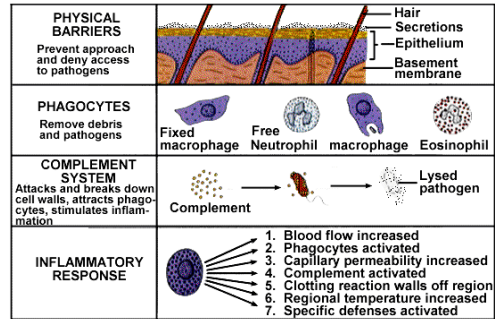


Nonspecific and specific host defenses

Non-specific defenses



Other resistance factors

- Physical and emotional stress
- Age
- General health and state of nutrition
- Socioeconomic conditions
- Occupational hazards
- Personal hygiene

Species, Racial, Individual Resistance

- Physiological and anatomical characteristics
- Genetic or racial factors
- Individual susceptibility to disease

Physical Barriers

- Skin
- mucous membranes
- Chemical secretions
- Hairs in the nose
- Cilia on the trachea
- Coughing and sneezing
- Urine flow
- Normal flora

Skin and mucous membranes

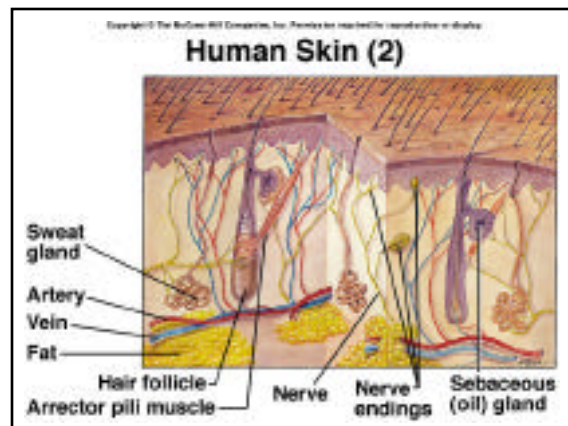
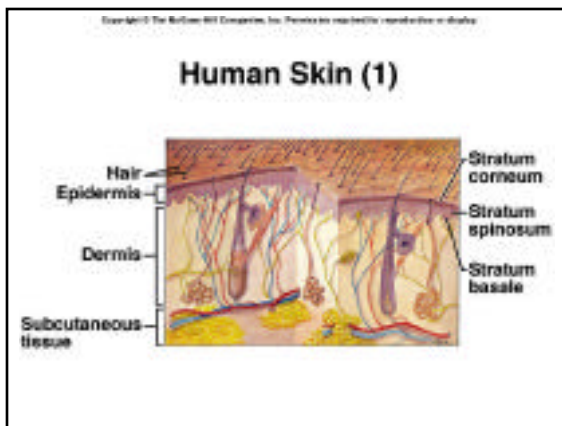
- Mechanical barrier
- Low moisture
- Low pH (3-5 pH)
- Inhibitory secretions
- Secretion of mucus

Normal flora

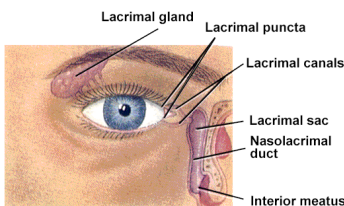
- Prevent colonization of pathogens.
 - Out compete for nutrients
 - Release of toxic substances that inhibit pathogens
- Stimulate the production of cross-reactive antibodies
- Stimulate the development of certain tissues, i.e. Peyer's patches

Chemical barriers

- Lysozyme is an enzyme that breaks down peptidoglycan
- Sebum is an oily secretion from the sebaceous glands of the skin
- Gastric juice contains hydrochloric acid
- Lactoferrin is protein found in body secretions that binds iron
- Peroxidase enzymes in saliva and milk



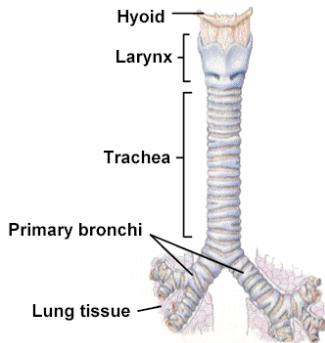
Lysozyme is excreted in tears and most body fluids



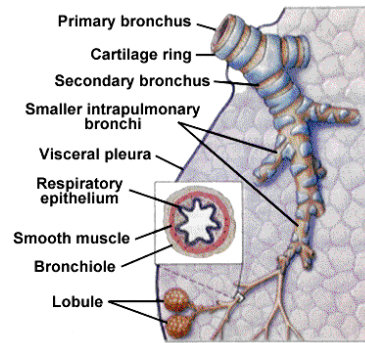
Other tissues



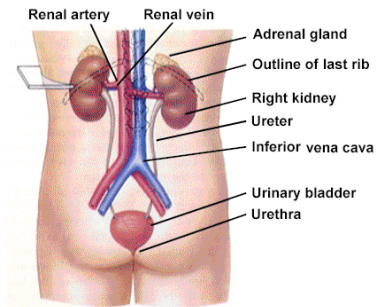
Trachea



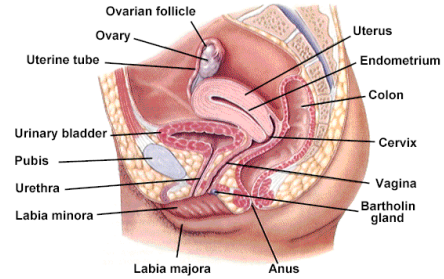
Bronchi



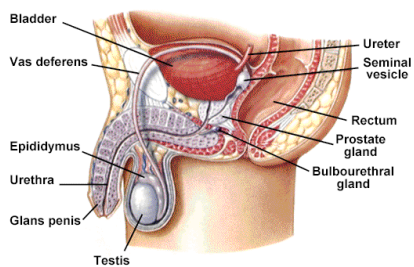
Distance of ureters prevents infection



Female are more prone to UTI



Male urethra is 20 cm vs 5 cm

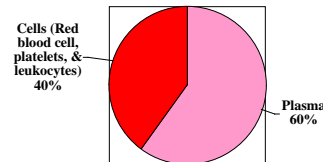


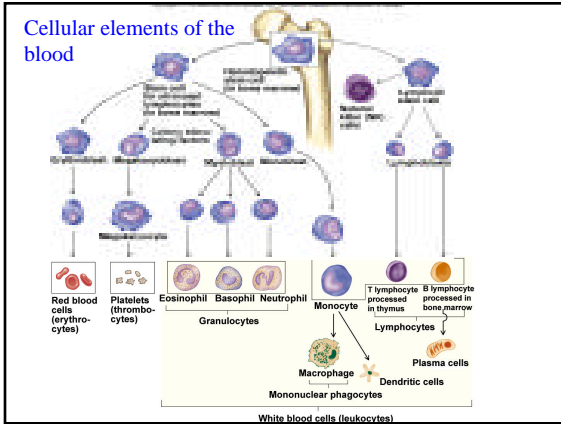
Cellular defenses

• Introduction

– Blood

- 60% plasma
- 40% cells (RBC, platelets, **WBC or leucocytes**)





