Introduction to The Human Immune System

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Table of Contents

Table of Contents (cont.)

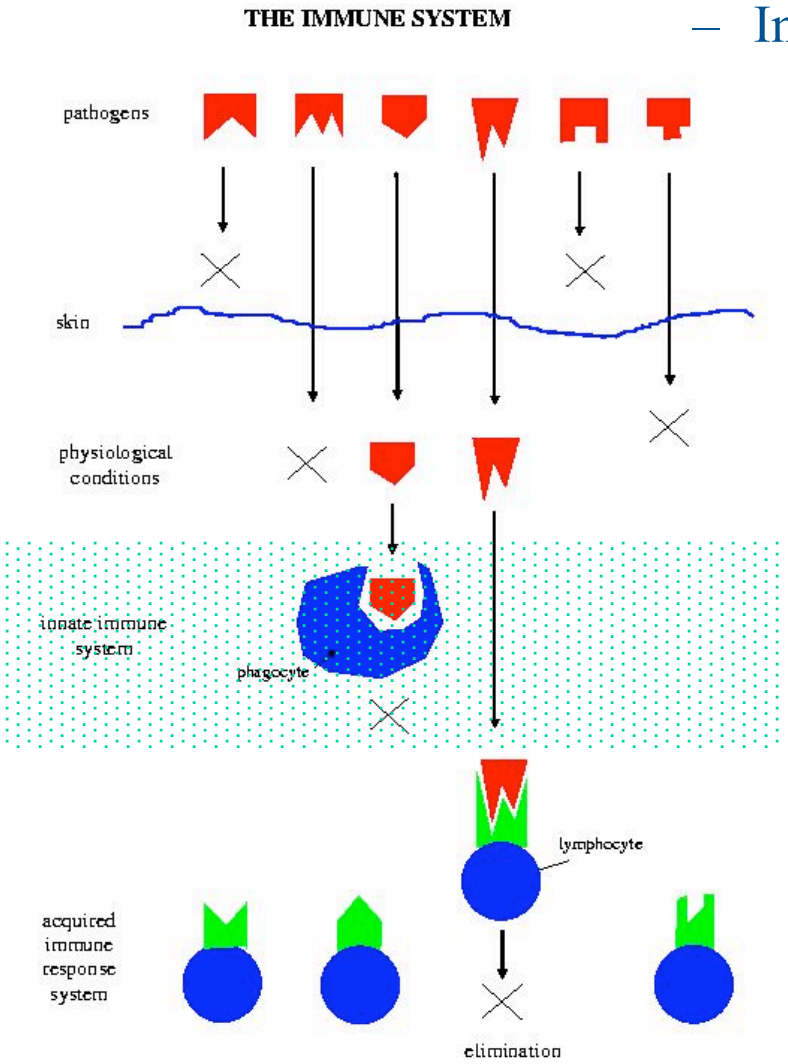
Table of Contents

Layers of Defense : The Skin

The body's first lines of defense against infection are nonspecific, i.e., they do not distinguish among intruder cells.

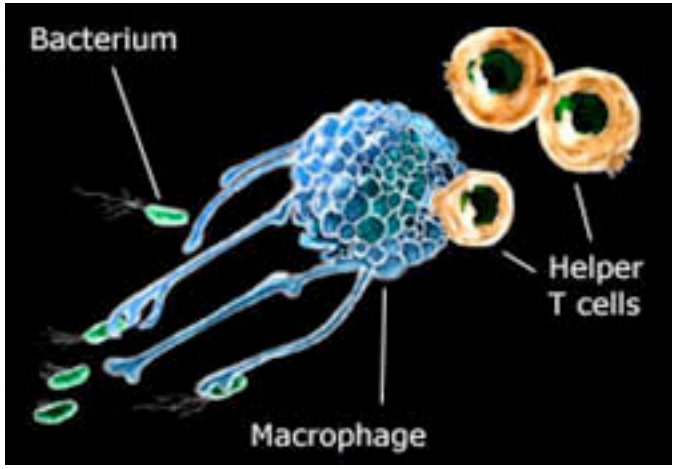
- **Skin**
  - Skin is a first tough barrier of dead cells, difficult to penetrate for most bacteria and viruses.
  - Acids in sweat and oils secreted by glands in the skin inhibit growth of many microorganisms.
  - Sweat, saliva, and tears contain lysozyme, an enzyme that attacks the cell walls of many bacteria.
  - Physiological conditions, such as pH and temperature provide inappropriate living conditions for foreign organisms.

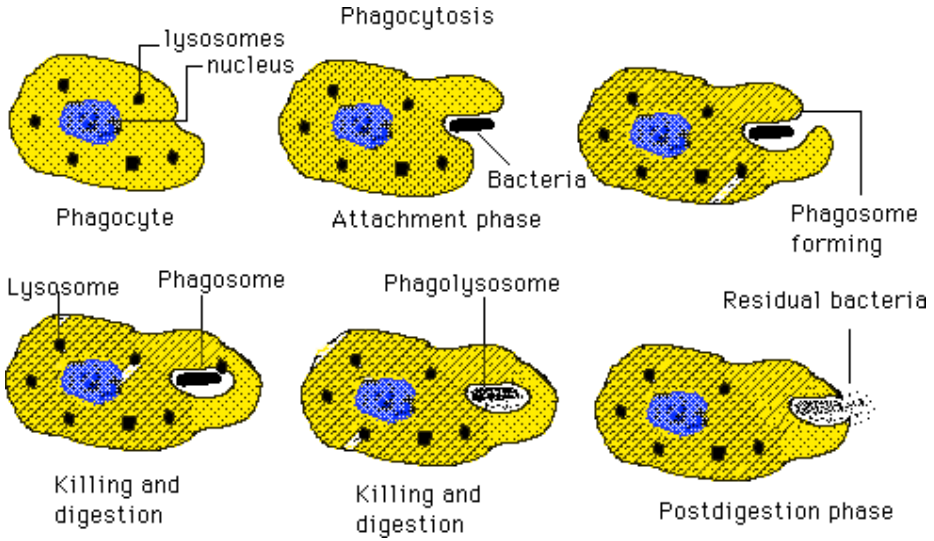
Layers of Defense: Innate Immune System



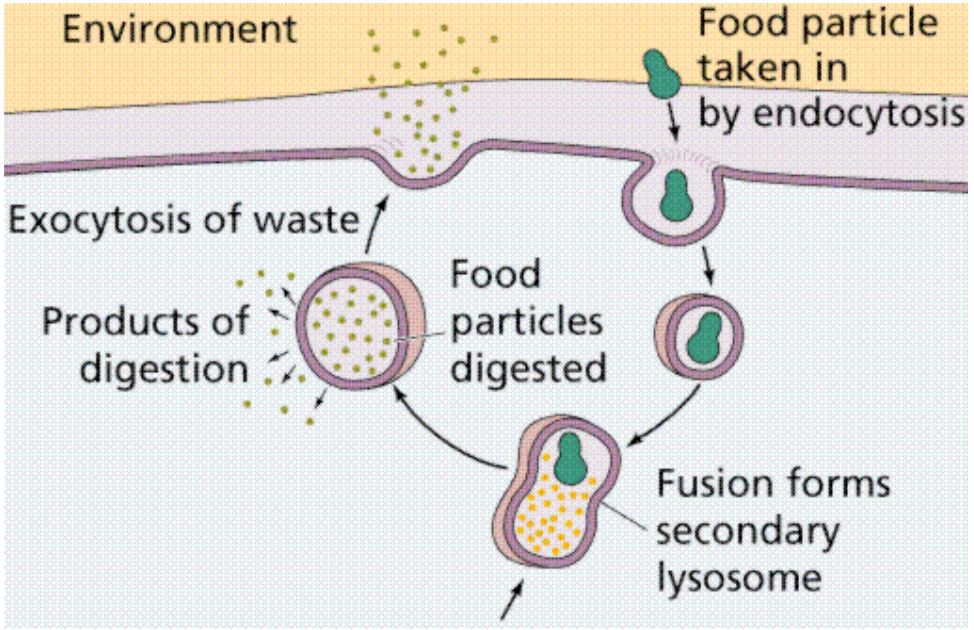
- Innate Immune System
  - Primarily consists of endocytic and phagocytic systems
    - Roaming scavenger cells (phagocytes), ingesting extracellular debris, molecules, and pathogens

