Defense Wins Games!
Nonspecific Host Defenses

Nonspecific Defenses of the Host

- Susceptibility- Lack of resistance to a disease
- Resistance- Ability to ward off disease
- Nonspecific resistance- Defenses against any pathogen
- Specific resistance- Immunity, resistance to a specific pathogen

Defense Mechanisms

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

First line of defense

- Barriers
  - Anatomical
  - Chemical
  - Genetic

Anatomical barriers

- Skin
  - Outermost layer
  - Hair follicles
  - Skin glands
  - Epidermis consists of tightly packed cells with keratin, a protective protein.
- Mucous membrane
  - Digestive
  - Urinary
  - Respiratory
  - Eye
  - Ciliary escalator: Microbes trapped in mucus are transported away from the lungs

Chemical barriers

- Sebaceous secretions
  - Fungistatic fatty acid in sebum
- Eyelid glands – meibomian gland
- Tears and saliva – lysozyme
- Acidic pH
  - Sweat
  - Stomach
  - Skin
  - Semen
  - Vagina

Genetic barriers

- Different level of sensitivity and resistance to infectious agents
  - Malaria
  - Tuberculosis
  - Leprosy
  - Fungal infections

Normal Microbiota

- Microbial antagonism/competitive exclusion: Normal microbiota compete with pathogens.
  - Remember *C. difficile*?
  - Yogurt?
  - Skin microflora?
- This is not true just in animals
  - Microbial symbiotic relationships

Second line and Third line of defense

- Defines immunology
- Protective cells

Immunology

- Study of the development of resistance to infectious agents by the body
  - Surveillance of the body
  - Recognition of foreign material
  - Destruction of foreign material or agent
- Involve nonspecific and specific immune defense systems
- White blood cells (WBCs) or leukocytes are involved

White Blood Cells

- WBCs recognize self markers on the host cell
  - Do not attack or do not respond to host cell
- WBCs recognize non-self markers on the invading microbe
  - Attack or respond to microbe

Systems

- All systems are integrated
  - Reticuloendothelial system (RES)
  - Extracellular fluids system (ECF)
  - Blood or circulatory
  - Lymphatic

Reticuloendothelial (RES)

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

Extracellular fluid (ECF)

- The spaces surrounding tissue cells and RES
- Enable immune cells to move

Blood

- Stem cells precursors
- Hematopoiesis
- Components

Stem cells

- From blood cells
  - Red blood cells (RBCs)
  - Platelets
- Hematopoietic stem cells in bone marrow
  - Neutrophils, basophils, eosinophils, monocytes
- Lymphoid stem cells
  - T cells
  - B cells

Hematopoiesis

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

Components of blood

- White blood cells or leukocytes
- Red blood cells
- Platelets

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 immune response (inflammation)

Eosinophils

- Nuclei – bi-lobed

- 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

- Specific immunity
  - T cells
  - B cells
- Present throughout the body

Monocytes

- Agranulocyte
- 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

Lymphatic system

- Fluids
- Vessels
- Nodes
- Spleen
- Thymus
- Miscellaneous

Fluids

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

Vessels

- Parallels the blood system
- Returns lymph to the blood system
- Movement of lymph depends on 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 channels and blood vessels
  - in the thoracic and abdominal cavity regions, armpit, groin and neck
- Filter for the lymph
- Provide environment for immune reactions

Spleen

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

Thymus

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

Gut-associated lymphoid tissue (GALT)

- Recognizes incoming microbes from food
- Supply lymphocytes for antibody response
- Ex. Appendix, lacteals, Peyer's patches

Non-specific Immunity

- Inflammation
- Phagocytosis
- Interferon
- Complement

Inflammation

- Five major symptoms
  - Heat
  - Redness

- Pain
- Swelling
- Loss of function

Inflammation

- Causes
- Function
- Stages

Causes

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

Function

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

Stages

- Vascular changes
- Edema
- Fever

Vascular changes

- Blood cells, tissue cells, and platelets release chemical mediators and cytokines
- Chemical mediators
  - Vasoactive
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines)
    - Affect WBC

Chemical mediators

- Cause fever, stimulate lymphocytes, prevent virus spread, cause allergic reactions
  - Vasoactive mediators
    - Affect endothelial cells, smooth muscles of blood vessels
  - Chemotactic (chemokines) mediators
    - Affect WBC

Edema

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

Fever

- Caused by pyrogens
  - reset the hypothalamic thermostat (increase temperature)
  - Vasoconstriction
- Pyrogens
  - Microbes and their products (ex. LPS)
  - Leukocyte products (ex. lnterleukins)
- Inhibits microbe and viral multiplication, reduces nutrient availability, increases immune reactions

Phagocytosis

- Neutrophils and eosinophils
- Macrophages
- Mechanism

Neutrophils and eosinophils

- Early responders to inflammation
- Neutrophils are primary components of pus
- Eosinophils are primary responders to parasitic infections

Macrophages

- Monocytes transform into macrophages
- Scavengers
  - Histiocytes – reside in one location (ex. Alveolar, Kupffer, Langerhans)
  - Drift throughout the RES
- Undergo phagocytosis
- Interact with B and T cells

Mechanism

- Chemotaxis
- Ingestion
- Phagolysosome
- Destruction

Chemotaxis

- Directed by
  - Pathogen-associated molecular patterns (PAMPs)
    - Peptidoglycan
    - LPS
  - Foreign debris

Ingestion

- Pseudopods enclose the pathogen or foreign material
- Form a phagosome

Phagolysosome

- Lysosomes fuse with the phagosome

- Other antimicrobials chemicals are released into the phagolysosome

Destruction

- Within the phagolysosome
  - Oxygen-dependent system
    - Oxidative burst (oxidizing agents)
  - Enzymes
  - Nitric oxide
- Undigestible debris are released

Interferon

- Produced due to viral infections, microbe infections, RNA, immune products, and antigens

Interferon

- Synthesis
- Classes
- Activity

Synthesis

- WBCs
- Tissue cells

Classes

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

Activity

- Ex. Virus - binds to host cell
- A signal is sent to the nucleus to synthesized (transcription and translation) interferon
- Interferon is secreted
- Binds to other host cells
- Host cells produce antiviral proteins
  - inhibit viral multiplication or translation
    - Not virus-specific

Other Roles of Interferon

- Activates and instructs T and B cell development
- Inhibits cancer cells
- Activates macrophages

Complement

- Consist of 26 blood proteins

- Produced by liver hepatocytes, lymphocytes, and monocytes
- Pathways
- Cascade reaction
- Stages

Pathways

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

Stages

- Initiation
- Amplification and cascade
- Polymerization
- Membrane attack

The Classical Complement System

- Serum proteins activated in a cascade.

Some bacteria evade complement

- Capsules prevent C activation
- Surface lipid-carbohydrates prevent MAC formation
- Enzymatic digestion of C5a