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TABLE 15.1 Human Leukocytes

Cell Type (% of Blood Leukocytes)	Morphology	Location in body	Functions
Granulocytes			
Neutrophils (polymorphonuclear neutrophils or PMNs, often called polys; 55%–65%)	Lobed nucleus; granules in cytoplasm; amboid appearance	Account for most of the circulating leukocytes; few in tissues except during inflammation and in reserve locations	Phagocytize and digest engulfed materials
Eosinophils (2%–4%)	Large eosinophilic granules; nonsegmented or bilobed nucleus	Few in tissues except in certain types of inflammation and by E-mediated allergies	Participate in inflammatory reaction and immunity to some parasites
Basophils (0%–1%), most cells	Lobed nucleus; large basophilic granules	Basophils in circulation; most cells present in most tissues	Release histamine and other inflammation-causing chemicals from the granules
Mononuclear phagocytes			
Monocytes (3%–8%), macrophages, dendritic cells	Single nucleus; abundant cytoplasm	Macrophages present in all tissues and in lining of vessels; monocytes less-mature circulating forms	Phagocytize and digest engulfed materials; can participate in killing foreign cells that are engulfed; play vital role in development of specific immunity
Lymphocytes			
Several types (25%–35%)	Single nucleus; little cytoplasm before differentiation	In lymphoid tissues such as lymph nodes, spleen, thymus, appendix, tonsils; also in circulation	Participate in specific immunological responses

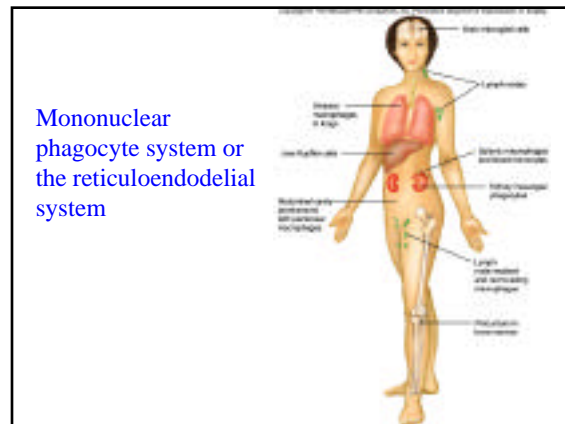
- ### Granulocytes
- **Neutrophils**
 - Polymorphonuclear leucocytes (PMNs).
 - Phagocytic cells
 - Can leave blood and enter tissues.
 - **Eosinophils**
 - Weakly phagocytic, can leave blood
 - Associated with allergies - release histamine
 - **Basophils**
 - Release heparin, serotonin, histamine.
 - Become mast cells and associated with allergies
 - Not phagocytic.

- ### Agranulocytes
- **Monocytes**
 - Monocytes become macrophages when induced by lymphokines and are phagocytic
 - Macrophages are big eaters
 - May wander or may reside in a tissue
 - **Lymphocytes**
 - Lymphocytes have role in specific immunity.
 - **NK cells - extracellular killing**

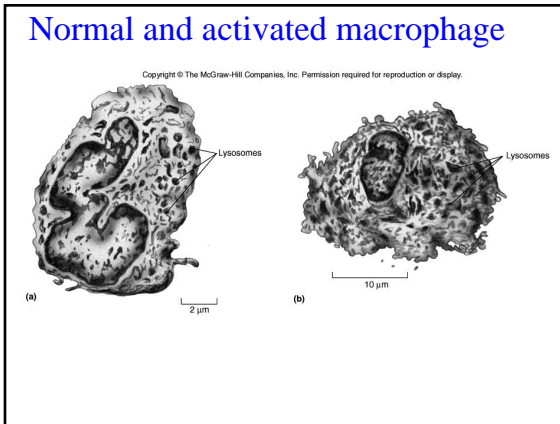
Macrophages in their tissues

> **Table 16.2 Names of fixed macrophages in various tissues**

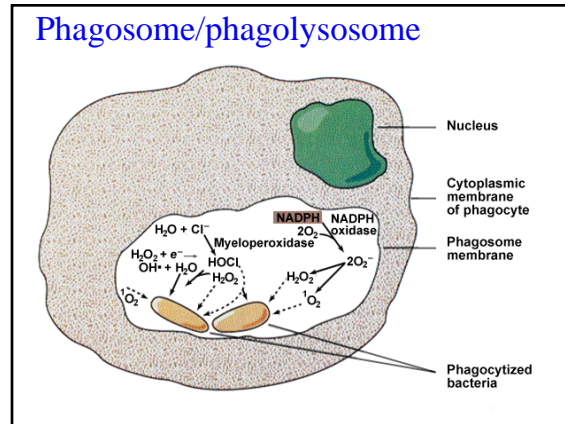
Name of macrophage	Tissue
Alveolar macrophage (dust cell)	Lung
Histiocyte	Connective tissue
Kupffer cell	Liver
Microglial cell	Neural tissue
Osteoclast	Bone
Sinusoidal lining cell	Spleen



Normal and activated macrophage

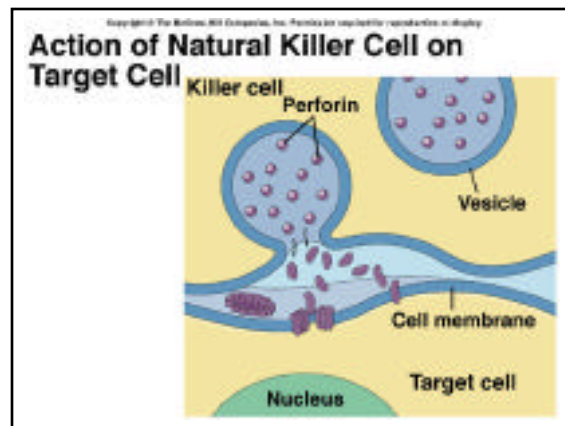


Phagosome/phagolysosome

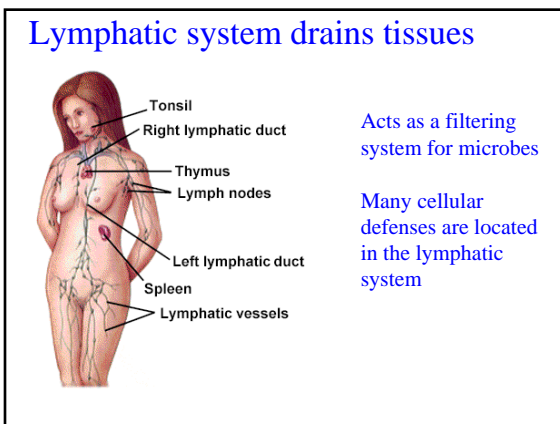


Natural killer cells

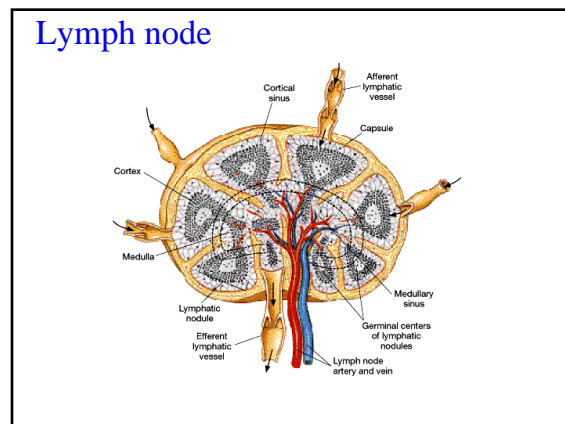
- NK cells are large lymphocytes that kill virus-infected cells or tumor cells.
- NK cells bind to target cells and release proteases and phospholipases.
- Maturation of NK cells is stimulated by interferon.
- Main role is surveillance.
- Not phagocytic.



