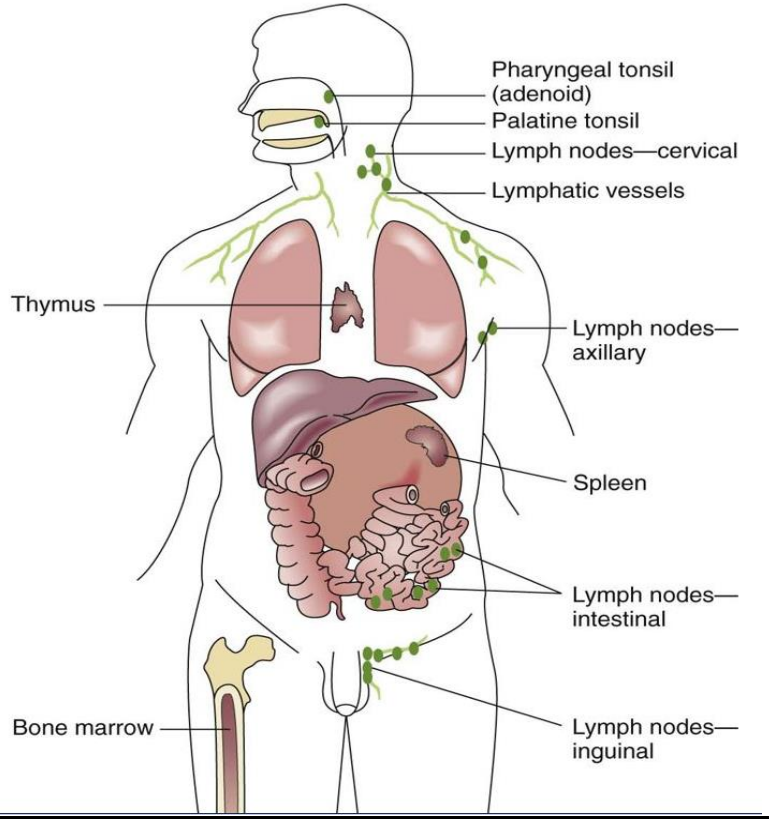
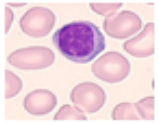
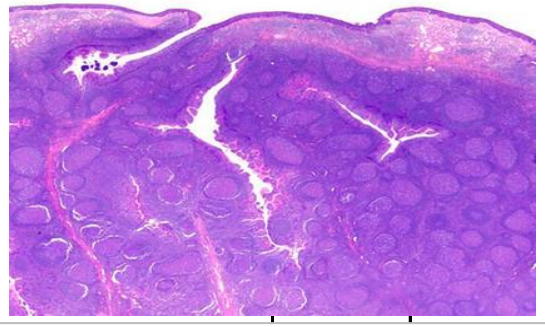
	BIOS 2015 … CHAPTER 7- Immunity	
Page	**Note**	
114	**BODY DEFENSES:**	
	First Line (*non-specific)*: mechanical, skin and mucous membranes and secretions (tears, saliva).	
	Second Line (*non-specific*): phagocytosis, inflammation, and interferon.	
	Third Line (*specific*): humoral and cellular immune systems - "Immunity"	
	"The specific immune response is intended to recognize and remove undesirable material from cells, tissues, and organs."	
	The immune system consists of:	
	1. Lymphoid structures: lymph nodes, the spleen and tonsils, the intestinal lymphoid tissue, and the lymphatic circulation **(see diagram on next page)**.	

