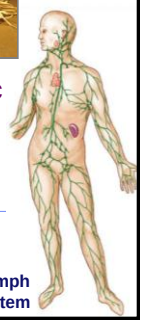
phagocytic leukocyte

Immune / Lymphatic System

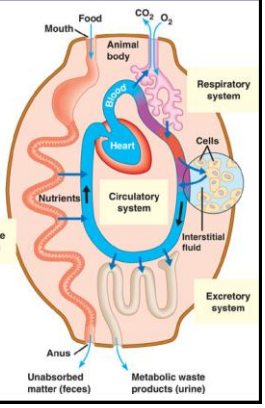
lymphocytes attacking cancer cell



lymph system

Avenues of attack

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

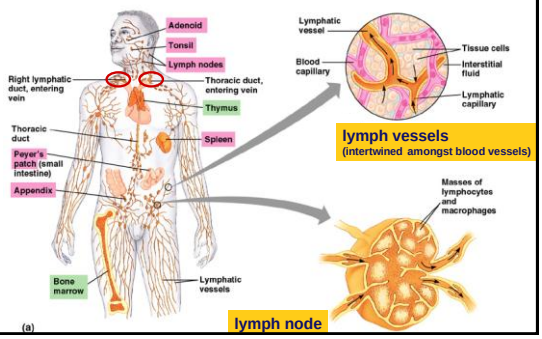


Why an immune system?

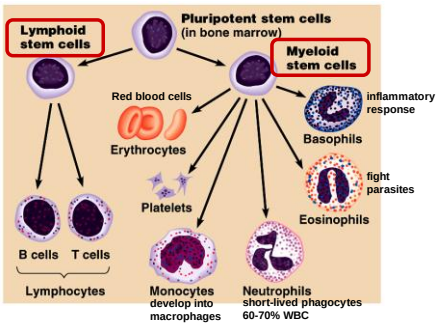
- Attack from outside
  - lots of organisms want you for lunch!
  - animals are a tasty nutrient- & vitamin-packed meal
    - cells are packages of macromolecules
    - no cell wall
      - traded mobility for susceptibility
  - animals must defend themselves against invaders
    - viruses
      - HIV, 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 = cancers

Lymph system

Production & transport of leukocytes
Traps foreign invaders



Development of Red & White blood cells



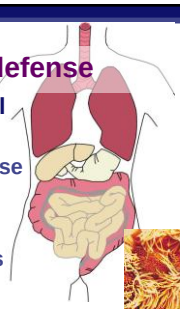
Lines of defense

- 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

Bacteria & insects inherit *resistance*. Vertebrates acquire *immunity*!

1st line: External defense

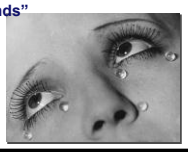
- Physical & chemical defenses
  - non-specific defense
- external barrier
  - epithelial cells & mucus membranes
    - skin
    - respiratory system
    - digestive system
    - uro-genital tract



Lining of trachea: ciliated cells & mucus secreting cells

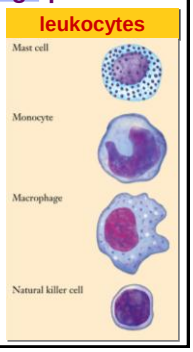
1st line: Chemical barriers on epithelium

- 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

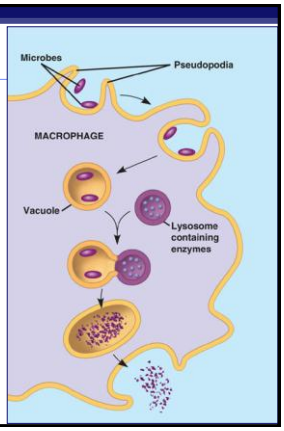
- Innate, general defense
  - rapid response
- Patrolling cells & proteins
  - attack invaders that penetrate body's outer barriers
    - leukocytes
      - phagocytic white blood cells
    - complement system
      - anti-microbial proteins
    - inflammatory response



Leukocytes: Phagocytic WBCs

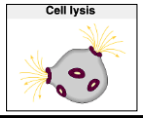
- Attracted by chemical signals released by damaged cells
  - enter infected tissue, engulf & ingest microbes
    - Lysosomes digest pathogens once engulfed
- Neutrophils
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- Macrophages
  - "big eater", long-lived
- Natural Killer Cells
  - destroy virus-infected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

Phagocytes

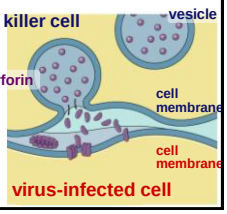


Destroying cells gone bad!

