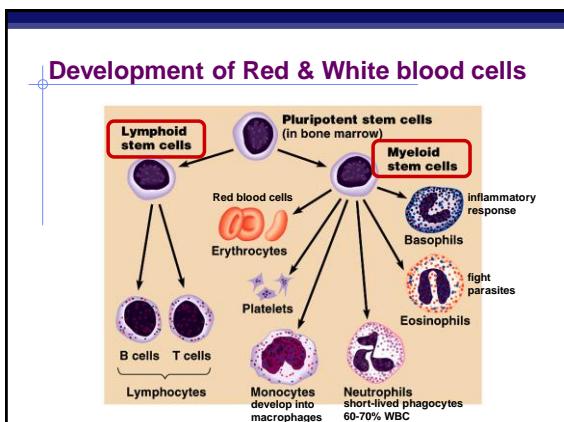
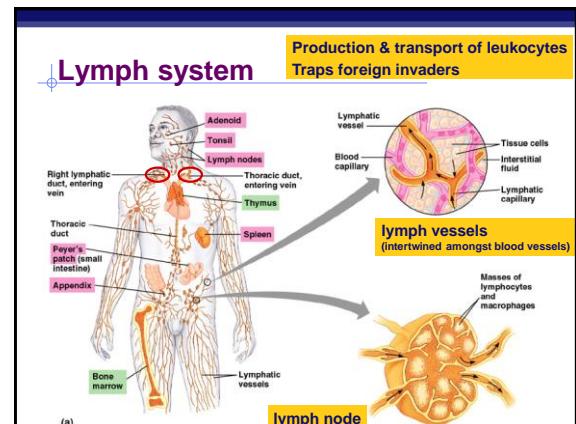


Why an immune system?

- 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



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

macrophage yeast

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**

Cell lysis
perforin punctures cell membrane
virus-infected cell
vesicle
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
 - complement proteins form cellular lesion

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
 - Pin or splinter
 - Bacteria
 - Chemical alarm signals
 - Blood vessel
 - Blood clot
 - swelling
 - Phagocytes

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
 - Surface glycoproteins
 - 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
 - ◆ an "immune response"
 - ◆ 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, concentrated in lymph nodes and spleen after maturing
 - 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
 - undergo "clonal expansion"
 - memory cells**
 - long term immunity—faster secondary response

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

The diagram illustrates the structure of an antibody molecule, showing four Y-shaped units. Each unit consists of four chains: two light chains (blue) and two heavy chains (green). The variable region (yellow) at the top of each arm contains the antigen-binding site. The constant region (purple) is embedded in the B cell membrane.