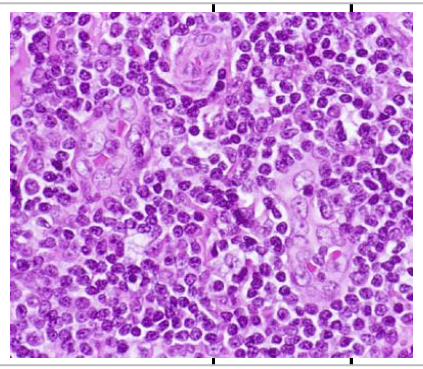




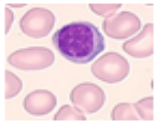
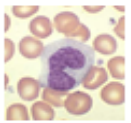
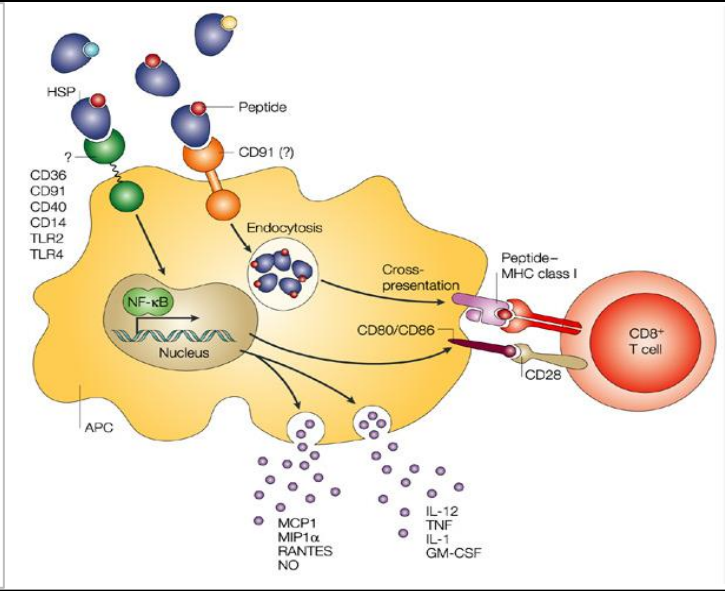
Lymphocyte

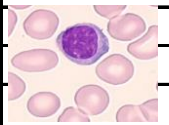
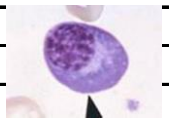


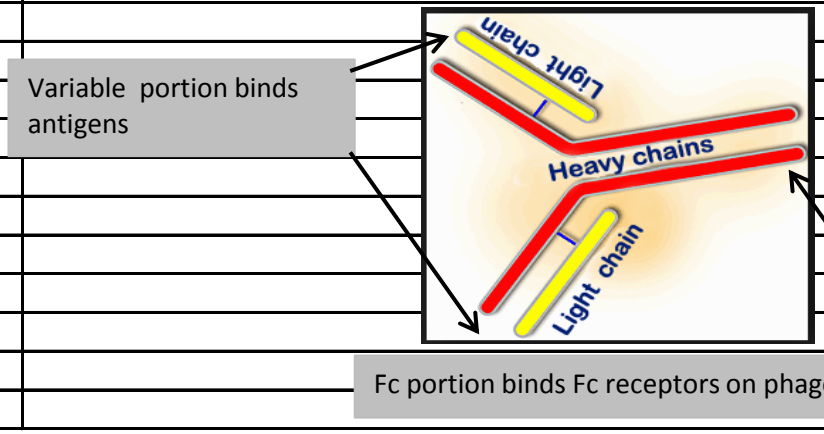
Lymphoid Tissue (Tonsil) - low magnification

