INNATE IMMUNITY
Non-Specific Immune Response
Physiology
Unit 3
Protection Against Infection

• The body has several defenses to protect itself from getting an infection
  • Skin
  • Mucus membranes
  • Serous membranes
  • Chemicals

• If a pathogen does breach the barriers at the entrances to the body, then your immune system is activated
  • 2 branches of your immune system
    • Innate immunity (non-specific immune response)
    • Adaptive immunity (specific immune response)
Defenses to Prevent Infection
Physical Barriers

• **Skin**
  • Water tight barrier
  • Kept clean and dry
  • Sweat glands secrete antibodies, lysozyme
  • Mostly impermeable to microbes
    • Certain microbes drill through (syphilis, hook worms, many arthropod borne pathogens)

• Cough and sneeze reflex

• Hairs at the entrance of the nose
Defenses to Prevent Infection
Physical Barriers

• *Mucous membranes*
• Non-keratinized epithelial membranes, often ciliated
• Lined with mucus
• Contain antimicrobial chemicals
• Excellent for trapping microbes for expulsion
Defenses to Prevent Infection
Physical Barriers

• *Serous membranes*
  • Lubricated with serum from “leaky capillaries”
  • Internal physical barrier to infection of vital organs
  • Heart, lungs, and abdominal viscera
  • Similar protection by the meninges of the brain and spinal cord
Defenses to Prevent Infection
Non-specific Chemical Defenses

- **pH levels**
  - Gastric secretions
  - Vaginal secretions
  - Urine
  - Low pH is damaging to most cells

- **Lysozyme**
  - Found in body secretions:
    - Tears
    - Saliva
    - Sweat
  - Found in granules of neutrophils and macrophages
  - Binds to microbes and perforates the cell wall
Response to Infection
Immune System

• The bodies defense against infectious disease
• 2 branches of your immune system
  • Innate Immunity:
    • Non-specific immune response
    • Encounter and recognition of antigen
    • Includes multiple types of immune cells
    • Includes inflammatory response
  • Adaptive Immunity:
    • Specific Immune response
    • Activated after presentation of antigen by an APC
    • Response of lymphocytes to specific antigen
Response to Infection
Cell Signaling

• Immune cells secrete more than 100 different cytokines
• Cytokines mediate every step of the immune response
• Allow communication between different immune cells and timing of cascade reactions
• Most cytokines have local actions
  • Paracrine/autocrine agents
• Some will circulate in blood to distant tissues
  • Hormones
Cells of the Innate Immune Response
Non-specific Immune Response

• Diverse collection of cells that are found in extracellular fluid
  • Plasma
  • Lymph
  • Interstitium

• Non-specific Immune Response Cells
  • Neutrophils, eosinophils, basophils, monocytes
  • Macrophage
  • Dendritic cells
  • Mast cells
  • NK Cells
  • **B cells
Cells of the Innate Immune Response
Non-specific Immune Response

- **Leukocytes (WBC’s)**
  - Neutrophils, eosinophils, basophils, monocytes
  - Different WBC’s have different actions
  - Transported in plasma and migrate into the tissues where they function

**Diapedesis and Extravasation**
Cells of the Innate Immune Response
Non-specific Immune Response

• **Neutrophils**
  • Voracious phagocytes
    • Opsonify pathogens
  • Use lysozymes and superoxide (reactive O$_2$ species) to dissolve microbes ingested
  • Granules contain anti-microbial agents
Cells of the Innate Immune Response
Non-specific Immune Response

• **Neutrophils**
  - First WBC at an infection site mediated by chemical messengers
    - Chemotaxis
    - Endothelium, mast cells, macrophage
  - Short lived
    - 5-90 hours in circulation
    - 1-2 days in tissue
Cells of the Innate Immune Response

Non-specific Immune Response

- **Eosinophils**
  - Slightly phagocytic
  - Major role in infections involving eukaryotic parasites (worms)
  - Also involved in
    - Some allergic responses
    - Dissolving clots
    - Detoxifying foreign substances
Cells of the Innate Immune Response
Non-specific Immune Response

• **Basophils**
  • Actions are similar to mast cells of loose connective tissue
  • Granules contain
    • Heparin
    • Histamine
      • vasodilator, increases capillary permeability
  • Important in inflammation, especially related to allergies
Cells of the Innate Immune Response

Non-specific Immune Response

• **Monocytes**

• Differentiate into macrophage and dendritic cells after migration into local tissues

• Stored in the red pulp of the spleen
Cells of the Innate Immune Response
Non-specific Immune Response

• **Macrophage**
  • Derived from monocytes
  • Activate to macrophage in interstitium
  • Resident populations found in all tissues
  • Strategically located
  • Epithelia in contact with the outside of the body
    • Skin, lining of digestive and respiratory tract
    • Line blood and lymph vessels
Cells of the Innate Immune Response
Non-specific Immune Response