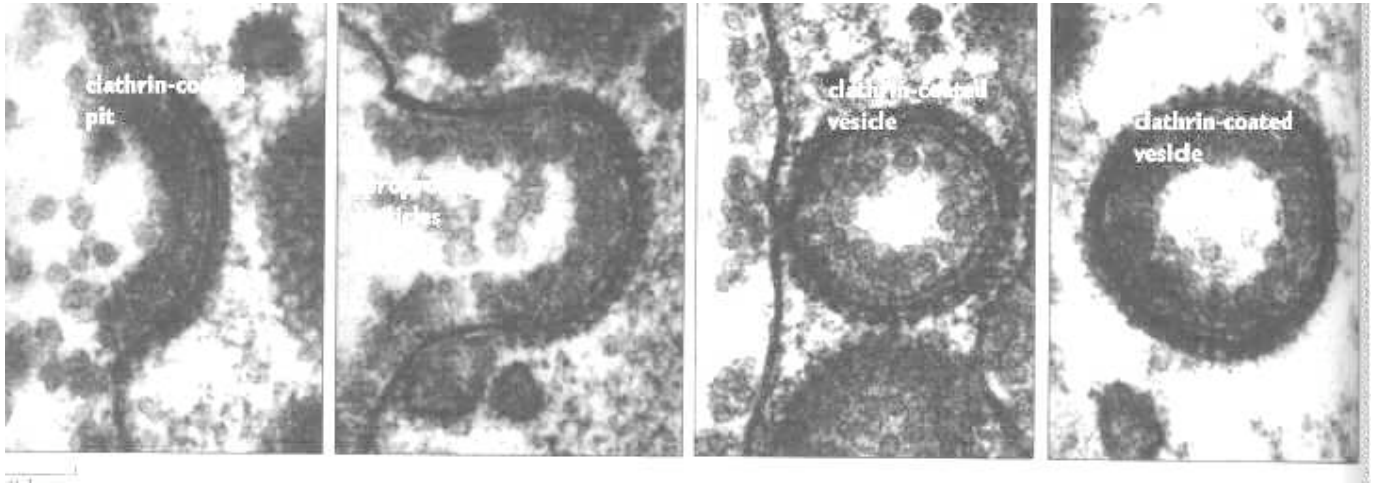
Phagocytosis



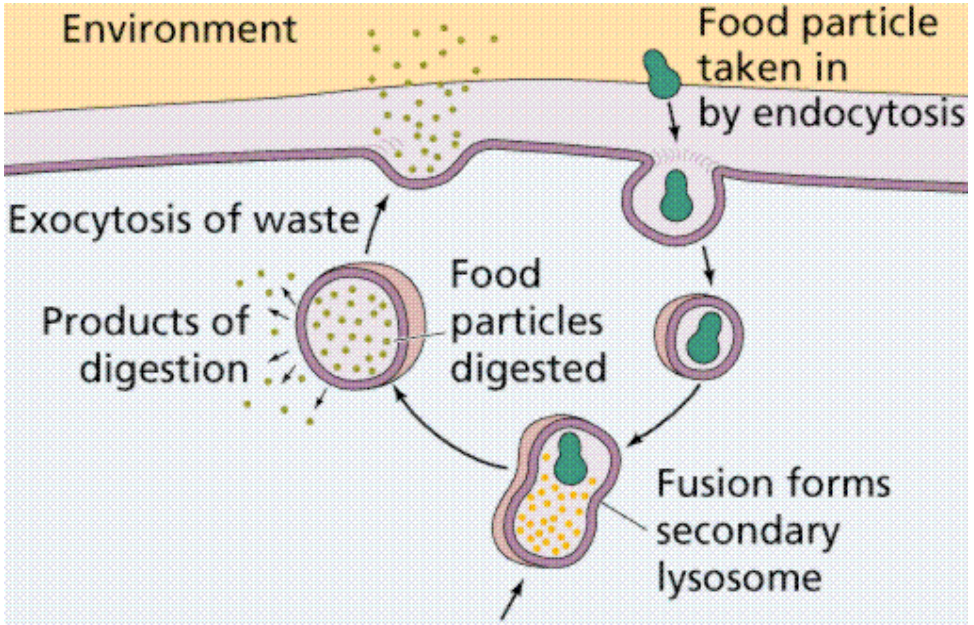


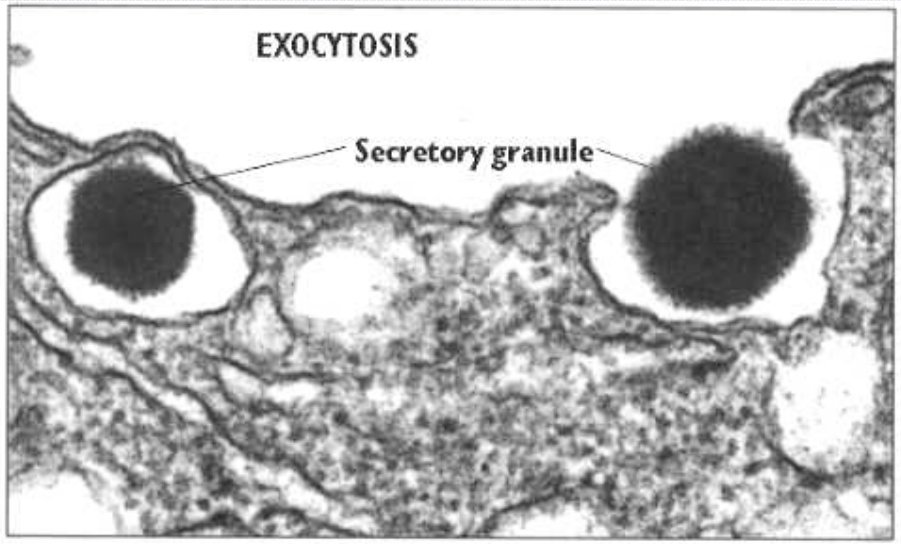
Endocytosis



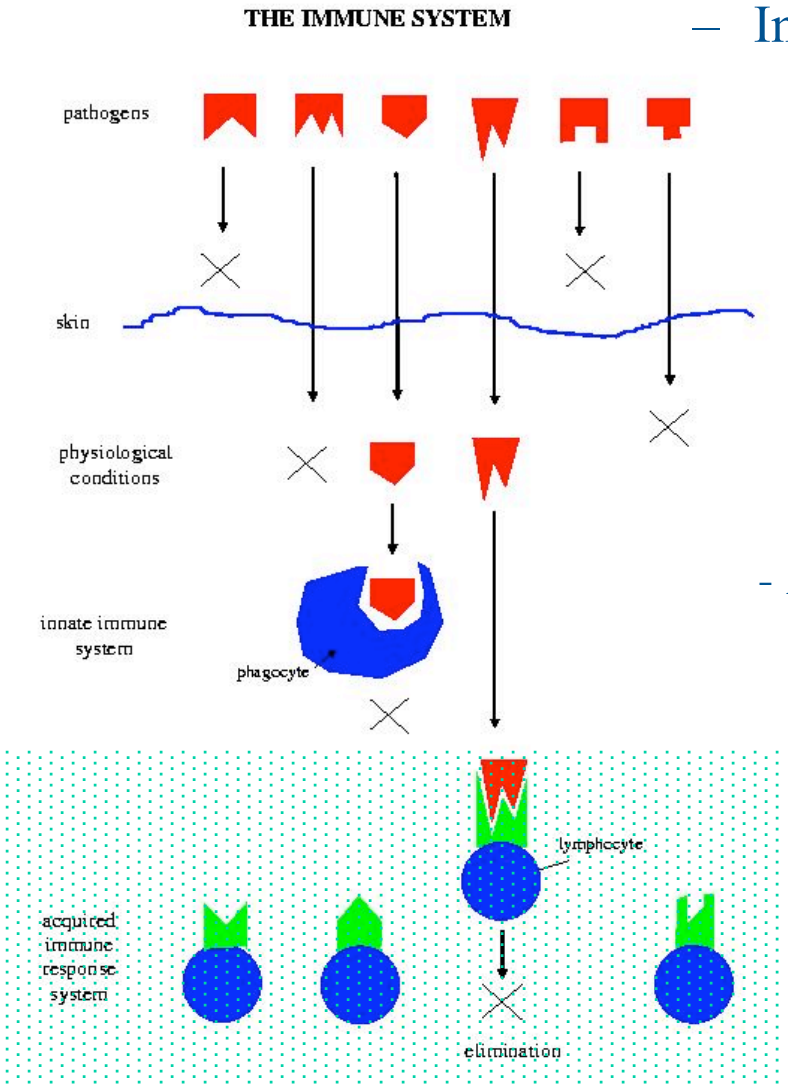


Exocytosis


Environment
Food particle taken in by endocytosis
Exocytosis of waste
Products of digestion
Food particles digested
Fusion forms secondary lysosome


EXOCYTOSIS
Secretory granule

Layers of Defense: Aquired Immune System



– Innate Immune System

- Primarily consists of endocytic and phagocytic systems
  – Roaming scavenger cells (phagocytes), ingesting extracellular debris, molecules, and pathogens

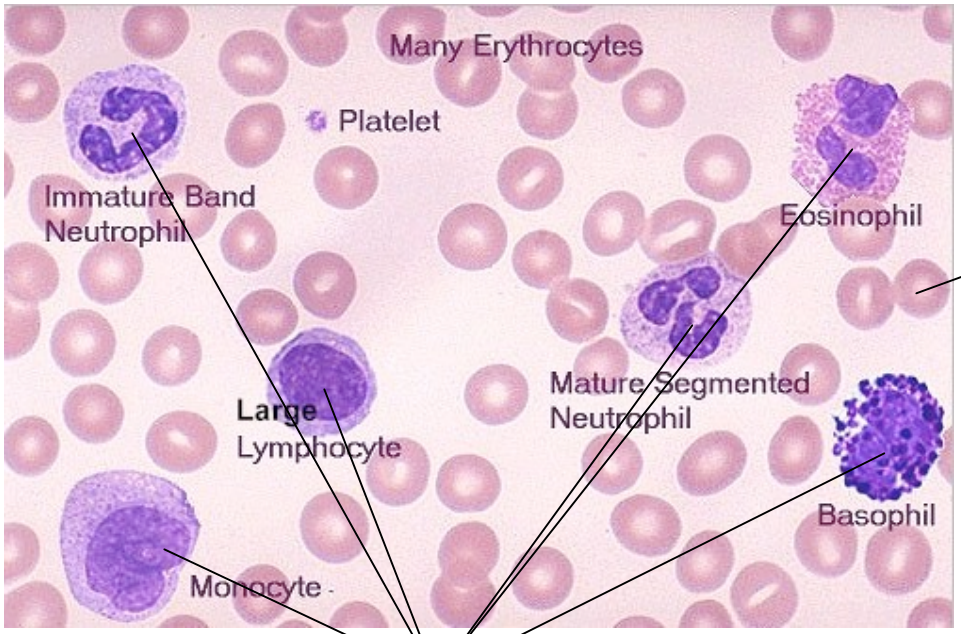
- Acquired Immune Response

Responsible for the immunity that is adaptively acquired during the lifetime of an organism

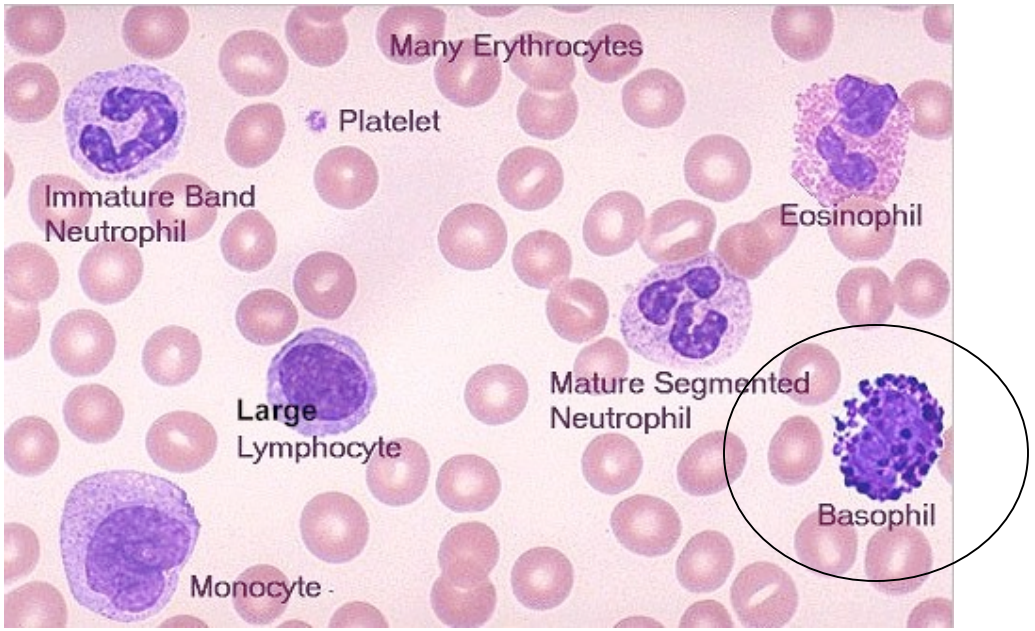
The main work force of the acquired immune system are lymphocytes, a specific type of white blood cells.

