Non-specific host defenses

Lecture 20 - Chapter 14

Topics

- Defense Mechanisms
- Components of immunity
- Non-specific immunity

Defense Mechanisms

- **Innate and nonspecific immunity**
  - First line of defense
  - Second line of defense
- **Acquired and specific immunity**
  - Third line of defense

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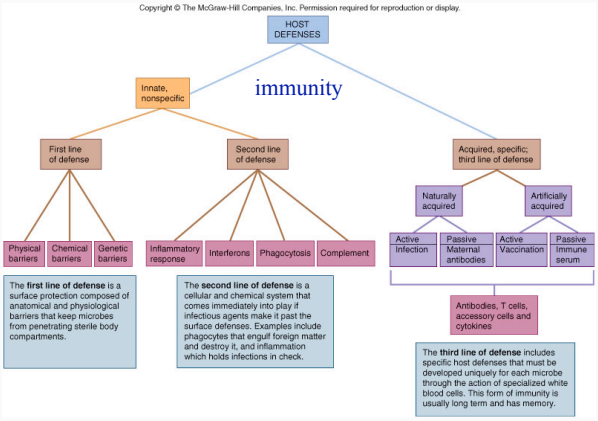

Fig. 14.1 Flowchart summarizing the major components of the host defenses.

Immunology

- **Study of immunity** - the host's resistance to infectious agents of disease

Immunity

- Involves nonspecific and specific components
- Has fluid-based (humoral) and cellular (white blood cells [wbc] = leukocytes) components
  - Surveillance of the host body
  - Recognition of foreign agents or material
  - Destruction of foreign agents or material

First line of defense

- Barriers of innate immunity
  - Anatomical
  - Chemical
  - Genetic

Anatomical barriers

- Intact Skin
  - Outermost layer
  - Hair follicles
  - Skin glands
- Mucous membrane
  - GI (digestive) tract
  - Urinary tract
  - Respiratory tract (also ciliatory escalator)
  - Outer Eye

Chemical barriers

- Sebaceous secretions
- Eyelid glands – meibomian gland
- Tears and saliva – lysozyme
- Menstruation
- Acidic pH
  - Sweat
  - Stomach
  - Skin
  - Semen
  - Vagina

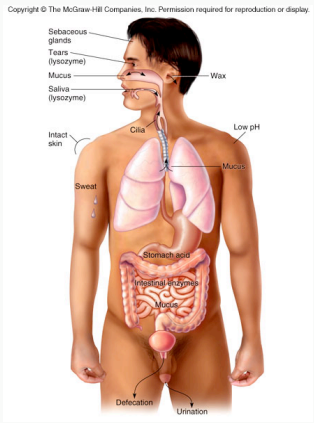

Fig. 14.2 The primary anatomical and chemical defense barriers.

Genetic barriers

- Different level of sensitivity and resistance to infectious agents
  - Malaria (sickle cells)
  - Tuberculosis
  - Leprosy
  - Fungal infections

Second and Third lines of defense

- Involves specific and non-specific contributions to host immunity
- Depends on activity of protective cells

WBC (Leukocyte)

- WBC recognize markers for "**self**" on the host cell
  - > Do not attack or do not respond to host cell
- WBC recognize markers for "**non-self**" on the invading agent or material
  - > Attack or respond to agent

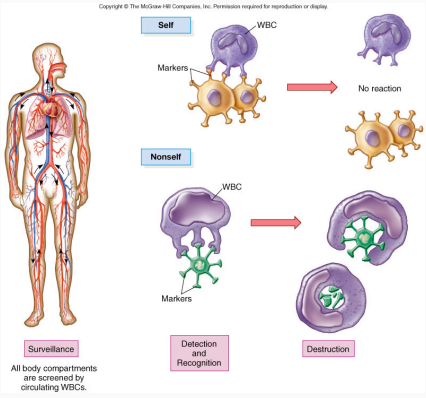

Fig. 14.4 Search, recognize, and destroy is the mandate of the immune system.