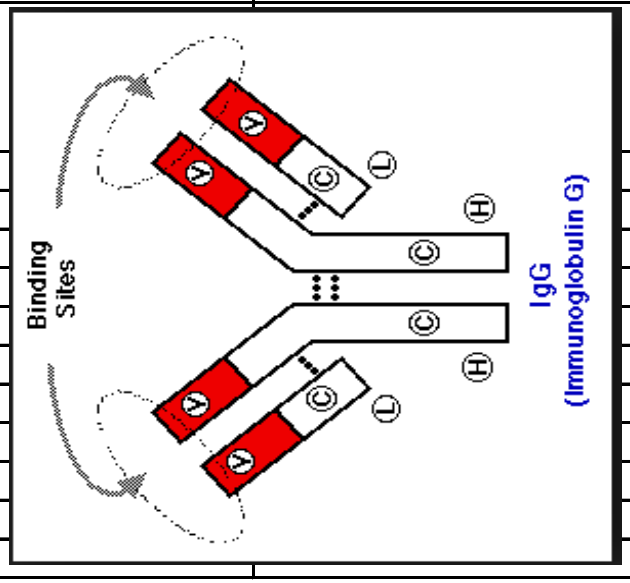


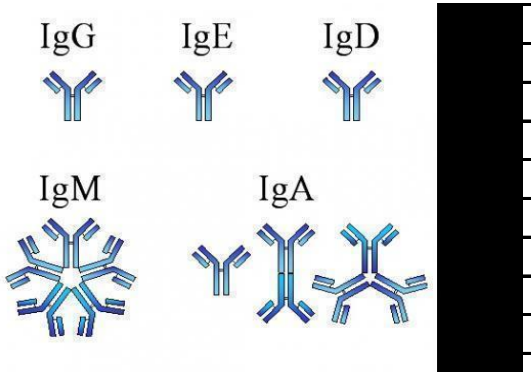
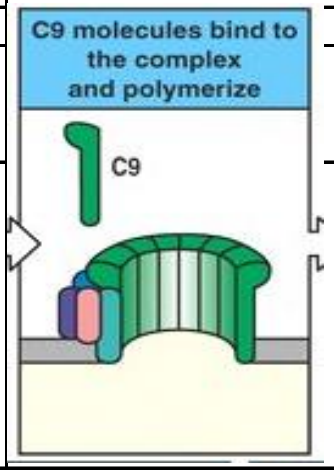
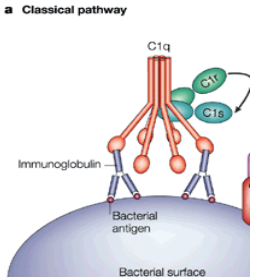
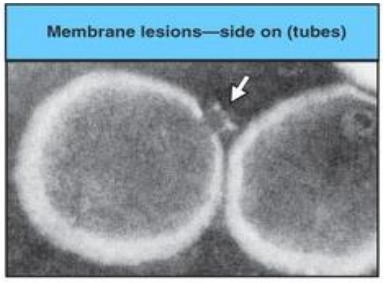
Lymphoid Tissue - high magnification

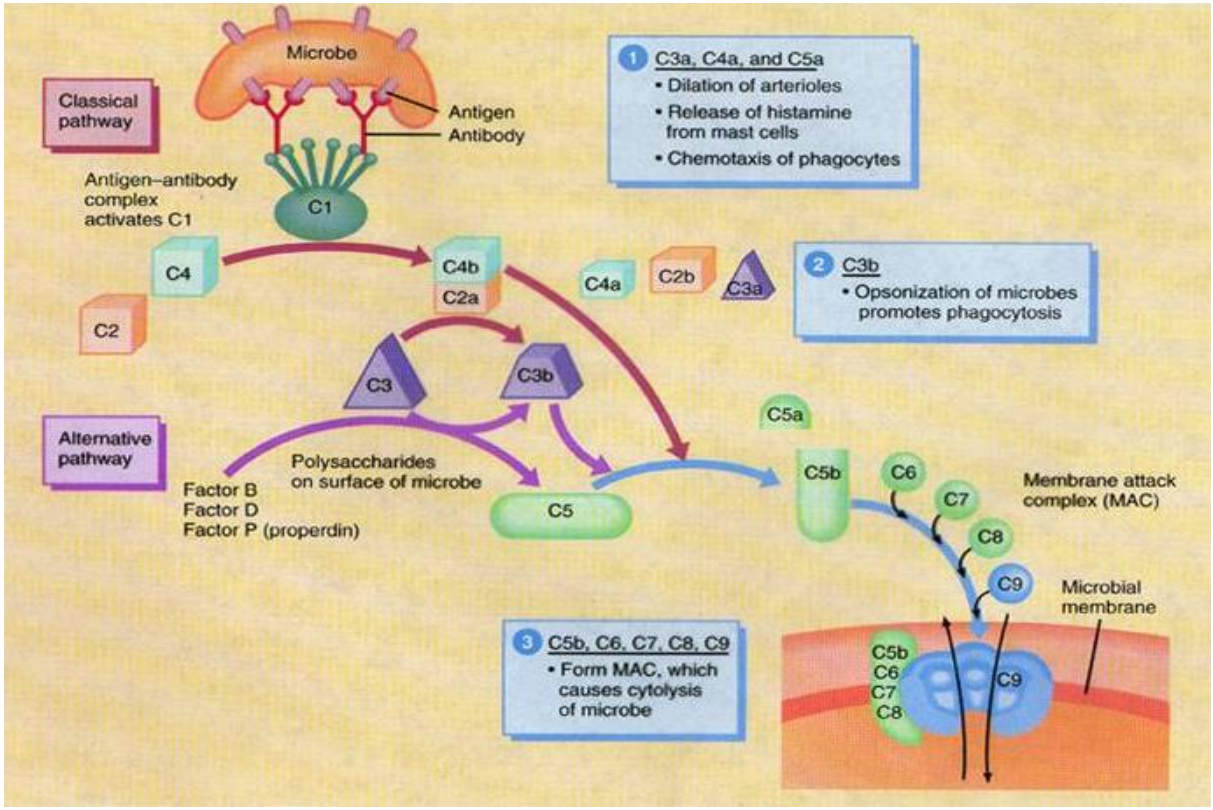
	2. Immune Cells: Lymphocytes and monocytes (macrophages).	  Lymphocyte Monocyte
	3. Tissues for immune cell development: Bone marrow and thymus. Sites of growth and maturation of immune cells. Thymus, in fetal development, educates lymphocytes to ignore self (otherwise the immune system would attack the body as a foreign material - this happens in a disease class called autoimmunity). **Ignoring self is called "Tolerance".**	
	4. Chemical Mediators: Complement, histamine, kinins, prostaglandins, leukotrienes, cytokines, tumor necrosis factor (TNF), and chemotactic factors.	
	How does the immune system work?	
	- it recognizes antigens (or immunogens) that may present as loose molecules or molecules on the surface membrane of a cell (bacteria, fungus, virus, virus infected cell, cancer cell).	
	- these molecules are often complex like proteins, polysaccharides, and glycoproteins.	
	- the antigens are detected by immune cells that trigger either a "Cellular" or "Humoral" immune response.	
	- antigens on the surface of out own cells known as the "Major Histocompatibility Complex" (MHC) are recognized by the immune cells to tell them the cells are self; so do not react to them.	
	- MHC molecules are inherited in combinations making most of us dissimilar, except for identical twins. This is why transplanted organs are rejected.	
115	**Antigen Presentation:** An immune process in which macrophages injest an antigen and then display a fragment of the antigen on their cell surface so that a lymphocyte can detect it and initiate an immune response. In this process, macrophages also secrete monokines and inter-leukins that activate additional lymphocytes in a secondary response. **Presentaion happens to T and B Cells, respectively initiating cell mediated and humoral immunity.** 	

