

phagocytic leukocyte

lymphocytes attacking cancer cell

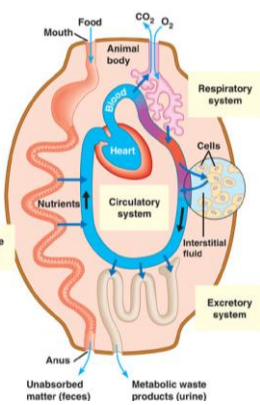
lymph system

Chapter 18

Immune System

Avenues of Attack

- Points of entry
 - digestive system
 - respiratory system
 - urogenital tract
 - break in skin
- Routes of attack
 - circulatory system
 - lymph system

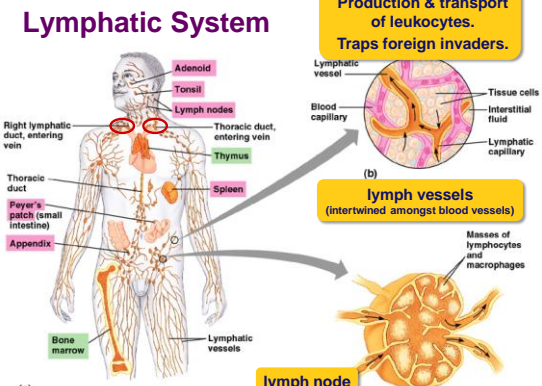


Why even have an immune system?

- Attack from outside
 - lots of organisms want you for lunch!
 - animals are a tasty nutrient- & vitamin-packed meal
 - cells are packages of macromolecules
 - no cell wall
 - traded mobility for susceptibility
 - animals must defend themselves against invaders
 - viruses: HIV, flu, cold, measles, chicken pox, SARS
 - bacteria: pneumonia, meningitis, tuberculosis
 - fungi: yeast ("Athlete's foot"...)
 - protists: amoeba, Lyme disease, malaria
- Attack from inside
 - defend against abnormal body cells: **cancer**

Lymphatic System

Production & transport of leukocytes. Traps foreign invaders.

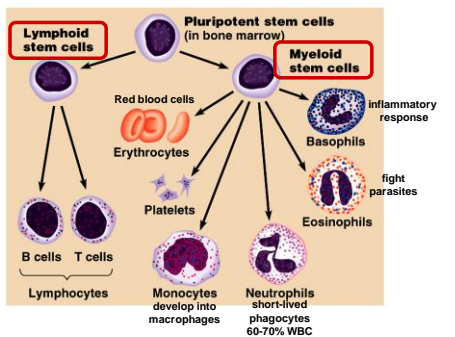


Adenoid, Tonsil, Lymph nodes, Thymus, Spleen, Thoracic duct, entering vein, Right lymphatic duct, entering vein, Thoracic duct, Peyer's patch (small intestine), Appendix, Bone marrow, Lymphatic vessels, Lymph node

lymph vessels (intertwined amongst blood vessels)

Masses of lymphocytes and macrophages

Development of Blood Cells



Pluripotent stem cells (in bone marrow)

Lymphoid stem cells → B cells, T cells → Lymphocytes


Myeloid stem cells → Erythrocytes, Platelets, Basophils, Eosinophils, Neutrophils (short-lived phagocytes 60-70% WBC), Monocytes (develop into macrophages)

inflammatory response

fight parasites


Lines of Defense

- 1st line: **Barriers**
 - broad, external defense
 - "walls & moats"
 - skin & mucus membranes
- 2nd line: **Non-specific patrol**
 - broad, internal defense
 - "patrolling soldiers"
 - leukocytes = **phagocytic WBC**
 - macrophages
- 3rd line: **Immune system**
 - specific, acquired immunity
 - "elite trained units"
 - lymphocytes & antibodies
 - B cells & T cells



1st line: External Defense

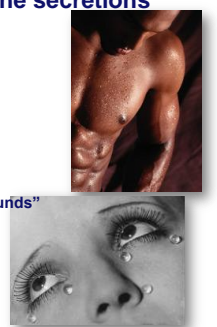
- Physical & chemical defenses
 - ◆ non-specific defense
- external barrier
 - ◆ epithelial cells & mucus membranes
 - skin
 - respiratory system
 - digestive system
 - uro-genital tract