Table of Contents

White Blood Cells (Leukocytes)

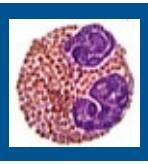


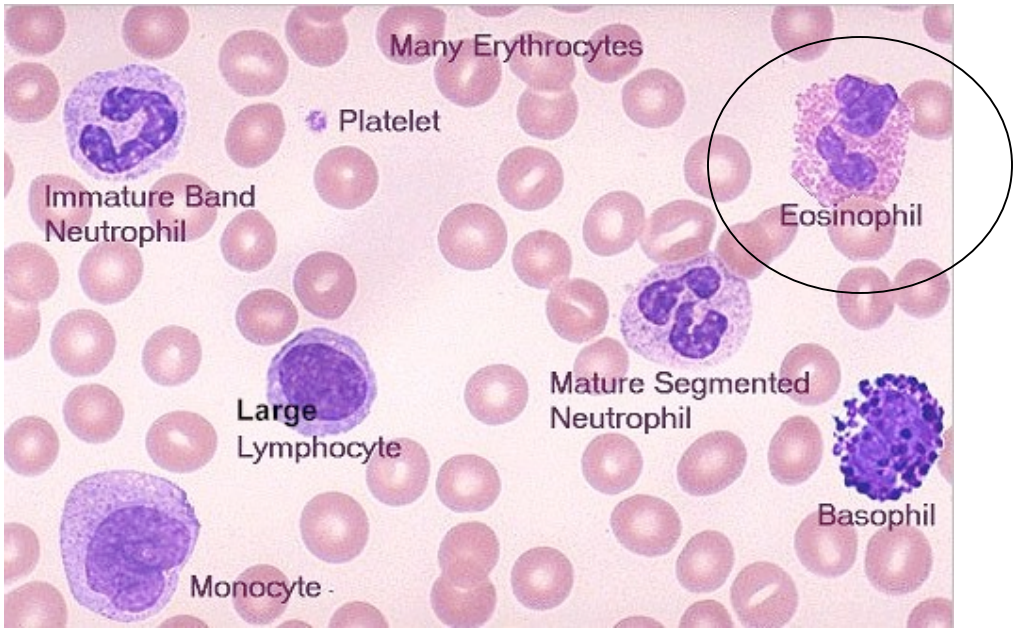
Leukocytes: Basophils



- Basophils
  - … comprise less than 1% of normal blood leukocytes.
  - … help fight infection by releasing chemicals—for example, histamine.
  - Histamine dilates blood vessels, thus allowing other white blood cells to move out of capillaries into surrounding tissues.

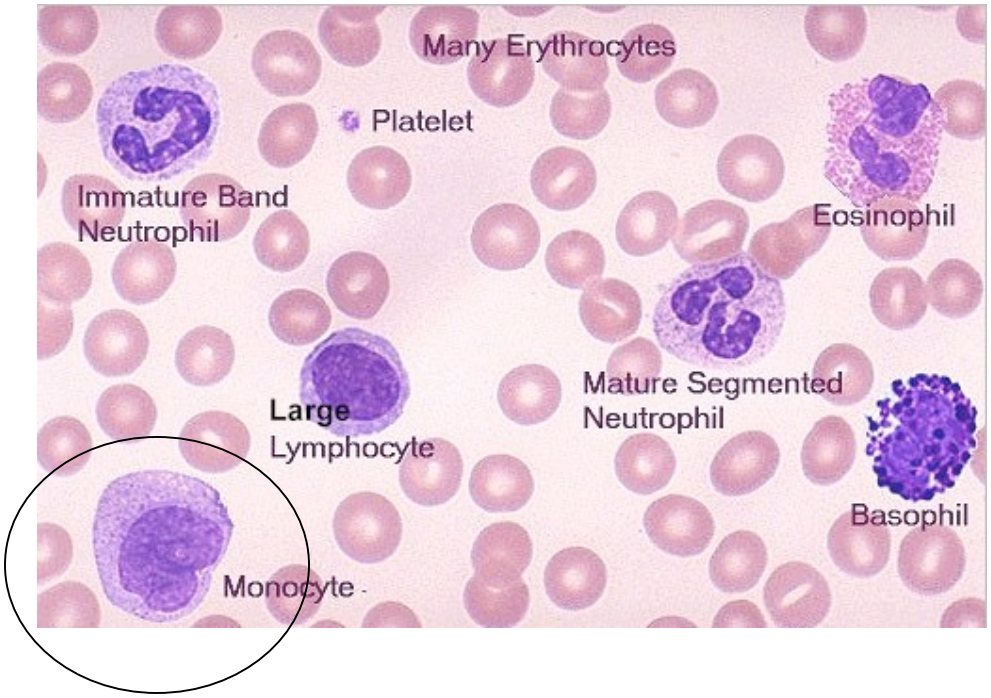
Leukocytes: Eosinophils





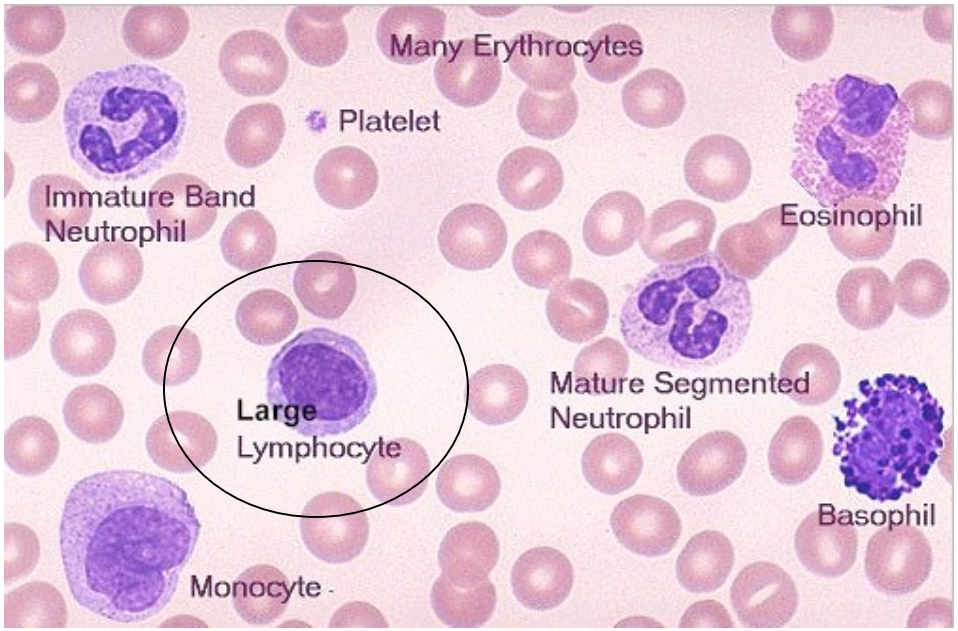
- Eosinophils
  - … comprise 3% of normal leukocytes population.
  - They spill their toxic granule contents out onto their targets.
  - They ingest antigen-antibody complexes, which are then destroyed by degradative enzymes.
  - They secrete enzymes which inactivate inflammatory mediators, limit inflammatory reactions.

Leukocytes: Monocytes



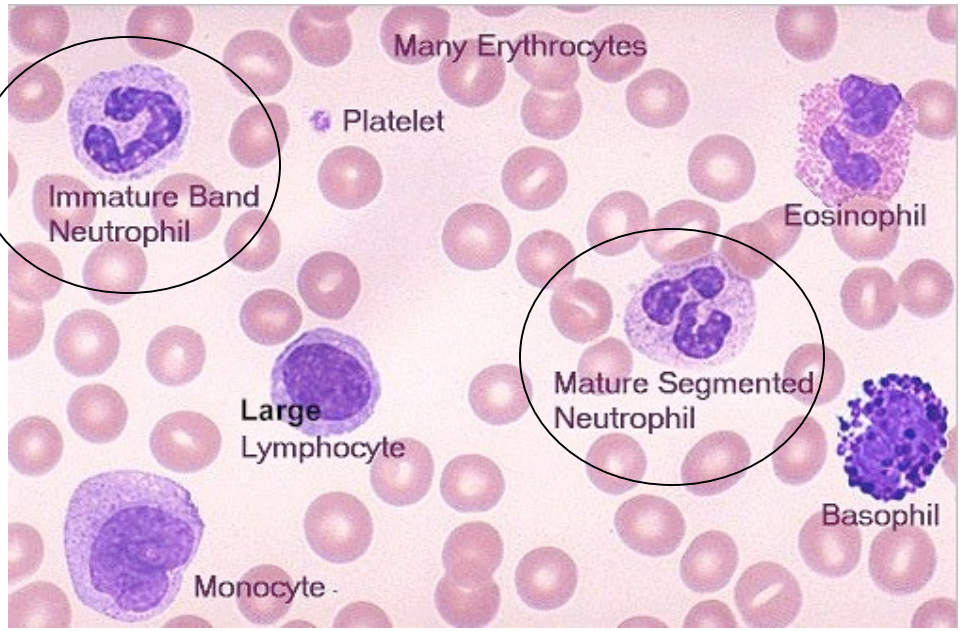
- Monocytes
  - … represent 4% of circulating leukocytes.
  - They are the garbage trucks, collecting and disposing of particulate debris..

