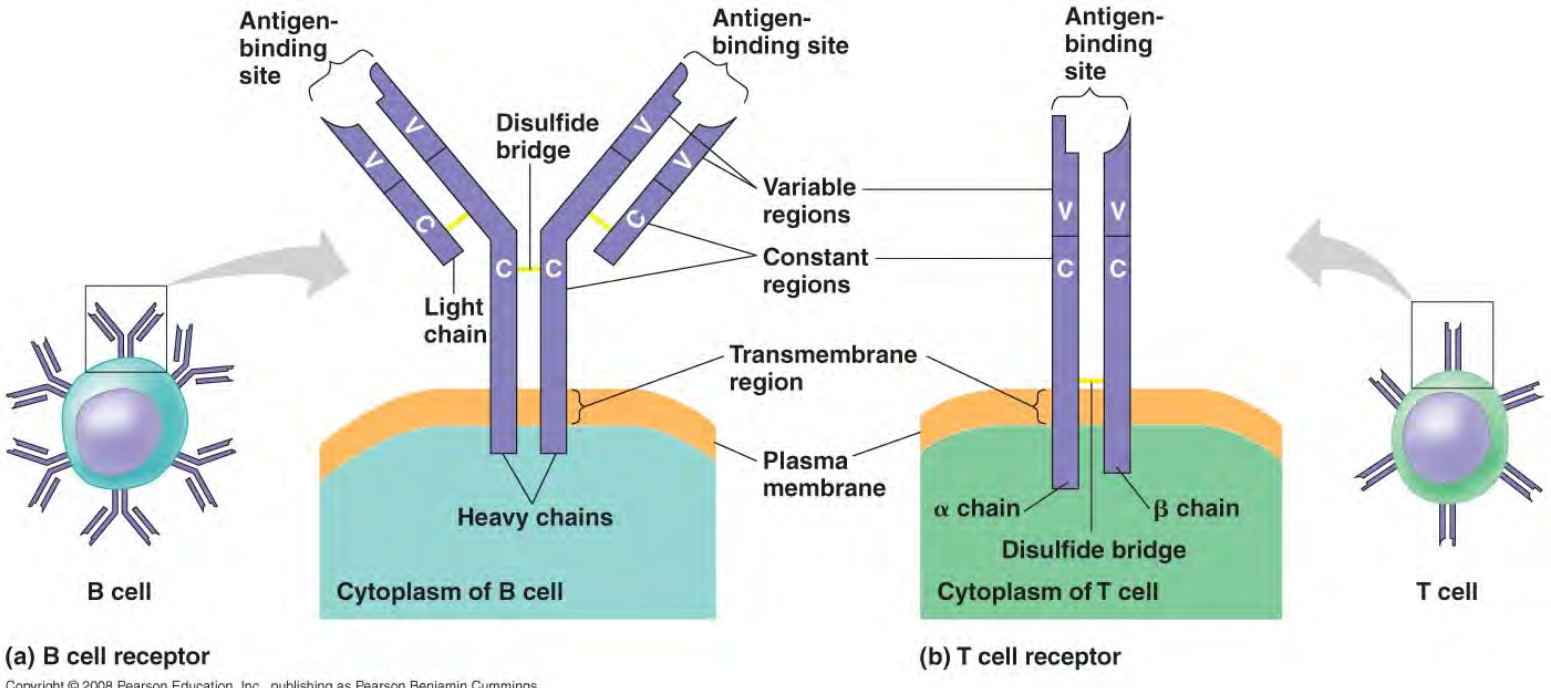


- Occur on both B and T cells
- Each B and T cell has ~100,000 identical antigen receptors
  - Thus, each T- or B-cell can only recognize 1 type of antigen

Figure 43.9 (Campbell 9th ed)

Figure 43.11 (Campbell 9th ed)

Antigen Receptor Structure



- All have 2 halves bound together;
- All have both a constant and a variable region;
  - Constant: Different B-cells have similar constant regions as do different T-cells.
  - Variable: Varies on different lymphocytes & thus different types recognize different antigens
    - 1,000,000 different B-cell antigen receptors
    - 10,000,000 different T-cell receptors
      - Thus T-cells recognize many more types of antigens than B-cells

Figure 43.9 (Campbell 9th ed)

Figure 43.11 (Campbell 9th ed)

Antibodies
(aka Immunoglobulins)

Secreted B-cell receptors (i.e. not attached to B-cell membrane)

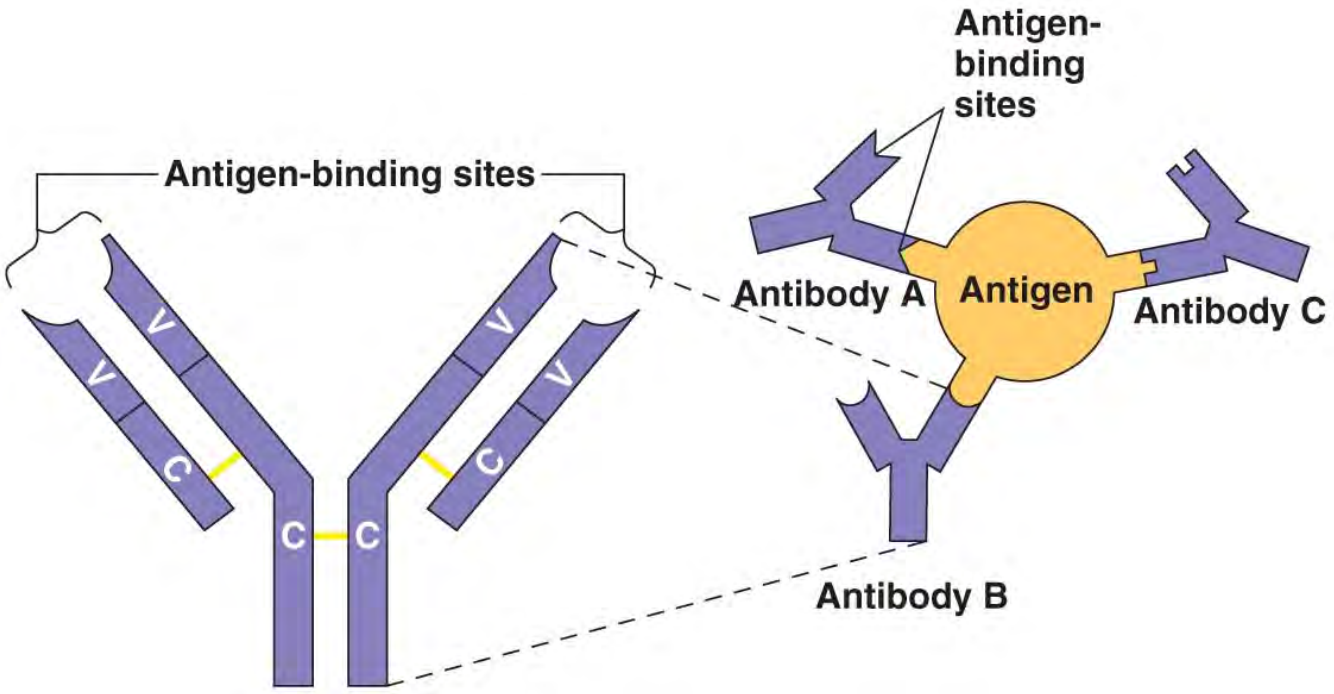
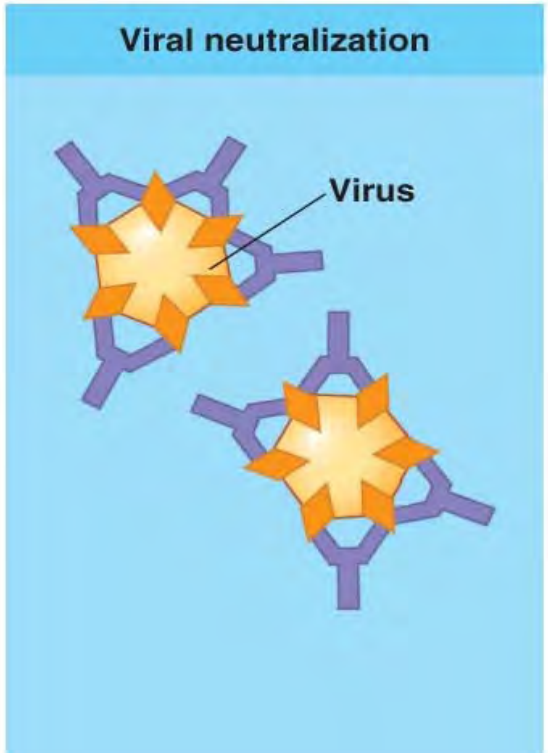