- Resident populations of macrophage
  - Kupfer Cells (liver)
  - Mesangial Cells (kidney)
  - Satellite Cells (PNS)
  - Microglia (CNS)
  - Dendritic Cells (skin)
  - Dust Cells (lungs)
  - Histocytes (c.t.)
  - Osteoclasts (bone)

- Macrophage are long lived
  - Several months

- Multiple actions of macrophage
  - Phagocytosis
  - Removal of cellular debris
  - Tissue repair
  - Wound healing
  - Inflammatory response

- APC
Cells of the Innate Immune Response
Non-specific Immune Response

• **Dendritic cells**
• Located in epithelium in contact with the external environment
• Macrophage function
• **APC**
Cells of the Innate Immune Response
Non-specific Immune Response

• **Mast cells**
  • Found in loose connective tissue
  • Are immature in circulation
  • Migrate into tissues where they mature
  • Undergo degranulation when activated
• Granules contain
  • Histamine
  • Eicosanoids
  • Chemokines
Cells of the Innate Immune Response

Non-specific Immune Response
Cells of the Innate Immune Response

Non-specific Immune Response

- **NK Cells**
  - Natural Killers
  - Lymphocyte like cell
  - Not immunologically specific
  - Performs tumor surveillance
Response to Infection
Inflammatory Response

• Inflammation accompanies many immune responses
  • Local response to infection or injury
  • Many immune processes
• Stimulated by the presence of infection or allergen
• Key mediators are phagocytic cells
  • Neutrophils, macrophages, dendritic cells
• Functions
  • To destroy foreign invaders
  • Prepare for tissue repair
• Signs: pain, heat, swelling, redness
Response to Infection
Inflammatory Response

Steps of the inflammatory response
1. Infection or injury causes release of chemicals
2. Local vasodilation
3. Increase in protein permeability resulting in diffusion of protein and filtration of fluid into interstitial fluid
4. Diapedesis and extravasation of leukocytes from venules into interstitial fluid of infected/injured area
5. Destruction of bacteria
6. Tissue repair
Response to Infection
Antigen Presentation

• Once antigen has been encountered and recognized by the cells of the non-specific immune response

• The antigen must be presented to a lymphocyte to initiate adaptive branch of the immune system (specific immune response)

• Antigen Presenting Cells (APC’s)
  • Macrophage
  • Dendritic cells
  • B cells
Response to Infection
Destruction of Antigen

• Once the specific immune response has been initiated, antibodies are produced for the antigen
• Antibodies neutralize antigen
• The antigen that is bound by antibody must be destroyed
• There are different ways to destroy antigen, depending on what the antigen is
  • Destruction of antigen is only specific to the type of antigen
  • Bacteria, virus, etc
Response to Infection
Destruction of Antigen

- **Destruction of Bacteria**
  - Compliment Pathway
  - Macrophage

- **Destruction of Virus**
  - Interferons (**)
  - Proteosomes
  - Macrophage
Response to Infection
Destruction of Bacteria

• **Compliment Pathway** (*classical pathway*)
  • Extracellular destruction of bacteria without phagocytosis
  • A suite (or family) of plasma proteins
    • Sequential activation of compliment proteins
    • C1 must be activated first
  • **Antibodies activate** the first complement protein (C1)
    • Can involve opsonization by the antibody
    • C1 binds to the constant arm of an antibody
    • The variable arms of the antibody are bound to a bacterium
  • The end result is the formation of a pore in the membrane of the bacterium
    • The contents of the bacterial cell leak out
    • The bacterium dies

Opsonization is a chemical attractant “To make tasty”
Response to Infection
Destruction of Bacteria
Response to Infection
Destruction of Bacteria
Response to Infection
Destruction of Virus (**)

- **Interferons**
  - Interferon family of cytokines
  - Released by virus infected body cells
  - Act as paracrine agents
  - Interferon released by a cell infected with virus
  - Interferon binds to cells in close proximity
  - Nonspecifically inhibits viral replication in cells before they become infected
    - Protection for healthy cells against newly released viruses
    - Host (tissue) specific, not virus specific
Response to Infection
Destruction of Virus
Response to Infection
Destruction of Virus

- Proteosomes
  - Protein complexes
  - Degrade un-needed, damaged, viral proteins
- Non-specifically destroy proteins
- Virus have a protein coat
- Proteases cleave peptide bonds
  - Proteolysis

How the proteasome acts?

[Diagram showing proteasome activity with ubiquitin ligase complex, polyubiquitylation, ATP, and proteolysis leading to antigen presentation]