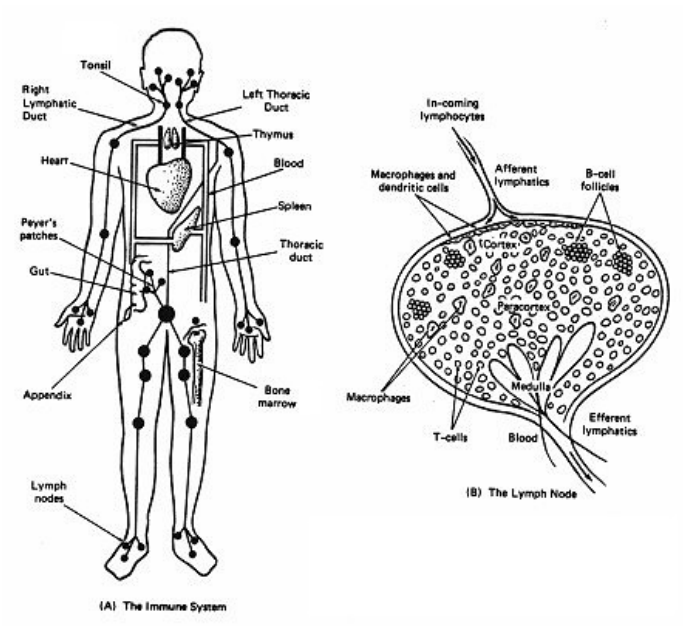
Chapter 16 Notes **Adaptive immune system response**

I. Introduction to Immunity

A. Vocabulary

1. Specific Immune System

The **immunological system** is comprised of the **lymphoid tissues and organs of the body**. Lymphoid tissues are widely distributed : they are concentrated in bone marrow, lymph nodes, spleen, liver, thymus, and Peyer's patches scattered in linings of the GI tract. The lymphoid system is encompassed by the **system of mononuclear phagocytes**. Lymphocytes are the predominant cells, but macrophages and plasma cells are present also. Lymphocytes are cells which circulate, alternating between the circulatory blood stream and the lymphatic channels. The distribution of lymphatic tissues that make up the immune system in humans is illustrated in the figure to the left.



2. ***Antigen***: a protein, toxin, or other substance of high molecular weight (5000 to100,000 daltons units), to which the body reacts by producing antibodies

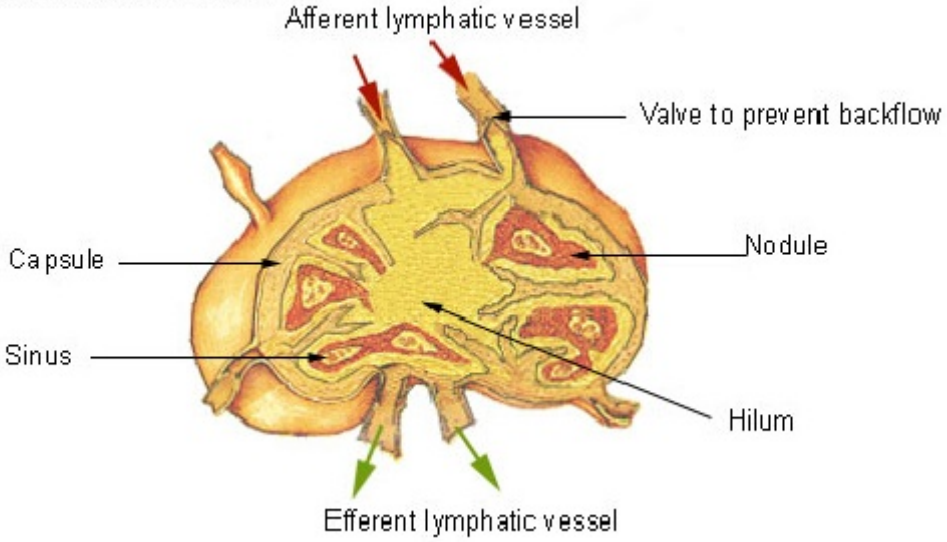
b. ***Antigenic determinant***: The body recognizes antigens by the three dimensional shapes of regions know ***epitopes***

c. ***Haptens***: small molecules of a mass less then 5000 daltons. Requires binding to larger molecular carrier to become antigentic. Ex.: penicillin molecular mass of 302 daltons triggers specific immune response when it binds to carrier protein in the blood.

d. Types of Antigens:

1) Exogenous: include toxins and other secretions and components of microbial cell walls, membranes, flagella, and pili

Lymph Node Structure



2) Endogenous: Protozoa, fungi, bacteria, viruses that reproduce inside a body's cell producing endogenous antigens.