Figure 43.10 (Campbell 9th ed)

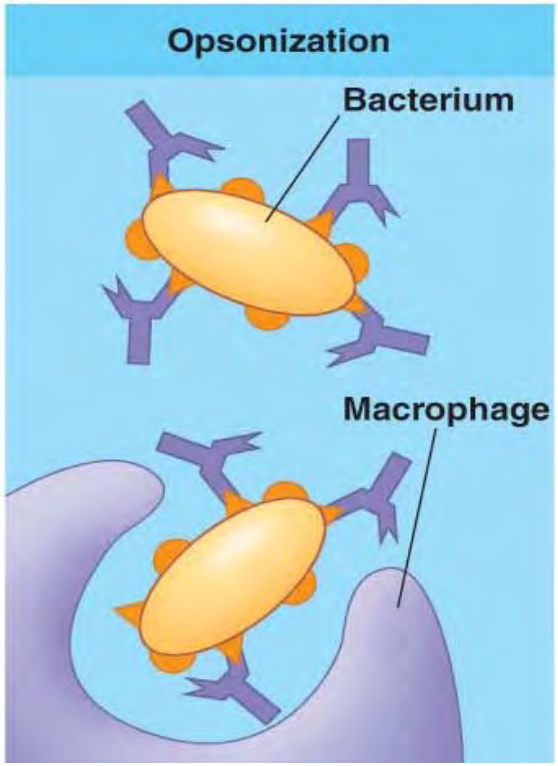
Antibodies inactivate antigens via several methods

1. Neutralization



Block all accessible surfaces of antigen

2. Opsonization



Make it easier for macrophages to phagocytose antigen

Figure 43.19 (Campbell 9th ed)

Antibodies inactivate antigens via several methods

3. Activation of complement system

Binding of antibodies to an antigen activates the complement system:

- Series of protein activations that constructs an attack complex to bore a hole in the antigen leading to lysis of pathogen.

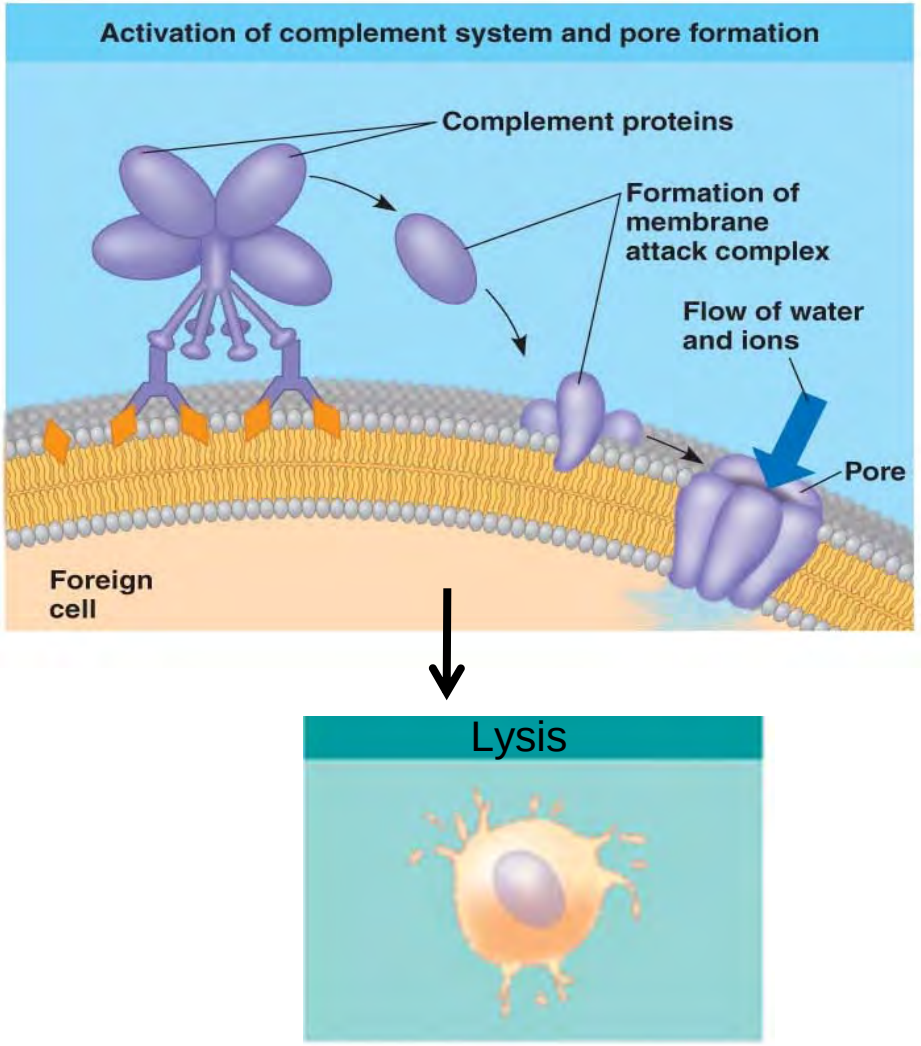
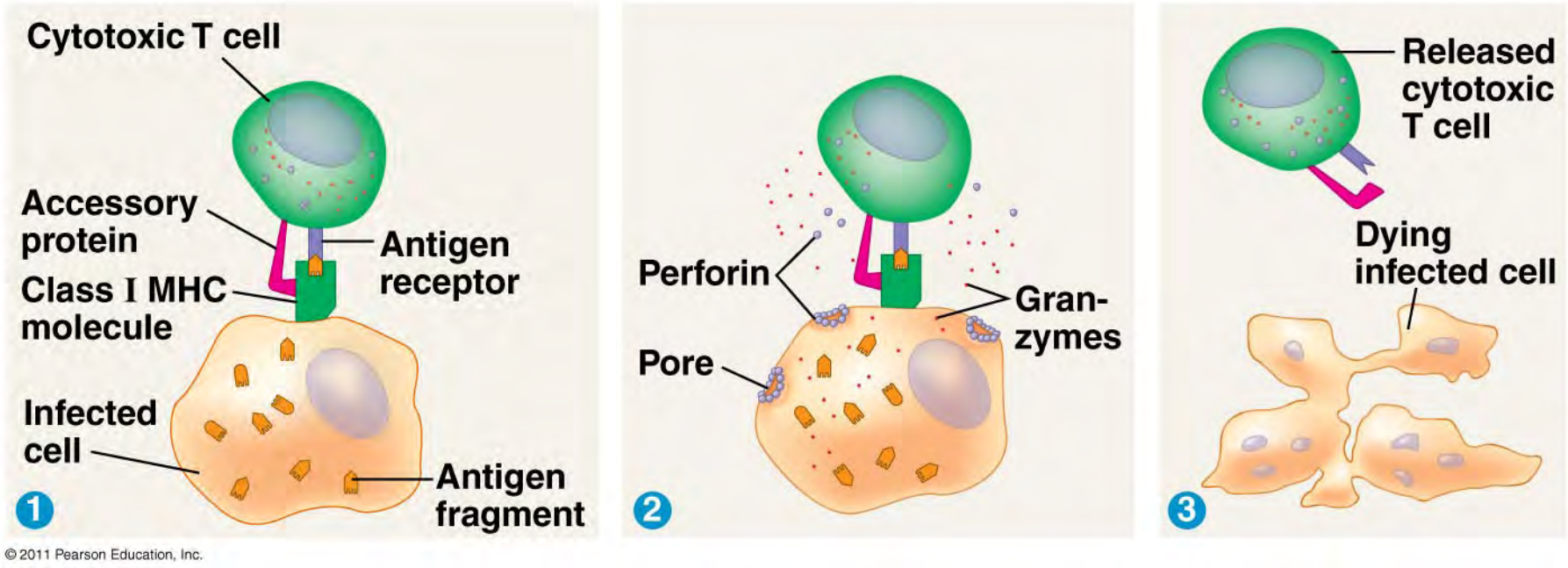


