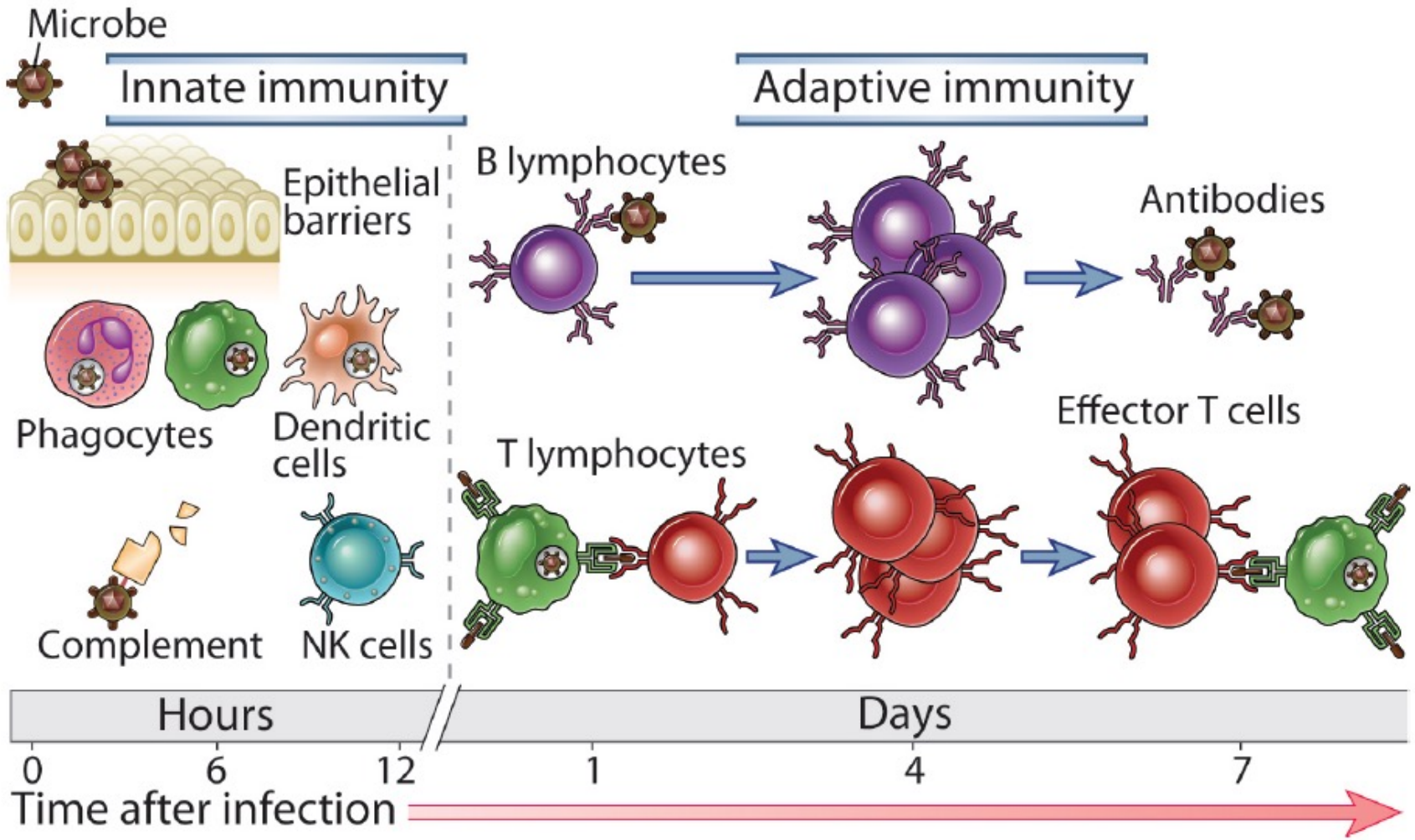
16 Oct 2023,
BT 304
Lecture 29

Immunity to different types of pathogens

Overview of Immunity



General features of Immune Responses to microbes

- **Effector mechanisms of innate and adaptive immunity**
  - Innate immune system: early defense (pathogens have evolved resistance mechanisms)
  - Adaptive immune system: more sustained and stronger response (more specific responses, expansion and memory)
- **Specialization of immune responses to types of microbes**
  - Generation of T_H1, T_H2, and T_H17 subsets of effector $CD4^+$ T cells -> production of different isotypes of antibodies
- **Microbes evade or resist the effector mechanisms of immunity**
  - Balance between host immune responses and microbial strategies for resisting immunity often determines the outcome of infections
- **Latent, or persistent, infections**
  - The immune response controls but does not eliminate the microbe and the microbe survives without propagating the infection
  - DNA viruses of the herpesvirus and poxvirus families, and some intracellular bacteria
  - Latent microbe may be reactivated, resulting in an infection
- **Tissue injury and disease may be caused by the host response**