3) Autoantigens: Antigenic molecules found on an individual's normal (uninfected) cells (self-antigens). Autoantigens recognized as foreign are normally eliminated during the development of the immune system.

3. Antibody

a. A protein produced by the body in response to an antigen, and capable of combining specifically with that antigen.

4. Immune Cells

a. Antibody Mediated Immunization (**Humoral)** lymphocyte: **B cells**

b. **Cell Mediated Immunization**: **T-cell**

c. Antigen-specific: acquired or specific immunity. This type of immune response is antigenic specific and has memory. Response becomes stronger with repeated encounters with the same antigen. This response system involves both immune cells and soluble proteins (antibodies) present in the host.

5. Innate Immunity (Non specific: Host defenses that afford protection against any kind of pathogen.

6. Acquired Immunity

Active Acquired Immunity

The host undergoes an immuological response and produces the cells and factor responsible for the immunity, i.e., the host produces its own antibodies and or immuno-reactive lymphocytes. Persist a long time in the host - up to many years.

Passive Acquired Immunity
is acquired by the host from immune factors raised in another animal, i.e., the receives antibodies and/or immuno-reative lymphocytes. Originally produced during an active response in another animal. Short-lived response

a. Active Natural Acquired Immunity

Antigens enter the body naturally; body produces antibodies and specialized lymphocytes

b. Passive Natural Acquired Immunity

Antibodies pass from mother to fetus via placenta or to infant in the mother's milk

c. Active Artificial Acquired Immunity

1. vaccinations

Antigens are introduced in vaccines; body produces antibodies and specialized lymphocytes

d. Passive Artificial Acquired Immunity

Preformed antibodies in immune serum introduced into body by injection

B. Levels & components of the Immune System

1. Complement (covered during chapter 15)

2. Phagocyte Components

a. Neutrophils & Macrophages

3. **Humoral system** (Antibody mediated immune system)
   a. Clonal selection
   b. Memory establishment

4. **Cell Mediated system** (T - cell mediated immune system)
   a. Major histo-compatibility complex (MHC-I)
   b. Antigen presenting cells (APC)

C. Development of the Immune system

1. Fetus: Yolk sack ------ later liver cells -------- later bone marrow.

D. Lymphocyte Receptors and Function

What are the major functions of immune system

A) Attachment to non-self or foreign antigens;

B) Binding receptors: to cell surface receptors that indicate self, such as MHC molecules

C) Receiving and transmitting chemical messages to coordinate the response;

a... B-cell receptors (BCR)

1) IgD antibodies attached to outer membrane

2) Each B-cell has upwards of 500,000 identical copies of BCR that bind to specific antigenic molecules.

a) It is calculated that there are over 10^9 different B lymphocytes

b. T-cell receptors (TCR)

(TCR) bind to foreign antigens. These receptor belong to the same protein family as B-cell receptors.

TCRs are variable like B-cell receptors.
Each T cell has identical copies of the same TCR
There are over 10^{11} different possible shapes which can act against antigens in a cell mediated response.

TCR also bind to Major histo-compatibility complex (MHCs) on macrophage and dendritic cells.

Dendritic cells have no other function than to become antigen-presenting cells (APC).

Following a macrophages phagocytisizing microbe, the microbe is broken up into fragments antigens of about 10 or so amino acids. These fragments are then displayed on the outer surface of the macrophage as a antigen-presenting cell (APC). A "T" cell will recognize an antigenic fragment on the APC only if its is in close association with certain cell-surface self molecules. These Self molecules are components of the major histo-compatibility complex (MHC I). **The particular MHC I protein a person carries are unique to the individual.** - thus, serving a signal for the immune system to distinguish self from non-self.

c. When TCR is bound to MHC containing foreign peptide TCR is phosphorylated.

Phosphorylated TCR send a signal to the T-cell nucleus to divide and produce interleukin IL-2.

d. T-cells form clones like B-cell.

e. The immune system must have specific clones of B-cells and T-cells to rapidly respond to foreign antigen.