Leukocytes: Lymphocytes



- Lymphocytes
  - 25% of the circulating leukocytes
  - Responsible for mounting immune responses to specifically recognized molecules (antigens)
  - **B** lymphocytes: produce specific antibodies
  - **T** lymphocytes: recognize specific antigens through T cell receptors.

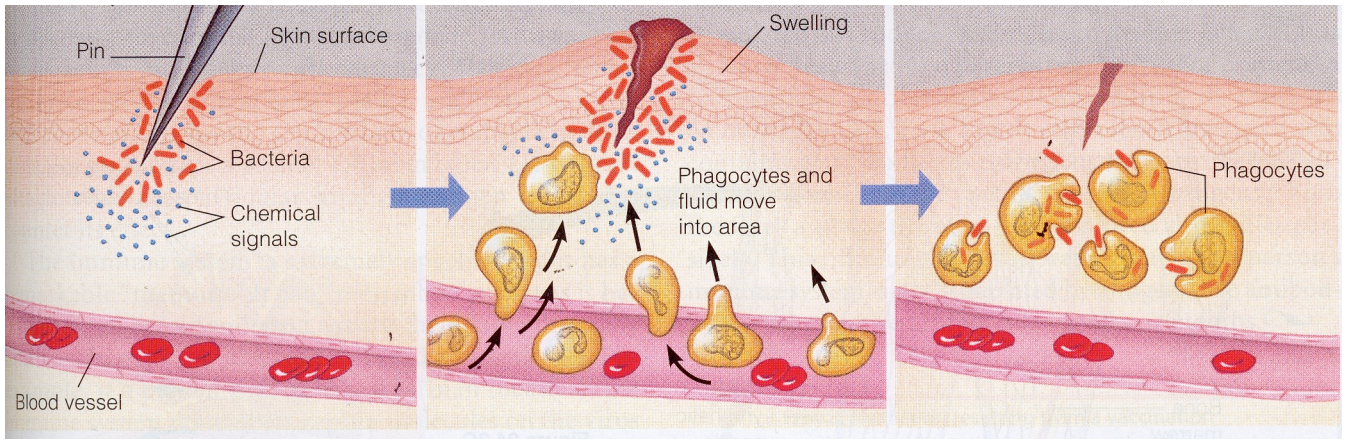
Leukocytes: Neutrophils



- Neutrophils
  - … are the most abundant white blood cells (60% of leukocytes).
  - … move into body tissues.
  - As phagocytes they "eat" bacteria and debris from other body cells.
  - Accumulate at a site of inflammation after a short time.

Table of Contents

Inflammatory Response



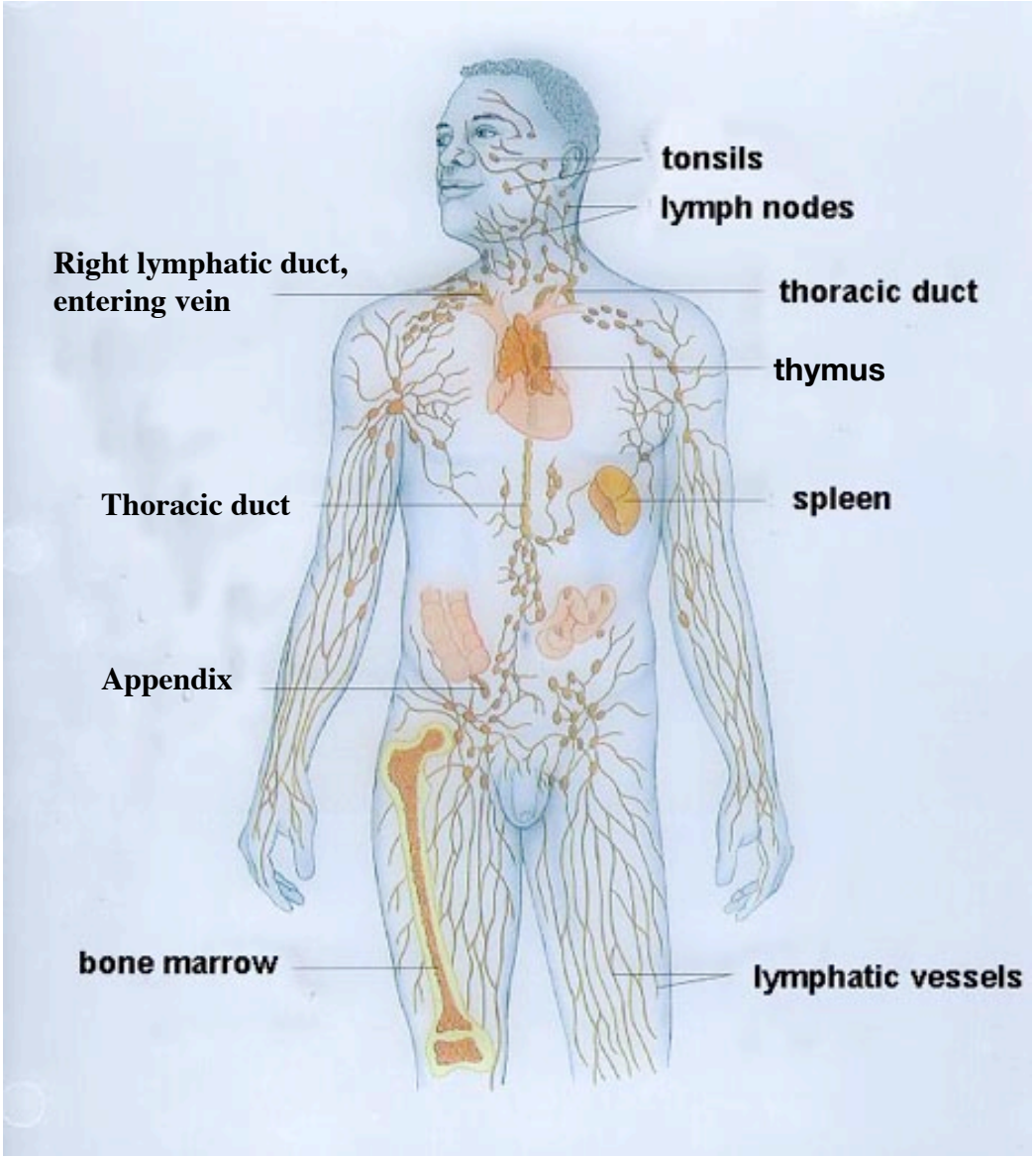
Tissue injury; release of chemical signals such as histamine (basophils help)

Dilation and increased leakiness of local blood vessels; migration of phagocytes to the area

Phagocytes (macrophages and neutrophils) consume bacteria and cell debris; tissue heals

