INNATE IMMUNITY
Non-Specific Immune Response
In Physiology Today

[Diagram showing mast cell with arrows labeled "injury," "complement," and "antibodies," and boxes listing products of degranulation (histamine, leukocyte chemotactic factors) and products of synthesis (prostaglandins, thromboxanes, leukotrienes).]
Resistance to Disease

• Body defenses against infectious disease

• Immune system has 2 arms:
  – Innate or non-specific immunity
  – Adaptive or specific immunity
Immune Cells

- Diverse collection of cells that are found in blood, lymph and tissues throughout the body
- **Cytokines**
  - Chemical messengers secreted by immune cells

- **Cells**
  - Leukocytes
  - Plasma cells
  - Macrophages
  - Dendritic cells
  - Lymphocytes
  - Mast cells
Immune Cells

• **Leukocytes**
  – Use blood primarily for transport and migrate to the tissues where they function

• **Plasma cells**
  – Found in tissues (lymph nodes) where they differentiate from B lymphocytes
  – Synthesize and secrete antibodies
Immune Cells

• **Macrophages**
  - Found in all organs and tissues strategically placed where they will encounter their targets
    - Epithelia in contact with the outside of the body
      - skin, lining of digestive and respiratory tract
      - Line blood and lymph vessels
  - Tissue specific resident populations
  - Derived from monocytes, transform into macrophages
  - Pass through walls of capillaries to enter tissues
    - Diapedesis and extravasation
Macrophage

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

- Macrophage are long lived (several months)
- APC role
- Removal of cellular debris
- Inflammatory response
- Tissue repair
- Wound healing
Diapedesis or Extravasation

- Bacteria
- Phagocytosis of bacteria
- Capillary wall
- Neutrophil
- Rolling
- Capture
- Adhesion and activation
- Spreading
- Extravasation
Immune Cells

- **Dendritic cells**
  - Epithelium in contact with the external environment,
  - Macrophage function
  - Migrate to lymph nodes
    - APC’s
    - Present to T Cells
    - Messengers between innate and adaptive immunity
Lymphocytes

Recognition cells in specific immune defenses and are essential for all aspects of specific immune responses.
Immune Cells

- **Mast cells**
  - Found in connective tissues (especially below epithelial surfaces of the body)
  - Move into tissues where they differentiate and divide
  - Contain vesicles that contain histamine and heparin
Cytokines

• Immune cells secrete more than 100 protein messengers that regulate host cell division
• Involved in non-specific and specific immune defenses
• Most of their actions act locally
  – Paracrine/autocrine agents
  – Some will circulate in blood and act as hormones on distant organs
• Allow communication between different immune cells and timing of cascade reactions
Nonspecific Immune Defenses

*Innate Immune Response*

- Against all “non-self” cells
- Recognize some general property marking the invaders as foreign
  - Antigens
- Not dependent upon exposure to disease
- Include: defenses at the body surfaces, the inflammatory response, interferons
Defenses at the Body Surface

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 at the Body Surface

Physical Barriers

• *Mucous membranes*
  • Nonkeratinized epithelial membranes, often ciliated
  • Lined with mucus
  • Contain antimicrobial chemicals
  • Excellent for trapping microbes for expulsion
Defenses at the Body Surface

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
Nonspecific Chemical Defenses

• pH levels
  – Gastric juice, vaginal secretions, urine

• Lysozyme
  – In tears, saliva, sweat
  – Binds to microbes and punches holes in the cell wall
  – Found in granules of neutrophils and macrophages
Nonspecific Cellular Defenses

- **Neutrophils**
- First WBC at an infection site
- Voracious phagocytes
- Microphage
- Use lysozymes and oxygen radicals to dissolve microbes
Nonspecific Cellular Defenses

- **Eosinophils**
- Slightly phagocytic
- Major role in infections involving eukaryotic parasites (worms)
- Also involved in certain allergies, dissolving clots, detoxifying foreign substances
Nonspecific Cellular Defenses

- **Basophils**
- Similar to mast cells of loose connective tissue
- Granules contain
  - Heparin
  - Histamine
    - vasodilator, increases capillary permeability
- Important to inflammation, especially related to allergies
Nonspecific Cellular Defenses

- **Monocytes**
- Transform when activated to macrophages
- “Eat” microbes and cellular debris
- Stored in the red pulp of the spleen
- *Link nonspecific body defenses to the specific immune responses*  
  – *APC*
Nonspecific Cellular Defenses

- Natural Killers
- NK Cells
- “lymphocyte like cell”, but not immunologically specific
- Performs tumor surveillance
Inflammation

• Local response to infection or injury
• Functions
  – To destroy foreign invaders
  – Prepare for tissue repair
• Key mediators are phagocytic cells
  – Neutrophils, macrophages, dendritic cells
Inflammation

• Inflammation accompanies many immune responses
• Involves phagocytosis and many immune processes
• First WBC at infection site: neutrophil
• Stimulated by the presence of infection or allergen
• Signs: pain, heat, swelling, redness
Inflammation

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: movement of leukocytes from venules into interstitial fluid of infected/injured area
5. Destruction of bacteria
6. Tissue repair
Complement Pathway

• A “suite” (or family) of plasma proteins
• Extracellular killing of bacteria without phagocytosis
• Sequentially bind to bacteria, forming a pore, causing lysis

• **Antibodies activate** the first complement protein (C1)

• Some form opsonins
  – Make microbes “tasty”
  – Chemical attractant for phagocytes
  – Molecule that enhances phagocytosis
Complement

1. Bacterial membrane
2. Antibody
3. Complement protein C4

Soluble complement (involved in chemotaxis)

Complement fixation

C4_a
C4_b
Complement
Interferons

• Nonspecific chemical defenses in plasma
• *Interferon* family of cytokines
• Nonspecifically inhibit viral replication in cells
  – Protection for healthy cells against newly released viruses
  – Host (tissue) specific, not virus specific
• Released by virus infected body cells
Interferon Action

1. Viral RNA
2. Nucleus
3. Interferon
4. Translation
5. Antiviral proteins (AVPs)

Virus-infected host cell

Transcription

Translation

Transcription