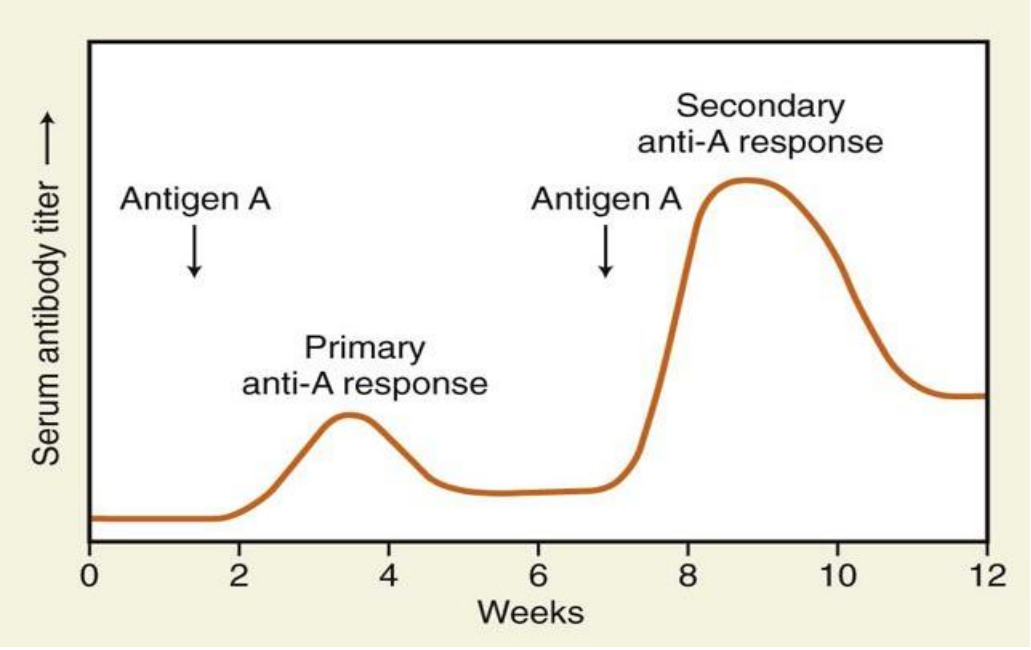
116	**IMMUNITY:**	
	- There are two types of immunity, "humoral" and "cellular"	
	- **T Lymphocytes** (thymus derived lymphocytes), arise from stem cells in the bone marrow and travel to the thymus gland to complete their maturation. They produce **cell mediated immunity.**	
	- **B Lymphocyte**s arise in the bone marrow, mature there, and travel to lymphoid tissues like the spleen, lymph nodes and tonsils where they produce **humoral immunity** (make antibodies).	
	Cell Mediated Immunity:	
	- T Cells have receptors that recognize antigens.	
	- When stimulated the T Cells attack the foreign cell and also divide to create an army of cells directed at the forein cells.	
	- The targets attacked by T Cells include virus infected cells, fungal cells, protozoa (one cell creatures), cancer cells, and transplant cells.	
117	- Subtypes of T Cells are CD4 + (Helper T Cells) and CD8+ (Cytotoxic T Cells)	
	- The normal ratio of CD4:CD8 is 2:1; this is reduced in HIV that selectively attacks CD4+ T Cells.	
	Humoral Immunity:	  Lymphocyte --> Plasma Cell
	- Macrophages present antigens to B Cells and with T Cell help become stimulated.	
	- Stimulated B Cells differentiate into Plasma Cells that produce antibodies (immunoglobulins) that specifically bind to the antigen that stimulated the B Cells.	
	- The antibodies coat bacteria and viruses marking them for ingestion by other cells, phagocytes, like macrophages and neutrophils. The structure facillitates this as these molecules have one region that recognizes another reason that binds to receptors on phagocytes.	