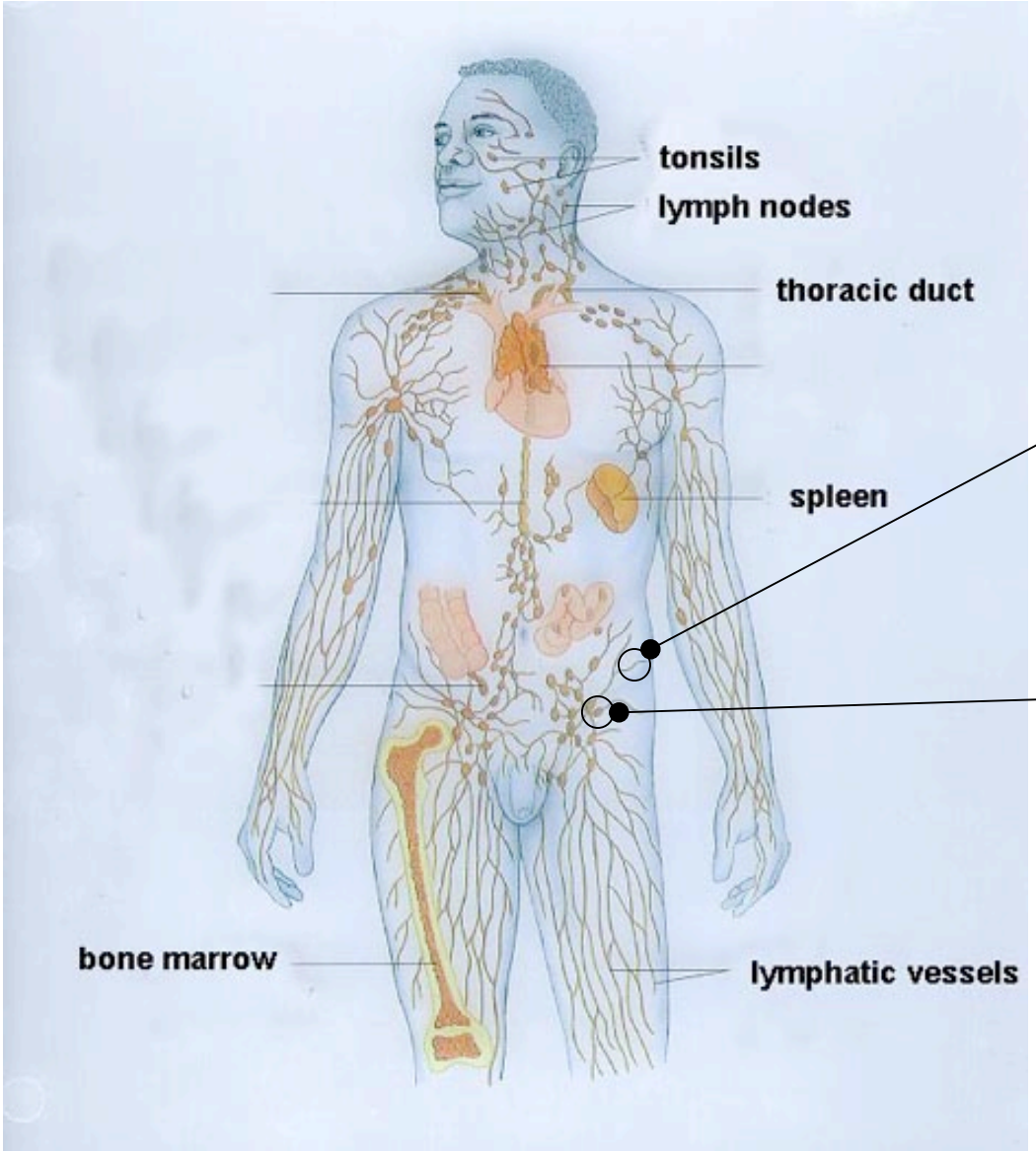
Table of Contents

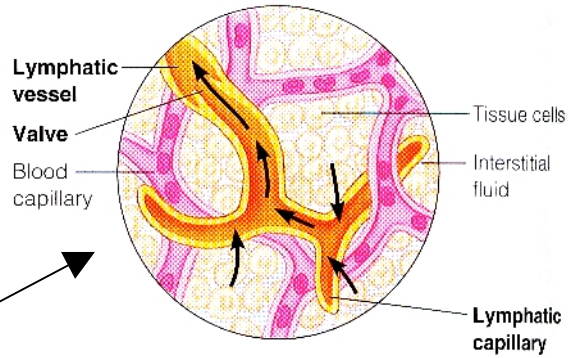
The Lymphatic System



- Branching network of vessels
- Numerous lymph nodes (saclike organs packed with lymphocytes)
- Thymus
- Tonsils
- Appendix
- Spleen
- Bone marrow

The Lymphatic System: More Details





Lymph node:

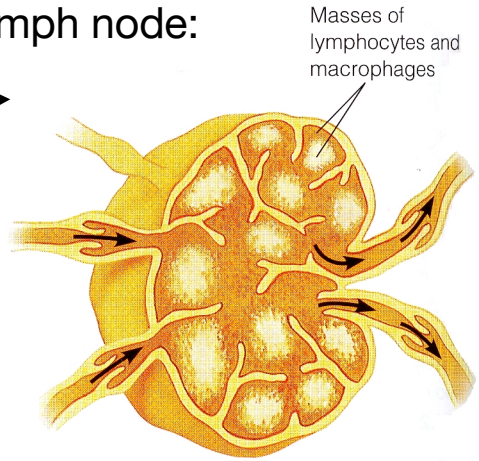


Table of Contents

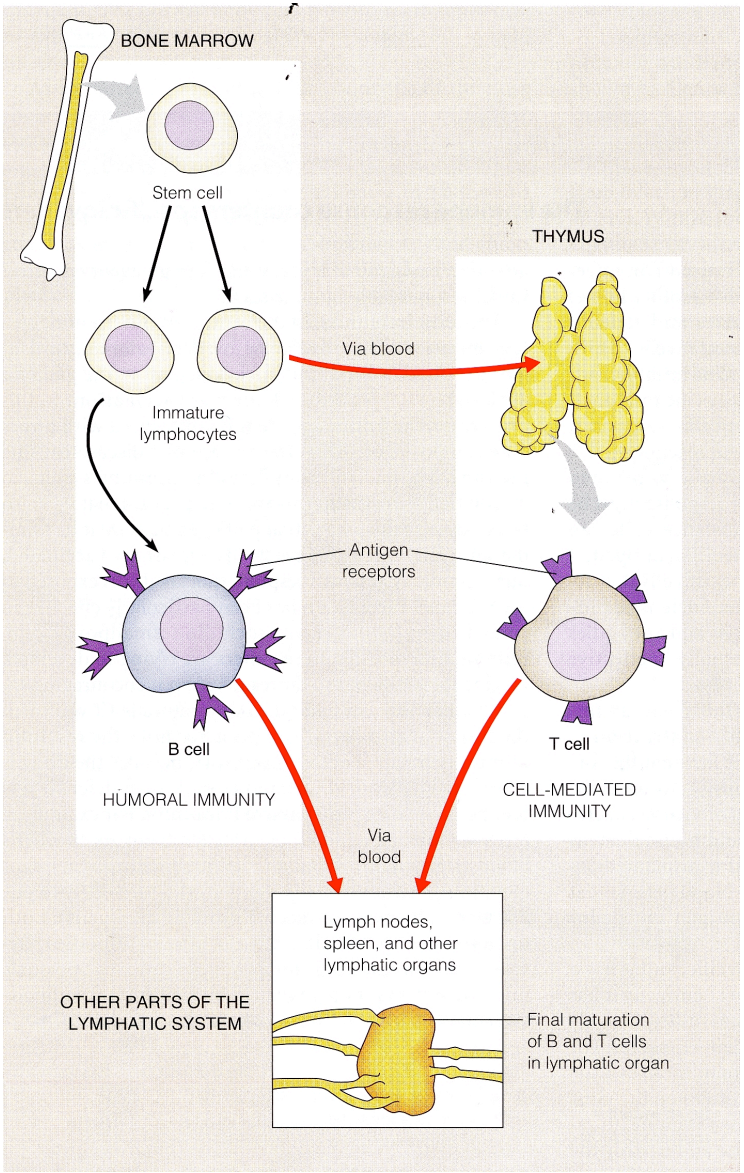
Immune Response Counters Invaders

- Acts more effectively than non-specific responses.
- Must be primed ("activated") by the presence of a foreign substance, called an antigen.
- An antigen is a molecule that elicits an immune response ("*anti*body-*gen*erating")
  - Molecules on the surface of viruses, bacteria, mold spores, cancer cells, pollen, house dust, …
- An antibody is a protein in blood plasma that attaches to one particular kind of antigen and helps counter its effect.

Table of Contents

B Cells and T Cells (Lymphocytes)

- Lymphocytes are white blood cells that spend most of their time in the tissues and organs of the lymphatic system.
- Lymphocytes originate from stem cells in the bone marrow.
- Some immature lymphocytes continue developing in the bone marrow and become specialized as B cells.
- Other lymphocytes are carried by the blood to the thymus, where they become specialized as T cells.
- Both B cells and T cells eventually make their way via the blood to the lymph nodes and other lymphatic organs.



Antigens and Antibodies

- Most antigens are proteins or large polysaccharides on the surfaces of viruses.
- Our immune system can recognize millions (billions?) of different antigens.
- Antibodies identify localized regions (antigenic determinants) on the surface of an antigen molecule.
- An antigen-binding site, a specific region on the antibody molecule, recognizes an antigenic determinant by a key-lock mechanism.