Components of immunity

- All systems are integrated
  - Recticulo-endothelial system (RES)
  - Extracellular fluids system (ECF)
  - Blood, vascular (circulatory) system
  - Lymphatic system

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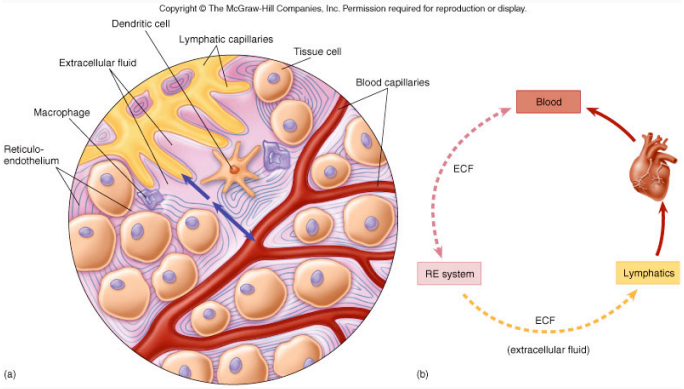

Fig. 14.5 Connection between the body compartments of the immune system.

Reticulo-endothelial (RES)

- Network of **connective tissue fibers** (Reticulum)
- Interconnects cells
- Allows immune cells to bind and move outside the blood and lymphatic system

Representation of the RES and the ECF, which surrounds the cells.

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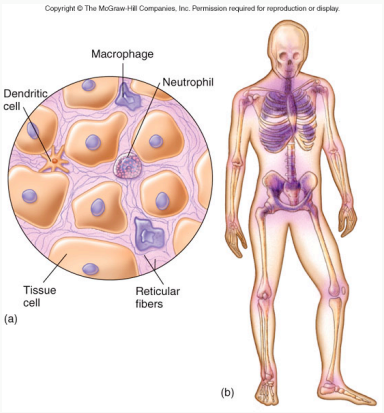


Fig. 14.6 The reticulo-endothelial system

Extracellular fluid (ECF)

- The spaces surrounding tissue cells and RES
- ECF enables immune cells to move

Blood

- Components
- Stemcells
- Hematopoiesis

The buffy coat layer from unclotted blood contains WBCs.

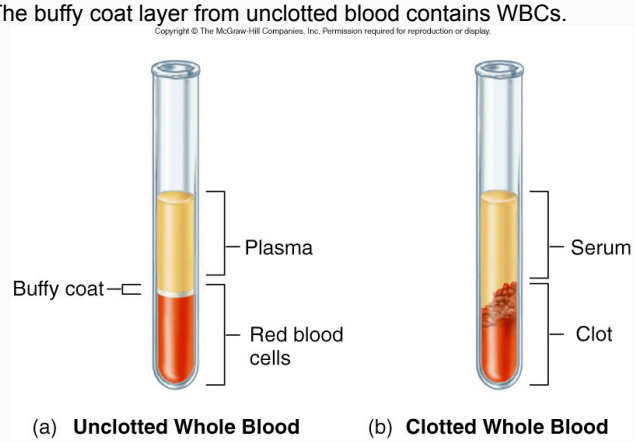


Fig. 14.7 The macroscopic composition of whole blood.

Hematopoiesis

- Production of blood
  - Starts at the embryonic stage
    - Yolk sac and liver
  - Continues throughout adult stage
    - Bone marrow

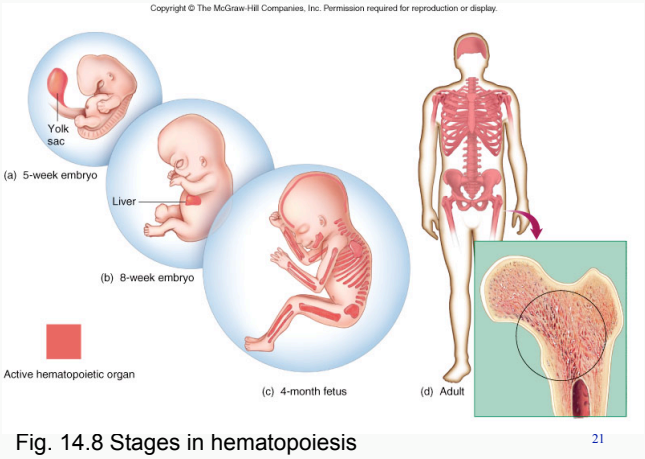


Fig. 14.8 Stages in hematopoiesis

Cellular components of blood

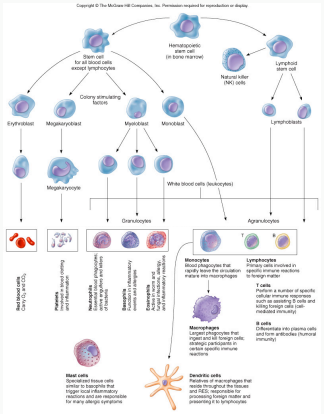
- White blood cells (WBC) or leukocytes
- Red blood cells (RBC)
- Platelets

The three types of stem cells differentiate into (within) blood: platelets, granulocytes, and agranulocytes.