- 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

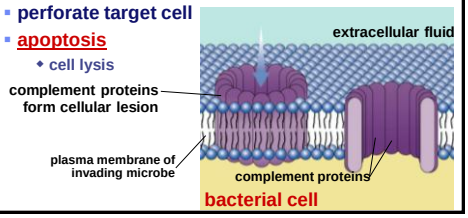


perforin punctures cell membrane



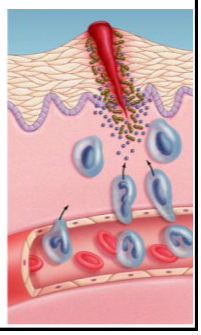
Anti-microbial proteins

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



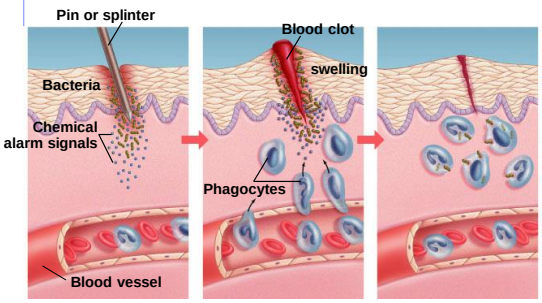
Inflammatory response

- 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

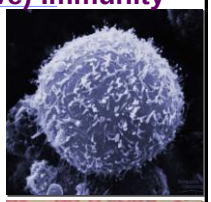


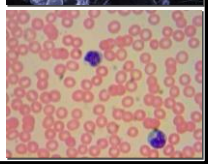
Fever

- 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)

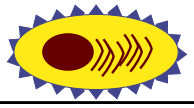




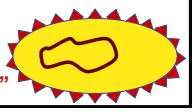
How are invaders recognized: antigens

- 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
- 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

"self"

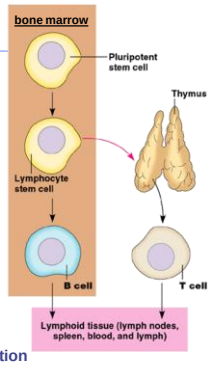


"foreign"



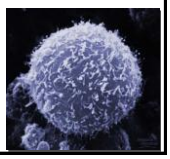
Lymphocytes

- 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



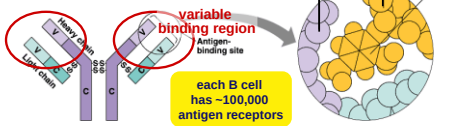
B cells

- 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

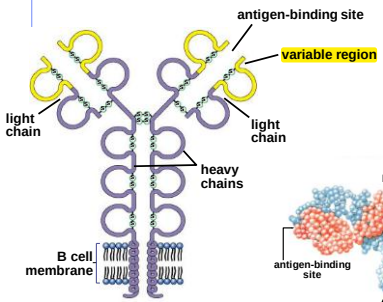


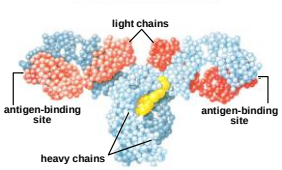
Antibodies

- 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!"



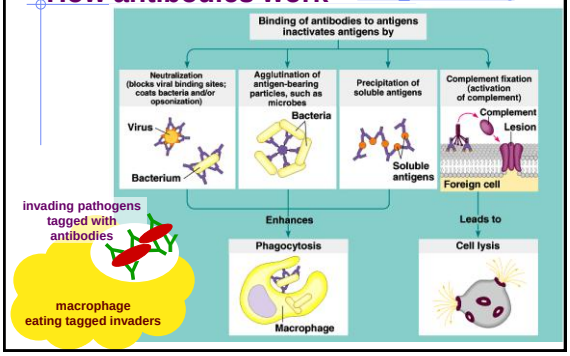
Structure of antibodies





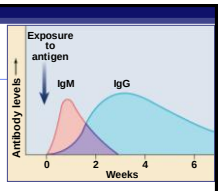
How antibodies work

http://www.youtube.com/watch?v=_49z0Xf235Q



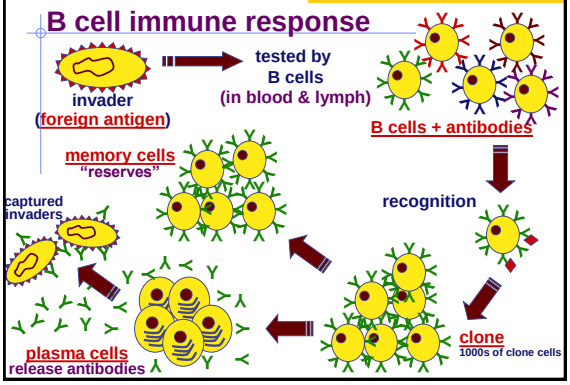
Classes of antibodies

- Immunoglobulins
  - IgM
    - 1st immune response
    - activate complement proteins
  - IgG
    - 2nd response, major antibody circulating in plasma
    - promote phagocytosis by macrophages
    - Most common, can pass placental barrier
  - 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??? Function unclear—found in belly