	Immunoglobulin Types:	
	Light chains - two types: kappa and lambda (κ, λ)	
	Heavy chains - five types: GAMED stands for gamma, alpha, mu, epsilon, and delta (γ, α, μ, ε, δ)	
	An antibody monomer (single molecule) is mad of two of the same light chains and two of the same heavy chains. It gets its name from the heavy chain:	
	IgG - gamma heavy chains and kappa or lambda light chains.	
	IgA - alpha heavy chains and kappa or lambda light chains. [dimers, mucosal associated]	
	IgM - mu heavy chains and kappa or lambda light chains. [pentamer]	
	IgE - epsilon heavy chains and kappa or lambda light chains.	
	IgD - delta heavy chains and kappa or lambda light chains.	
		
118	**Complement System:**	
	A family of nine proteins (C1-C9) that are activated in a cascade starting with an antigen-antibody complex with C1 and ending in a polymer of C9 that forms a pore (effectively a hole) in the target cell. In the cascade, some products act as inflammatory mediators, stimulating inflammation.	
	 	

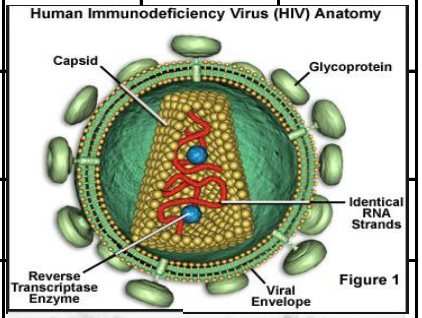
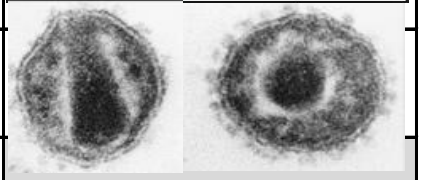
	Complement Cascade (illustrative only, not on test):	
		
	Memory Cells: Recognize antigen and stimulate and immune response. If a small number of cells was available to recognize the antigen in the primary infection, an expanded pool of "memory cells" is available to recognize the antigen on re-exposure (making the response quicker and stronger). B Cells that form in a humoral response facillitate antibody producion if the host is re-exposed to the antigen at a future date. Likewise sensitized T Cells generate a Cell Mediated response on re-exposure.	
	Natural killer cells are lymphocytes distinct from the T and B lymphocytes. They destroy, without any prior exposure and sensitization, tumor cells and cells infected with viruses.	
	Vacines and Booster Shots: The first time the immune system sees an antigen, the response time and delay time until antibodies are available is longer that if the host is re-exposed. A vaccination is an artificial exposure to an antigen, and a booster shot is a re-exposure, geared to prime the host so that a natural infection will generate a rapid and strong immune response.	

119	**Titer:** is a term that reflects the concentration of an antibody in the plasma. If you have a test for the antibody, an antibody at high concentration can be diluted until the test is no longer positive. The highest dilution that still reads positive for the antibody is the titer. If your test was positive at a dilution of 1:1000 and negative at 1:10,000, then the titer is 1:1000.	
	- using titer as a measure, the titer is higher in a re-exposure (or secondary response) when compareed to the original exposure (primary response).	
		