Lymphatic system drains tissues



Lymph node

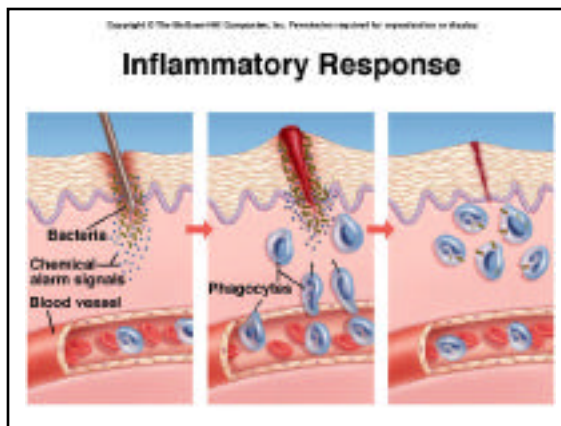


Inflammation

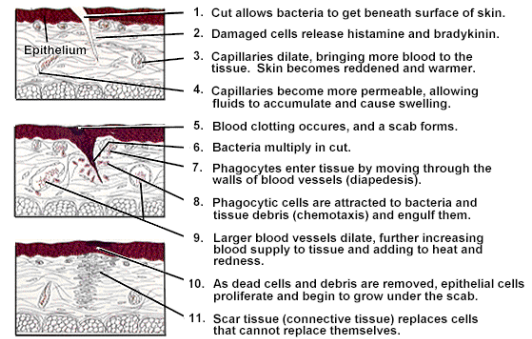
- A vascular and cellular response to presence of invading microorganisms or inanimate irritants.
- Symptoms include redness, swelling and pain and increased temperature.
- Symptoms are due to vasodilation.

Process of inflammation

- Initiation
- Tissue response
 - Histamines, TNF, bradykinin, prostaglandins released.
 - Vasodilation occurs
- Leucocyte response.
 - Vasodilation allows movement of phagocytes (*diapedesis*).



Repair and regeneration



Inflammation

- pus formation
 - Dead phagocytes, damaged cells, dead organisms
 - *Streptococcus pyogenes* produces leukocidins that kill phagocytes
- Abscesses - hollowed out due to tissue damage
 - Boils
 - Pimples

Inflammation

- Harmful effects
 - Meninges
 - Airways
 - Walling off
- Chronic inflammation
 - Granuloma

Fever

- Normal body temperature is 98.6°F (37° C)
 - 100.5°F (37.8°C) orally
 - 101.5°F (38.4°C) rectally
- Fever is a systemic response to chemicals
- Endotoxins (pyrogens) & IL-1 cause fever because they affect the hypothalamus
- Other substances raise the metabolic activity of the body

Benefits of fevers

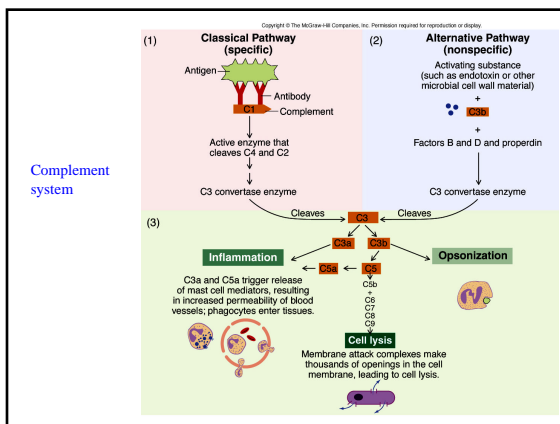
- Body temp. is higher than optimum for pathogens
- Microbial enzymes and toxins are inactivated
- Increase immune response
- Patient feels ill and rests

Complement

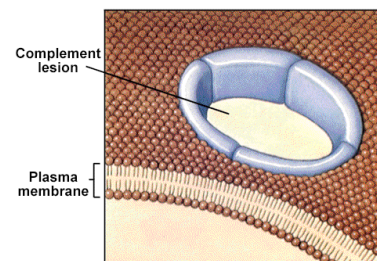
- A group of ~20 proteins that act in a cascade in response to an antibody-antigen interaction.
 - opsonization
 - Enhance phagocytosis by phagocytes
 - membrane attack
 - Lyse invading bacterial cells and some viruses
 - Stimulates inflammatory response
 - Releasing of histamines and other substances by basophils and mast cells

Complement system

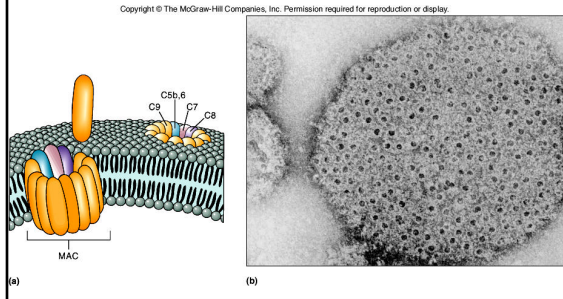
- **Classical pathway**
 - Antibody-antigen stimulation
- **Alternative pathway**
 - Pathogen surface stimulation



Complement forms pores in the pathogen



Membrane Attack Complex



Deficiencies in complement lead to disease susceptibilities

DISEASE STATE	COMPLEMENT DEFICIENCIES
Severe recurrent infections	C3
Recurrent infections of lesser severity	C3, C2, C5
Systemic lupus erythematosus (a bodywide immunologic disease)	C1, C2, C4, C5, C8
Glomerulonephritis (an immunologic disease of the kidneys)	C1, C8
Gonococcal infections	C6, C8
Meningococcal infections	C6

Lymphokines

- Soluble proteins secreted by activated T lymphocytes.
 - Inhibit macrophage migration.
 - Activate macrophages.
 - Poison foreign cells or virus-infected cells.
 - Can damage tissue in inflammation.

Interferon

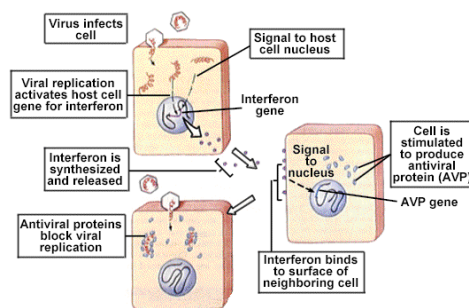
- Inhibits intracellular viral replication.
- Protein in nature.
- Secreted by infected cells and alerts other uninfected cells.
- Are not virus-specific.
- Are species specific.

Interferons

Table 16.3 Properties of type I and type II human interferons

Class	Cell source	Subtypes	Stimulated by	Effects
Type I				
Alpha-interferon (INF- α)	Leukocytes	20	Viruses	Production of antiviral proteins in neighboring cells
Beta-interferon (INF- β)	Fibroblasts	1	Viruses	Same as INF- α
Type II				
Gamma-interferon (INF- γ)	T lymphocytes and NK cells	1	Viruses and other antigens	Activates tumor destruction and killing of infected cells

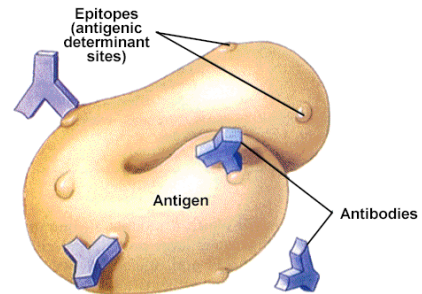
Antiviral effect of interferon



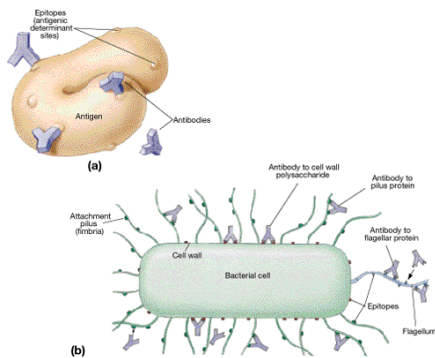
Antigens

- Foreign matter that triggers the immune response.
- Epitopes are small portions of an antigen that are recognized by antibody.