Myeloid sc

blast

cyte



Lymphoid sc

Fig. 14.9 The development of blood cells and platelets.

Stem cells

- Hematopoietic stem cells in bone marrow
- Myeloid stem cells
  - Wbc: neutrophils, eosinophils, basophils; monocytes
  - Rbc: erythrocytes
  - platelets
- Lymphoid stem cells
  - Agranular wbc: T lymphocytes; B lymphocytes

White blood cell

- Leukocytes
  - Granulocytes (large cytoplasmic granules)
    - Neutrophils
    - Basophils
    - Eosinophils
  - Agranulocytes (very small granules)
    - T cells
    - B cells
    - Monocytes

Neutrophils

- Nuclei - horse shoe or polymorphic nuclei
- Present in high numbers in blood and tissue
- Phagocytizes bacteria – granules are digestive enzymes
- First to arrive during an inflammatory immune response

Eosinophils

- Nuclei – bilobed
- Present in the bone marrow and spleen
- Attach and destroy eukaryotic pathogens
- Associated with inflammation and allergies

Basophils

- Nuclei – constricted
- Present in low in number in the body
- Function is similar to eosinophils
- Localized basophils are called mast cells

Lymphocytes

- Agranular
- Present throughout the body
- Contribute to specific (adaptive) immunity
  - T cells
  - B cells

Monocytes

- Agranular and motile
- Differentiate into macrophages (circulation and lymphatics) and dendritic cells (tissue associated)
- Phagocytosis

Lymphatic system

- Network of vessels that extend to most body areas
- Connected to the blood system
- Provides an auxiliary route for the return of extracellular fluid to the circulatory system
- “Drain off” system for inflammatory response
- Contains lymphocytes, phagocytes and antibodies

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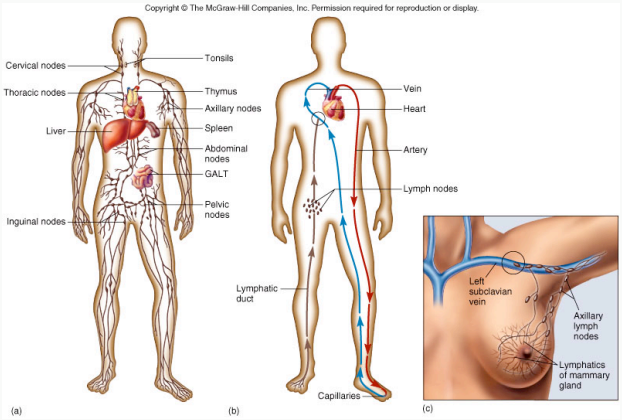

Fig. 14.11 General components of the lymphatic system.

Fluids

- Plasma-like fluid (lymph) - formed from blood components
  - Water
  - Dissolved salts
  - Proteins (antibodies, albumin)
  - White blood cells
  - No red blood cells
- Diffuses into the lymphatic capillaries

Lymph Vessels

- Parallels the blood system
- Returns lymph to the blood system
- Movement of lymph depends on (smooth) muscle contractions
- Permeate all parts of the body except the central nervous system, bone, placenta, and thymus.

Lymph Nodes

- Exist in clusters
- Located
  - along the lymphatic and blood vessels
  - in the thoracic and abdominal cavity regions, armpit, groin and neck
- Filter for the lymph fluid
- Provide environment for immune reactions

Spleen

- Located in the upper left portion of the abdominal cavity
- Filter for lymph fluid and blood
  - traps pathogens
- Adults can survive without spleen
- Asplenic children are severely immunocompromised

Thymus gland

- Embryo
  - two lobes in the pharyngeal region
  - High activity (releases mature **T** cells) until puberty
- Adult
  - Gradually shrinks
  - Lymph nodes and spleen supply mature **T** cells

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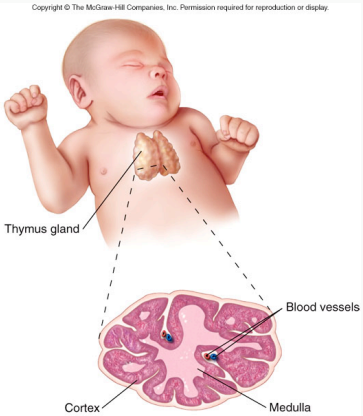

Fig. 14.12 In the thymus gland immature T cells differentiate into mature T cells.