Figure 43.19 (Campbell 9th ed)

INFECTED body cells use special molecules (MHC I) to present antigen fragments to CYTOTOXIC T-cells



"Major Histocompatibility Complex" I (MHC I) molecules occur in almost all body cells

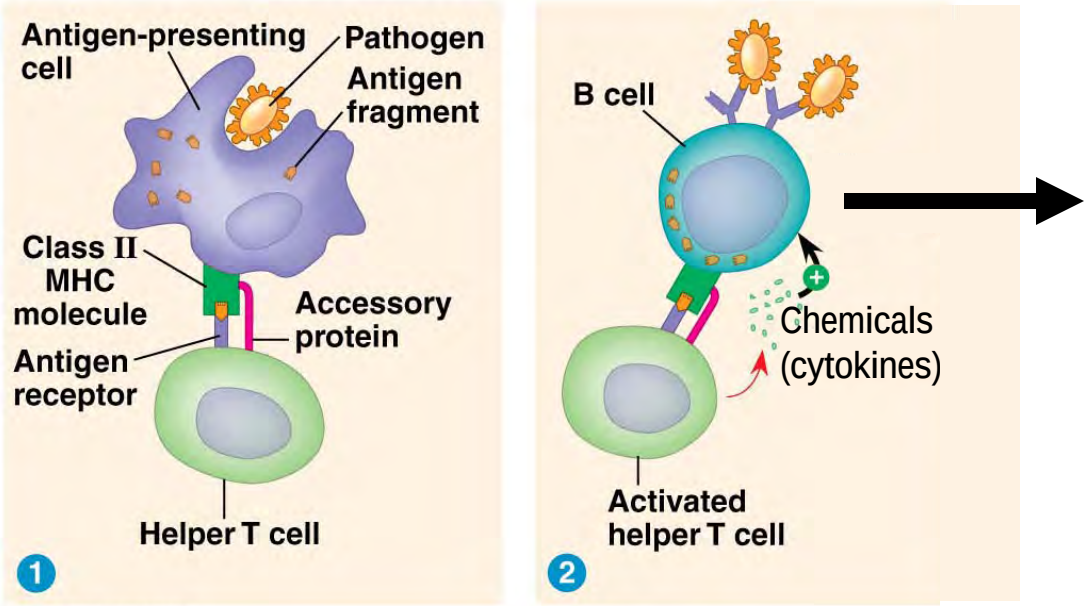
1A. Infected body cells use MHC I to present intracellular antigen fragments to cytotoxic T-cell

1B. Cytotoxic T-cell then binds to MHC I/ antigen fragment complex

2. Binding activates the cytotoxic T-cell causing it to kill the infected cell

Figure 43.17 (Campbell 9th ed)

PHAGOCYTIC cells use different molecules (MHC II) to present antigen fragments to HELPER T-cells



"Major Histocompatibility Complex" II (MHC II) molecules only occur on phagocytic cells (e.g. macrophages & B-cells (yes B-cells phagocytose too!)

1a. Macrophage phagocytoses antigen & presents fragments on its surface using MHC II molecules;

1b. Helper T-cell activated by binding to MHC II/ antigen fragment complex and then releases;

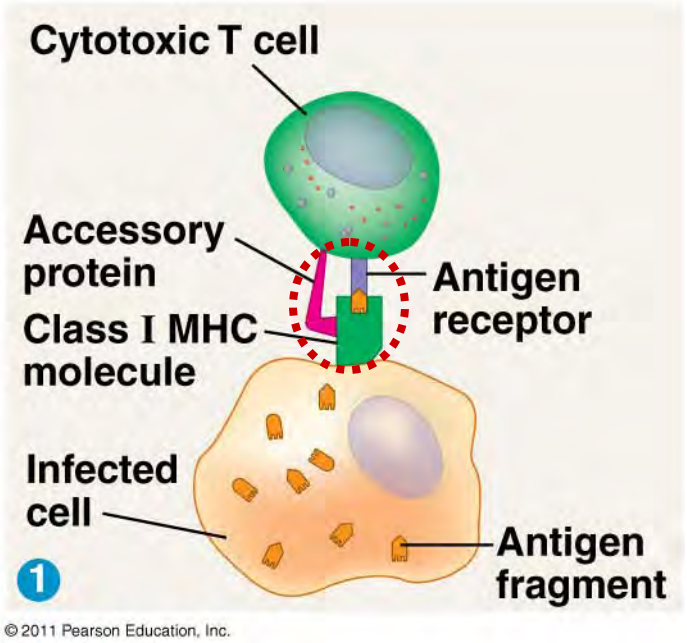
2a. B-cell binds to and phagocytoses same kind of antigen and also presents fragments using MHC II

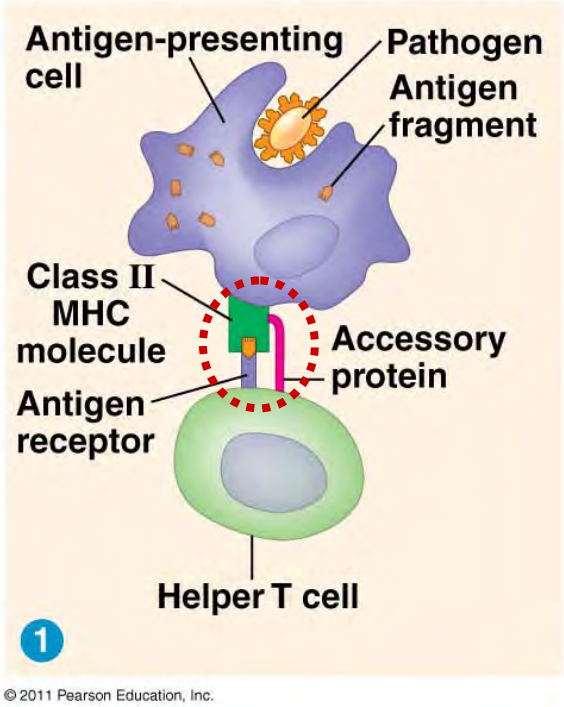
2b. Activated helper T-cell binds to B-cell MHC II/ antigen complex presenting same kind of antigen

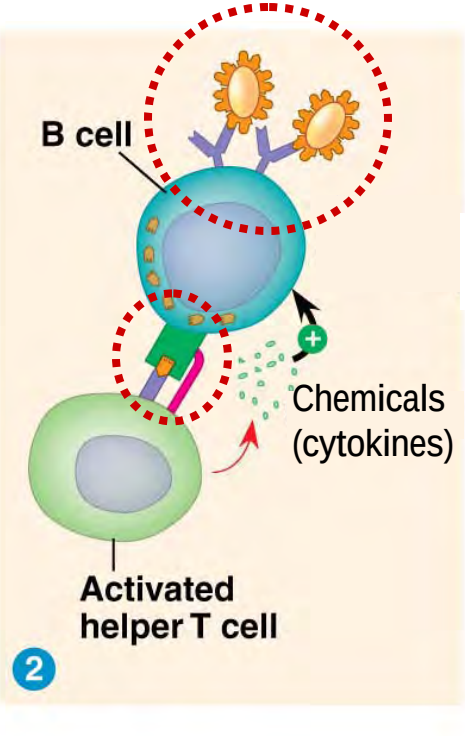
2c. Activated helper T-cell releases chemicals which activates the B-cell

Figure 43.18 (Campbell 9th ed)