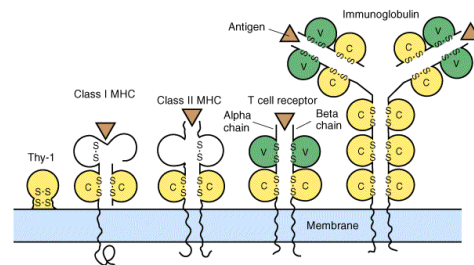
Antibodies bind to epitopes



Flagella, pili, & cell walls may have several antigens



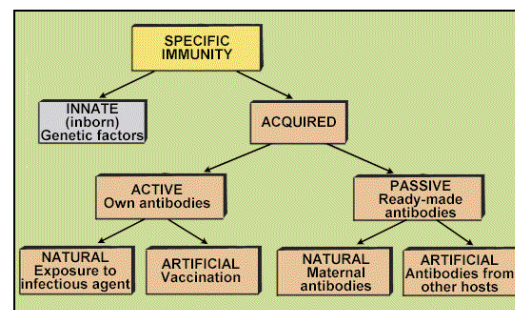
Antibodies and receptors

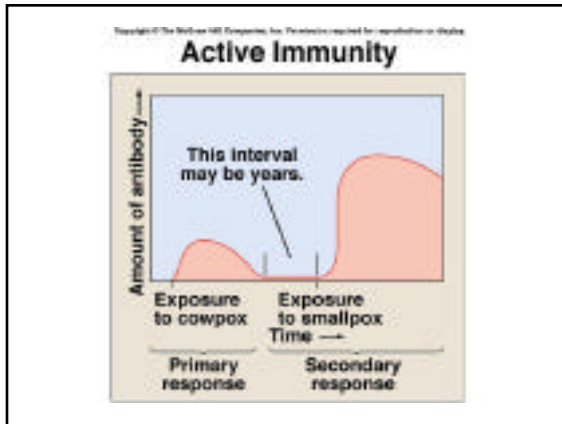


Acquired Specific Immunity

- Active immunity
 - Produced by the host
 - Natural--exposure to infection or free antigens.
 - Artificial--vaccination or transfusion.
- Passive immunity
 - Produced by a donor.
 - Natural--transplacental or in breast milk
 - Artificial--from serum or specific lymphocyte products.

Immunity





Active immunization

- Toxoid
 - May require a booster
- Killed pathogen
- Live but attenuated pathogens
 - Usually life long immunity
- Vaccinations
 - DPT, poliomyelitis, MMR, Hib

Immunizations

DISEASE	VACCINE	DOSAGE SCHEDULE
Diphtheria	Toxoid	2, 4, and 6 months, 1 1/2 and 4 to 6 years
Tetanus	Toxoid	Same as diphtheria, administered in DPT vaccine
Pertussis	Killed bacteria	Same as diphtheria, administered in DPT vaccine
Poliomyelitis	Live viruses Types I, II, and III	2, 4, and 6 months, 1 1/2 and 4 to 6 years
Haemophilus (HIB) infection	Polysaccharide-protein conjugate	2, 4, 6, and 15 months
Measles	Live virus	15 months, booster at school age, 11-12 years
Mumps	Live virus	15 months, 11-12 years
Rubella	Live virus	15 months, 11-12 years

Passive immunization

- Immune serum globulin
 - Gamma globulin
 - Portion of the serum containing antibodies
- Hyperimmune serum
 - Gamma globulin from a person recovering from an illness
- Antitoxin
 - Antibodies against specific toxins

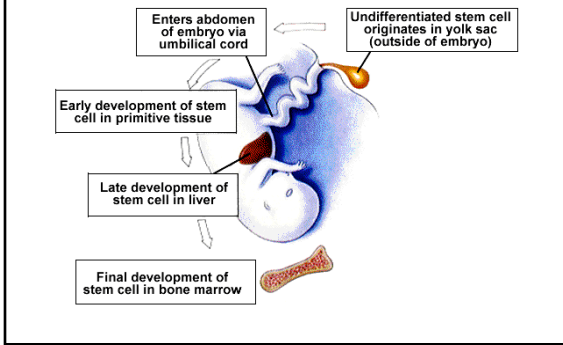
Immune response

- **Humoral Immunity**
 - Found in blood serum and lymphoid organs
 - pathogens outside of cells, bacteria, bacterial toxins, viruses in body fluids
 - Antibodies in serum comprise “humoral” component
- **Cellular Immunity**
 - White blood cells in blood and lymphoid tissue
 - Defends host from bacteria, viruses within cells, fungi, protists, other parasites
 - Immune surveillance

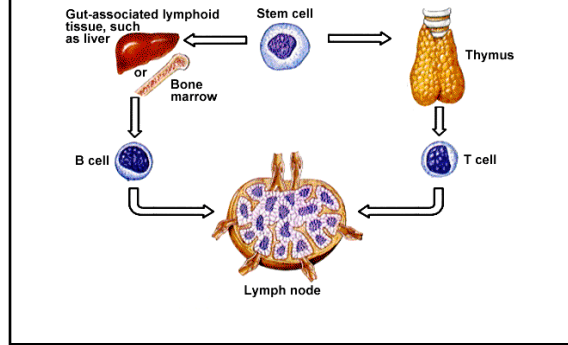
Properties of the immune response

- “self” verses “non-self”
 - “self” is normal host tissue
 - Major Histocompatibility (MHC) proteins.
 - “non-self” is foreign substances
- Specific antigen-antibody response.
- Heterogeneity
 - many different kinds of antibodies
- immunologic memory
 - anamnesic response (secondary or recall)

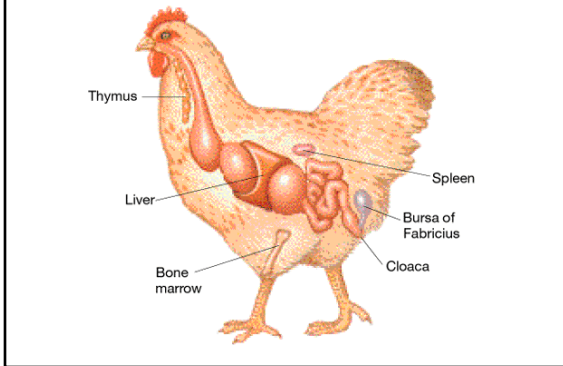
Embryonic stem cells reside in bone marrow