Lining of trachea: ciliated cells & mucus secreting cells

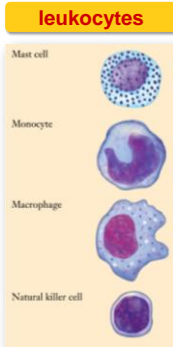
1st line: Epithelial Chemical Barriers

- Skin & mucous membrane secretions
 - ◆ sweat
 - pH 3-5
 - ◆ tears
 - washing action
 - ◆ mucus
 - traps microbes
 - ◆ saliva
 - anti-bacterial = "lick your wounds"
 - ◆ stomach acid
 - pH 2
 - ◆ anti-microbial proteins
 - lysozyme enzyme
 - digests bacterial cell walls



2nd line: Internal, Broad Range Patrol

- Innate, general defense
 - ◆ rapid response
- Patrolling proteins & cells
 - ◆ attack invaders that penetrate body's outer barriers
 - complement system
 - ◆ anti-microbial proteins
 - inflammatory response
 - **leukocytes**
 - ◆ **phagocytic** white blood cells

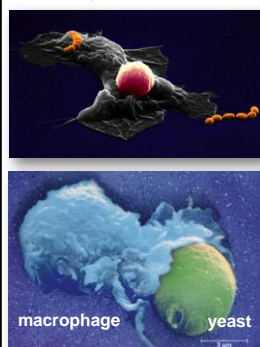
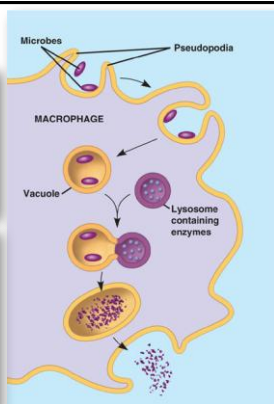


Leukocytes: Phagocytic WBCs

- Attracted by chemical signals released by damaged cells
 - ◆ enter infected tissue, engulf & ingest microbes
 - **lysosomes**
- **Neutrophils**
 - ◆ most abundant WBC (~70%)
 - ◆ ~ 3 day lifespan
- **Macrophages**
 - ◆ "big eater", long-lived
- **Natural Killer Cells**
 - ◆ destroy virus-infected cells & cancer cells

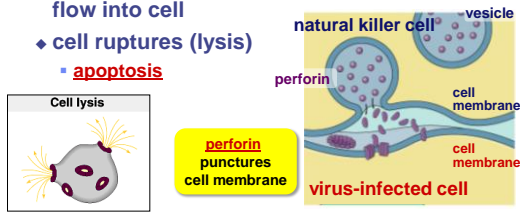


Phagocytes

Destroying cells gone bad!

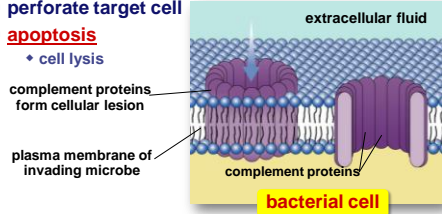
- "Natural Killer Cells" perforate cells
 - ◆ release **perforin** protein
 - ◆ insert into membrane of target cell
 - ◆ forms pore allowing fluid to flow into cell
 - ◆ cell ruptures (lysis)
 - **apoptosis**



Anti-microbial Proteins

Complement system

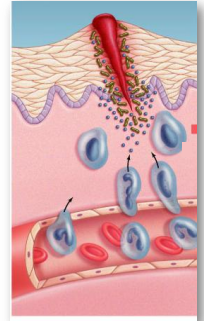
- ◆ ~20 proteins circulating in blood plasma
- ◆ attack bacterial & fungal cells
 - form a **membrane attack complex**
 - perforate target cell
 - **apoptosis**
 - ◆ cell lysis



