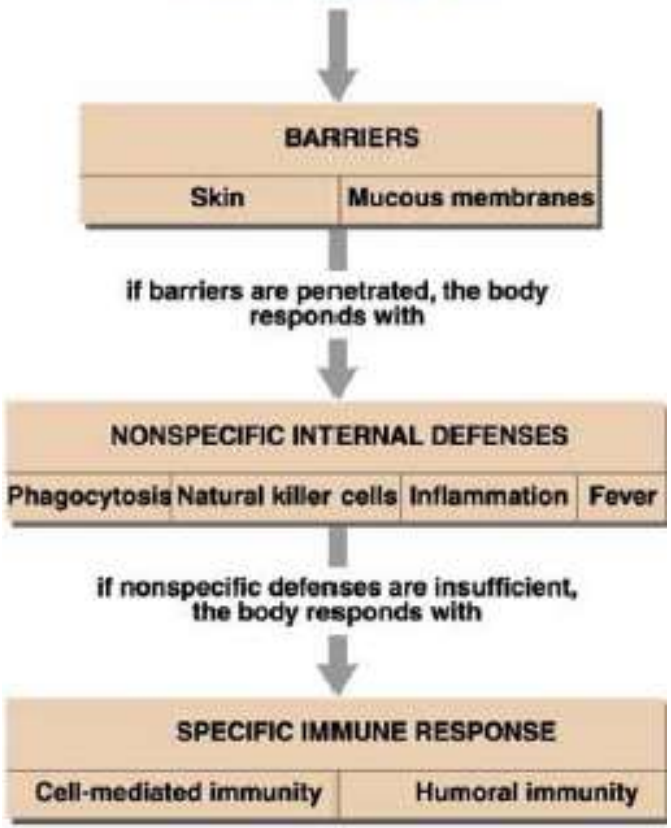
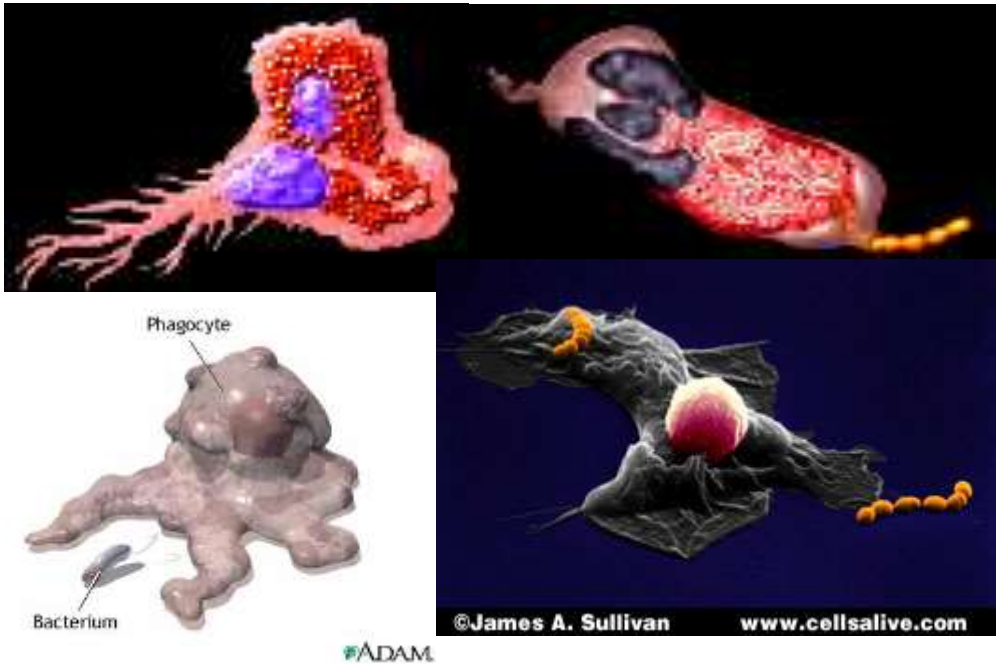
Immune Response

Cell Biology and Its Application

BI-1202

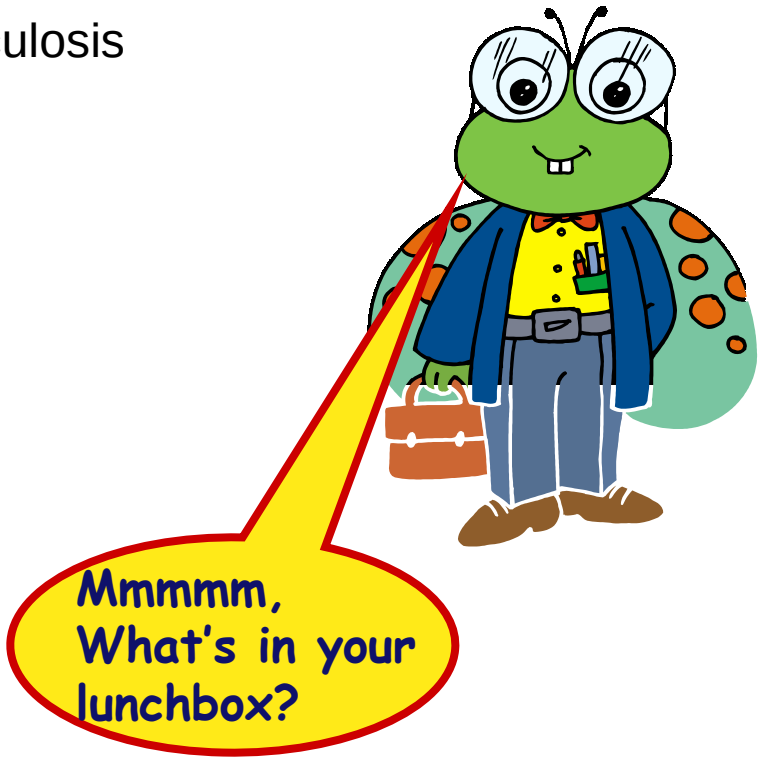




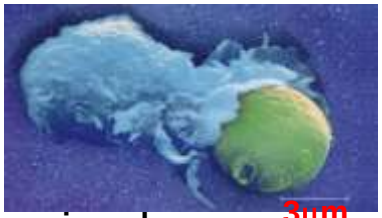
MIT, EGR, RRE & AB, SITH ITB

Why an immune system?

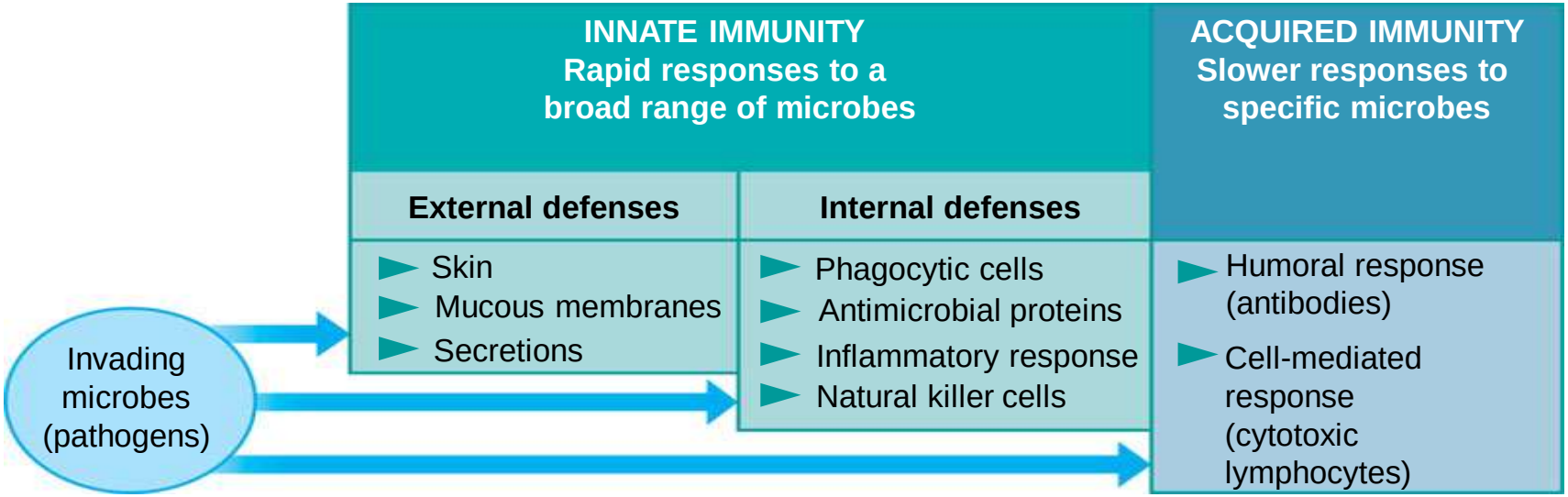
- Attack from outside
  - Everybody must defend himself from many dangerous pathogens
    - viruses
      - HIV, flu, cold, measles, chicken pox
    - bacteria
      - pneumonia, meningitis, tuberculosis
        Lyme disease
    - fungi
      - yeast (“Athlete’s foot”…)
    - protists
      - amoeba, malaria
- Attack from inside
  - cancers = abnormal body cells



- Two major kinds of defense have evolved that counter these threats
  - Innate immunity and acquired immunity
- Innate immunity
  - Is present before any exposure to pathogens and is effective from the time of birth
  - Involves nonspecific responses to pathogens
- Acquired immunity/adaptive immunity
  - Develops only after exposure to inducing agents such as microbes, toxins, or other foreign substances
  - Involves a very specific response to pathogens



A summary of innate and acquired immunity



1st line: Non-specific External defense

- Barrier
  - skin
- Traps
  - mucous membranes, cilia, hair, earwax
- Elimination
  - coughing, sneezing, urination, diarrhea
- Unfavorable pH
  - stomach acid, sweat, saliva, urine
- Lysozyme enzyme
  - digests bacterial cell walls
  - tears, sweat