Stem cell can become T or B cells



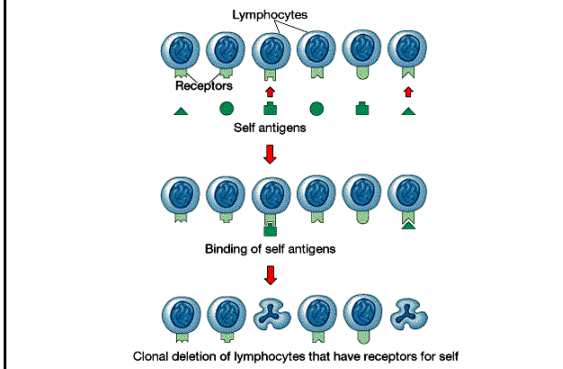
The bursa of Fabricius



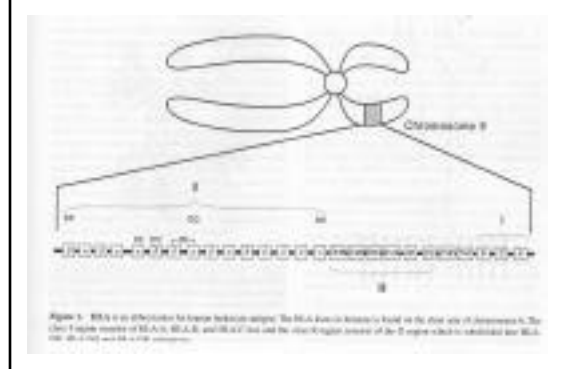
Percent B & T cell in tissues

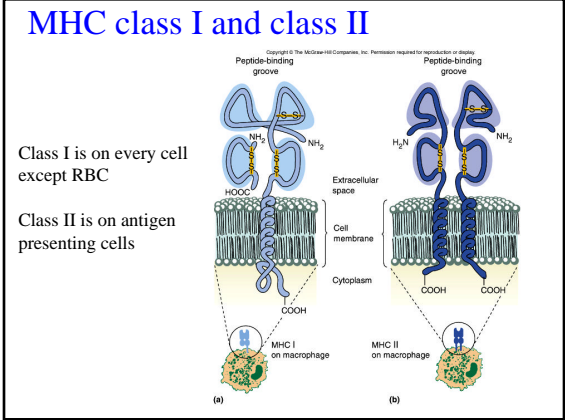
LYMPHOID TISSUE	% B CELLS	% T CELLS
Peyer's patches and nodules in digestive tract	60	25
Spleen	45	45
Lymph nodes	20	70
Blood	25	75
Thymus	1	99

Clonal deletion (eliminates lymphocytes that recognize self)

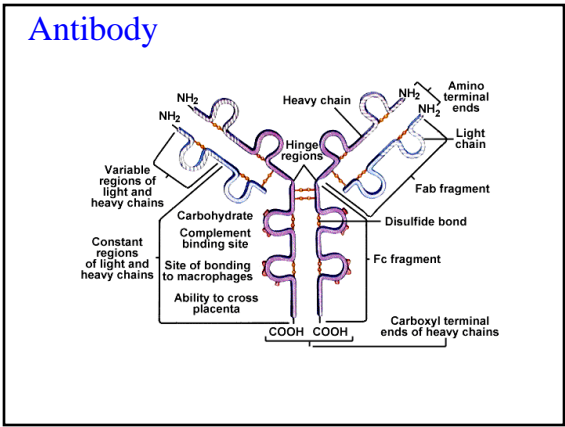
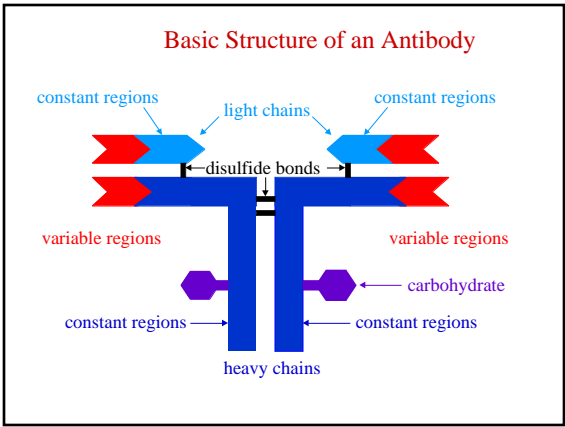


Class I and II MHC antigens





- ### Antibody
- Immunoglobulin (Ig)
 - Globular glycoprotein comprised of 2 “light” chains and 2 “heavy” chains.
 - 5 kinds: IgM, IgG, IgA, IgD, IgE.
 - 2 antigen-binding sites.



- ### IgG
- Most common antibody (80% in serum).
 - Major humoral defense protein.
 - Largest during the secondary response
 - Fix complement, lyse bacteria, viruses, old cells.
 - Transferred across placenta.
 - Production follows formation of IgM.

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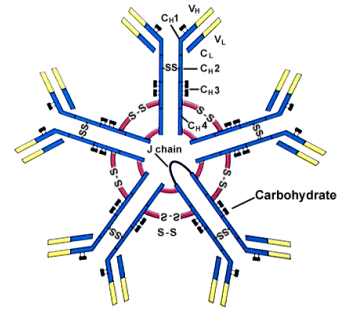
TABLE 16.1 Characteristics of the Various Classes of Human Immunoglobulins

Class and Molecular Weight (daltons)	Structure	Percent of Total Serum Immunoglobulin (Half-life in serum)	Properties	Functions
IgG 146,000	Monomer	80%–85% (21 days)	Specific attachment to pathogens; complement fixation; ability to cross placenta	Agglutination; precipitation; opsonization; ADCC; complement fixation
IgM 970,000	Pentamer	5%–10% (10 days)	Complement fixation; major class produced by some polysaccharides; first antibody produced during immune response	Agglutination; precipitation; complement fixation leads to opsonization and inflammation
IgA monomer 160,000; secretory IgA 390,000	Dimer in secretions	10% (6 days)	Secreted into saliva, milk, mucus, and other secretions; secretory form resists enzymatic degradation	Protection of mucous membranes by preventing attachment of organisms
IgD 184,000	Monomer	<1% (3 days)	Antigen receptor on B lymphocytes	Facilitates development and maturation of the antibody response
IgE 198,000	Monomer	<0.01% (2 days)	Attaches to mast cells and basophils; antigen reacts with cell-bound IgE to release granule contents	Involved in many allergic reactions; functions in ADCC; helps to expel parasites

IgM

- First immunoglobulin to be produced in response to antigen (primary)
- Short life span
- 5 units connected together
- Fix complement, lyse bacteria, viruses, old cells
- 5-10% serum

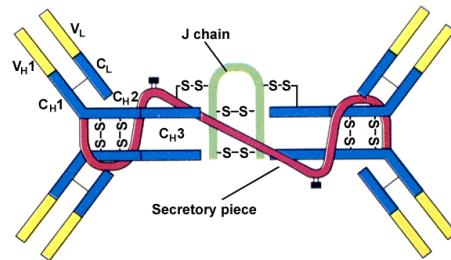
IgM



IgA

- Humoral immunity in mucous secretions (tears, saliva, semen, colostrum)
- Contains secretory piece
- Dimeric
- Neutralizes toxins, allergens, bacteria, viruses
- 10% in serum

IgA



IgE

- Allergic antibody
- Attached to surface of mast cells (basophils)
 - causes the release of histamines
- 0.005% in serum

IgD

- Function is not well known.
- Associated with unactivated B cells.
- Perhaps a cell receptor.
- 0.2% in serum

Antibody response: Macrophage

- Macrophage engulf foreign substance and process antigens.
- Macrophage present antigens to T and B lymphocytes.

Antibody response: T cells

- Helper T cells produce interleukins.
 - they “help” the B cells.
- Suppressor T cells moderate/suppress the activity of the B cells.

Lymphocytes

- Mediators of both humoral and cellular immunity.
- T cells: thymus-derived.
- B cells: bone marrow-derived.
- Null cells: include natural killer (NK) cells and killer (K) cells.