Inflammatory Response

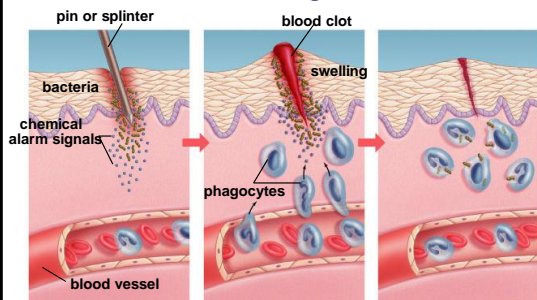
Damage to tissue triggers local non-specific inflammatory response

- ◆ release **histamines** & **prostaglandins**
- ◆ capillaries dilate, more permeable (leaky)
 - increase blood supply
 - delivers WBC, RBC, platelets, clotting factors
 - fight pathogens
 - clot formation
 - accounts for swelling, redness & heat of inflammation & infection



Inflammatory Response

Reaction to tissue damage



Fever

When a local response is not enough

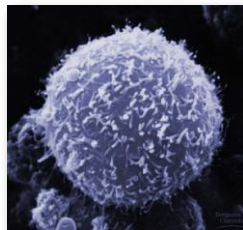
- ◆ systemic response to infection
- ◆ activated macrophages release **interleukin-1**
 - triggers **hypothalamus in brain** to readjust body thermostat to raise body temperature
- ◆ higher temperature helps defense
 - inhibits bacterial growth
 - stimulates phagocytosis
 - speeds up repair of tissues
 - causes liver & spleen to store iron, reducing blood iron levels
 - ◆ bacteria need large amounts of iron to grow



3rd line: Acquired (active) Immunity

Specific defense

- ◆ **lymphocytes**
 - B lymphocytes (**B cells**)
 - T lymphocytes (**T cells**)
- ◆ **antibodies**
 - **immunoglobulins**



Responds to...

- ◆ **antigens**
 - specific pathogens
 - specific toxins
 - abnormal body cells (**cancer**)

How are invaders are recognized...

Antigens

- ◆ proteins that serve as cellular name tags
 - **foreign antigens** cause response from WBCs
 - ◆ viruses, bacteria, protozoa, parasitic worms, fungi, toxins
 - ◆ non-pathogens: pollen & transplanted tissue
 - ◆ **antigenic determinants** are the sites on the antigens that the immune system recognizes

B cells & T cells respond to different antigens

- ◆ B cells recognize **intact antigens**
 - pathogens in blood & lymph
- ◆ T cells recognize **antigen fragments**
 - pathogens which have already infected cells



Lymphocytes

- B cells**
 - mature in **bone marrow**
 - humoral** response system
 - "humors" = body fluids
 - produce antibodies
- T cells**
 - mature in **thymus**
 - cellular** response system

Learn to distinguish "self" from "non-self" antigens during maturation

- if they react to "self" antigens, they are destroyed during maturation

B cells

- Humoral response** = "in fluid"
 - defense against attackers circulating freely in blood & lymph
- Specific response**
 - produce specific **antibodies** against specific **antigen**
- Types of B cells**
 - plasma cells**
 - immediate production of antibodies
 - rapid response, short term release
 - memory cells**
 - long term immunity

Antibodies

- Proteins that bind to a specific antigen**
 - multi-chain proteins produced by B cells
 - binding region matches molecular shape of antigens
 - each antibody is unique & specific
 - millions of antibodies respond to millions of foreign antigens
 - tagging "handcuffs"
 - "this is foreign...gotcha!"

each B cell has ~100,000 antigen receptors

Structure of Antibodies

How do vertebrates produce millions of antibody proteins, if they only have a few hundred genes coding for those proteins?