Gut-associated lymphoid tissue (GALT)

- Recognized incoming microbes from food
- Supply lymphocytes for antibody response
- Examples: Appendix, Lacteals, Peyer's patches

Non-specific Immunity

- Inflammation
- Phagocytosis
- Cytokines (i.e., Interferon)
- Complement

Inflammation

- Five major symptoms
  - Redness (Rubor)
  - Warmth (Calor)
  - Swelling (Tumor)
  - Pain (Dolor)
  - Loss of function

The typical symptoms that occur after injury.

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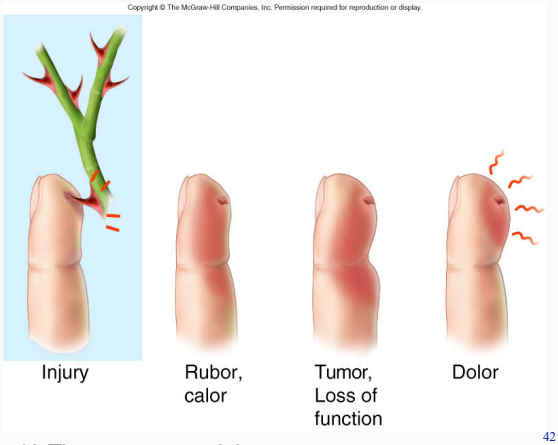

Fig. 14.13 The response to injury

Inflammation - Causes

- Trauma
- Tissue injury due to physical or chemical agents
- Specific immune reactions

Inflammation - Function

- Mobilize and attract immune components to the site of injury (second line of defense)
- Localized and remove harmful substances
- Destroy microbes and block their invasion
- Aid in the repair of tissue damage

The major events in inflammation are injury, vascular reactions, edema, and resolution.

- Vascular changes
- Edema
- Fever
- Phagocytosis

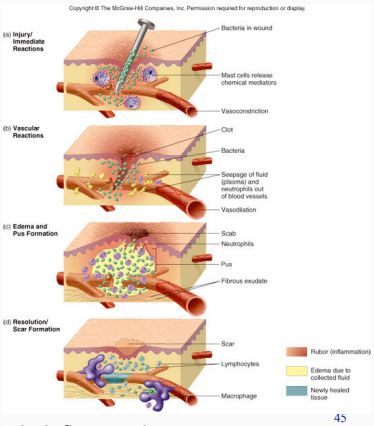

Fig. 14.14 The major events in inflammation

Vascular changes

- Blood cells, tissue cells, and platelets release **chemical mediators** and **cytokines**, which cause fever, stimulate lymphocytes, prevent virus spread, cause allergic reactions
- **Chemical mediators**
  - Vasoactive
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines)
    - Affect WBC
- **Cytokines**
  - Interferon, interleukins

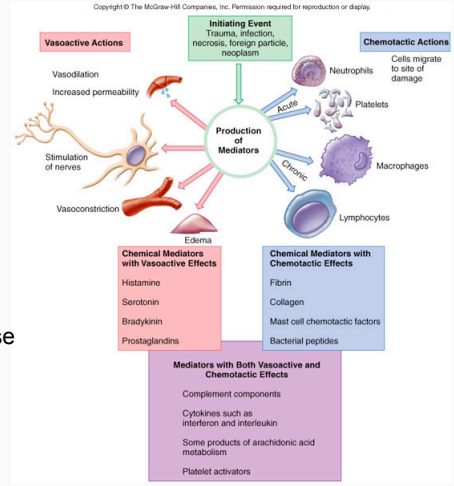

Fig. 14.15 Chemical mediators of the inflammatory response and their effects.

Edema

- Leakage of vascular fluid (exudate) into tissue
- Exudate - plasma proteins, white blood cells (wbc), debris, and pus
- Migration of wbc is called diapedesis or transmigration
- Chemotaxis - response Chemokines

The transmigration of WBCs is followed by chemotaxis.