Summary of T-cell vs. B-cell receptor function







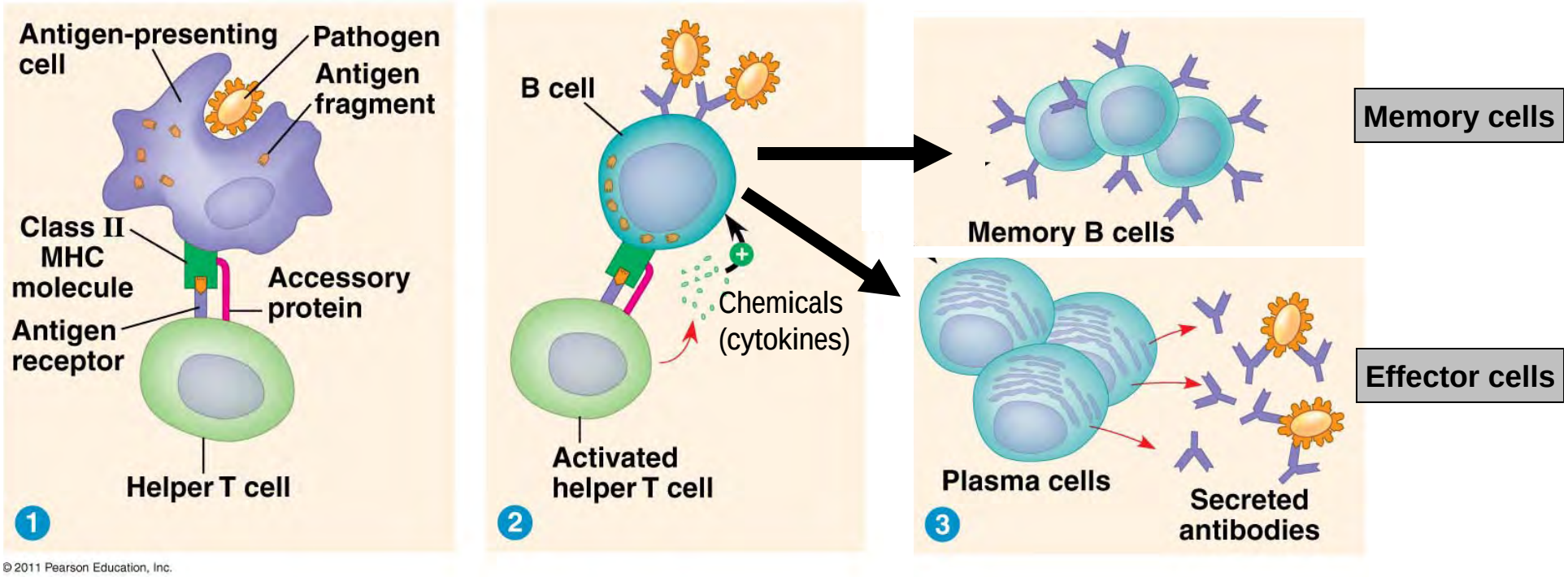
T-cell
- Bind to antigen FRAGMENT
  - presented by:
    - infected cell (which uses MHC I)
    - phagocytic cell (which uses MHC II)
    - B-cell (which uses MHC II)

B-cell
- Bind to INTACT antigen
  - free floating or
  - on pathogen surface

Figure 43.17 (Campbell 9th ed)

Figure 43.18 (Campbell 9th ed)

Activated B-cells rapidly reproduce



- Once activated by the T-cell, the B-cell actively clones itself.
- Clones differentiate into two types of cells:
  - Plasma B-cells (an effector cell) – short-lived antibody secreting cells
    used immediately to fight against present antigen
  - Memory B-cell – long-lived copies of the original B-cell
    used for fighting future infections by same type of antigen

Figure 43.18 (Campbell 9th ed)

Many B-cells can also be activated by binding to the antigen

Binding to the antigen is enough to induce cloning of many B-cells

i.e. some memory and plasma B-cells can be produced w/o the help of a helper T-cell

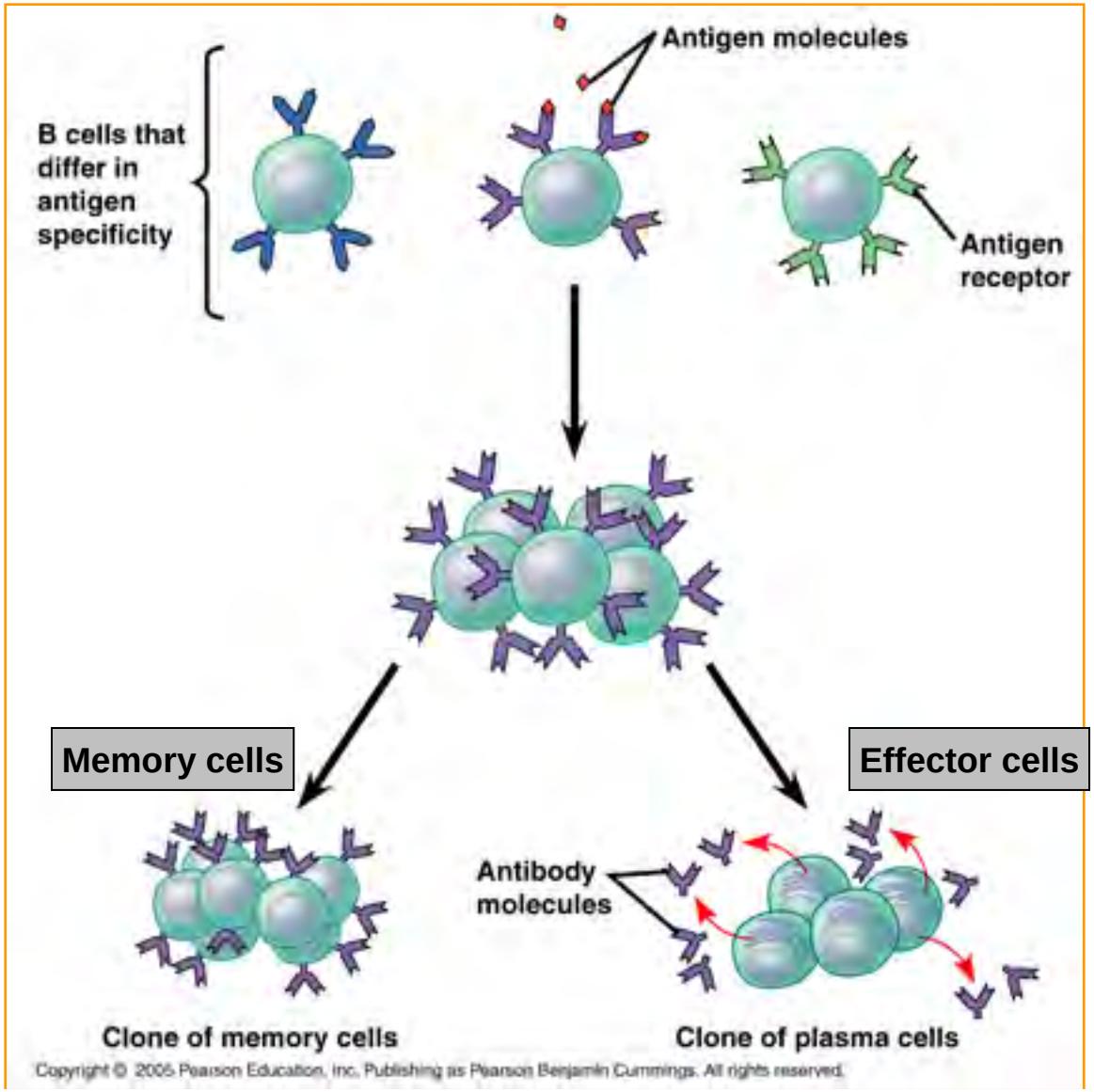


Figure 43.14 (Campbell 9th ed)

Activated helper and cytotoxic T-cells also clone themselves

Like activated B-cells,
activated cytotoxic and helper T-cells
clone themselves.