By **DNA rearrangement** & **somatic mutation** vertebrates can produce millions of B & T cells

How Antibodies Work

Binding of antibodies to antigens inactivates antigens by:

- Neutralization** (blocks viral binding sites; coats bacteria and/or spores)
 - Virus
 - Bacterium
- Agglutination of antigen-bearing particles, such as microbes**
 - Bacteria
- Precipitation of soluble antigens**
 - Soluble antigens
- Complement fixation (activation of complement)**
 - Foreign cell
 - Leads to **Cell lysis**

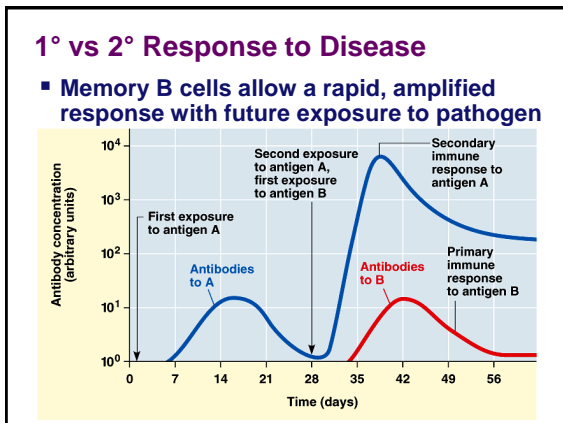
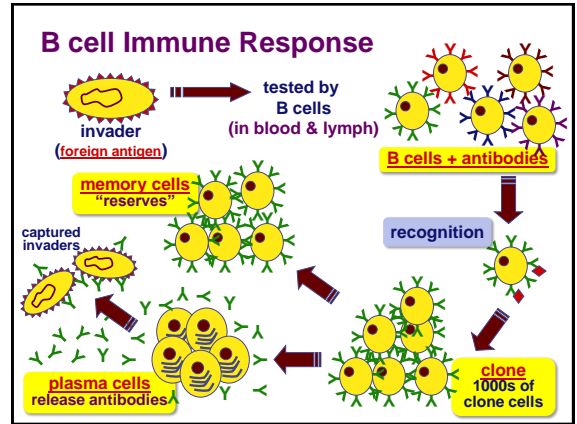
invading pathogens tagged with antibodies

macrophage eating tagged invaders

Enhances **Phagocytosis** (Macrophage)

Classes of Antibodies

- Immunoglobulins
 - IgM**
 - 1st immune response
 - activate complement proteins
 - IgG**
 - 2nd response, major antibody circulating in plasma
 - promote phagocytosis by macrophages
 - IgA**
 - in external secretions, sweat & mother's milk
 - IgE**
 - promote release of histamine & lots of bodily fluids
 - evolved as reaction to parasites
 - triggers allergic reaction
 - IgD**
 - receptors of B cells



Jonas Salk

- Developed first vaccine
 - against polio
 - attacks motor neurons

Albert Sabin
1962
oral vaccine

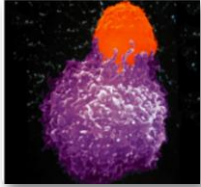


Passive Immunity

- Obtaining antibodies from another individual
- Maternal immunity
 - antibodies pass from mother to baby across placenta or in mother's milk
 - critical role of breastfeeding in infant health
 - mother is creating antibodies against pathogens baby is being exposed to
- Injection
 - injection of antibodies
 - short-term immunity

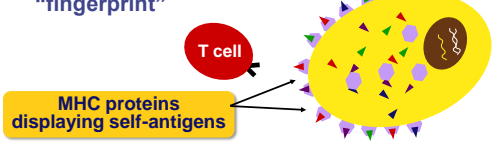
T cells

- **Cell-mediated response**
 - ◆ immune response to infected cells
 - viruses, bacteria & parasites (pathogens) within cells
 - ◆ defense against “non-self” cells
 - cancer & transplant cells
- **Types of T cells**
 - ◆ helper T cells
 - alerts immune system
 - ◆ killer (cytotoxic) T cells
 - attack infected body cells



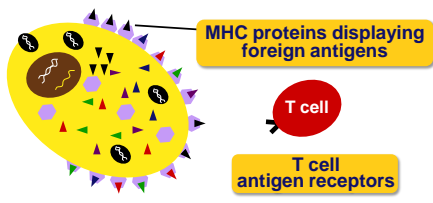
How Cells Are Tagged With Antigens

- **Major histocompatibility (MHC) complex**
 - ◆ antigen glycoproteins
- MHC proteins constantly carry bits of cellular material from the cytosol to the cell surface
 - ◆ “snapshot” of what is going on inside cell
 - ◆ give the surface of cells a unique label or “fingerprint”