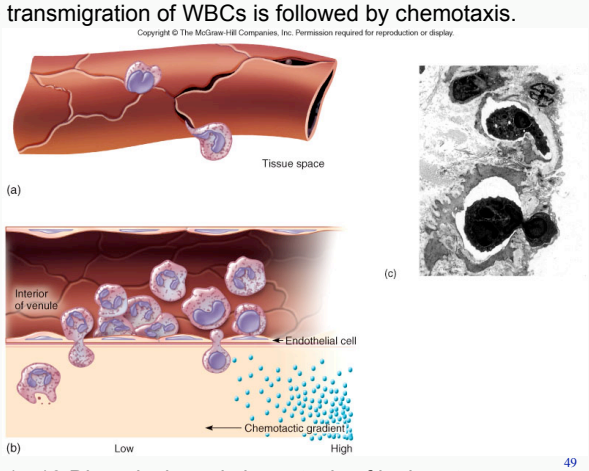

Fig. 14.16 Diapedesis and chemotaxis of leukocytes.

Fever

- Fever is caused by ***pyrogens***
- Pyrogens
  - Microbes and their products (ex. LPS)
  - Leukocyte products (called Interleukins)
- Fever:
  - Causes a reset of the hypothalamic thermostat (Hypothalamus) to a higher temperature
  - Causes Vasoconstriction
  - Inhibits microbe and viral multiplication, reduces nutrient availability, increases immune reactions

Phagocytosis

- Neutrophils
- Macrophages & Dendritic Cells

Neutrophils

- Early responders to inflammation
- Neutrophils are primary responders to bacterial infections and components of pus
- **Eosinophils,** the primary responders to parasitic infections (eukaryotes), are non-phagocytotic and recruited by players in the third line of defense.

Macrophages & Dendritic Cells

- Monocytes transform into scavenger cells that can reside in one particular location
  - Alveolar Cells, Kupffer Cells - Macrophages
  - Langerhans Cells - Dendritic cells

  or drift throughout the Reticuloedothelial System
- Macrophages & Dendritic cells
  - perform phagocytosis,
  - interact with B and T cells

Stem cells differentiate into macrophages in the bone marrow and peripheral blood, and then either migrate or take residence in a specific location.

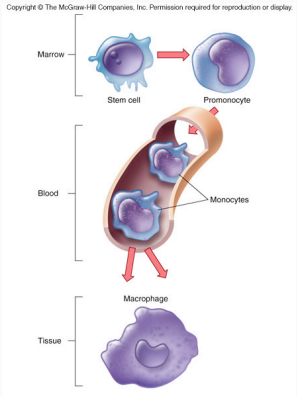

Fig. 14.17 The development stages of monocytes and macrophages.

Macrophages can take-up permanent residence in the lung (alveolar), liver (Kupffer) and skin (Langerhans).

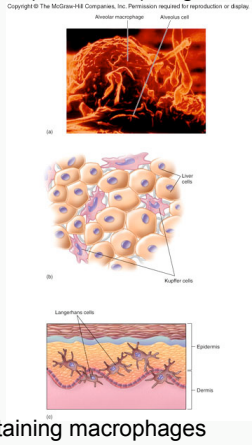

Fig. 14.18 Sites containing macrophages

Mechanism of phagocytosis

- Chemotaxis (Peptidoglycan, LPS, foreign debris))
- Ingestion (Phagocytes enclose the pathogen or foreign material, form a phagosome)
- Phagolysosome (Phagosomes fuse with the Lysosome forming the the Phagolysosome, where antimicrobial chemicals are released
- Destruction (Enzymes: Oxidative burst; Nitrosative burst

A summary of the mechanism of phagocytosis.