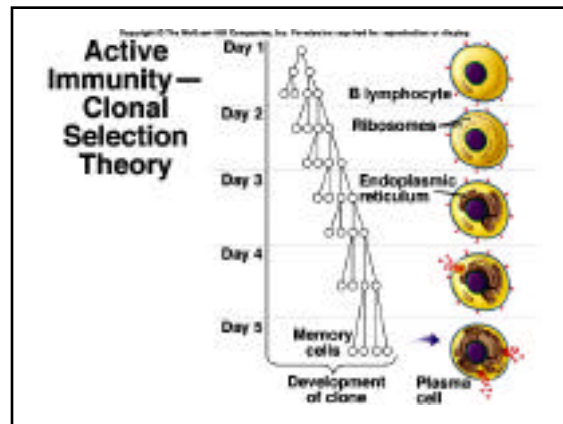
Lymphocytes

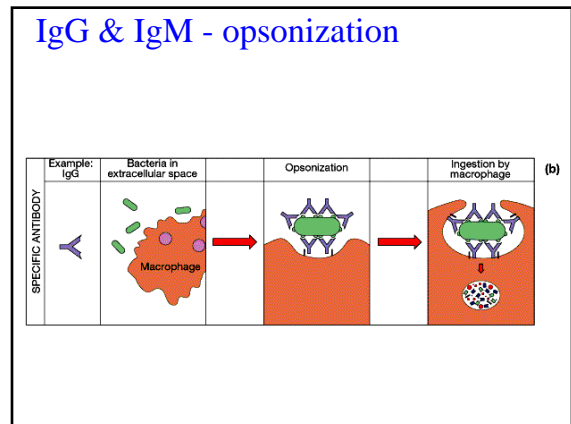
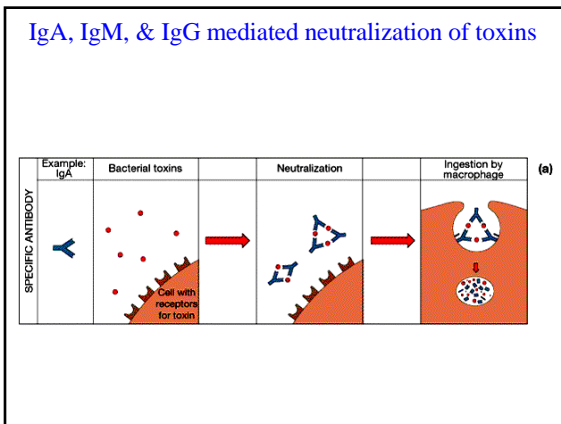
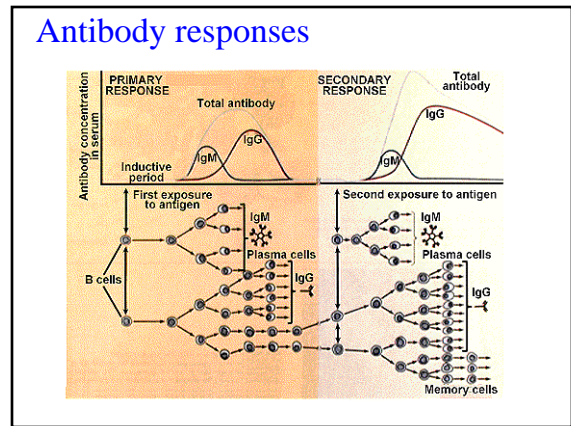
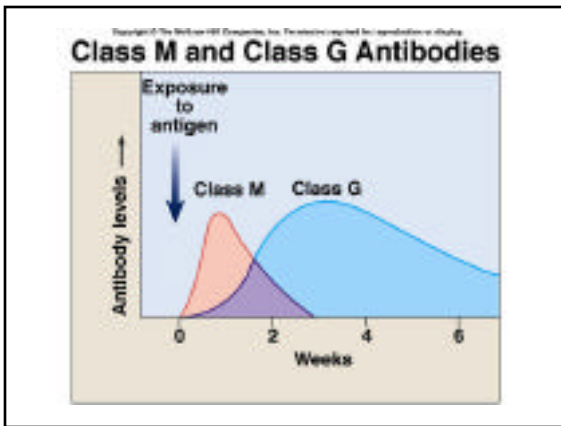
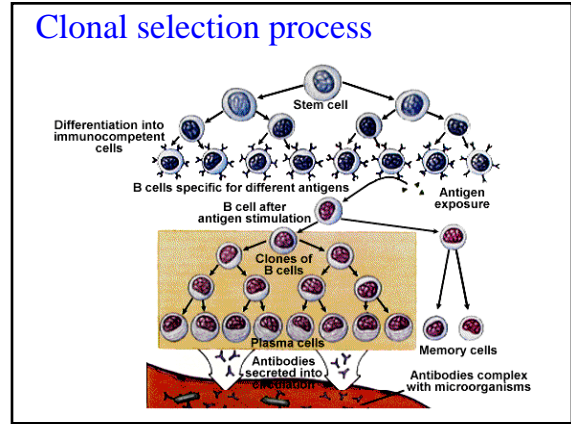
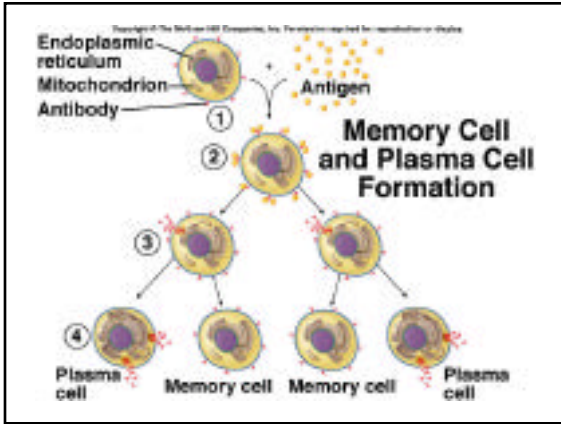
CHARACTERISTIC	B CELLS	T CELLS
Site of production	Bursal-equivalent tissues	Thymus or under thymic hormones
Type of immunity	Humoral	Cell-mediated and assist humoral
Subpopulations	Plasma cells and memory cells	Cytotoxic, helper, suppressor, delayed hypersensitivity, and memory cells
Presence of surface antibodies	Yes	No
Presence of foreign surface antigens	No	No
Presence of receptors for antigens	Yes	Yes
Life span	Some long, most short	Long and short
Secretory product	Antibodies	Lymphokines
Distribution (% leukocytes)		
Peripheral blood	15-30	55-75
Lymph nodes	20	75
Bone marrow	75	10
Thymus	10	75

TABLE 1 Some Characteristics Used to Distinguish Lymphoid Cells

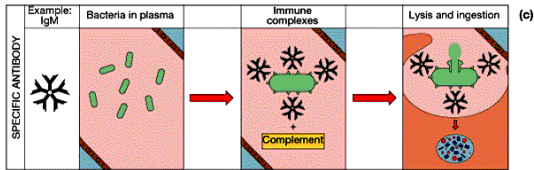
Cell Type	Surface Ig	Exhaustive Surface Ig	CD3	CD4	CD8	HLA
B cells	+	+	-	-	-	Class II
Plasma cells	+	+	-	-	-	Class II
T cells	-	-	+	+	+	Class I