How antibodies work

<http://www.youtube.com/watch?v=49z0Xf235Q>

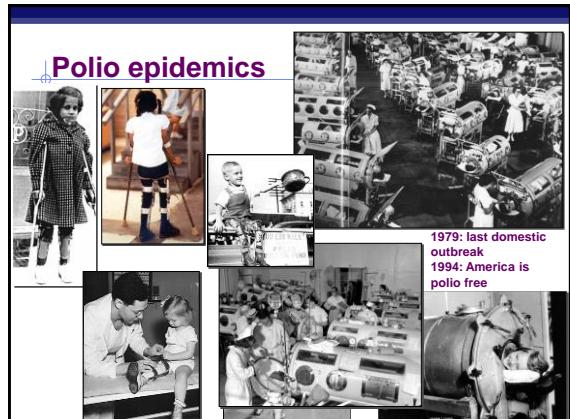
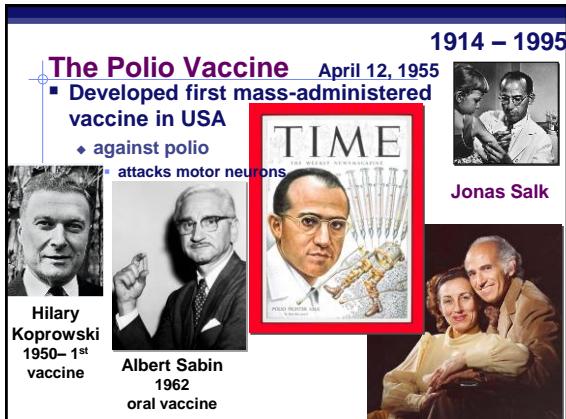
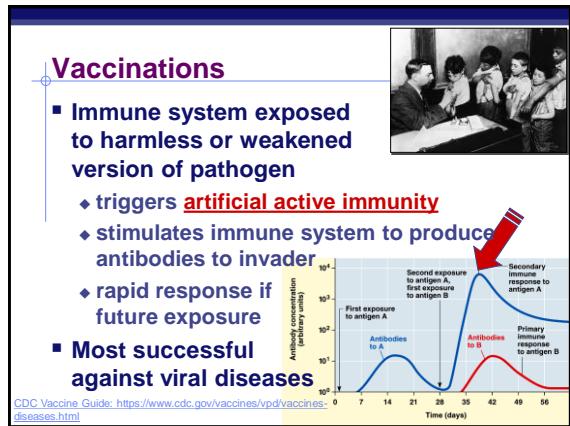
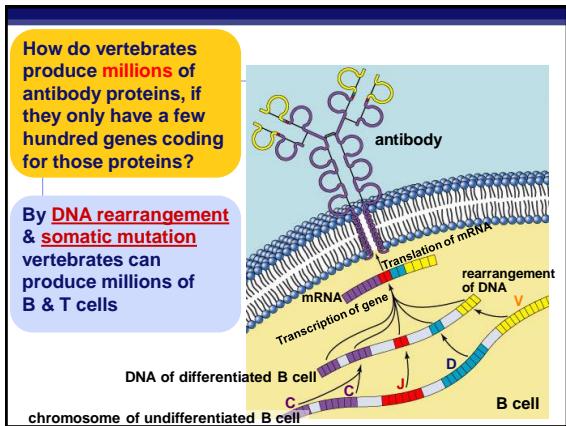
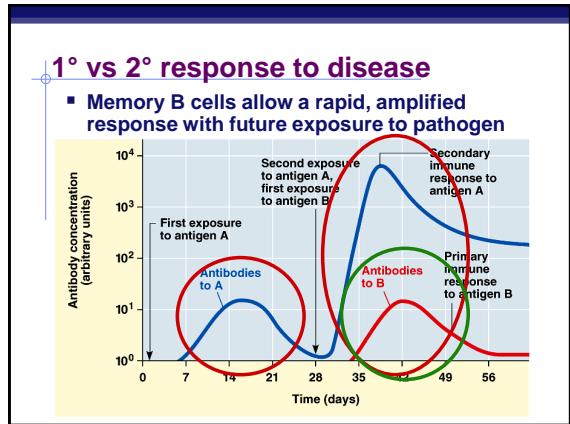
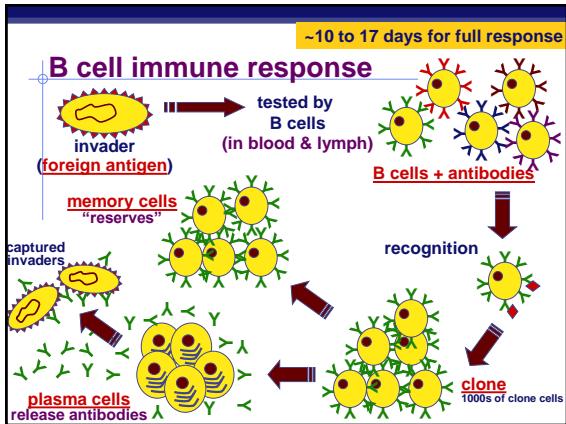
The flowchart details the mechanisms of antibody action:

- Binding of antibodies to antigens inactivates antigens by:**
 - Neutralizing viral binding sites; coats bacteria and/or opsonization
 - Aggregation of antigen-bearing particles, such as microbes
 - Precipitation of soluble antigens
 - Complement fixation (activation of complement)
- Enhances Phagocytosis:** Macrophages eat tagged invaders.
- Leads to Cell lysis:** Foreign cells are destroyed.

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

The graph shows antibody levels (y-axis) versus time in weeks (x-axis). IgM peaks early (around week 1) and then declines. IgG peaks later (around week 4) and remains at a higher level for a longer duration.



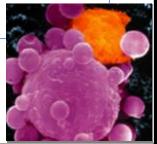
Passive immunity

- 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



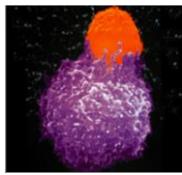
What if the attacker gets past the B cells in the blood & actually infects some of your cells?

You need trained assassins to kill off these infected cells!



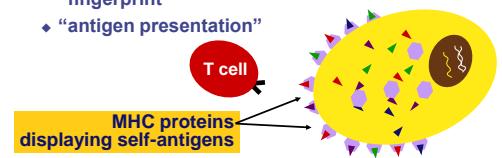
T cells

- **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



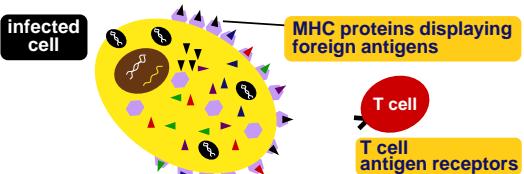
How are cells tagged with antigens

- **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"
 - ◆ "antigen presentation"

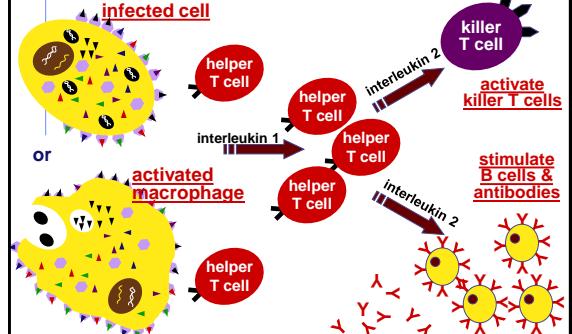


How do T cells know a cell is infected

- 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 or other chemicals
 - punctures cell membrane of infected cell

Cell lysis

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	
B	I ^B I ^B or I ^B i	Anti-A	
AB	I ^A I ^B	—	
O	ii	Anti-A Anti-B	