Lining of trachea:
ciliated cells & mucus secreting cells

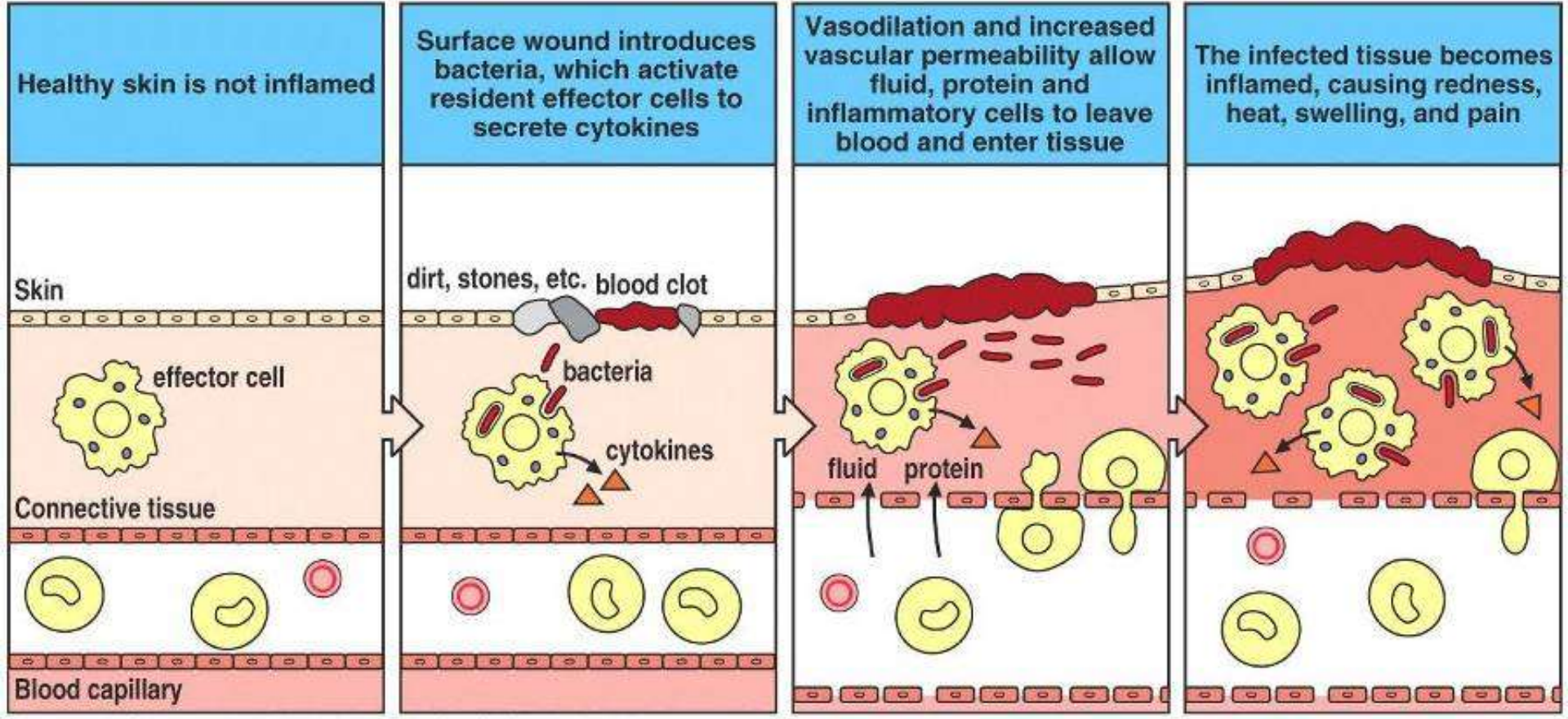
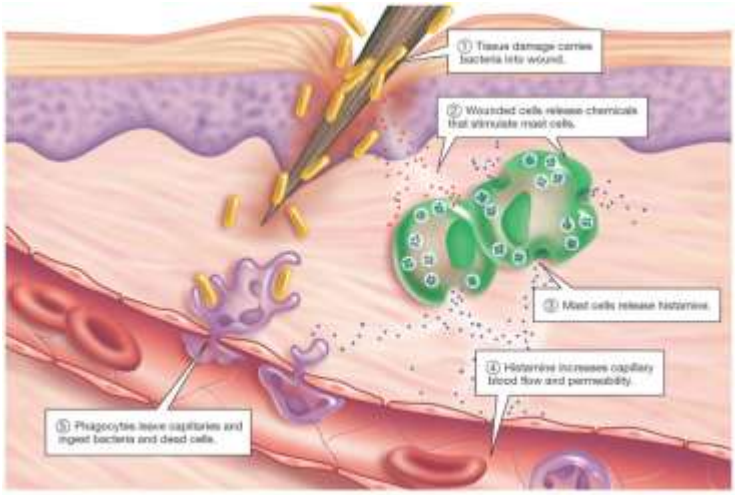


Figure 1-6 The Immune System, 2/e (© Garland Science 2005)



2nd line: Non-specific internal defenses

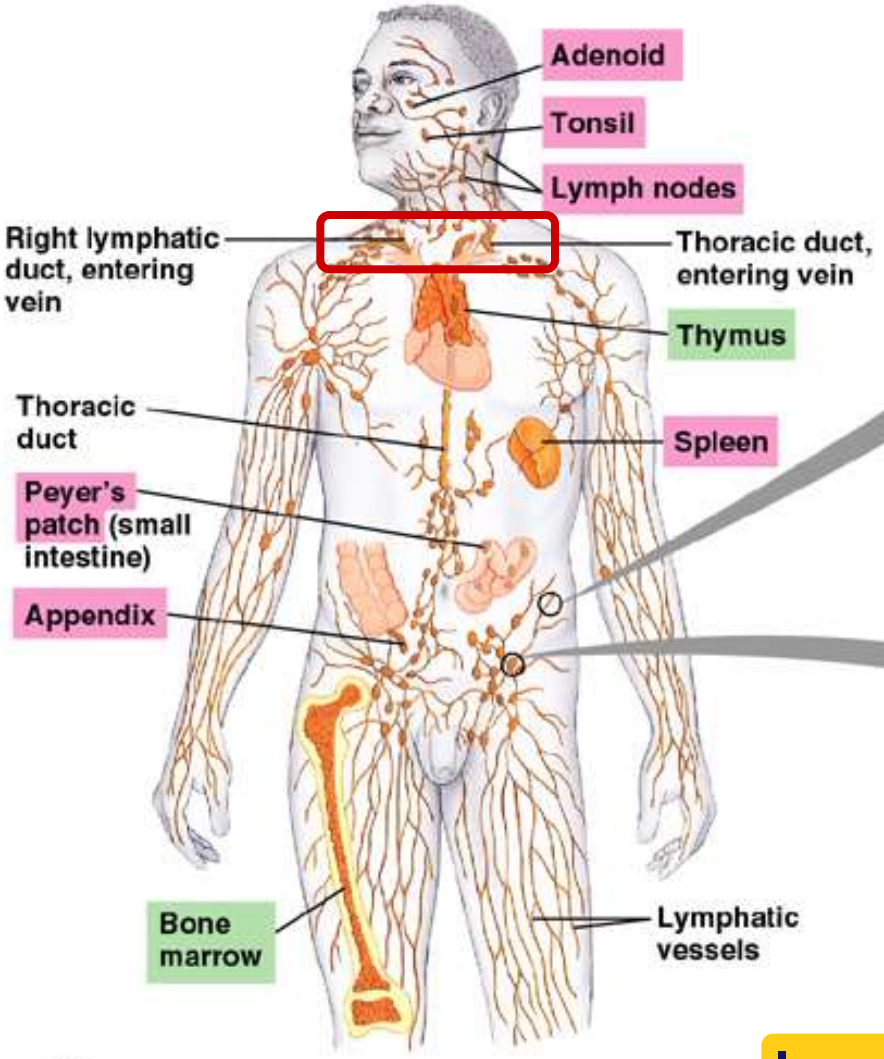
- Patrolling cells & proteins
  - attack pathogens, but don't "remember" for next time
    - leukocytes
      - phagocytic white blood cells
      - macrophages, neutrophils, natural killer cells
    - complement system
      - proteins that destroy cells
    - inflammatory response
      - increase in body temp.
      - increase capillary permeability
      - attract macrophages