Clones differentiate into active (effector)
and memory T-cell forms

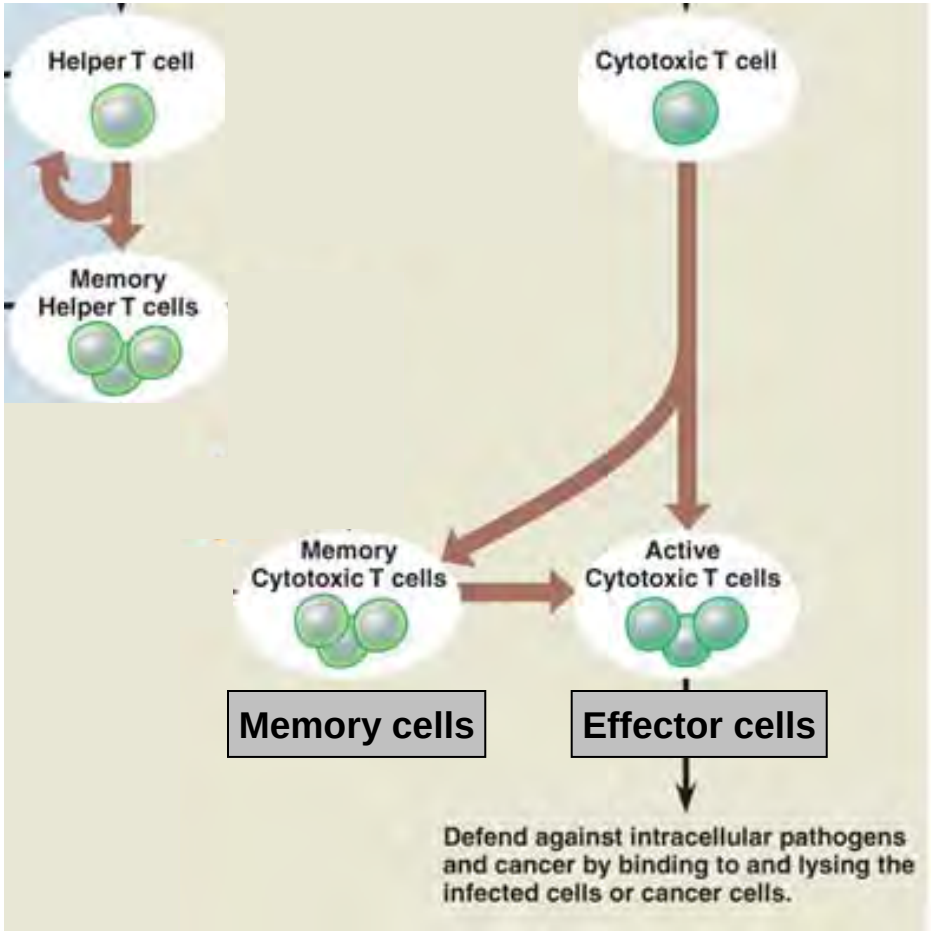
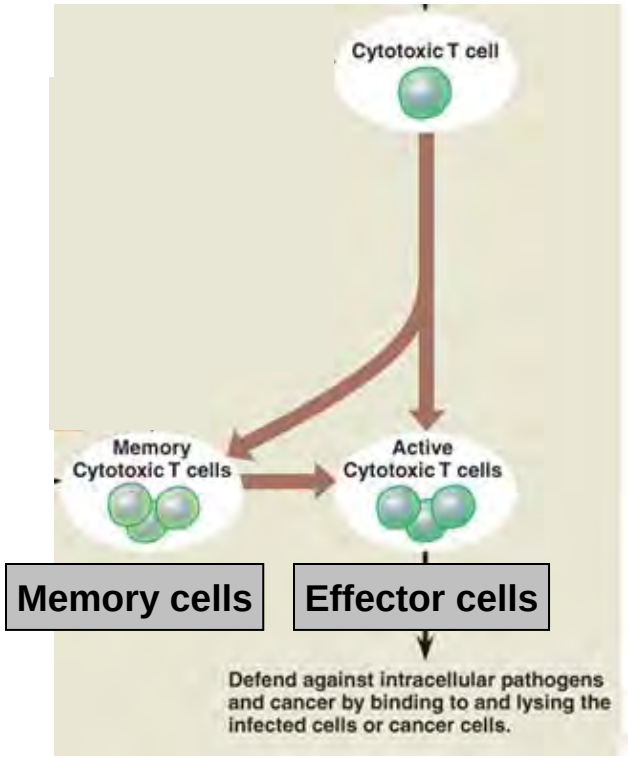
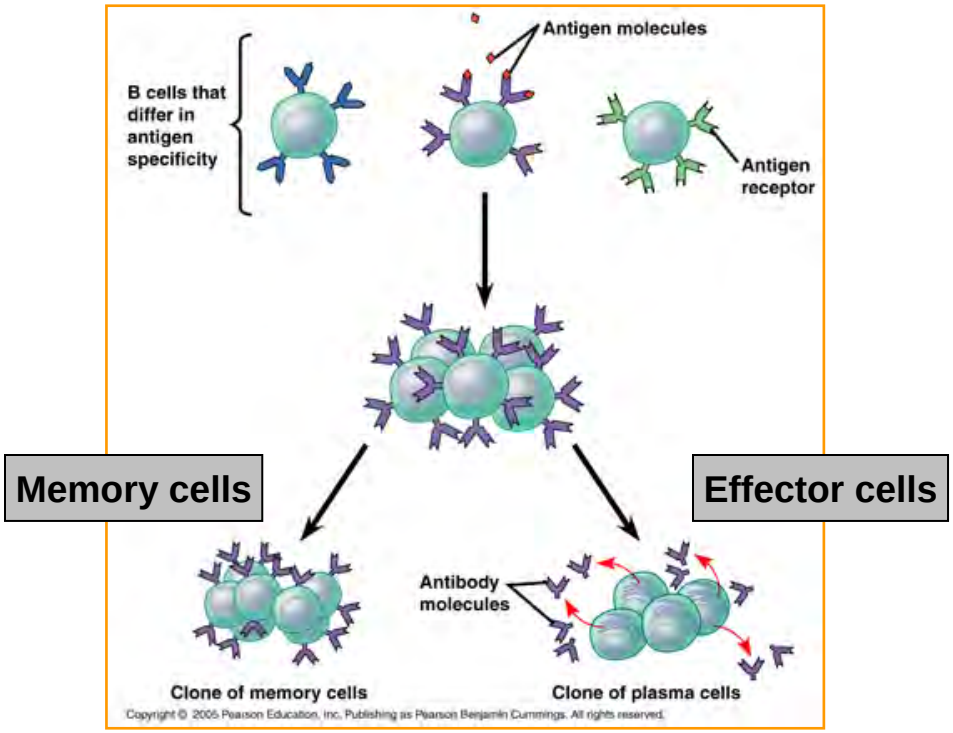


Figure 43.16 (Campbell 9th ed)

Figure 43.20 (Campbell 9th ed)

Effector vs Memory Cells





Effector cells

1. Plasma cell (antibody secreting B-cell)
2. Active cytotoxic T-cell
3. Helper T-cell

•Short lived
•Numerous once activated
•Attack antigens

Memory cells

1. Memory B-cell
2. Memory helper T cell
3. Memory cytotoxic T cell

•Live a long time (10-20 yrs)
•Less numerous than effector cells
•Activate effector cells & give rise to effector and memory cells

Memory cells result in immunological memory

① 1st exposure to antigen “A”

- Few antigen “A” antibodies

② 1° response to “A”

- Slow and mild

③ 2nd exposure to antigen “A”
1st exposure to antigen “B”