Principal categories of pathogenic microbes

- Extracellular bacteria
- Intracellular bacteria
- Fungi
- Viruses
- Protozoan and multicellular parasites

Immunity to Extracellular Bacteria

Microbe	Examples of Human Diseases	Mechanisms of Pathogenicity
Staphylococcus aureus	Skin and soft tissue infections, lung abscess Systemic: toxic shock syndrome, food poisoning	Skin infections: acute inflammation induced by toxins; cell death caused by pore-forming toxins Systemic: enterotoxin ("superantigen")-induced cytokine production by T cells causing skin necrosis, shock, diarrhea
***Streptococcus pyogenes* (group A)**	Pharyngitis Skin infections: impetigo, erysipelas; cellulitis Systemic: scarlet fever	Acute inflammation induced by various toxins, e.g., streptolysin O damages cell membranes
Streptococcus pyogenes (pneumococcus)	Pneumonia, meningitis	Acute inflammation induced by cell wall constituents; pneumolysin is similar to streptolysin O
Escherichia coli	Urinary tract infections, gastroenteritis, septic shock	Toxins act on intestinal epithelium chloride and water secretion; endotoxin (LPS) stimulates cytokine secretion by macrophages
Vibrio cholerae	Diarrhea (cholera)	Cholera toxin ADP ribosylates G protein subunit, which leads to increased cyclic AMP in intestinal epithelial cells and results in chloride secretion and water loss
Clostridium tetani	Tetanus	Tetanus toxin binds to the motor end plate at neuromuscular junctions and causes irreversible muscle contraction
Neisseria meningitidis (meningococcus)	Meningitis	Acute inflammation and systemic disease caused by potent endotoxin
Corynebacterium diphtheriae	Diphtheria	Diphtheria toxin ADP ribosylates elongation factor 2 and inhibits protein synthesis

Pathogenicity of Extracellular Bacteria

- Capable of replicating outside host cells

- Two principal mechanisms of disease:

  - ✓ Induce inflammation- Tissue destruction at site of infection
  - ✓ Release toxins- diverse pathologic effects

Endotoxins vs Exotoxins

- Endotoxins:
  - components of bacterial cell walls
  - strong inducers of inflammation
- Exotoxins:
  - actively secreted by the bacteria
  - cytoxic
  - interfere with normal cellular functions without killing cells
  - production of cytokines that cause disease

CHARACTERISTIC	GRAM-POSITIVE BACTERIA	GRAM-NEGATIVE BACTERIA
Structural		
Outer membrane	Absent	Present
Peptidoglycan layer	Thick	Thin
Lipopolysaccharide	Absent	Present
Teichoic acids	Present in many species	Absent
Capsule, pili, flagella	Present in some species	Present in some species
Functional		
Lysozyme sensitivity	Very sensitive	Largely resistant
Antibiotic permeability	Very permeable to most	Impermeable to many
Sporulation	Some species	None
Exotoxin production	Some species	Some species

Rapid Review Microbiology and Immunology, Rosenthal & Tan, 3rd Edition

Innate Immunity to extracellular bacteria

- Complement activation
  - Alternative pathway: direct binding of C3b (Gram+ peptidoglycan, Gram- LPS)
  - Lectin pathway: Bacteria that express mannose
  - Enhanced phagocytosis of the bacteria
  - Membrane attack complex (*Neisseria species*)
  - Complement byproducts stimulate inflammatory responses by recruiting and activating leukocytes
- Phagocyte receptors
  - Promote phagocytosis
    - Mannose receptors and scavenger receptors
    - Fc receptors and complement receptors
  - Activation and stimulate microbicidal activities
    - Toll-like receptors (TLRs)
    - Fc and complement receptors
    - Secretion of cytokines and chemokines -> recruitment of leukocytes