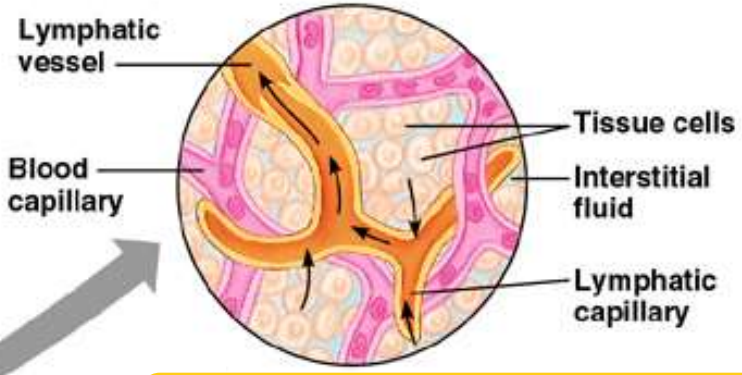
bacteria

macrophage

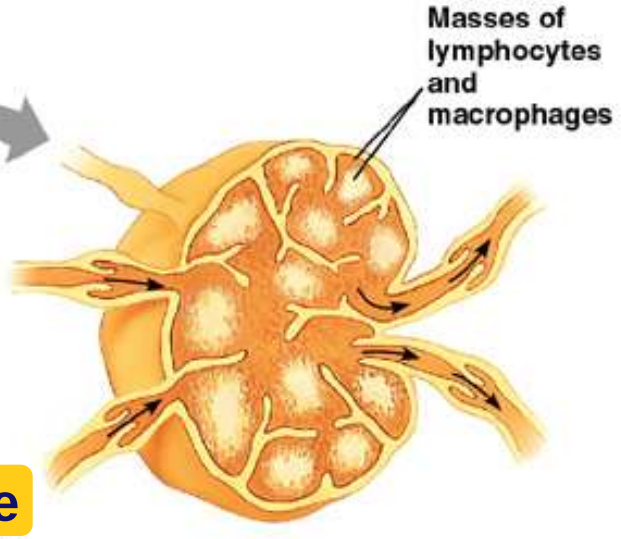
Lymph system

Production & transport of leukocytes
Traps foreign invaders



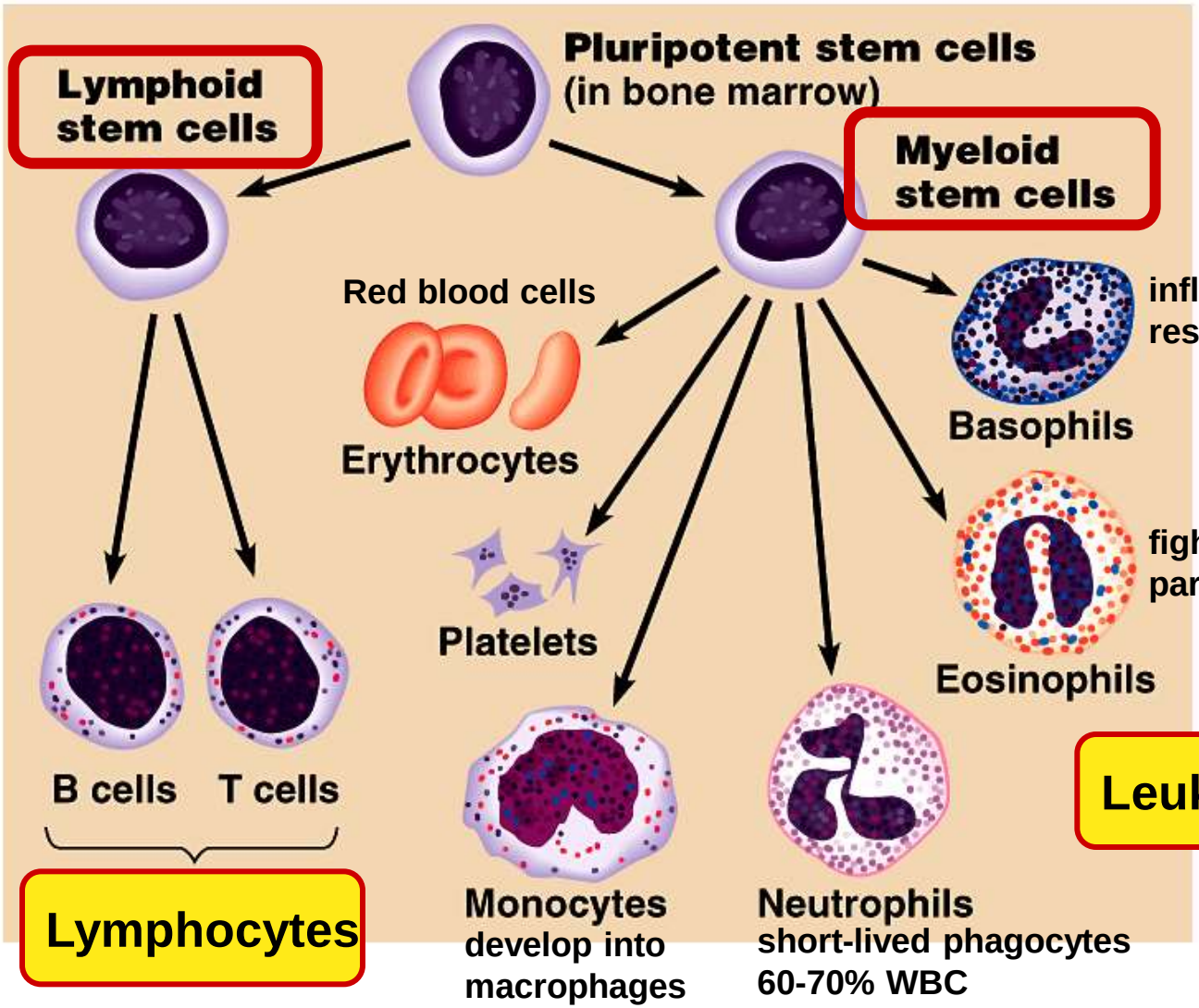


lymph vessels
(intertwined amongst blood vessels)



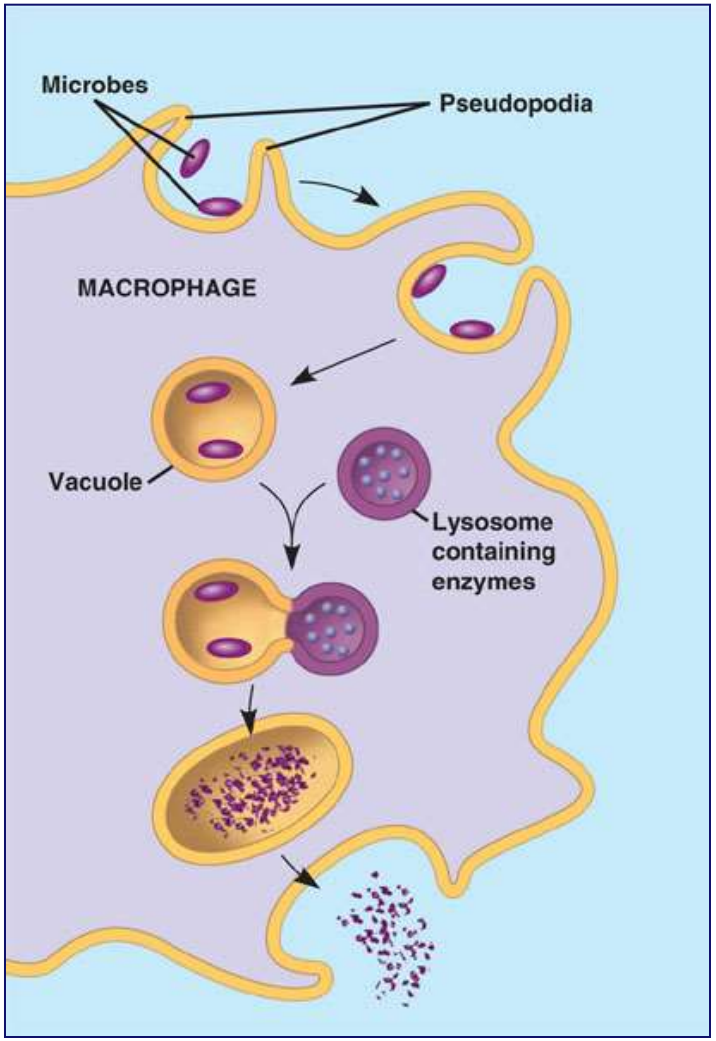
lymph node

Development of Red & White blood cells



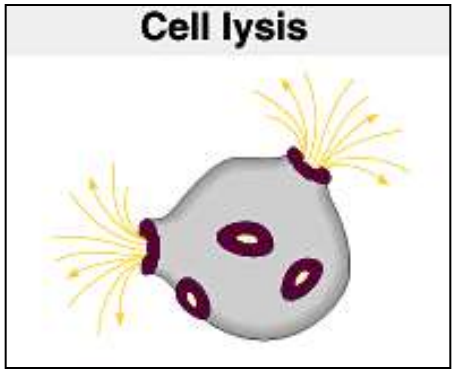
Leukocytes: Phagocytic WBCs

- Attracted by chemical signals released by damaged cells
  - ingest pathogens
  - digest in lysosomes
- Neutrophils
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- Macrophages
  - “big eater”, long-lived
- Natural Killer Cells
  - destroy virus-infected cells & cancer cells

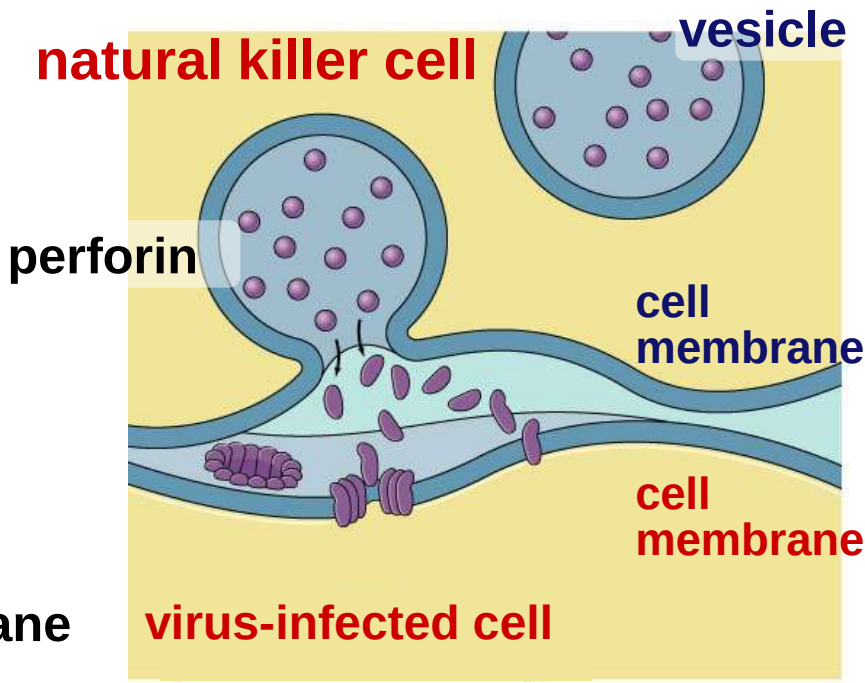


Destroying cells gone bad!