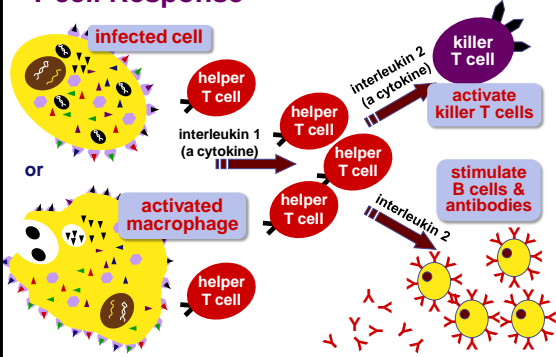


How do T cells know a cell is infected?

- Infected cells digest pathogens & MHC proteins bind & carry pieces to cell surface
 - ◆ antigen presenting cells
 - ◆ alerts Helper T cells

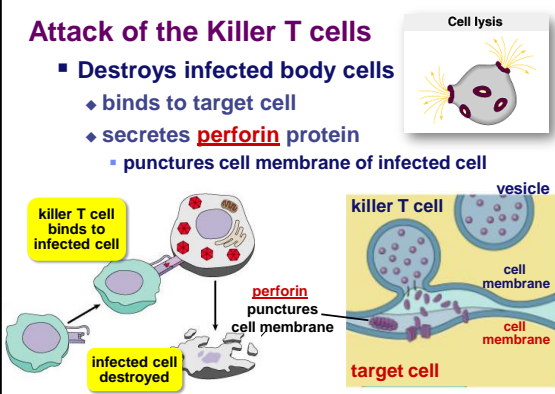


T cell Response

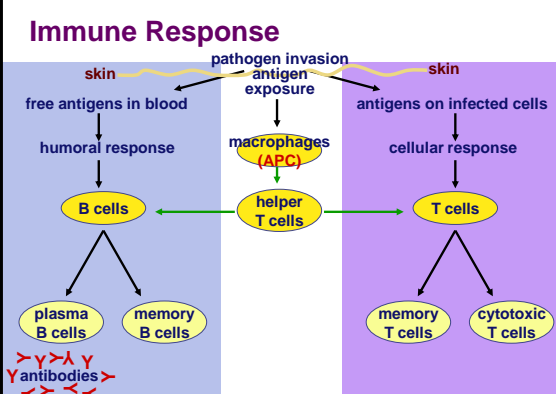


Attack of the Killer T cells

- **Destroys infected body cells**
 - ◆ binds to target cell
 - ◆ secretes perforin protein
 - punctures cell membrane of infected cell

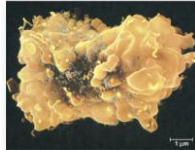


Immune Response



HIV & AIDS

- **Human Immunodeficiency Virus**
 - ◆ virus infects **helper T cells**
 - ◆ helper T cells don't activate rest of immune system: T cells & B cells
 - also destroy T cells
- **Acquired ImmunoDeficiency Syndrome**
 - ◆ infections by opportunistic diseases
 - ◆ death usually from other infections
 - pneumonia, cancer



Immune System Malfunctions

- **Auto-immune diseases**
 - ◆ immune system attacks own molecules & cells
 - lupus
 - ◆ antibodies against many molecules released by normal breakdown of cells
 - rheumatoid arthritis
 - ◆ antibodies causing damage to cartilage & bone
 - diabetes – Type I
 - ◆ beta-islet cells of pancreas attacked & destroyed
 - multiple sclerosis
 - ◆ T cells attack myelin sheath of brain & spinal cord nerves
- **Allergies**
 - ◆ over-reaction to environmental antigens
 - allergens = proteins on pollen, dust mites, in animal saliva
 - stimulates release of histamine

Key Attributes of Immune System

- 4 attributes that characterize the immune system as a whole
 - ◆ **specificity**
 - antigen-antibody specificity
 - ◆ **diversity**
 - react to millions of antigens
 - ◆ **memory**
 - rapid 2^o response
 - ◆ **ability to distinguish self vs. non-self**
 - maturation & training process to reduce auto-immune disease