	Types of Acquired Immunity:	

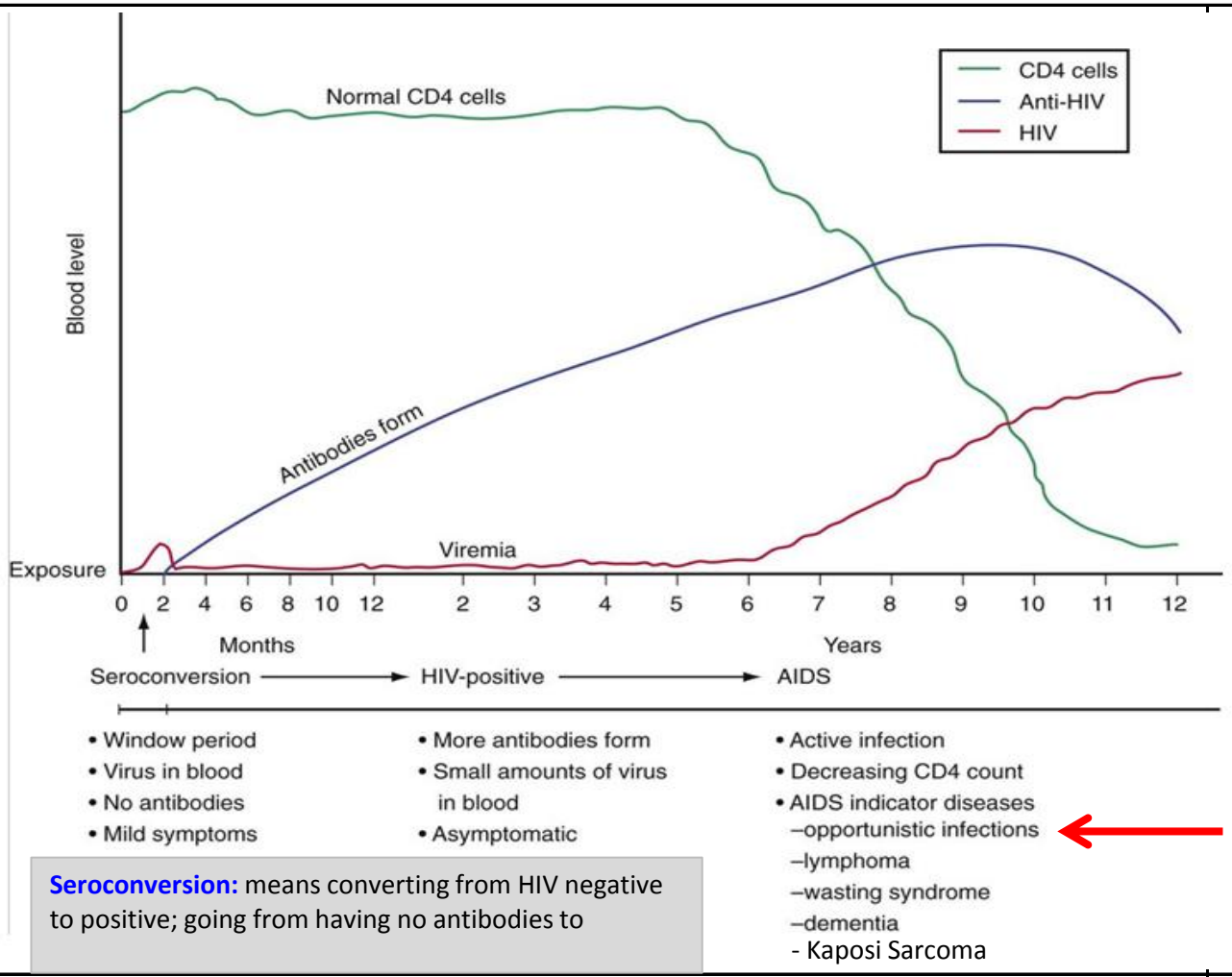
Type	Mechanism	Memory	Example
Natural active	Pathogens enter body and cause illness; antibodies form in host	Yes	Person has chickenpox once
Artificial active	Vaccine (live or attenuated organisms) is injected into person. No illness results, but antibodies form	Yes	Person has measles vaccine and gains immunity
Natural passive	Antibodies passed directly from mother to child to provide temporary protection	No	Placental passage during pregnancy or ingestion of breast milk
Artificial passive	Antibodies injected into person (antiserum) to provide temporary protection or minimize severity of infection	No	Gammaglobulin if recent exposure to microbe