- Natural Killer Cells perforate cells
  - release perforin protein
  - insert into membrane of target cell
  - forms pore allowing fluid to flow in & out of cell
  - cell ruptures (lysis)
    - apoptosis

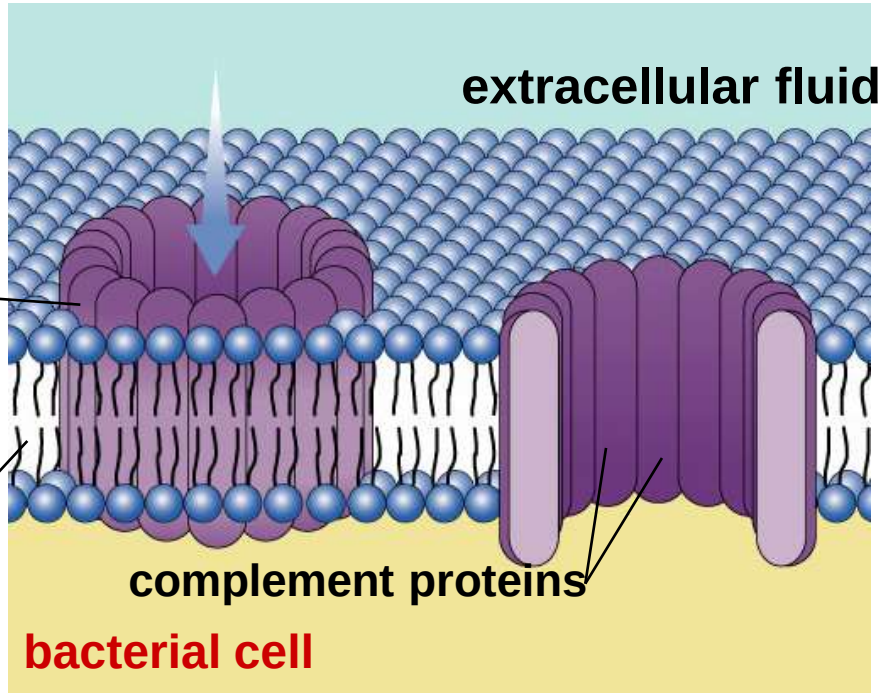


perforin
punctures
cell membrane



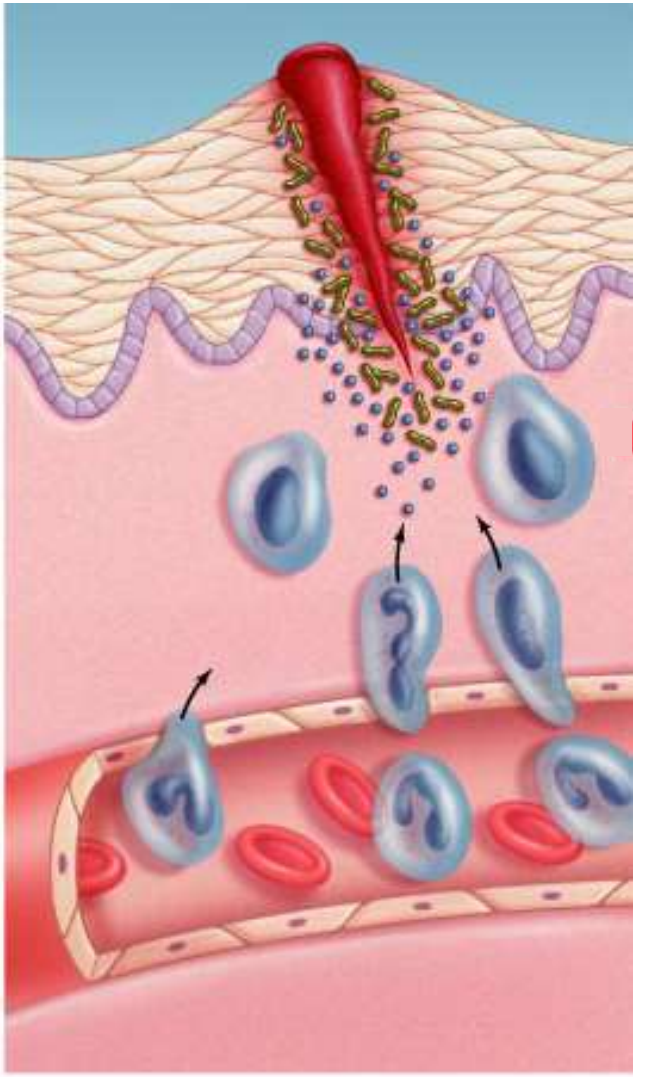
Anti-microbial proteins

- Complement system
  - ~20 proteins circulating in blood plasma
  - attack bacterial & fungal cells
    - form a membrane attack complex
    - perforate target cell
    - apoptosis
      - cell lysis



Inflammatory response

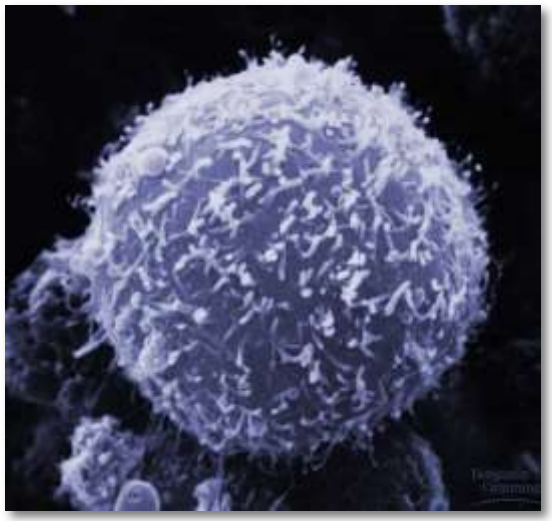
- Damage to tissue triggers local non-specific inflammatory response
  - release chemical signals
    - histamines & prostaglandins
  - capillaries dilate, become more permeable (leaky)
    - delivers macrophages, RBCs, platelets, clotting factors
      - fight pathogens
      - clot formation
  - increases temperature
    - decrease bacterial growth
    - stimulates phagocytosis
    - speeds up repair of tissues

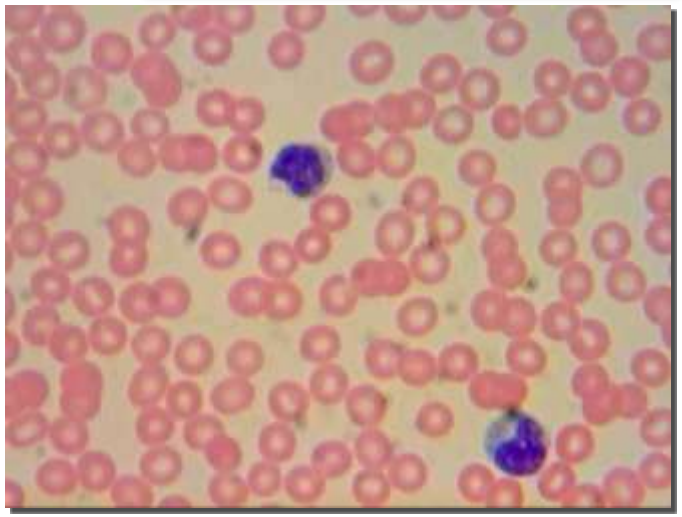


3rd line: Acquired (active) Immunity

- Specific defense with memory
  - lymphocytes
    - B cells
    - T cells
  - antibodies
    - immunoglobulins
- Responds to…
  - antigens
    - cellular name tags
      - specific pathogens
      - specific toxins
      - abnormal body cells (cancer)

B cell

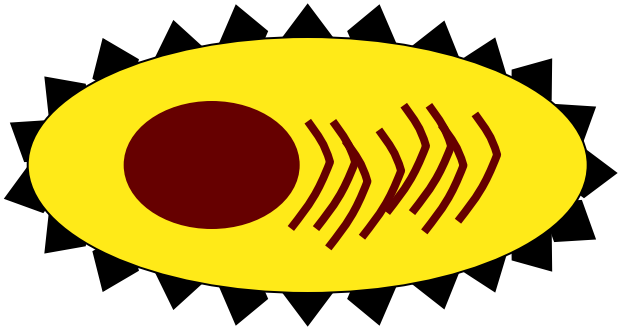




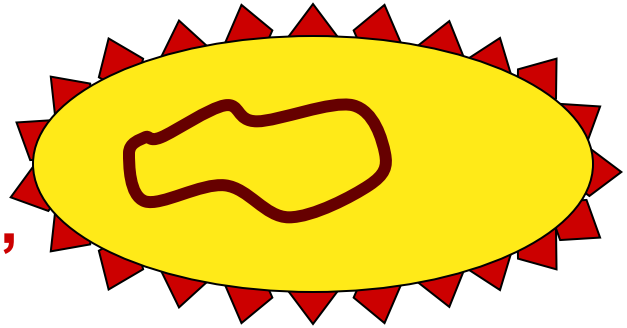
How are invaders recognized?

- Antigens
  - cellular name tag proteins
    - "self" antigens
      - no response from WBCs
    - "foreign" antigens
      - response from WBCs
      - pathogens: viruses, bacteria, protozoa, parasitic worms, fungi, toxins
      - non-pathogens: cancer cells, transplanted tissue, pollen

"self"

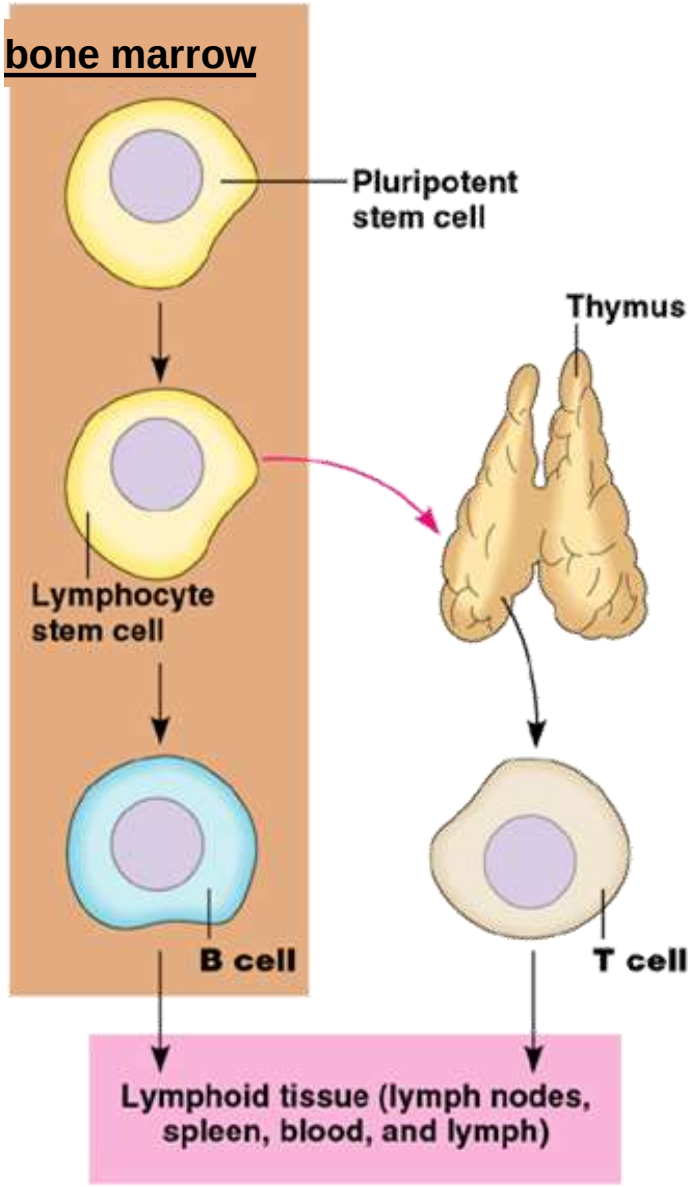


"foreign"