④a 2° response to “A” – fast and strong

④b 1° response to “B” – slow and mild

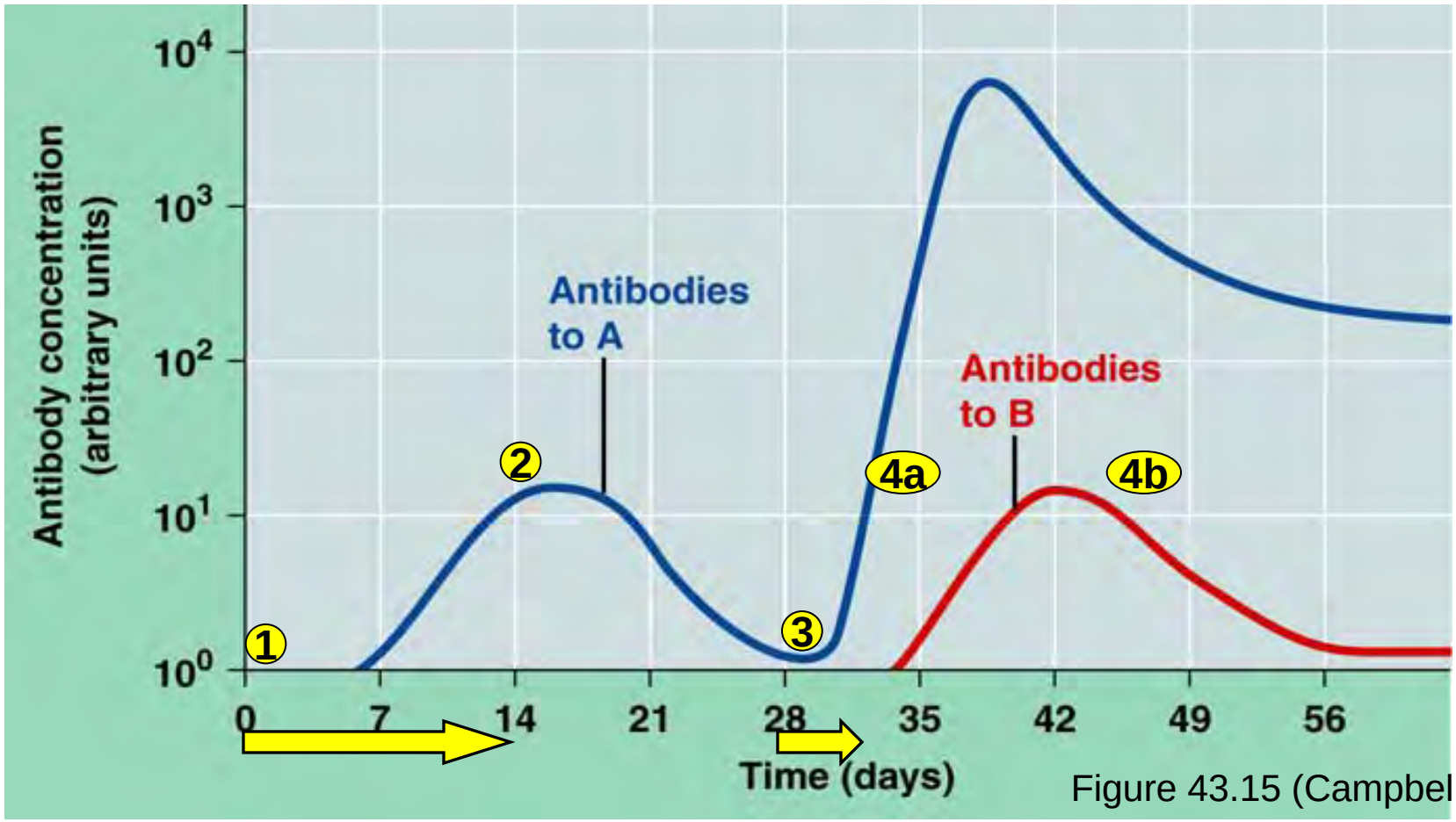
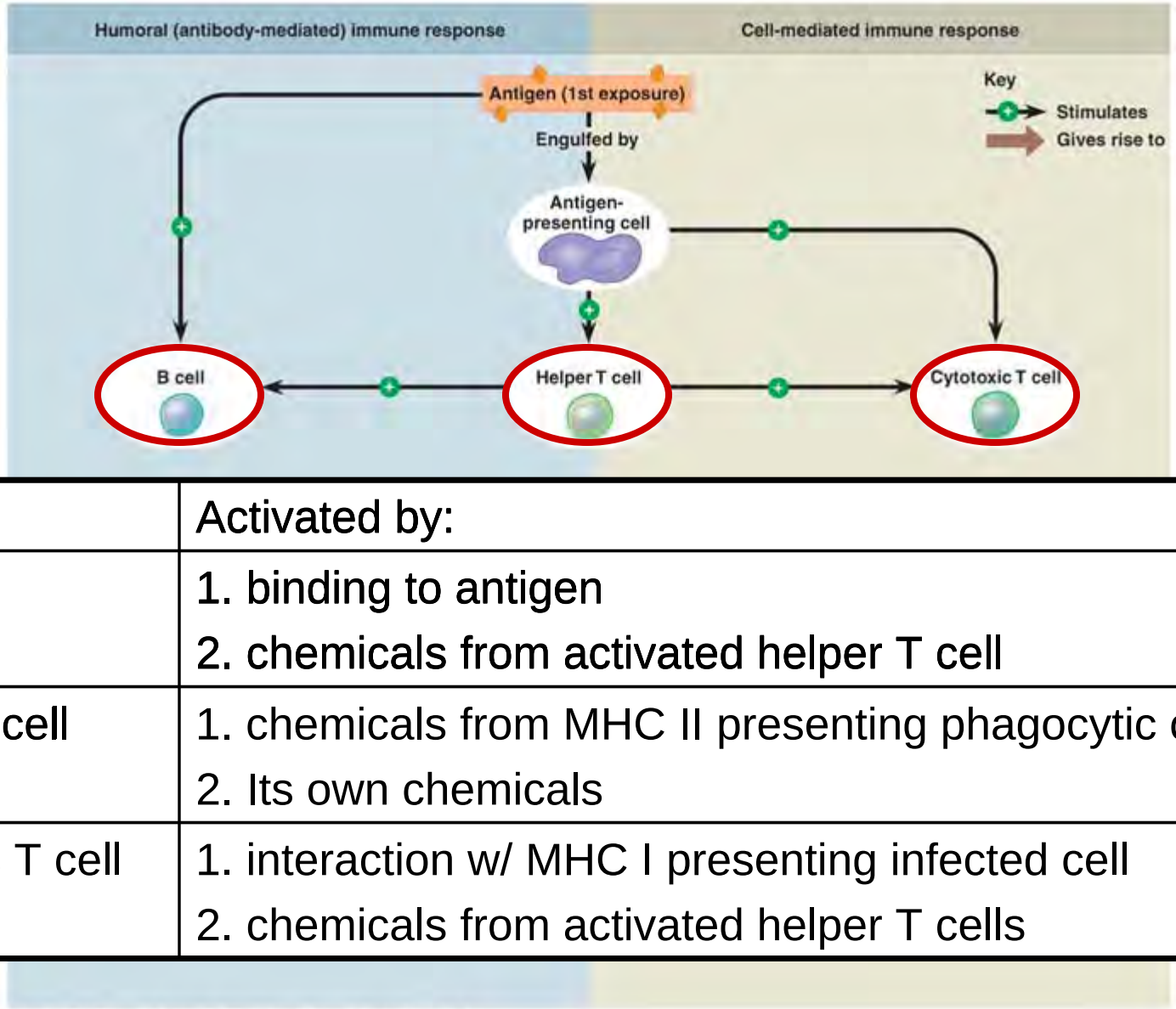


Figure 43.15 (Campbell 9th ed)

40 Acquired response Overview



	Activated by:
B cell	1. binding to antigen 2. chemicals from activated helper T cell
Helper T cell	1. chemicals from MHC II presenting phagocytic cell 2. Its own chemicals
Cytotoxic T cell	1. interaction w/ MHC I presenting infected cell 2. chemicals from activated helper T cells

Figure 43.20 (Campbell 9th ed)

Activated Helper T-cells clone & then differentiate into more active Helper T-cells & Memory Helper T-cells

