Nonspecific Defense

- **Barriers** – first line of defense
  - **Physical (anatomical) barriers**
    - Skin
    - Mucous membranes
    - Respiratory cilia
  - **Chemical barriers** – antimicrobial properties factors contained in:
    - Secretions from sebaceous and sweat glands give the skin a pH ranging from 3 to 5,
    - Lysozymes in:
      - Mucus
      - Tears
      - Saliva
      - HCl
  - **Biological barriers** – the actual presence of symbionts prevents other microbes from establishing residence

- **INNATE IMMUNITY**
  - Recognition of traits shared by broad ranges of pathogens, using a small set of receptors
  - Rapid response

- **Barrier defenses:**
  - Skin
  - Mucous membranes
  - Secretions

- **Internal defenses:**
  - Phagocytic cells
  - Antimicrobial proteins
  - Inflammatory response
  - Natural killer cells

- **ACQUIRED IMMUNITY**
  - Recognition of traits specific to particular pathogens, using a vast array of receptors
  - Slower response

- **Humoral response:**
  - Antibodies defend against infection in body fluids.

- **Cell-mediated response:**
  - Cytotoxic lymphocytes defend against infection in body cells.
Inflammatory response – second line of defense when first line breached by bacteria for example
  - Locally - cells in area of breach release mast cells histamines and other chemicals which:
    - Increase blood flow to area
    - Localized temperature
    - Increase permeability of capillary endothelium
      - Fluid accumulates – swelling
      - White blood cells (macrophages, neutrophils and macrophages) squeeze through the wall of blood vessels into tissue
    - Engulf invading bacteria literally killing microbes and eventually self
      - Neutrophils 60-70% of leukocytes in blood (short-lived)
      - Monocytes 5% of leukocytes in blood enter tissue to become macrophages (long-lived)
    - Release chemicals
      - Chemokines – attract more phagocytes
      - Interleukin – stimulates cells associated with immune response to proliferate
      - Lactoferrin – directly kills bacteria
      - Endogenous pyrogen – trigger release of prostaglandins that increase set point for “thermostat” in hypothalamus
  - Clotting cascade walls off area
  - Symptoms – area becomes swollen, hot, red and painful; pus may form
    - Systemic changes – to prevent microbes such as bacteria from spreading beyond local area
      - Fever
      - Proliferation of phagocytic white blood cells (elevated WBC count)
• Role of lymph system

- Some macrophages migrate throughout the body
- Others reside permanently in certain tissues, including the lung, liver, kidney, connective tissue, brain, and especially in lymph nodes and the spleen
- The fixed macrophages in the spleen, lymph nodes, and other lymphatic tissues are particularly well located to contact infectious agents
  - Interstitial fluid taken up by lymphatic capillaries, flows as lymph, eventually returning to the blood circulatory system
  - Along the way, lymph must pass through numerous lymph nodes, where any pathogens present encounter macrophages and lymphocytes
  - Also, microorganisms, microbial fragments, and foreign molecules that enter blood encounter macrophages when they become trapped in netlike architecture of spleen

• Interferons
  - Produced in response to viral infections
  - Do not act directly on the invading viruses but rather stimulate the body’s own cells to resist
  - Three different classes of interferons – all small proteins
  - Cells attacked by viruses release interferon – doesn’t help the cell but binds to other cells to:
    - Stimulate healthy cells to produce antiviral enzymes that block viral reproduction.
    - Stimulate certain white blood cells involved in both inflammatory & immune responses

Immune System – Specific Response
• Antibody mediate immunity
  - B lymphocytes or B cells
    - Produced in red bone marrow
    - Capable of producing antibodies (immunoglobulins)
    - Production triggered by presence of antigens – chemicals (usually foreign protein or polysaccharides) that the body recognizes as “not self”
      - Surface proteins and polysaccharides of cell of foreign cell
      - Proteins such as toxins produced by pathogens
    - Antibodies “fit” antigens and bind to them - very specific
Action

- Inactive B cells circulate everywhere (about 2 trillion present at any one time)
- Antigen receptors protrude from surface of B cells can match up to specific antigen
- Problem: huge number of possible antigens – would need incredible numbers of B cells to be able to fight all possible antigens
- Solution – activation of a few inactive B cells for a particular antigen – clonal selection

- Come in contact with antigen – cell enlarges and begins synthesizing proteins
- Under the influence of a prostaglandin called interleukin (il-2), cells divide rapidly to make many more of this particular B cell which begins to differentiate into two types of B cell -
  - Plasma or effector cells – specialized to synthesize and secrete antibodies (3,000 – 30,000 molecules/sec.) Which are released into blood – short lived cells
  - Memory cells – long lived cells that are responsible for immunity to future infections
- **Types of immunity**
  - Active
    - Natural – experience with actual pathogen
    - Artificial – vaccines
  - Passive
    - Natural – transfer of antibodies from mother to fetus/baby
    - Artificial – antitoxins, immunoglobulin shots
- **Structure and action of antibodies**
  - Y shaped
    - Heavy and light chains
    - Constant and variable regions
  - An antibody interacts with a small, accessible portion of the antigen called an epitope or antigenic determinant
  - A single antigen such as a bacterial surface protein usually has several effective epitopes, each capable of inducing the production of specific antibody
  - 5 classes of immunoglobulins are made
  - Action
Cell-mediated immunity

- T lymphocytes or T cells – attack eukaryote cells
  - Two primary types
    - Destroyers of foreign eukaryote cells (e.g. parasites) and body’s own cells
      - Cytotoxic T (T_C) cells (CD8 glycoprotein on surface)
    - Regulators of the immune response
      - Helper T cells (T_H) (CD4 glycoprotein on surface) – HIV attacks these!
- Produced in red bone marrow during development but move to thymus where they differentiate
- Like B cells very specific; mature in a similar fashion to B cells (memory and plasma cells) but role played is different – do not make antibodies
- Recognition not based on antigens on surface of cells but on special glycoproteins found on surface of eukaryote cells – coded by genes called MHC
  - As many as twenty different types
  - Many different versions of each type
  - Many possible combinations – no two humans likely to have same combination except identical twins
- Tissue typing and transplant rejection
  - Two types
    - Class I MHC – found throughout body – recognized by T_C cells
    - Class II MHC – found only on immune system cells – recognized by T_H cells

Functions of T cells

- Cytotoxic T cells – how do we destroy foreign cells or our own infected cells (e.g., cells infected with viruses)
- Foreign cells have foreign class I MHCs – infected cells have class I MHCs that have been modified by antigen
- Receptor on inactive cytotoxic T cell matches to these MHCs
- Activation, proliferation and differentiation produce active cytotoxic T cells and memory cells
- Active cytotoxic T cells bind to class I MHCs and lyse the cell
- Active cytotoxic T cells also make lymphokines, another prostaglandin
  - Lymphokines attract macrophages which clean up debris and destroy things such as viruses that were in the infected cell
- Helper T cells – react to modified class II MHCs found on surface of macrophages or B cells that have encountered foreign microorganisms
  - Inactive T cell encounters modified (by presence of antigen) class II MHC on surface of macrophage or inactive B cell
  - Activation, proliferation and differentiation produce active helper T cells and memory cells
  - Active helper T cells secrete interleukins which stimulate cytotoxic T cells and B cells following their activation

- Active helper T cells are also essential in directly establishing full activation of B cells
HIV knocks out these T helper cells and therefore immune response greatly diminished

- Rare cancers karposi’s sarcoma – compromised cytotoxic T cell production
- Rare infections compromised B cell production