Lymphocytes

- B cells
  - mature in bone marrow
  - humoral response system
    - "humors" = body fluids
    - attack pathogens still circulating in blood & lymph
  - produce antibodies
- T cells
  - mature in thymus
  - cellular response system
    - attack invaded cells
- "Maturation"
  - learn to distinguish "self" from "non-self" antigens
    - if react to "self" antigens, cells are destroyed during maturation



- The roles of the major participants in the acquired immune response

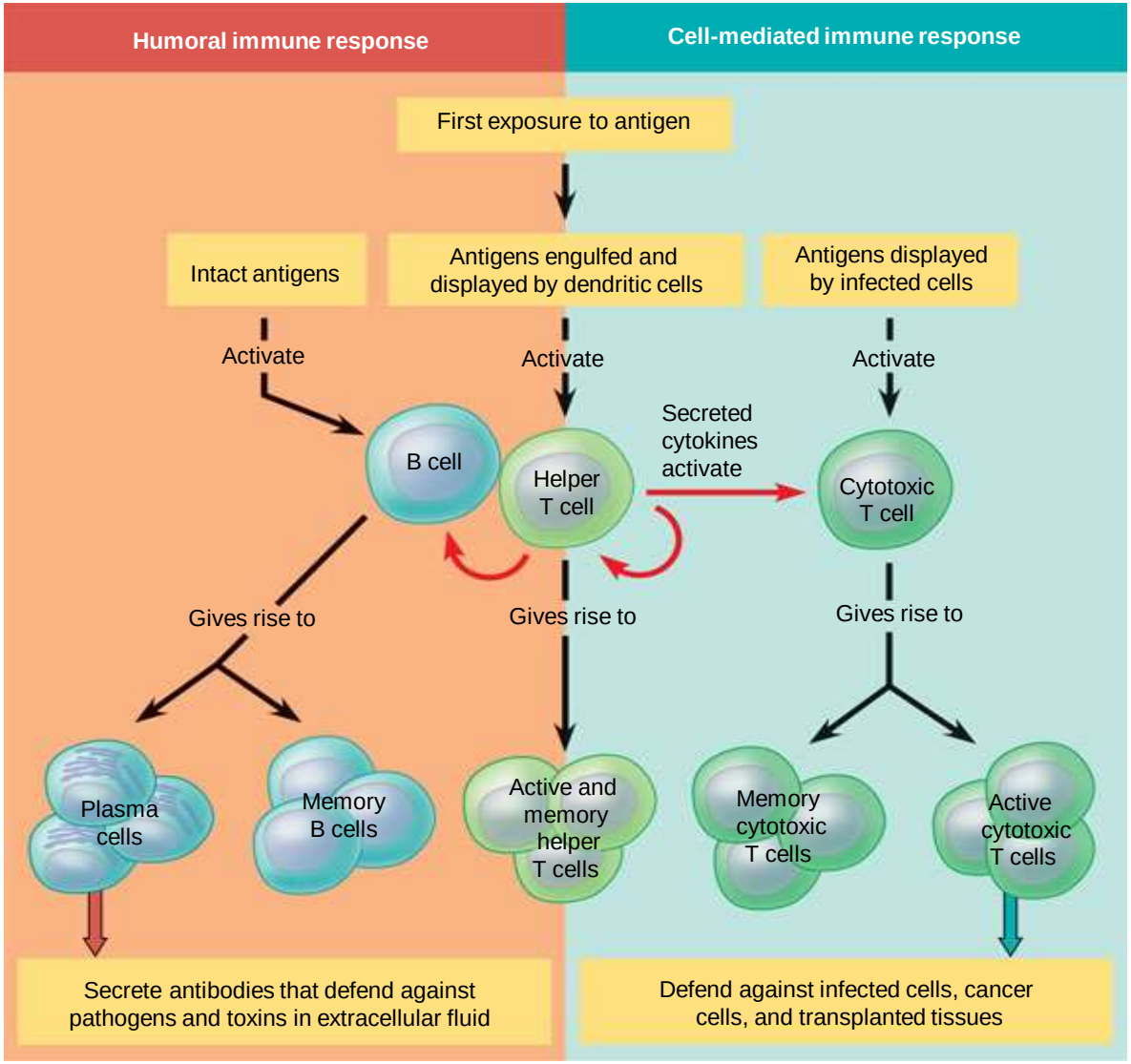
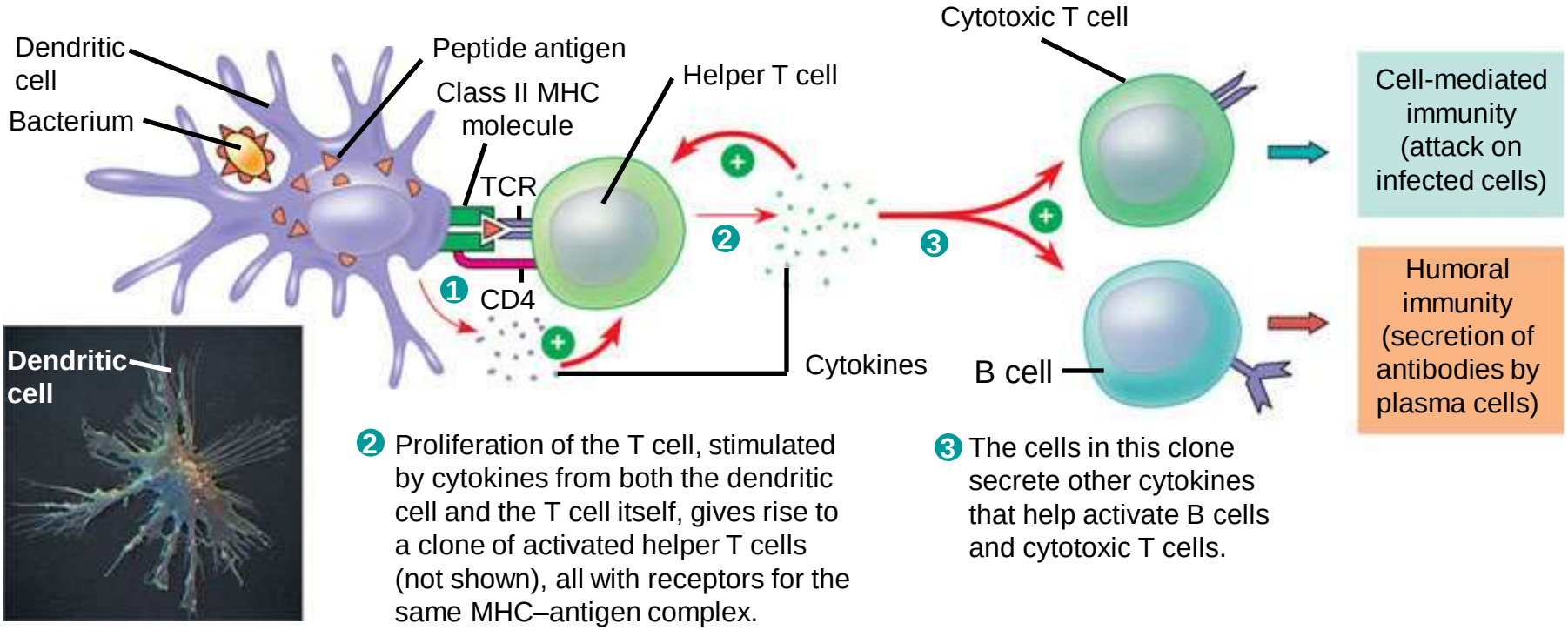


Figure 43.14

The role of helper T cells in acquired immunity

1 After a dendritic cell engulfs and degrades a bacterium, it displays bacterial antigen fragments (peptides) complexed with a class II MHC molecule on the cell surface. A specific helper T cell binds to the displayed complex via its TCR with the aid of CD4. This interaction promotes secretion of cytokines by the dendritic cell.



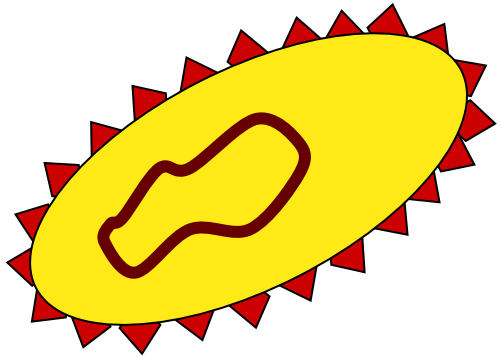
2 Proliferation of the T cell, stimulated by cytokines from both the dendritic cell and the T cell itself, gives rise to a clone of activated helper T cells (not shown), all with receptors for the same MHC–antigen complex.