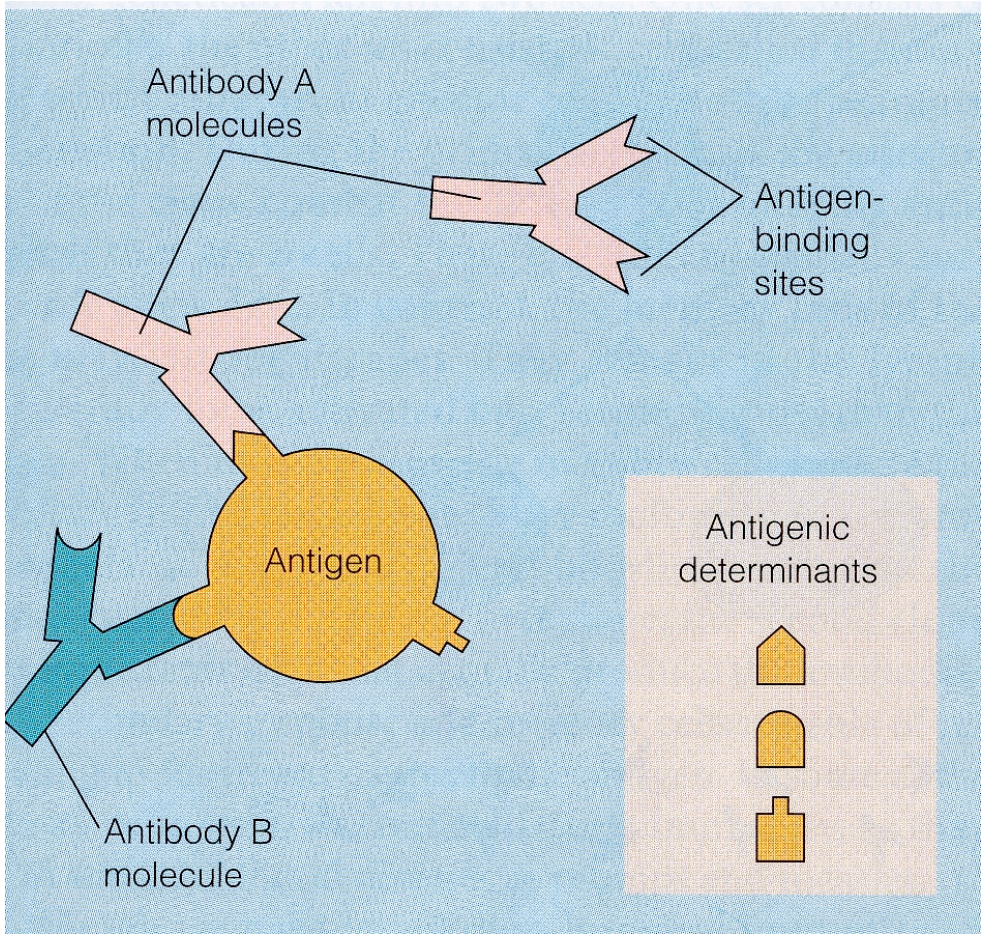


Table of Contents

Clonal Selection of B Cells

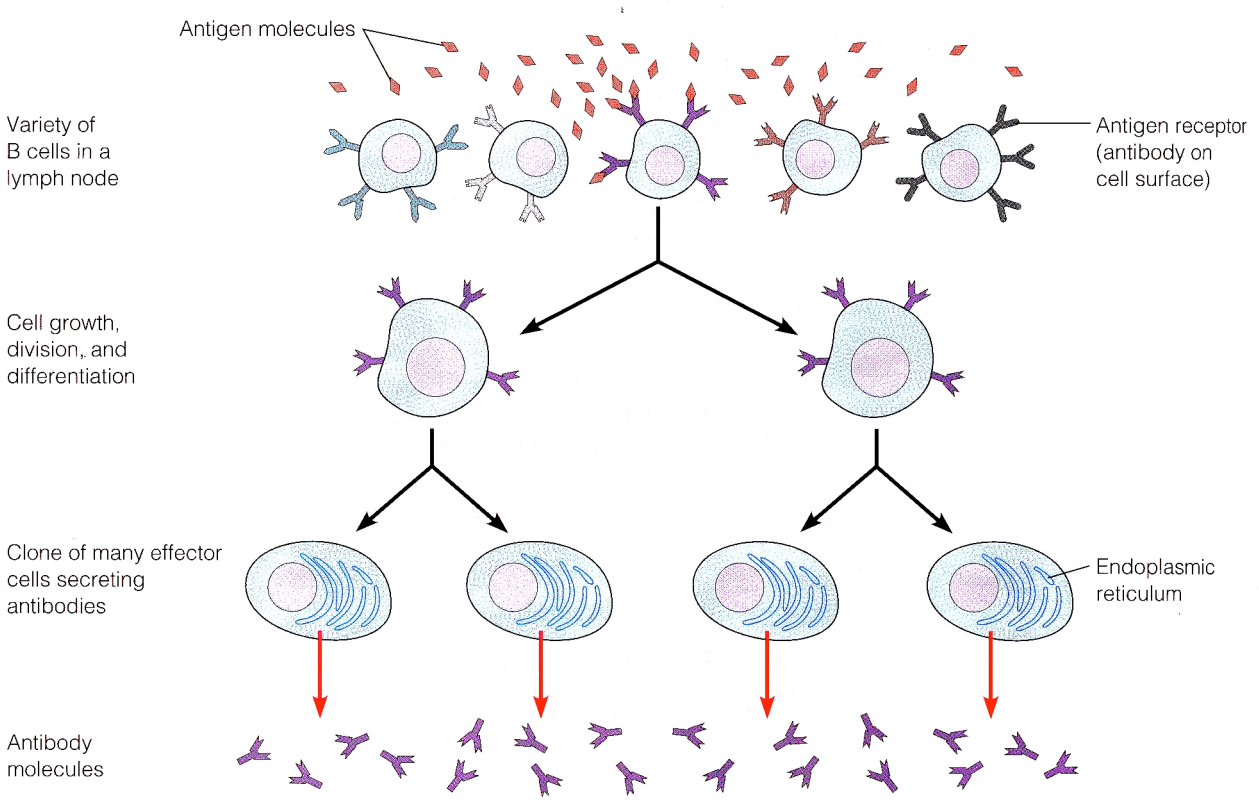
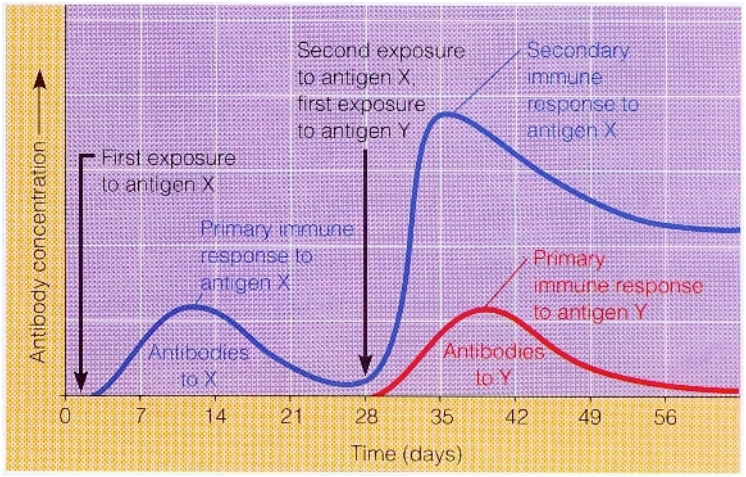
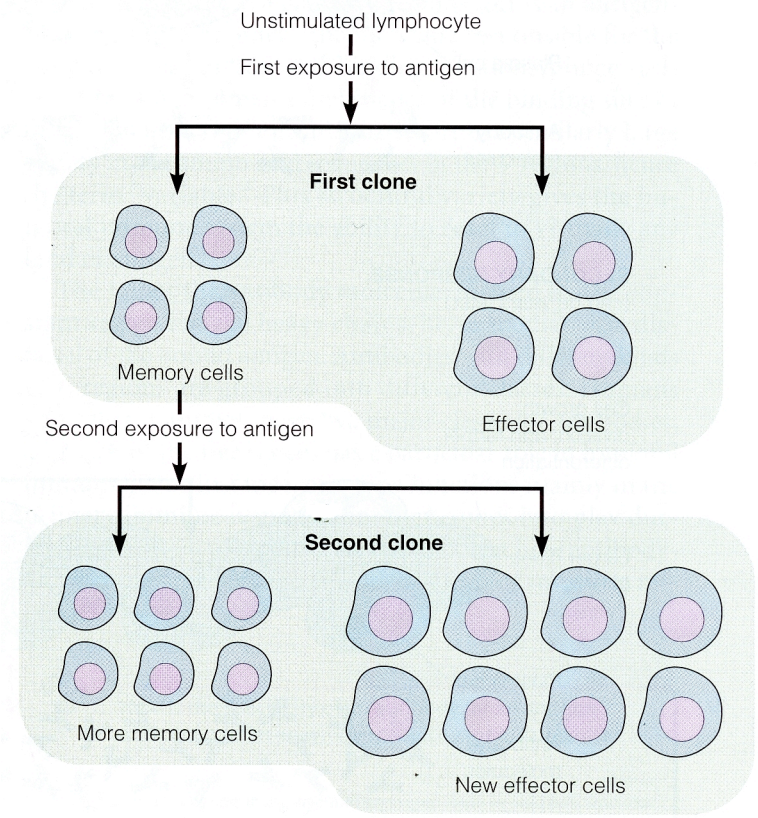


Table of Contents

Immune System Memory



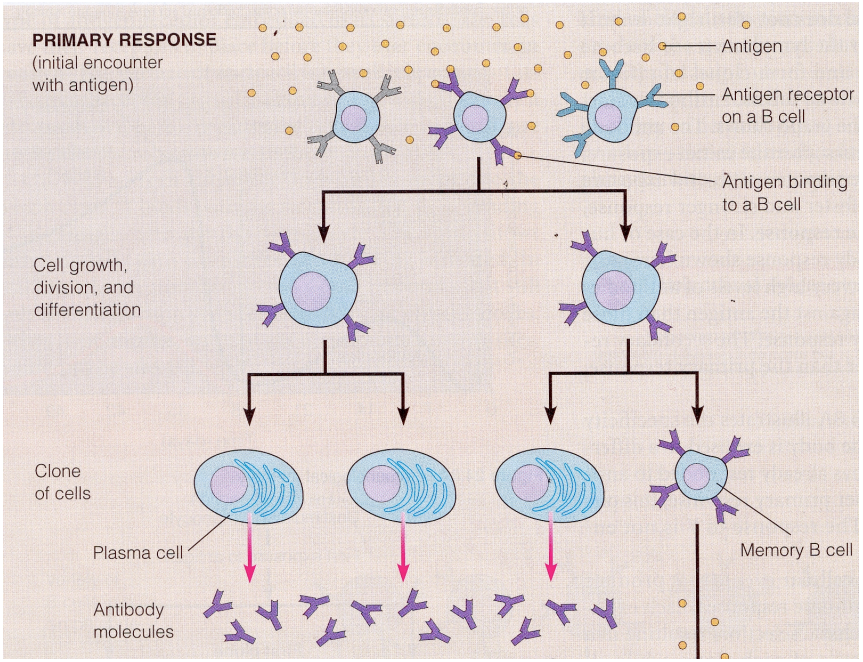
Immunological Memory Response



Cellular Basis if Immunological Memory

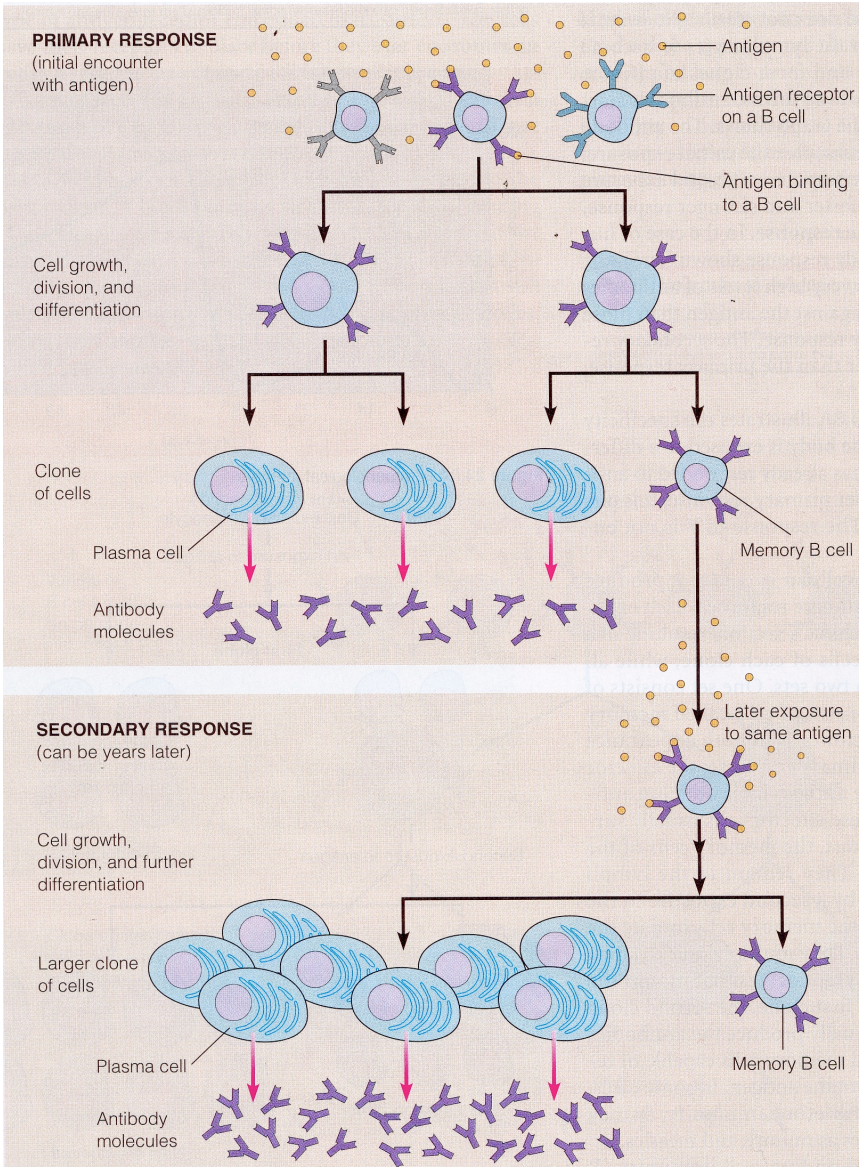
Table of Contents (Part 2)