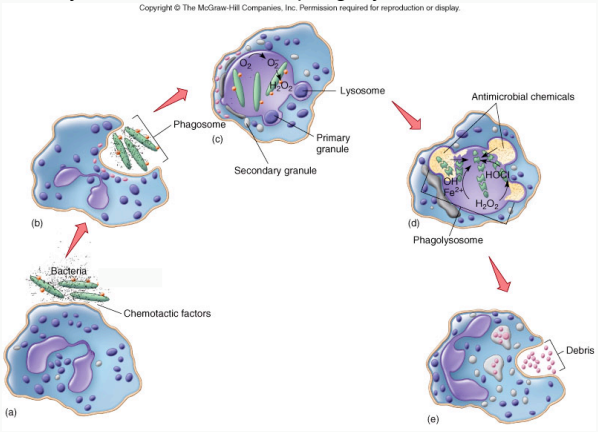

Fig. 14.19 The phases in phagocytosis

Interferon

- Synthesis: in WBCs & Tissue cells
- Produced in response to viral infections, microbe infections and other antigens, increased nucleic acid contents, immune products

Classes

- Interferon alpha
  - Product of lymphocytes and macrophages
- Interferon beta
  - Product of fibroblasts and epithelial cells
- Interferon gamma
  - Product of T lymphocytes

Activity

- A signal (induced by virus-cell interaction) is sent to the nucleus to synthesize (transcription and translation) interferon
- Interferon is secreted from cell
- Interferon binds to other host cells and induces production antiviral proteins (leads to inhibition of viral multiplication; I.e., by inhibition of translation)

Interferon is produced, released, and taken-up by a near-by cell, where by original cell is not protected but the recipient cell is protected.

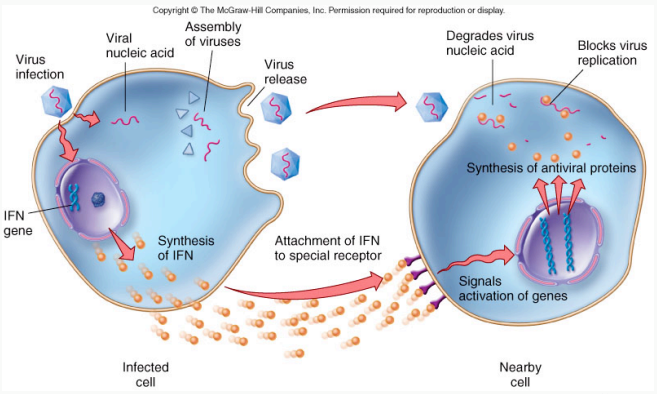

Fig. 14.20 The antiviral activity of interferon.

Other Roles of Interferon

- Activates and instructs T and B cell development
- Activates macrophages
- Inhibits tumor cell growth

Complement

- Consist of 26 blood proteins
- Produced by liver hepatocytes, lymphocytes, and monocytes

Pathways

- Classical
  - activated by the presence of antibody bound to microbes
- Lectin
  - activated when a host serum protein binds a particular sugar in the wall of fungi and other microbes
- Alternative
  - activated when complement proteins bind to cell wall or surface components of microbes

The three complement pathways, their activators, and the complement proteins involved.

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TABLE 14.1 Complement Pathways

Pathway	Activators	Host Components That Initially Bind	Complement Proteins Involved
Classical (Rapid, efficient)	Complement-fixing antibodies (IgG, IgM) (sometimes microbe surface components)	C1 complex	C1 complex, C4, C2, C3 → C5, C6, C7, C8, C9, Membrane Attack Complex
Lectin	Mannans	Mannose-binding lectin	→ C5, C6, C7, C8, C9, Membrane Attack Complex
Alternative (Slower, less efficient)	Bacterial or fungal cell wall, Viruses, Parasite surfaces	C3	C3, Factor B, Factor D, Properdin

Table 14.1 Complement pathways

Stages

- Initiation
- Amplification and cascade
- Polymerization
- Membrane attack

The classical pathway begins with C1 components binding to antibodies, and ends by puncturing small pores through the membrane, leading to lysis.

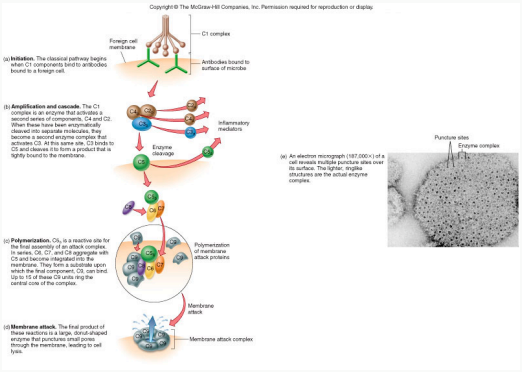

Fig. 14.21 Steps in the classical complement pathway at a single site.

Summary: Complement

- Different activators
- Different inflammatory mediators
- Formation of membrane attack complex
- Perforation and lysis of cells