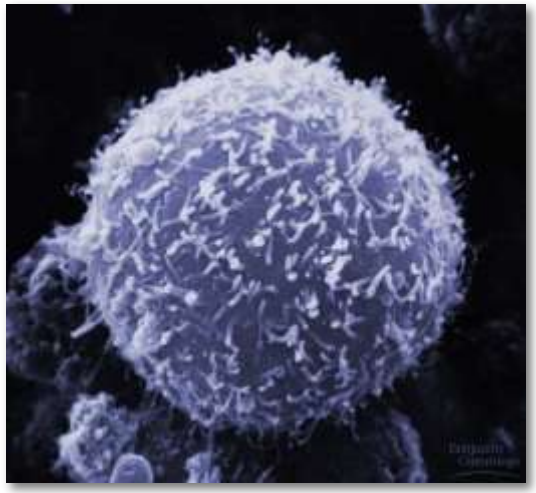
3 The cells in this clone secrete other cytokines that help activate B cells and cytotoxic T cells.

Figure 43.15

B cells

- Attack, learn & remember pathogens circulating in blood & lymph
- Produce specific antibodies against specific antigen
- Types of B cells
  - plasma cells
    - immediate production of antibodies
    - rapid response, short term release
  - memory cells
    - continued circulation in body
    - long term immunity





1 After a macrophage engulfs and degrades a bacterium, it displays a peptide antigen complexed with a class II MHC molecule. A helper T cell that recognizes the displayed complex is activated with the aid of cytokines secreted from the macrophage, forming a clone of activated helper T cells (not shown).

2 A B cell that has taken up and degraded the same bacterium displays class II MHC–peptide antigen complexes. An activated helper T cell bearing receptors specific for the displayed antigen binds to the B cell. This interaction, with the aid of cytokines from the T cell, activates the B cell.

3 The activated B cell proliferates and differentiates into memory B cells and antibody-secreting plasma cells. The secreted antibodies are specific for the same bacterial antigen that initiated the response.

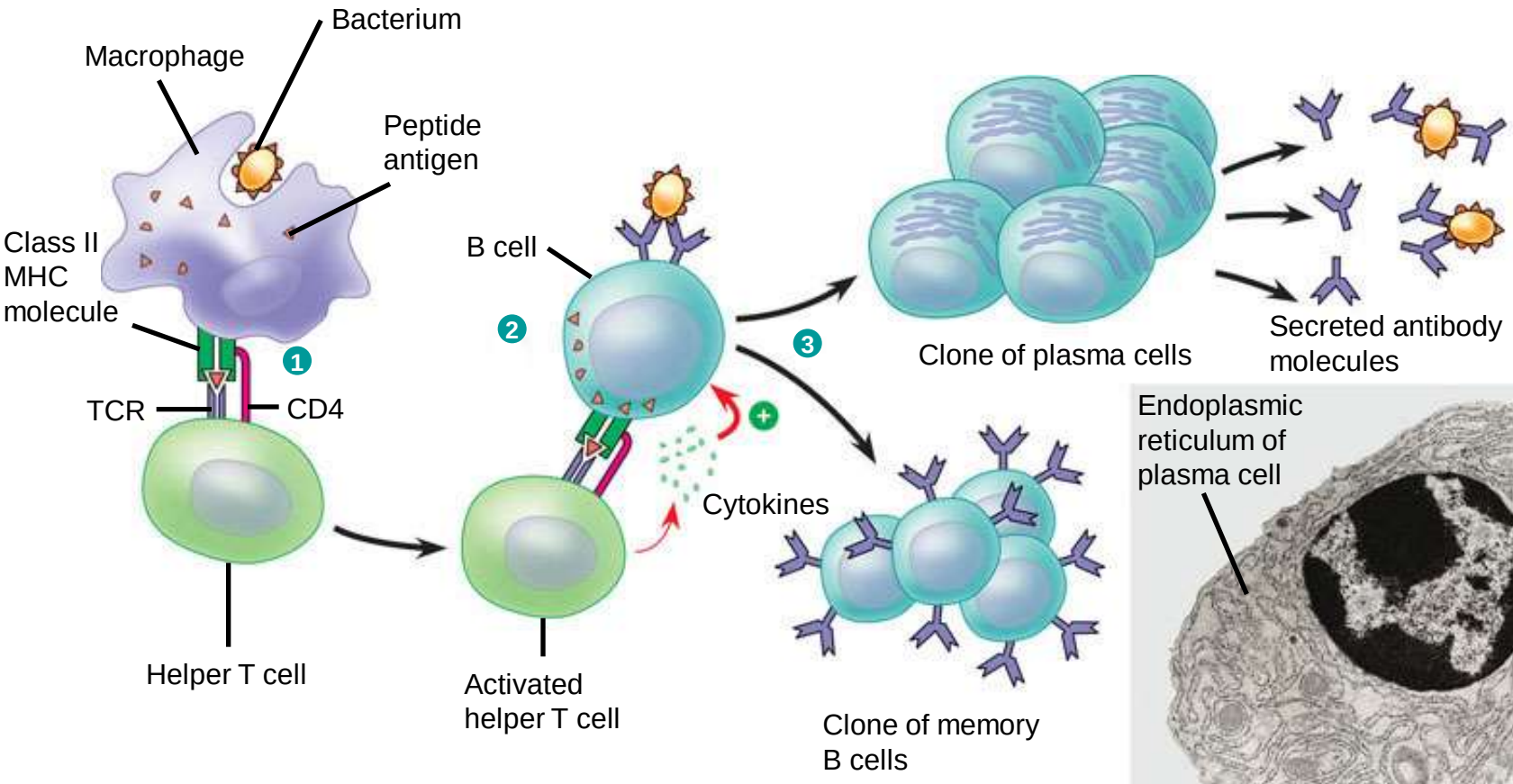
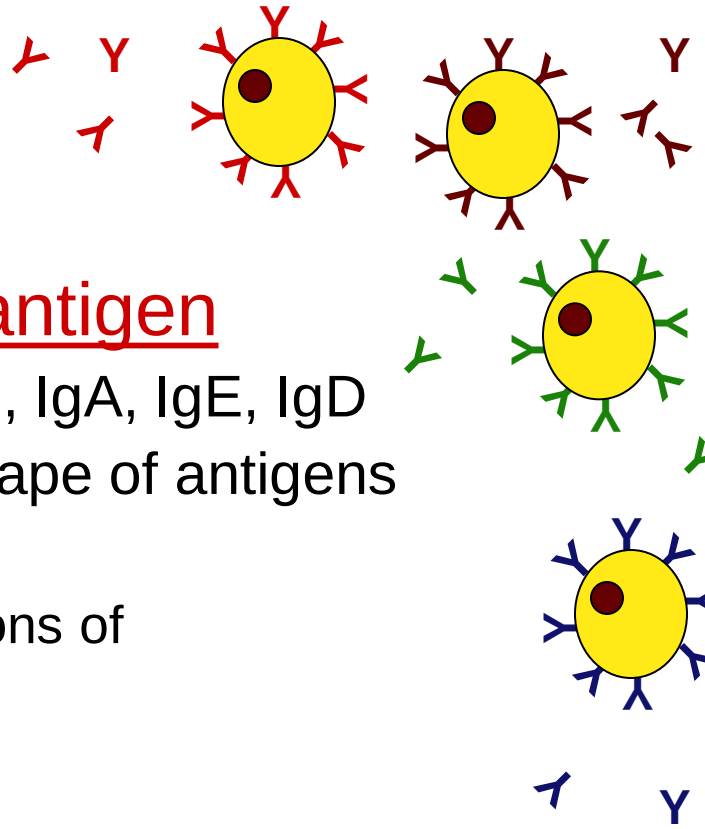
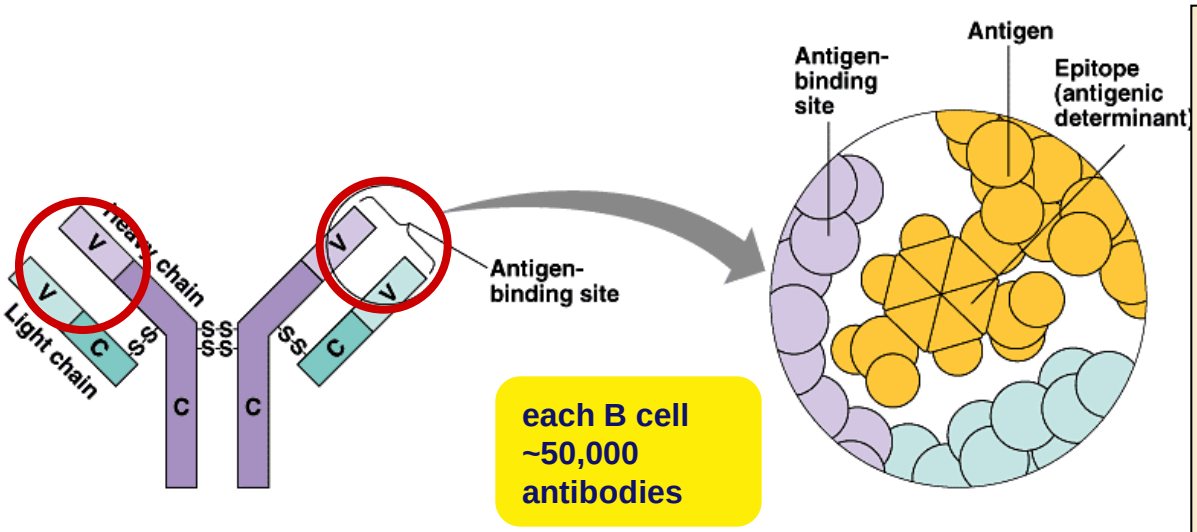