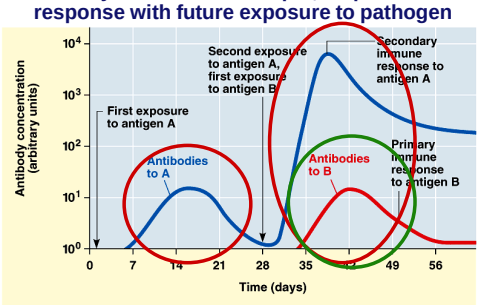
10 to 17 days for full response

B cell immune response



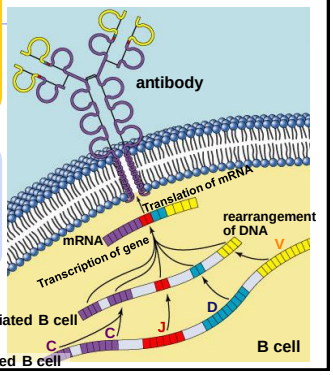
1° vs 2° response to disease

- Memory B cells allow a rapid, amplified response with future exposure to pathogen



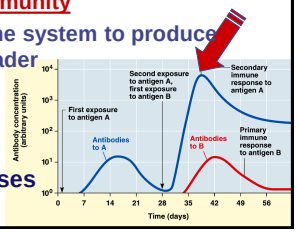
How do vertebrates produce millions of antibody proteins, if they only have a few hundred genes coding for those proteins?

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



Vaccinations

- Immune system exposed to harmless or weakened version of pathogen
  - triggers active immunity
  - stimulates immune system to produce antibodies to invader
  - rapid response if future exposure
- Most successful against viral diseases

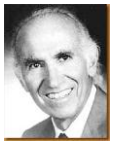


Jonas Salk

1914 – 1995

April 12, 1955

- Developed first vaccine
  - against polio
    - attacks motor neurons



Albert Sabin
1962
oral vaccine

Polio epidemics

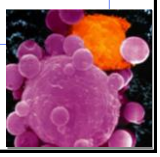
1994:
America is polio free

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

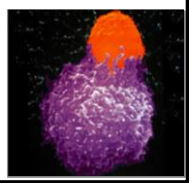
What if the attacker gets past the B cells in the blood & actually infects some of your cells?

You need trained assassins to kill off these infected cells!



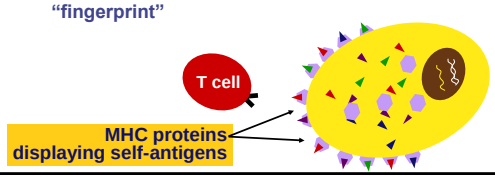
T cells

- 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



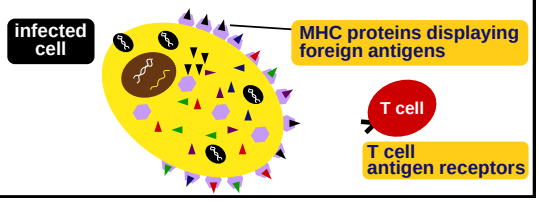
How are cells tagged with antigens

- Major histocompatibility (MHC) proteins
  - 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"

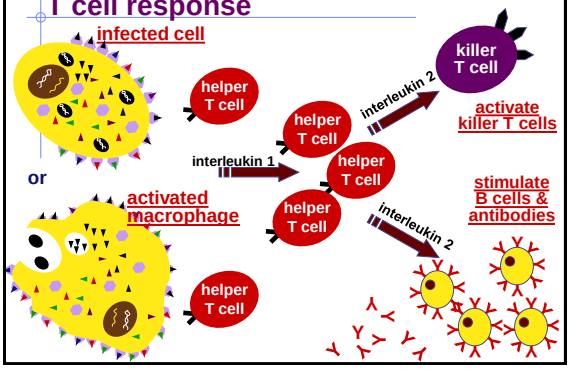


How do T cells know a cell is infected

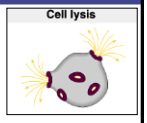
- Infected cells digest pathogens & MHC proteins bind & carry pieces to cell surface
  - antigen presenting cells (APC)
  - alerts Helper T cells



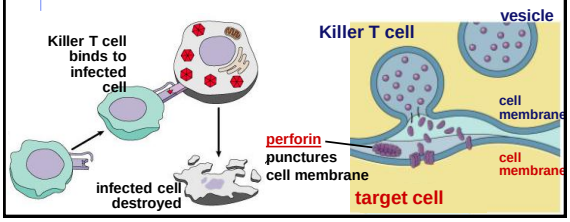
T cell response



Attack of the Killer T cells



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



Blood type

blood type	antigen on RBC	antibodies in blood	donation status
A			__
B			__
AB			
O			

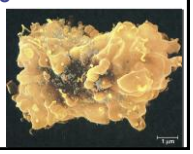
Matching compatible blood groups is critical for blood transfusions
A person produces antibodies against foreign blood antigens

Blood donation

(a) Phenotype (blood group)	(b) Genotypes	(c) Antibodies present in blood serum	(d) Results from adding red blood cells from groups below to serum from groups at left			
			A	B	AB	O
A	$I^A I^A$ or $I^A i$	Anti-B		clotting	clotting	
B	$I^B I^B$ or $I^B i$	Anti-A	clotting		clotting	
AB	$I^A I^B$	—				
O	ii	Anti-A Anti-B	clotting	clotting	clotting	

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



How to protect yourself…

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
      - 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° response
  - ability to distinguish self vs. non-self
    - maturation & training process to reduce auto-immune disease