Humoral Immunity: B Cell Warriors



- *Humors* = body fluids (blood, lymph, interstitial fluid)
- The defensive machine of humoral immunity is achieved by a combination of clonal selection and immunological memory.
- Primary response:
  - B cell is "selected" by antigen.
  - This triggers its growth, division, and further differentiation.
  - Resulting clone contains
    - Many effector B cells: plasma cells: secrete antibody molecules (2000/sec, 4-5 days), which circulate in blood and lymph
    - Smaller number of memory B cells:
      - They await future exposure to the same antigens that triggered their production.
      - If contact with antigens occurs, the **secondary response mechanism** is triggered.

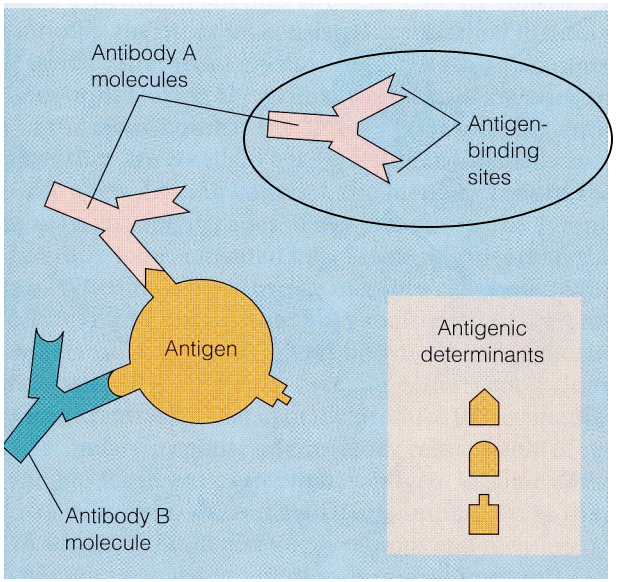
Humoral Immunity: B Cell Warriors

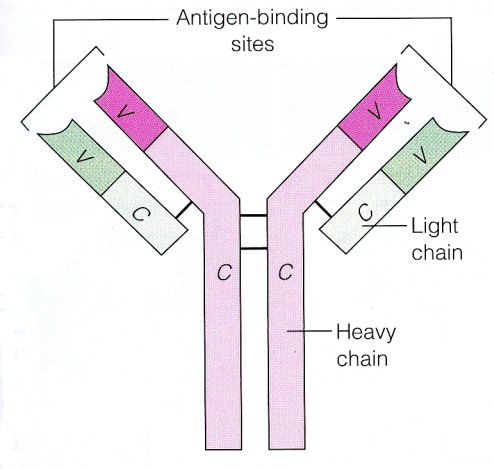


- Secondary response:
  - Memory cells bind antigens.
  - This stimulates the production of a large number of new clones.
  - This occurs more rapidly and produces more plasma cells than in the primary response.
  - Consequently, antibody levels in the blood and lymph are much higher.
  - Antibodies differing in structure are involved.

Table of Contents (Part 2)

The Antibody Weapons





- Each antibody is made up of four polypeptide chains:
  - Two fairly long, heavy chains (Y shape, with bonds at the fork), help mediate disposal
  - Shorter, light chains (bonded to heavy chains):
    - V(ariable) region: antigen binding site
    - Different amino acid sequences result in different 3D shapes

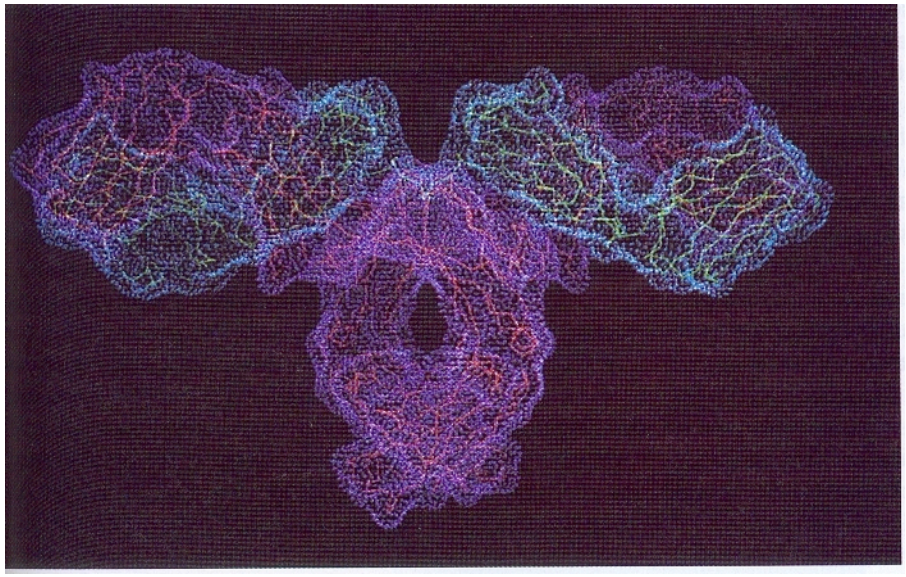


Table of Contents (Part 2)