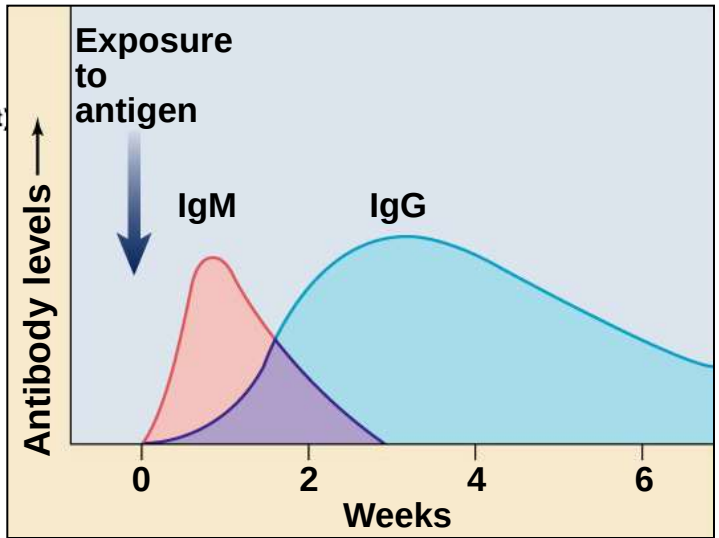
Figure 43.17

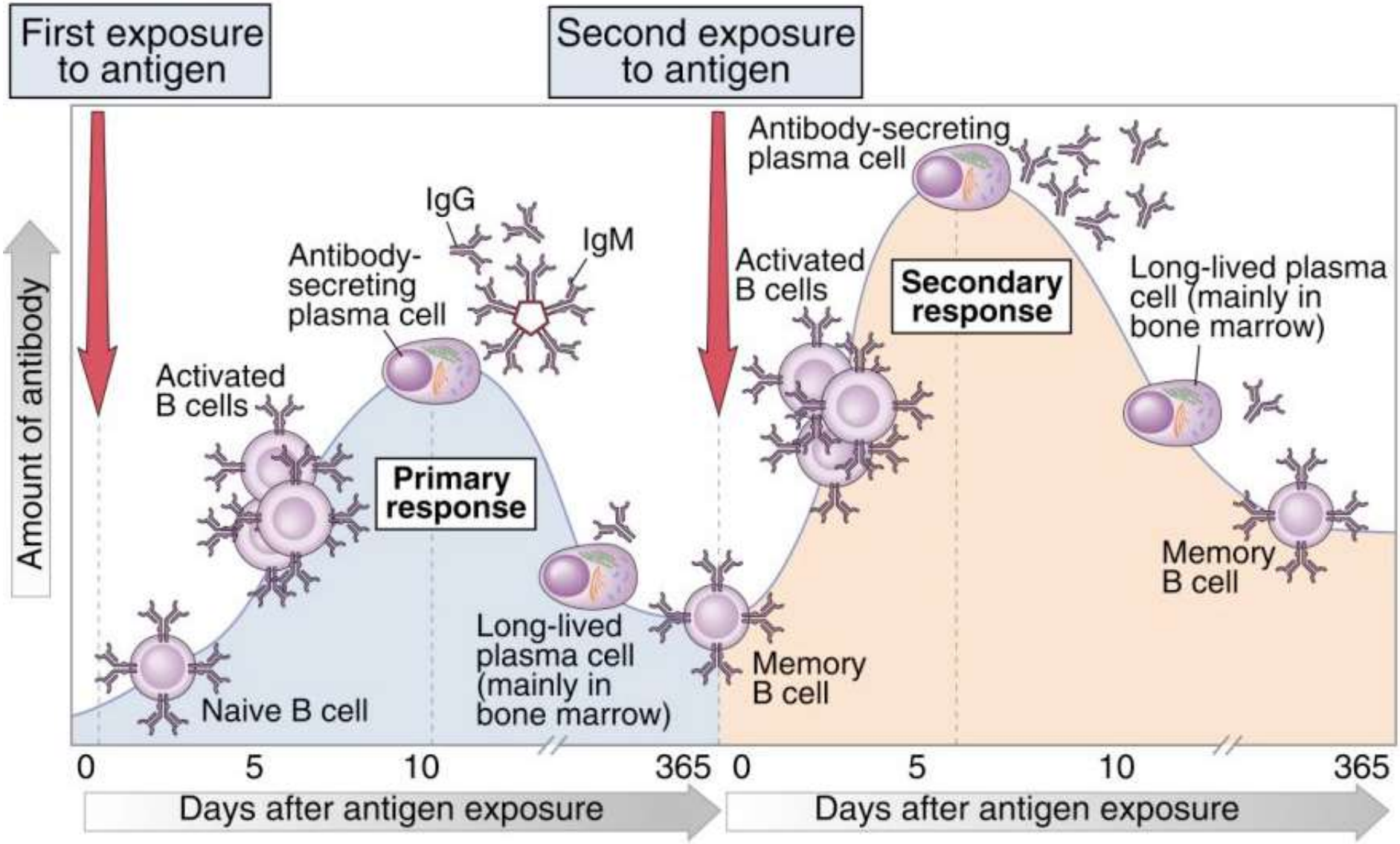
Antibodies



- Proteins that bind to a specific antigen
  - Classes of Immunoglobulin: IgM, IgG, IgA, IgE, IgD
  - binding region matches molecular shape of antigens
  - each antibody is unique & specific
    - millions of antibodies respond to millions of foreign antigens

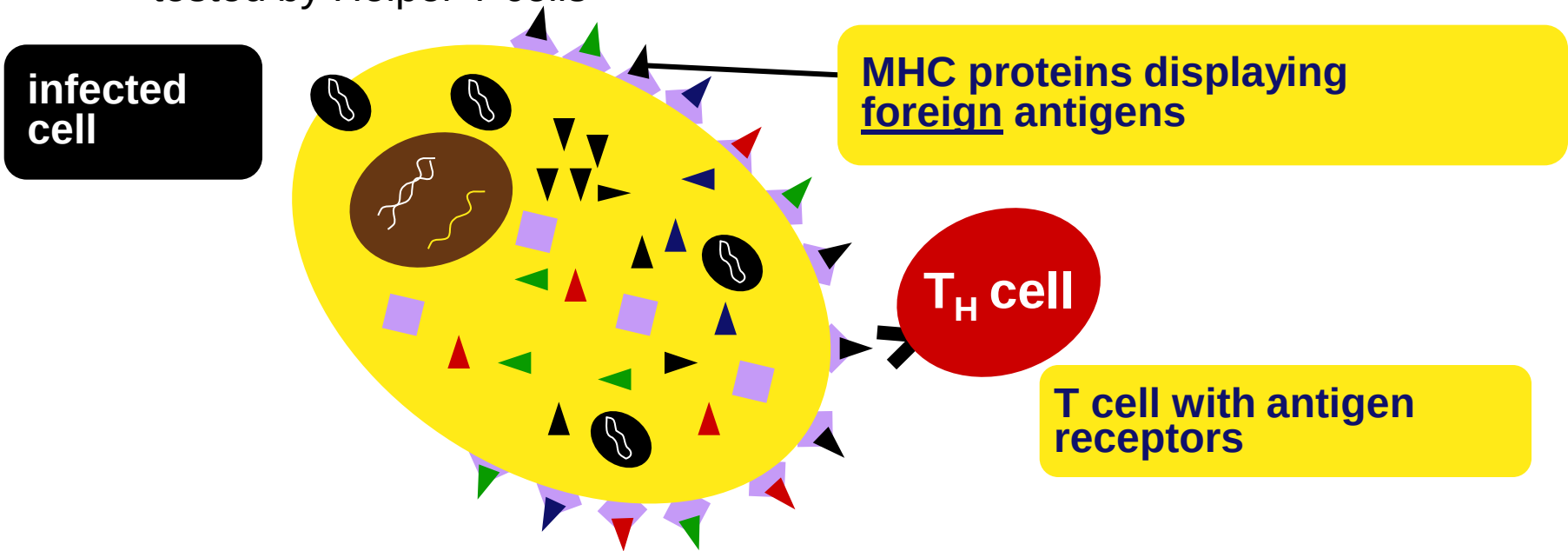





First exposure to antigen
Second exposure to antigen
Amount of antibody
IgG
IgM
Antibody-secreting plasma cell
Activated B cells
Primary response
Naive B cell
Long-lived plasma cell (mainly in bone marrow)
Memory B cell
Secondary response
Long-lived plasma cell (mainly in bone marrow)
Memory B cell
0
5
10
365
Days after antigen exposure

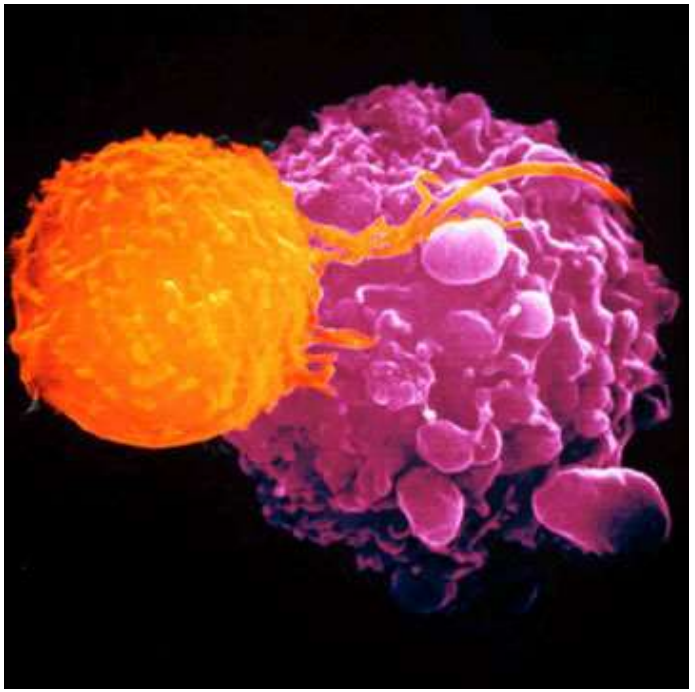
How do T cells know a cell is infected?