Labels: n or duffy, Nucleus, Rough endoplasmic reticulum

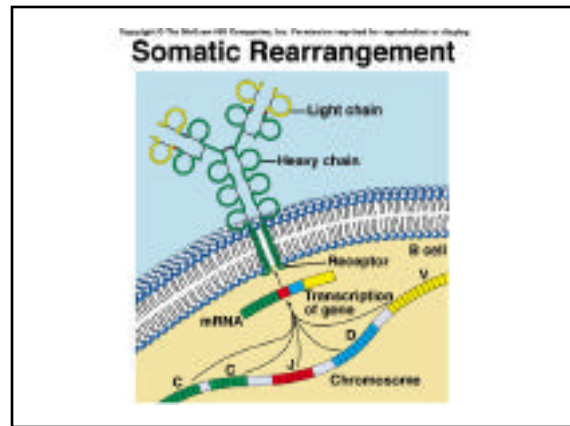
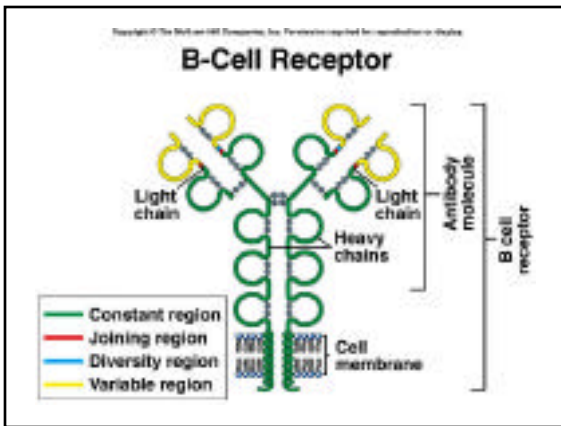
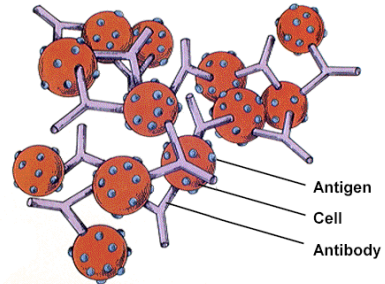




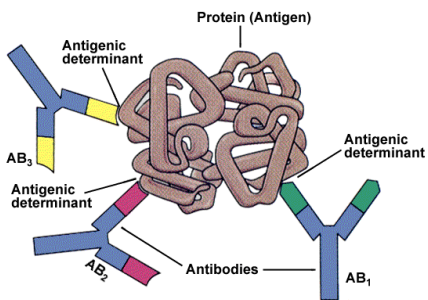
IgM & IgG formation of immune complexes



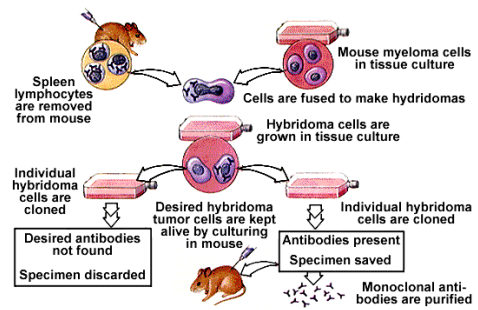
Immune complexes

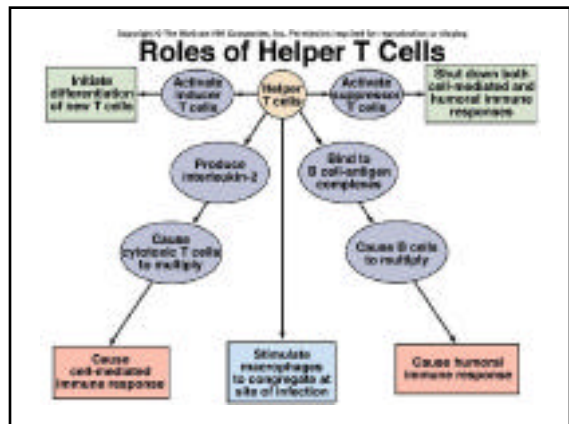
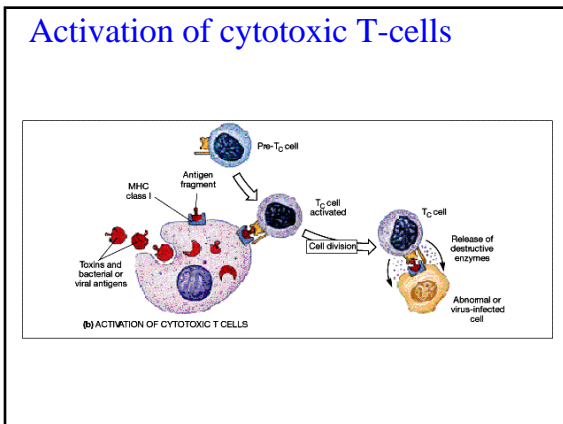
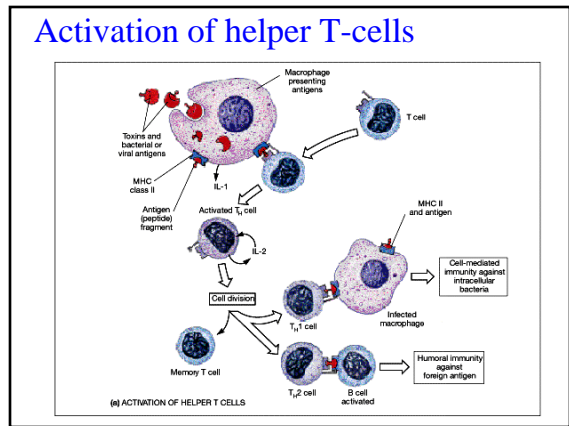
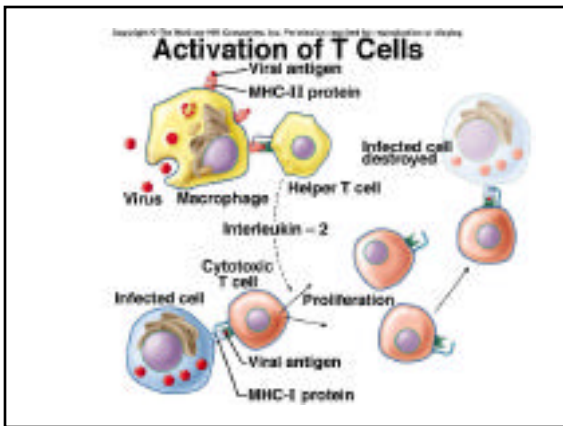
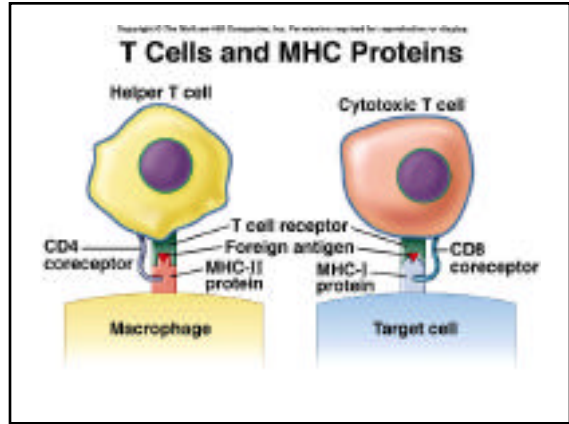
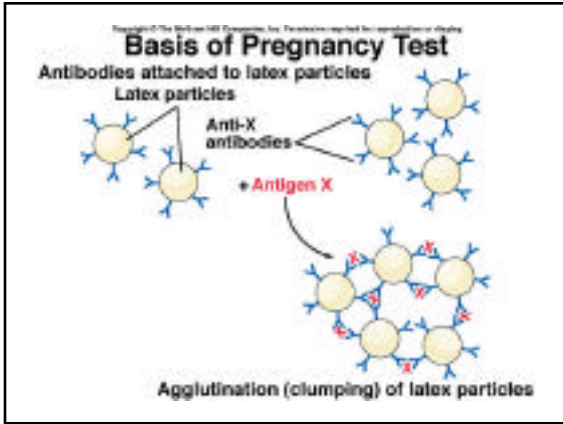