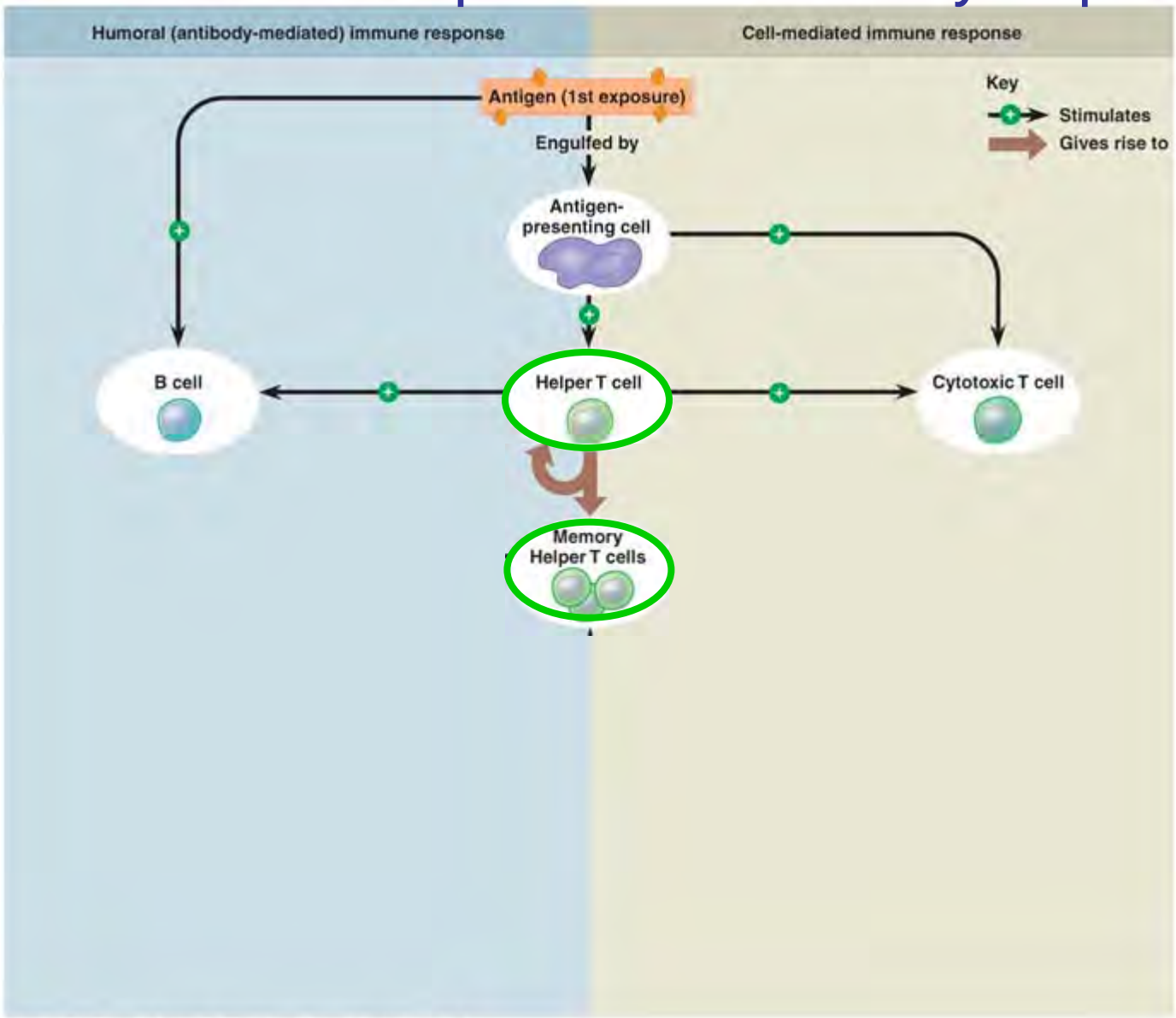


Figure 43.20 (Campbell 9th ed)

Activated B and Cytotoxic T-cells clone. Clones differentiate into effector and memory cells

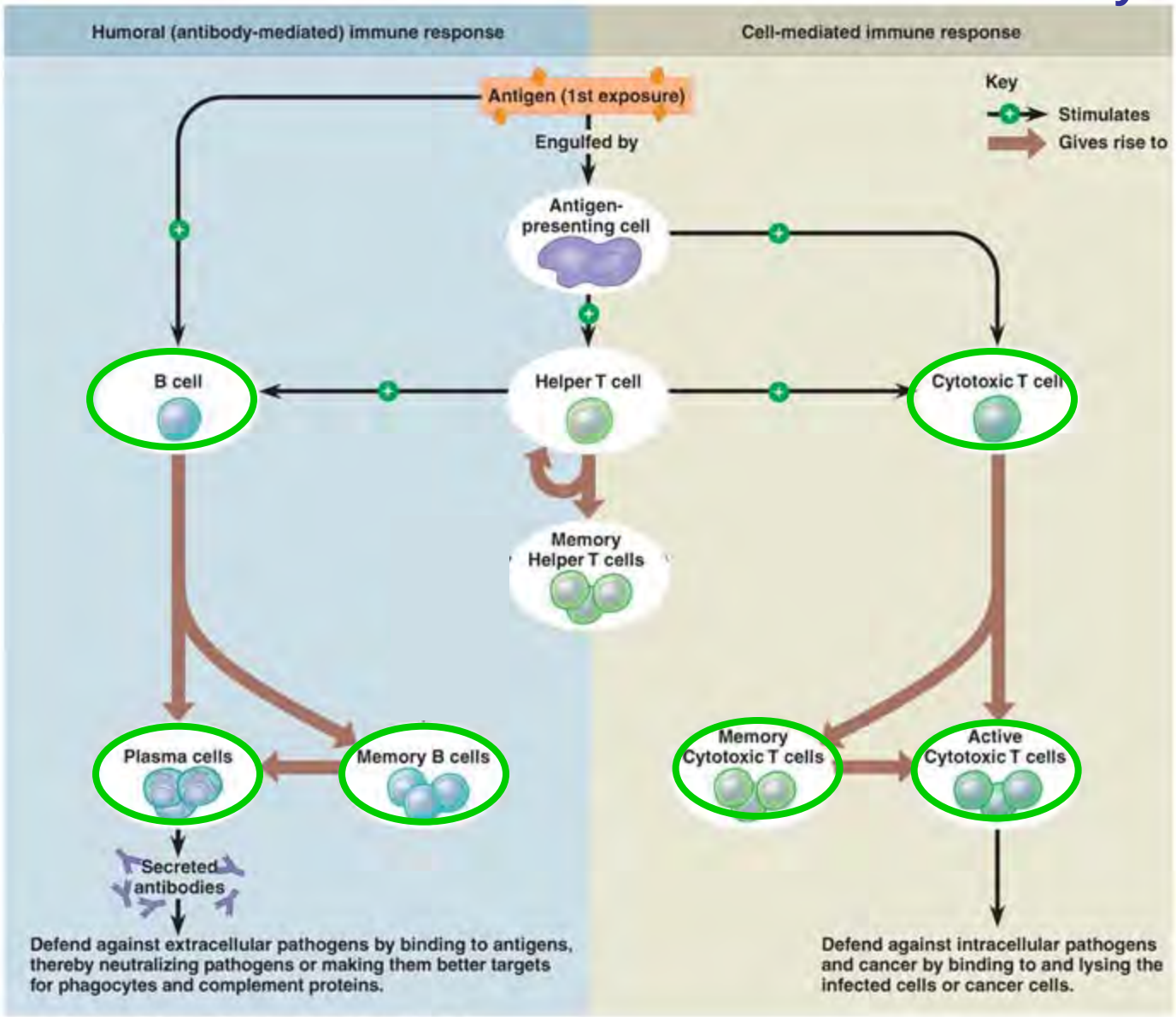


Figure 43.20 (Campbell 9th ed)

2nd exposure

Memory Helper T-, Memory B- and Memory Cytotoxic T-cells activated.

Memory Helper T-cells further activate Memory B- & Memory cytotoxic T-cells.