	ORGAN TRANSPLANTS:	
	Graft - the transplanted organ.	
	Allograft (heterograft) - organ comes from same species, genetically different (not an identical twin).	
	Isograft - organ from identical twin.	
	Autograft - tissue transferred from one part of the body to another part in the same body.	
	Xenograft - tissue comes from a different species (example: pig heart valve used in a human).	
	Graft Rejection:	
	- is an immmune response to foreing antigens in the graft.	
	- the foreign antigens targeted are the "Major histocompatibility antigens" (MHC). These are also known as Human Leukocyte Antigens (HLA).	
	- minimal rejection of transplants that are not vascular like cartilage and corneas.B109	
	- transplants last longer when they are HLA matched more closely to host, the organ is from a living donor, and immunosuppresive medications are taken as directed.	
	Graft vs Host Disease: this is a form of rejection whereby the graft rejects the host rather than the opposite. This can occur in a bone marrow transplant were the transpplanted marrow sees the host as foreign and attacks it.	
121	**Types of Rejection:**	
	- Hyperacute: immediately after transplant (humoral response with pre-existing antibodies)..	
	- Acute: several weeks after transplant (lymphocytes attack organ cells).	
	- Chronic: months or years after transplant (involves chronic blood vessel damage).	
	Treatment of Rejection:	
	- relies on immunosupressive drugs.	
	- depressed immune system predisposes the host to opportunisitc infections.	
	- depressed immune system also leaves the host more vulnerable to cancer.	
122	**Types of Hypersensitivity Reactions:**	
	Type I: Allergic Reactions	
	- antigen is an allergan (food, chemical, pollen, drug, etc …)	
	- primary exposure results in IgE anibody response.	

	- secondary exposure finds the IgE bound to mast cells triggering them to release histamines that result in itch (if on skin), vasodilatation-congestion (if in nasal cavity) or bronchoconstriction and mucus secretion (if in bronchi). This is why we take "anti-histamines".	
	- an exaggerated form of this reaction is a life threatening emergency known as "Anaphylactic Shock" that can obstruct airways and be fatal. The treatment is epinephrine (can be carried in an emergency injector called an "epi pen"). Triggers include latex in gloves and cosmetics, insect stings, ingestion of nuts or shellfish, administration of penicillin, or local anesthetic injections. The reaction usually occurs within minutes of the exposure.	
124	**Type II: Cytotoxic Hypersensitivity**	
	- antigen is a cell surface protein detected by circulating IgG.	
	- an example is an **incompatibile blood transfusion** where circulaing antibodies attack and lyse the incompaible circulating red blood cells. Lysing or breaking open red cells is called **"Hemolysis".**	
125	**Type III: Immune Complex Hypersensitivity**	
	- immune complexes (antigen-antibody complexes) deposit in tissue and initiate an immune response that results in tissue destruction.	
	- glomerulonephritis and rheumatoid arthritis are examples.	
	- serum sickness with immune complex deposition in muliple tissues can happen if injections of animal serum are given as therapy.	
126	**Type IV: Cell-Mediated or Delayed Hypersensitivity**	
	- This type of hypersensitivity is a delayed response by sensitized T lymphocytes to antigens, resulting in release of lymphokines or other chemical mediators that cause an inflammatory response and destruction of the antigen.	
	- the TB skin test is an example; **Contact Dermatitis** is an example.	
	- other examples include reactions to chemicals, cosmetics, dyes, soaps, metals, and poison ivy.	
127	**Autoimmune Disorders**	
	- antibodies to one's own tissues develop (called "autoantibodies").	
	- can involve a single organ or be systemic ivolving multiple organs and sites.	
	- Examples, Hashimoto's thyroiditis, systemic lupus erythematosus, rheumatic fever, myasthenia gravis, scleroderma, pernicious anemia, and hyper-thyroidism (Graves' disease)	
	- treated with steroids and cytotoxic agents.	