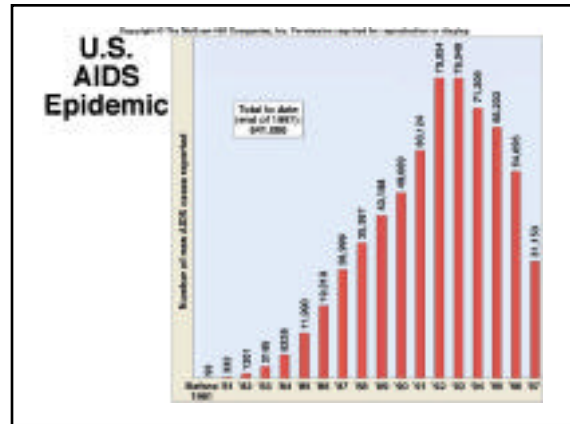
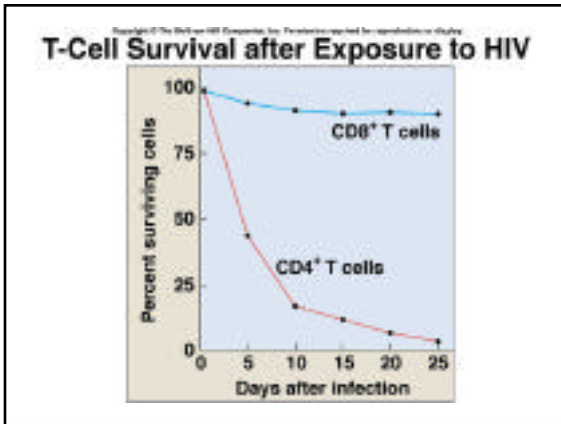
Polyclonal antibodies



Monoclonal antibody production

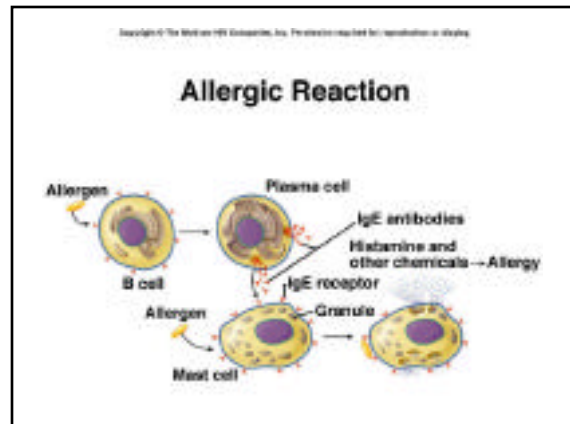






Hypersensitivity

- Extreme sensitivity to foreign antigens.
- Allergic responses.



Immediate/Anaphylactic Type I

- Hay fever and insect stings
- When antigen binds to bound IgE, granules are released
- Histamine, heparin, prostaglandins, PAF, ECF-A, serotonin, hyaluronidase
- Acute phase ends within 20 minutes to a few hours.
- Symptoms: reddening and swelling, anaphylaxis (local or systemic)

Cytolytic Type II

- Stimulates complement-IgG/IgM complex
- Directed against cell antigens
- Causes lysis of red blood cells if antigen is bound to rbc's
- Erythroblastosis fetalis, blood transfusion, drug reactions
- Can lead to anaphylaxis when mast cells are activated

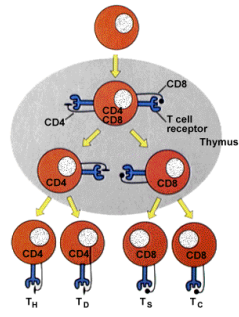
Immune-Complex/Arthus Type III

- Antibody complexes are formed
- Attracts PMNs that damage tissues
- Arthus reaction (joints), vasculitis, glomerulonephritis,

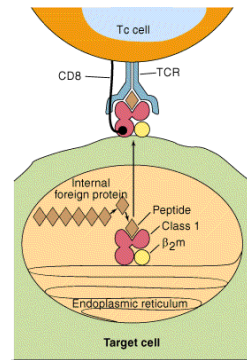
Delayed Type IV

- T-cell mediated
- Skin reaction over 24-48 hours: reddening, then diminishes
- Macrophage flood site, some host cells may be killed
- TB skin test, poison ivy/oak, transplant rejection

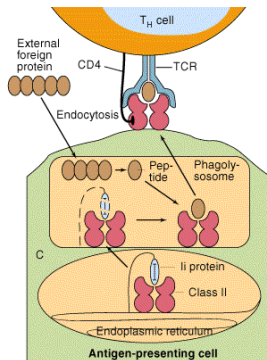
T-cell differentiation



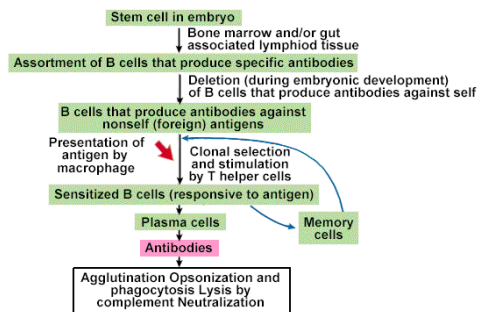
Cytotoxic T-cell targeting a cell



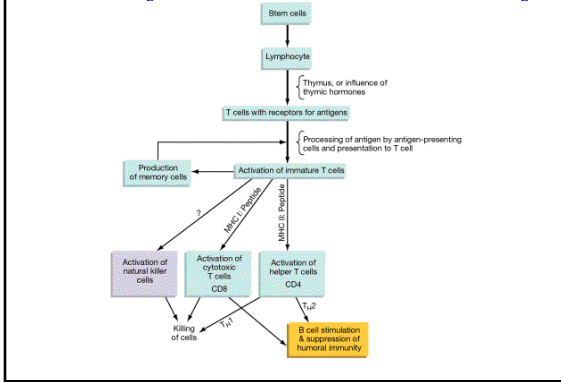
Antigen presenting cell (APC)



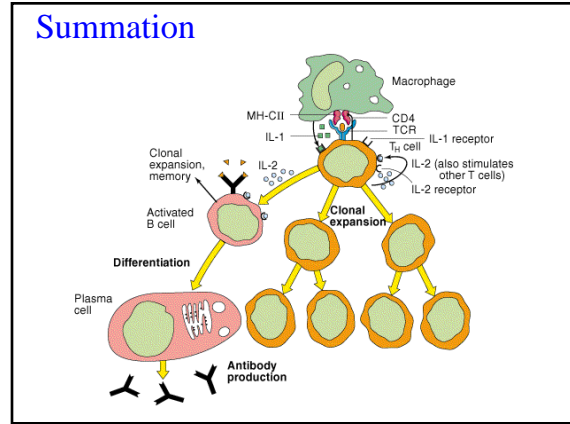
Summary of humoral immunity



Summary of cell-mediated immunity



Summation



Taxing the immune system