Memory B- & Memory Cytotoxic T-cells clone & differentiate into effector cells

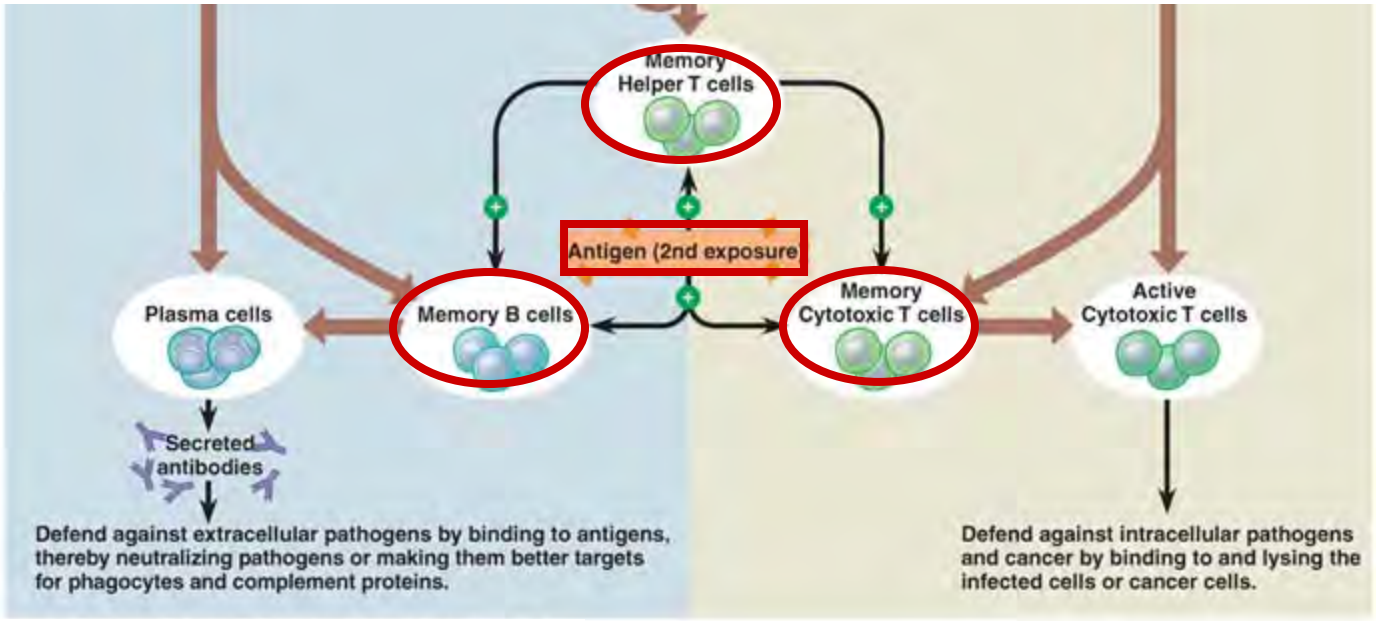
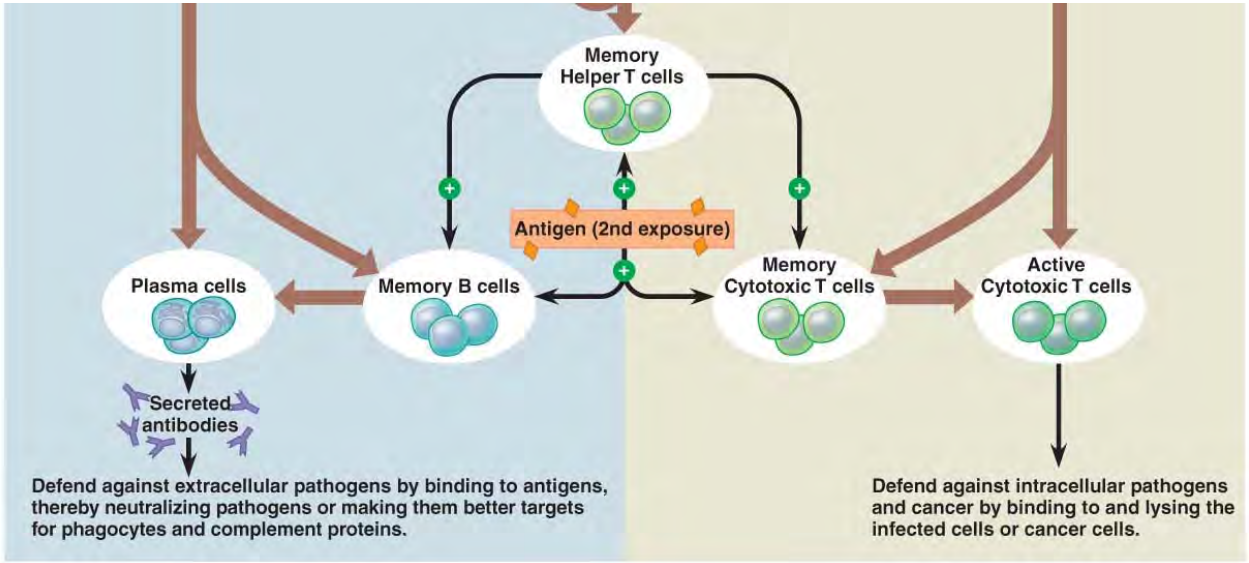


Figure 43.20 (Campbell 9th ed)

Active Immunity

Creation of memory B- and T-cells effective against specific antigens

Can be induced by: A) natural exposure B) immunization



Immunization:

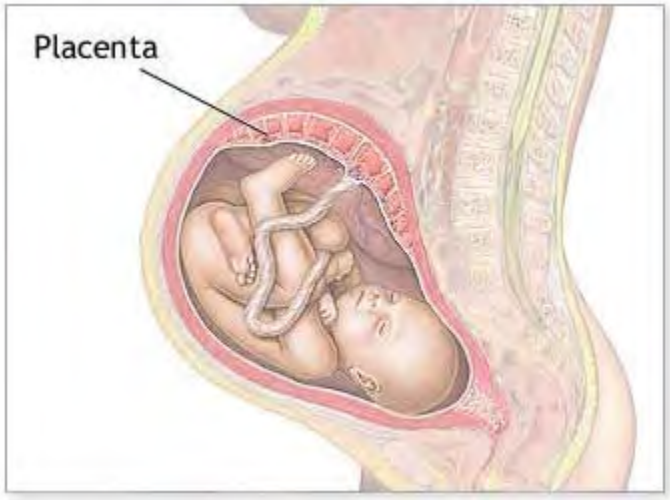
- Allows for fast and stronger response against a disease
- Multiple immunizations may be needed to induce a sufficient # of memory cells
- Reimmunization needed prior to death of memory cells

Figure 43.20 (Campbell 8th ed)

Passive immunity

- Transfer of antibodies from one individual to another

  A. Transfer of mother's antibodies prior to birth (across placenta) and from breast milk gives short-term protection to baby's developing immune system



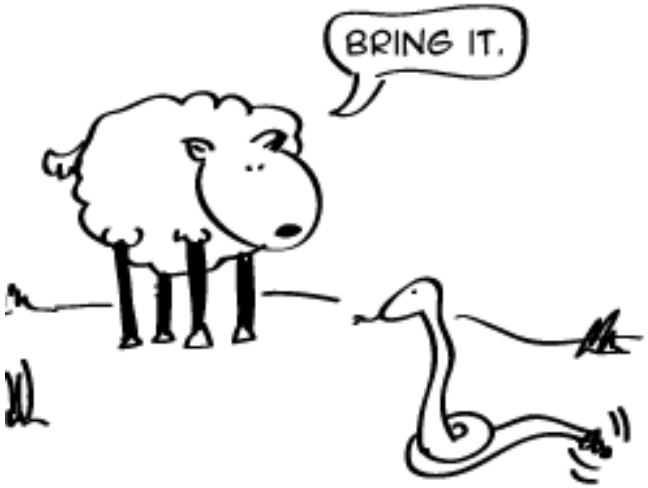
Placenta

Breast milk

Thus breast milk offers innate (lysozyme) and acquired immunity

Passive Immunity

B. Antivenin contains **antibodies**
that can give immediate protection against venomous bites



Readings on which you will NOT be tested

- **Innate immunity of invertebrates (930-931)**
- **Figure 43.5 (931)**
- **Generation of lymphocyte Diversity (937-938)**
- **Figure 43.13 (938)**
- **Antibodies as Tools and Figure 43.21 (945)**
- **Immune Rejection (945-946)**
- **Section 43.4 (946-950)**

In general:

- You are NOT responsible for definitions of terms or sections included in the text but which were not discussed in lecture
- You are not responsible for the details of examples used in the text but not discussed in lecture. HOWEVER, these additional examples will help your understanding of concepts discussed and may be used on exams to test if you understand the general concepts.
- You ARE responsible for material covered in lecture but not included in the readings

Next Lecture

Osmoregulation and Excretion

Chapter 44