Antibodies Mark Antigens

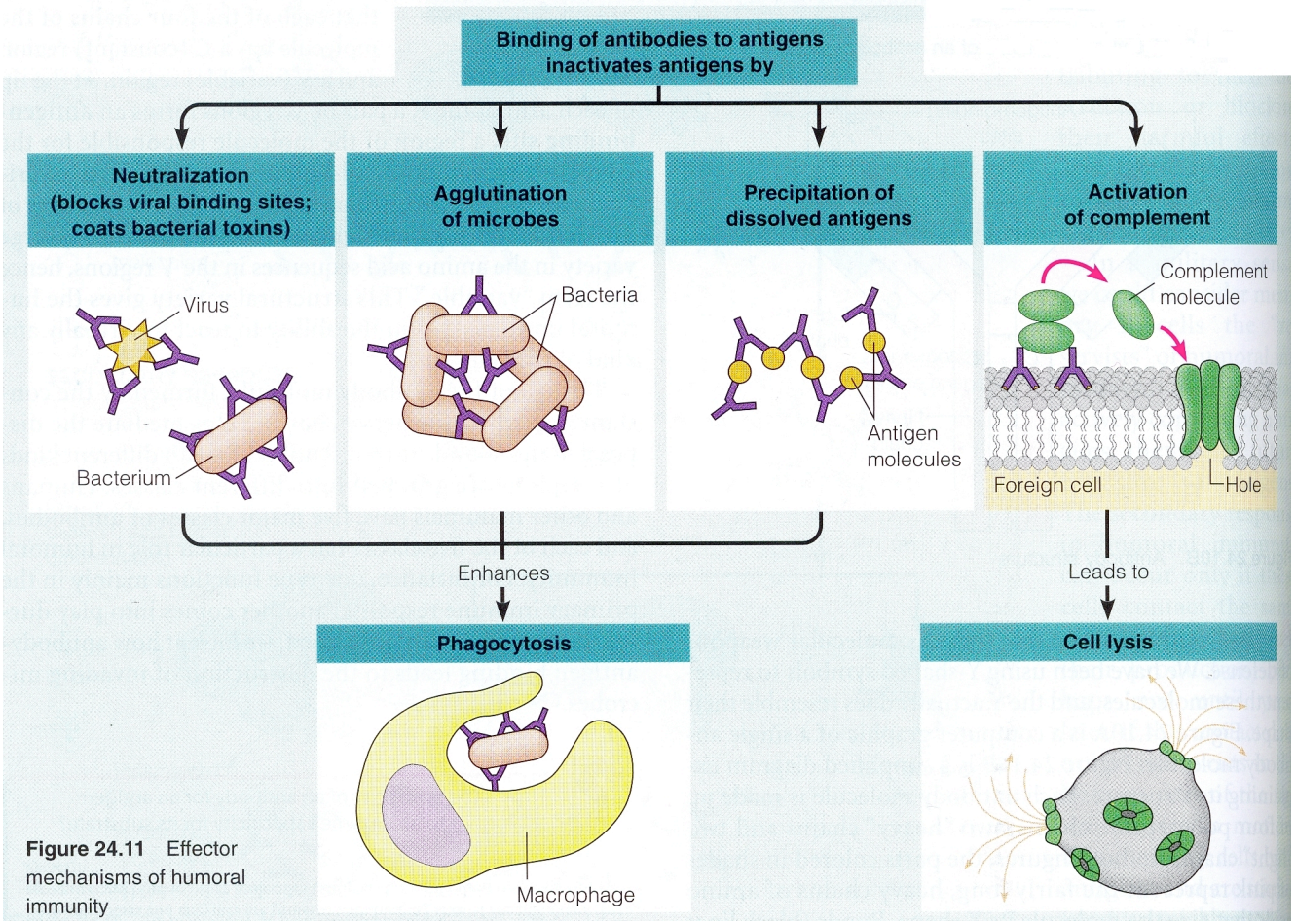


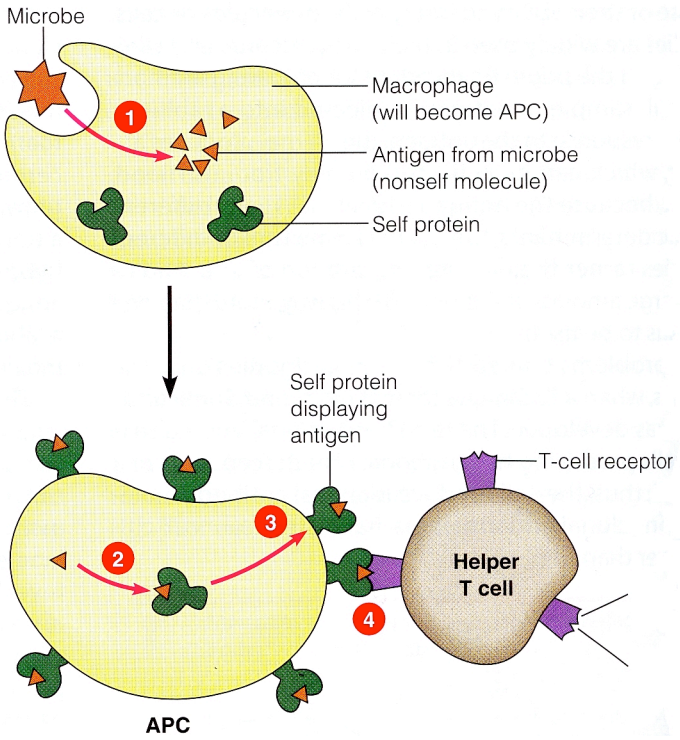
Figure 24.11 Effector mechanisms of humoral immunity

Table of Contents (Part 2)

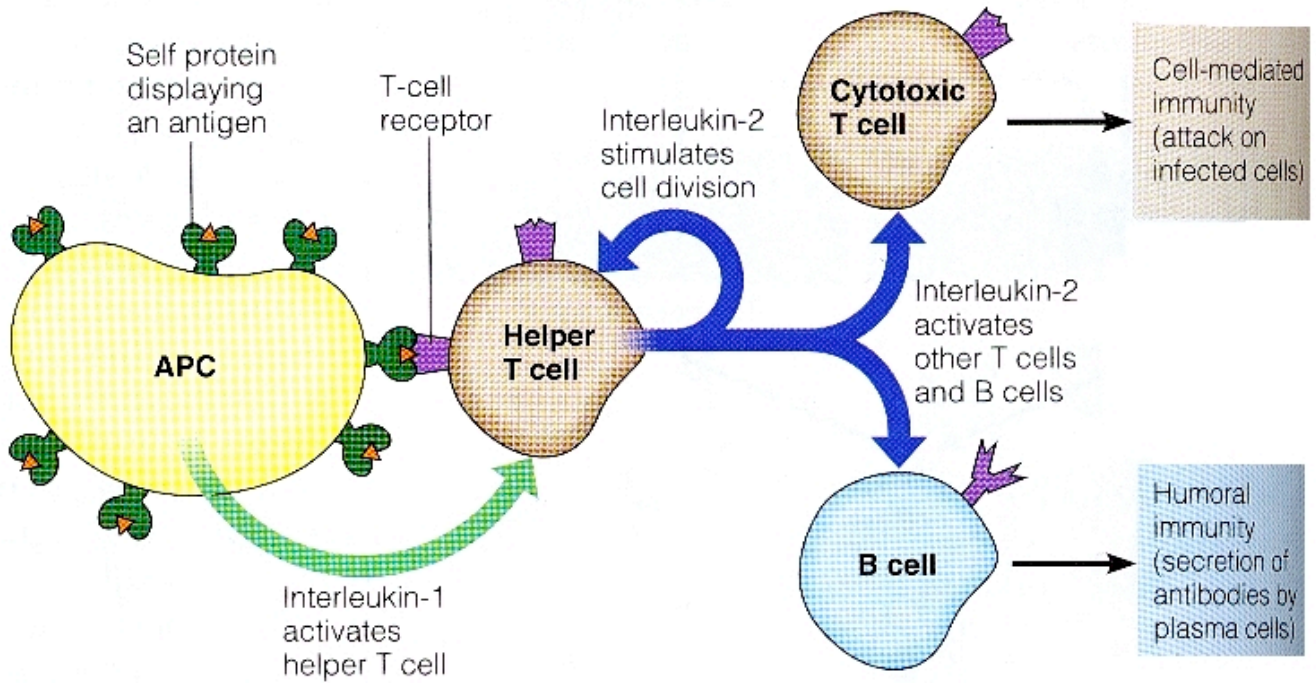
APC and Helper T Cell Interaction

- APC:
  antigen-presenting cell
- Helper T cell:
  activates cytotoxic T cells
  and microphages

1. The microphage ingests a foreign particle and breaks it into fragments—antigens.
2. Self-proteins bind the foreign antigens (non-self molecules) and …
3. … display them on the cell surface.
   The set of self-proteins is unique for each individual human.
4. Helper T cells recognize and bind to the *combination* of a self-protein and a foreign antigen.
   (analogy: safety box bank system)



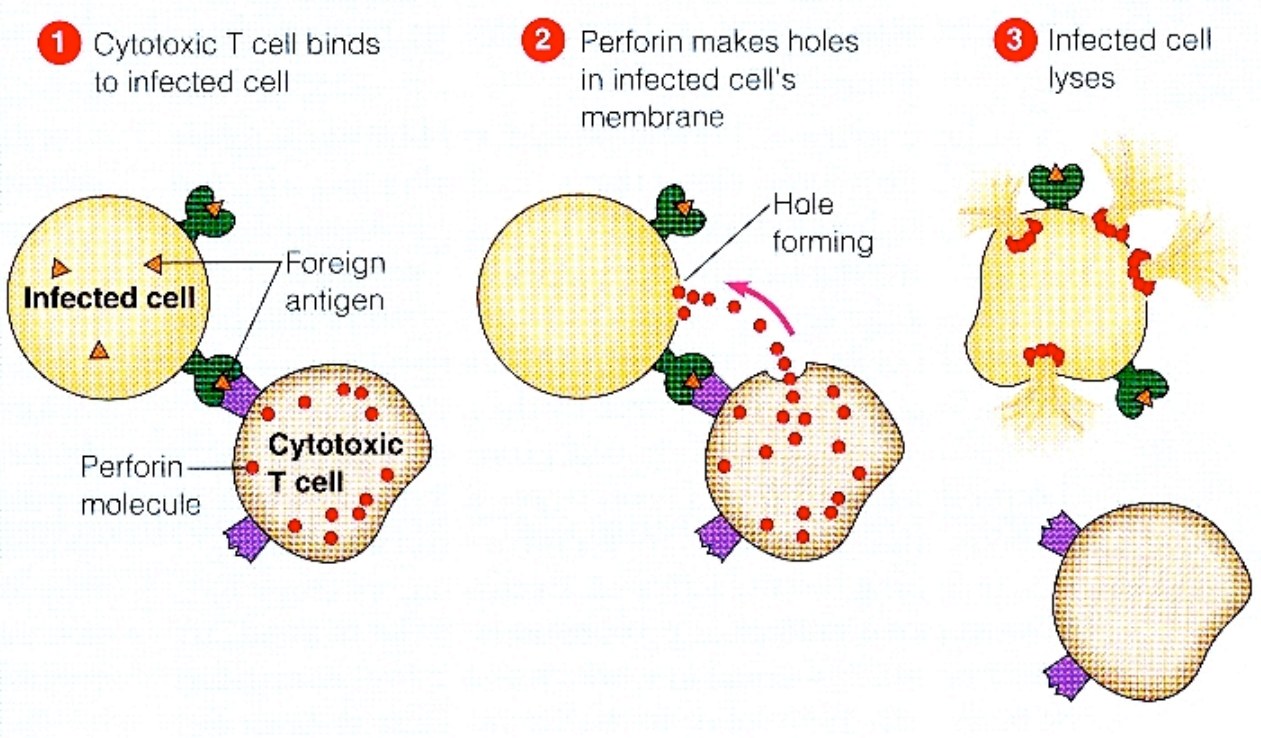
Helper T Cell Activation



- Binding of T cell receptor triggers a signal transduction pathway.
- This activates the helper T cell (enhanced by secreted proteins: Interleukin-1).
- Activated helper T cells secrete additional stimulatory proteins; Interleukin-2:
  - Makes helper T cell grow and divide (>>> memory cells and active helper T cells).
  - Stimulates activity of cytotoxic T cells.
  - Helps activate B cells, thus stimulating humoral immunity as well.

Table of Contents (Part 2)

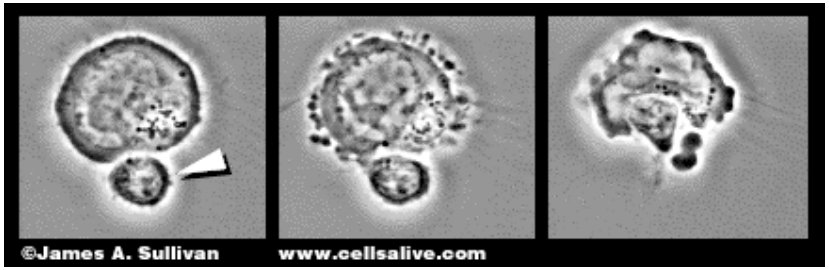
Cytotoxic T Cell Kills Infected Cell



Cytotoxic T Cells Attacking …

Cytotoxic T cell attacks cancer cell

CYTOTOXIC T-LYMPHOCYTE:
A specialized white blood cell responsible for eliminating unwanted body cells (e.g. cancer) is killing a cell infected with the influenza virus



Cytotoxic T Lymphocyte

Why are Immune Systems interesting

for Computer Scientists

and Engineers?

http://www.cs.unm.edu/~immsec/html-imm/

References

- Campbell, Mitchell, and Reece: *Biology: Concepts and Connections*, 3rd Edition, Addison-Wesley Longman.