	Immunodeficiency			
130	Immunodeficiency results from a loss of function, partial or total, of one or more components of the immune system leading to increased risk of infection and cancer.			
	Primary Immunodeficiency - a genetic disorder, born with it, manifests in infnats and children,			
	Examples include an inherited X-linked hypogammaglobulinemia (low antibody levels because of a B-cell defect) or a developmental defect known as DiGeorge syndrome (hypoplasia of the thymus).			
	Secondary or acquired immunodeficiency refers to loss of the immune response resulting from specific causes and may occur at any time during the lifespan. Loss of the immune response can occur with infection, particularly viral infection, splenectomy (removal of the spleen), malnutrition or liver disease (hypoproteinemia—low serum protein level), use of immunosuppressive drugs in clients with organ transplants, and radiation and chemotherapy for cancer treatment.			
	- It is essential that prophylactic antimicrobial drugs (preventive antibiotics) be administered to anyone in an immunodeficient state before undertaking an invasive procedure that carries an increased risk of organisms entering the body.			
131	**Acquired immunodeficiency syndrome (AIDS)** is a chronic infectious disease caused by HIV, which destroys helper T-lymphocytes, causing loss of the immune response and increased susceptibility to secondary infections and cancer.	**NOTE: Fetus can get HIV, but antibodies in newborn are mother's antibodies that crossed the placenta.**		
	An individual is considered **HIV-positive** when the virus is known to be present in the body, but few if any clinical signs have developed. **Acquired immunodeficiency syndrome** is the stage of active infection, with marked clinical manifestations and multiple complications. **An individual may be HIV positive for many years before he or she develops AIDS.**			
	Homosexual males, prostitutes, prisoners and IV drug abusers are high risk groups, but also seen in women, children, and in transmission to the fetus. Anal or vaginal sex can transmit the disease.			
	The first sporadic cases of AIDS in the US appear to have occurred as early as the 1950s, but a significant presence of the disease began in the early 1980's. Acquired immunodeficiency syndrome is now considered a worldwide pandemic, and cases still are multiplying.			
	Human immunodeficiency virus is not transmitted by casual contact (touching or kissing an infected person), sneezing and coughing, fomites such as toilet seats or eating utensils, or insect bites.			
	Anti-retrovirals are the treatment, but globally, 90% of those infected are not being treated with anti-retrovirals. Figures in 2011: 34 million people world wide living with HIV (70% in Subsaharan Africa).			
	The core of HIV contains two strands of RNA and the enzyme reverse transcriptase, and the coat is covered with a lipid envelope studded with "spikes" of glycoproteins that the virus uses to attach to human cells.			
	- viral RNA must be converted by the viral enzyme into viral DNA, which is then integrated with the human DNA. The virus then controls the human cell and uses its resources to produce more virus particles, and subsequently the host cell dies	 Diagram and Electron Microscope images of HIV virus.		

	Steps in infection:			
	1. HIV attaches to CD4+ Lymphocyte (**Helper T Cell**) and enters cell			
	2. Reverse transcriptase converts the viral RNA to DNA. [blocked by AZT].			
	3. Viral DNA integrates into human DNA.			
	4. Host cell makes more virus parts.			
	5. Virus parts are assembled [blocked by Anti-HIV protease inhibitor drugs].			
	6. Virus is shed and cell dies.			
	Window Period: time from virus entering body and antibodies appearing.			
	Infectivity: When there are antibodies present (HIV positive), the virus is present and the patient can infect others.			
	Phase 1 of Infection (3-6 weeks) flu like symptoms. HIV positive in 2-10 weeks.			
	Phase 2 of Infection. Latent phase, may last years.			
	Phase 3 of Infection. AIDS with low CD4+ lymphocytes, severe opportunistic infections, cancer, wasting, and CNS deficits.			
	CD4+ Lymphocytes (**"Helper Cells**") are necessary for **Cell Mediated Immunity and Humoral Immunity**; so **both are affected in HIV/AIDS**.			



Seroconversion: means converting from HIV negative to positive; going from having no antibodies to

Opportunistic Infections: Organisms like flora that normally may not be pathogenic act as pathogens in an immunosuppressed host. **Pneumocystis carinii** is an opportunistic pulmonary infection that is the **most common cause of death in AIDS patients.**

Treatment for AIDS:

Antiviral drugs can reduce the replication of viruses, but they do not kill the virus, and thus are not a cure.

Combinations of three to five drugs in a "cocktail" are being used successfully to prolong the latent phase as well as reduce the viral load during the final phase.

As patients with HIV live longer, new disease processes and social challenges are arising.