- Infected cells digest some pathogens
- Major histocompatibility (MHC) proteins
  - proteins which constantly carry bits of cellular material from the cytosol to the cell surface
  - "snapshot" of what is going on inside cell
  - give the surface of cells a unique label or "fingerprint"
  - MHC proteins carry pieces to cell surface
    - foreign antigens now on cell membrane
    - called Antigen Presenting Cell (APC)
      - macrophages can also serve as APC
    - tested by Helper T cells



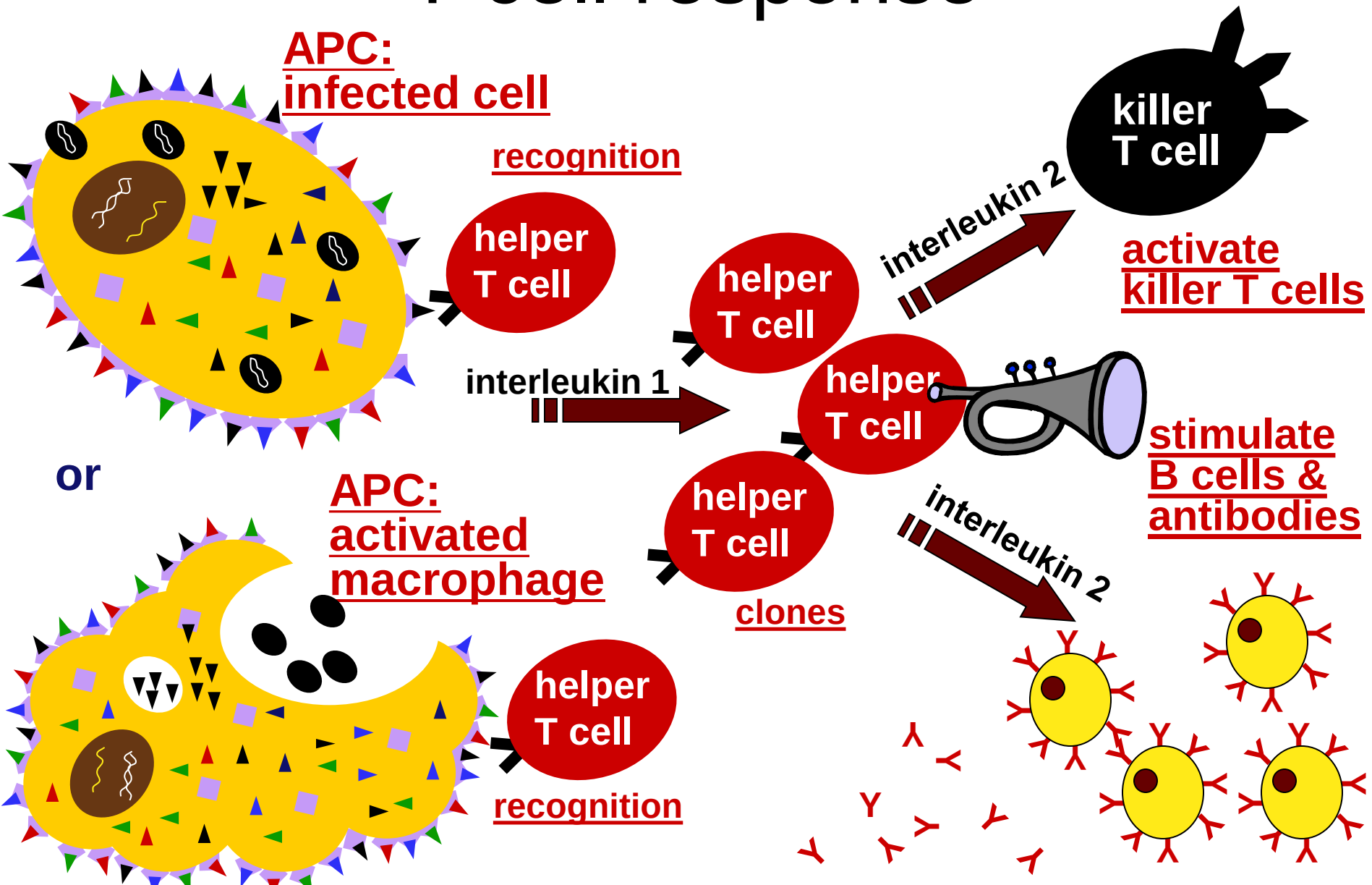
T cells

- Attack, learn & remember pathogens hiding in infected cells
  - recognize antigen fragments
  - also defend against “non-self” body cells
    - cancer & transplant cells
- Types of T cells
  - helper T cells
    - alerts rest of immune system
  - killer (cytotoxic) T cells
    - attack infected body cells
  - memory T cells
    - long term immunity



T cell attacking cancer cell

T cell response



- The activated cytotoxic T cell
  - Secretes proteins that destroy the infected target cell

1 A specific cytotoxic T cell binds to a class I MHC–antigen complex on a target cell via its TCR with the aid of CD8. This interaction, along with cytokines from helper T cells, leads to the activation of the cytotoxic cell.

2 The activated T cell releases perforin molecules, which form pores in the target cell membrane, and proteolytic enzymes (granzymes), which enter the target cell by endocytosis.

3 The granzymes initiate apoptosis within the target cells, leading to fragmentation of the nucleus, release of small apoptotic bodies, and eventual cell death. The released cytotoxic T cell can attack other target cells.

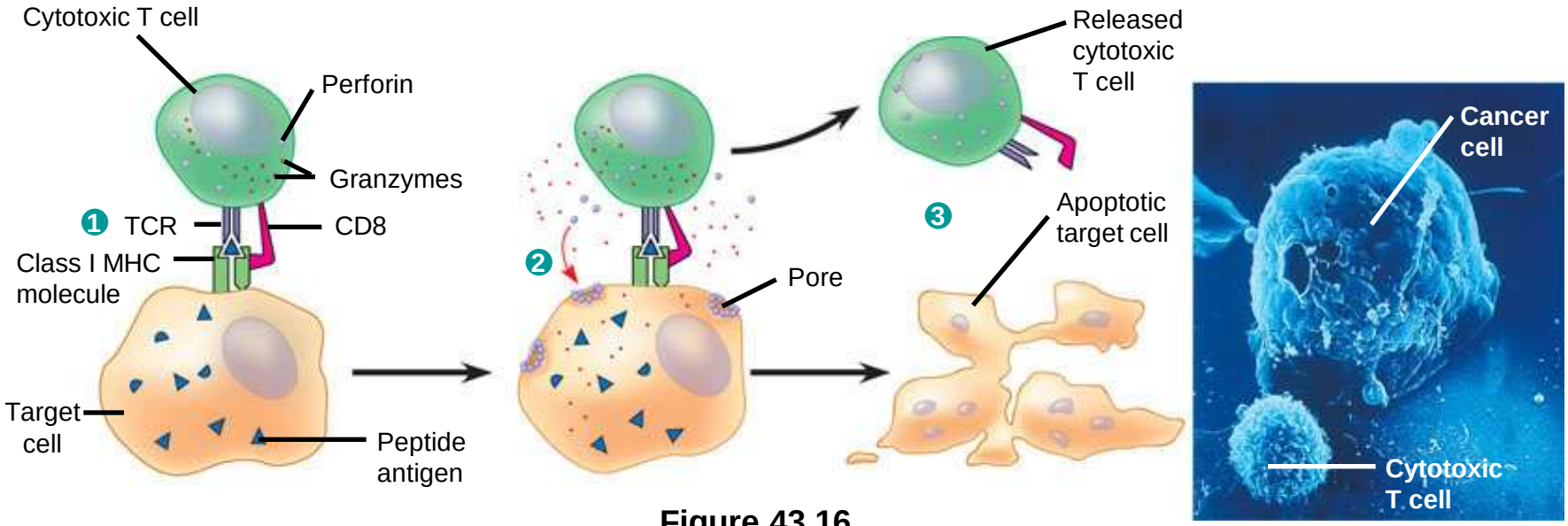


Figure 43.16

Acquired immunity

Acquired Immunity

Natural Immunity
is acquired through the normal life experiences of a human and is not induced through medical means.

Active Immunity
is the consequence of a person developing his own immune response to a microbe.

Passive Immunity
is the consequence of one person receiving a performed immunity made by another person.

Artificial Immunity
is that produced purposefully through medical procedures (also called immunization).

Active Immunity
is the consequence of a person developing his own immune response to a microbe.

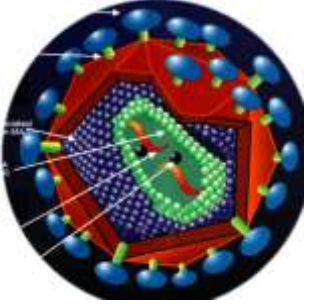
Passive Immunity
is the consequence of one person receiving a performed immunity made by another person.

Active natural (contact with infection): develops slowly, is long term, and antigen specific.

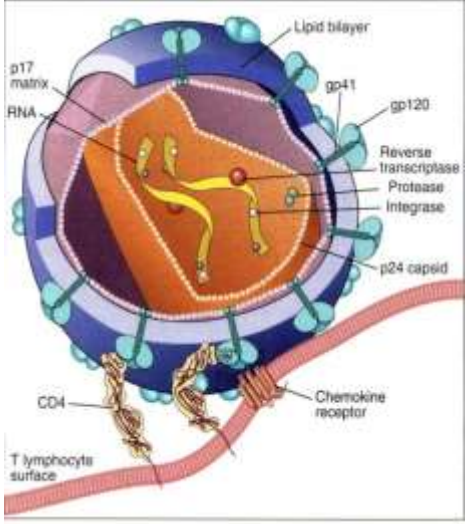
Passive natural (transplacental= mother to child): develops immediately, is temporary, and affects all antigens to which the mother has immunity.

Active artificial (immunization): develops slowly, lasts for several years, and is specific to the antigen for which the immunization was given. A vaccine can be a weakened (non-lethal) form of invader or a toxic by-product of an invader.

Passive artificial (injection of gamma globulin): develops immediately, is temporary, and affects all antigens to which the donor has immunity.



HIV & AIDS



- Human Immunodeficiency Virus
  - virus infects helper T cells
    - helper T cells don't activate rest of immune system: killer T cells & B cells
    - also destroys helper T cells
- AIDS: Acquired ImmunoDeficiency Syndrome
  - infections by opportunistic diseases
  - death usually from "opportunistic" infections
    - pneumonia, cancers