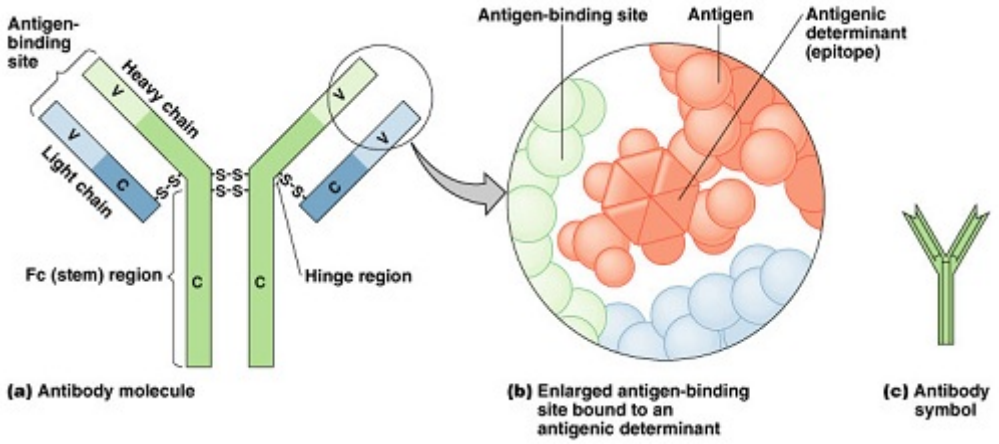
f. Antibody Formation

1). B cell - Plasma cell produce 2000 antibody **proteins per second**.

E. Antibody classes and function

1. Five classes

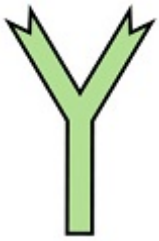
1. IgG; 2. IgA 3. IgM 4. IgE 5. IgD



The heavy chain of the define the Ig antibody defines the type and response of the antibody. Light chain: Kapa and lambda chain, Mu, Delta (five classes)

Upwards of 3.6 million response can be marshaled against microbes from the five classes of antibodies collectively: IgG, IgM, IgD, IgE IgA

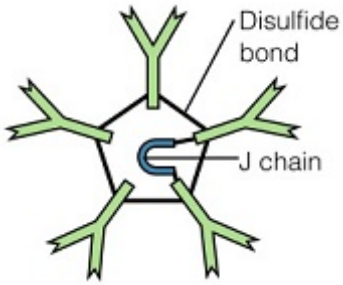
IgG



Monomer
80% of serum antibodies
Fix complement
In blood, lymph, intestine Cross placenta
Enhance phagocytosis; neutralize toxins & viruses; protects fetus & newborn
Half-life = 23 days

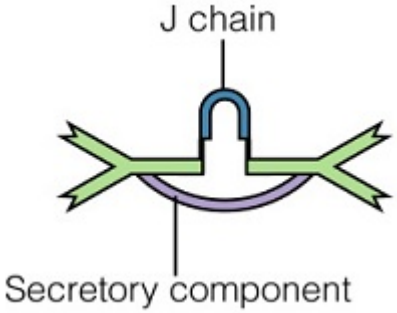
IgM

Pentamer
5-10% of serum antibodies
Fix complement
In blood, lymph, on B cells
Agglutinates microbes; first Ab produced in response to infection
Half-life = 5 days



IgA

Dimer
10-15% of serum antibodies
In secretions
Mucosal protection
Half-life = 6 days



IgD

Monomer
0.2% of serum antibodies
In blood, lymph, on B cells
On B cells, initiate immune response
Half-life = 3 days

IgE

Monomer
0.002% of serum antibodies
On mast cells and basophils, in blood
Allergic reactions; lysis of parasitic worms
Half-life = 2 days

2. Antibody Variability

Antibodies: Soluble molecule protein with great host specificity to bind to a particular antigen

F. Modes of Actions for various Types of Antibody (Ab)

a. Agglutination:

1) Antibodies gluing together multiply bacteria as a larger cluster thereby increasing the likelihood that phagocytosis.

b. Antibody-dependent cell mediated cytotoxcity

1) antibody attach to target cell cause destruction by non-specific immune system cells

c. Neutralization

1) toxoid bound by antibodies prevent either bacterial or viral toxins causing damage

d. Opsonization:

1) the coating of antibody to antigen

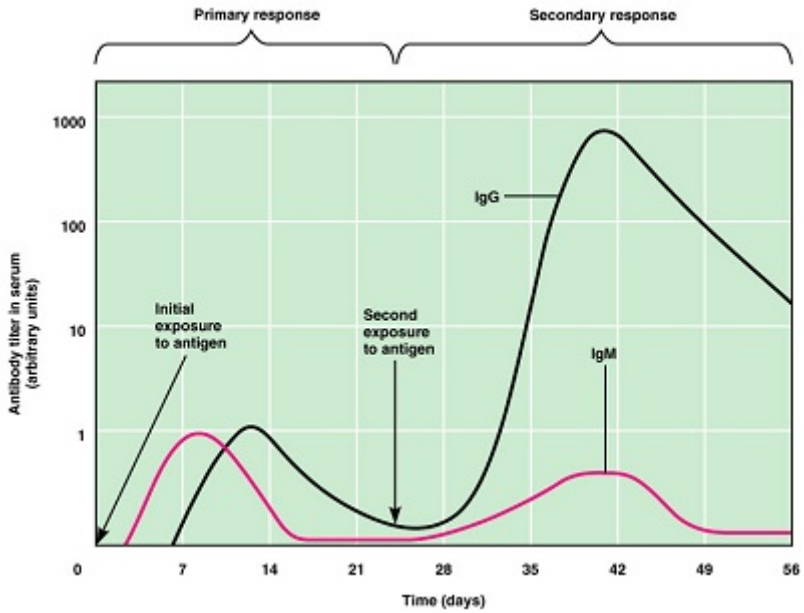
e. Inflammation

1) Disruption of cell by complement/reactive protein attracts phagocytic and other defensive immune system cells

f. Active Complement system

1) Bacterial cell lysis by Neutrophil C3b antibody complex

G. Vaccination



Primary and secondary responses to antigens.

1. Initial exposure to novel antigen at zero time.
2. Between zero time and 3 days (**latent period**) **clonal selection** takes place where a unique fit between antigen and IgD antibody B-cell receptor takes place.
3. Upon T-cell mediated B-cell activation occurs (B-cells become either B-plasma cells or B-memory cells) resulting in the synthesis of IgM. This titer rapidly increases over the next several days soon to be replaced by the synthesis of IgG.
4. B-cells remain active for 2 to 3 days then burn out.
5. Upon the second exposure of the immune system to the same antigen followed by a variable time period, B-memory cells act immediately without T-cell mediation bifurcating into B-plasma and B-memory cells (**Anamnestic response**). This second contact results in a significant increase in the total antibody titer while increasing the number of reside B-memory cells.

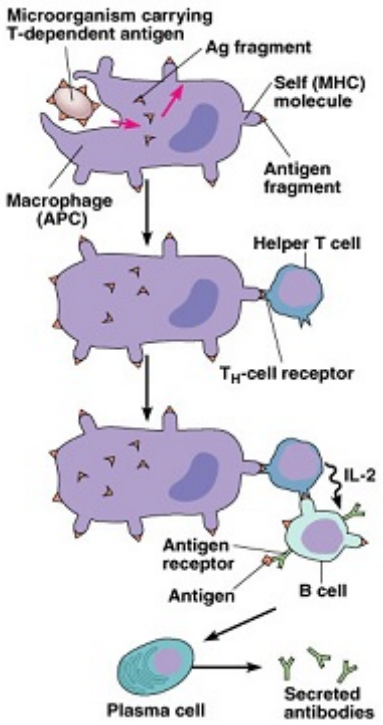
H. T-cell Cellular Immunity

Cells communicated with each other, triggering their activity or causing them to differentiate.

Cytokines function as a chemical messenger cell with in the immune system.

Cytokines may have a variable response within the immune system either inhibiting or stimulating a response.

Chemokines, a form of cytokines, causes chemotaxis leukocytes into infected tissue (See attached addendum)



1. Types of T cells

Antibody or reactive "T" cell will react specifically with the antigen that induced its formation; it will not react with other antigens. However, cross-reactivity is possible

2. Cluster of differentiation cells (CD cells types) are glycoprotein used in the immune response (over 250 types identified)

CD4, CD8, CD95 and CD95L cells

a. CD4 cells are primarily helper T cells (T_H) which include the long lived memory cells

1) Bind T_4 to major histo-compatibility complex II (MHC II) found on B-cell and specialized antigen presenting cell (APC)

b. CD8, CD95, and CD95L include both cytotoxic and suppressor T cells.

1) Major histo-compatibility complex I (MHC I) binds cytotoxic cell (T_c) (also known as Natural Killer cells (NK's)) and suppressor T-cell (T_s) to body cell expressing abnormal MHC I self marker.
Every cell in the human body will have an identical MHC I as selfing marker against auto-destruction by NK cell. NK cell attack cells expressing endogenous viral particles and abnormal markers resulting from cancer or tumor cells.

3. **Function of T cells**

Mature T cells of these four types can be identified by their characteristic cell-surface molecules

1) T - helper cells (T_H) ;

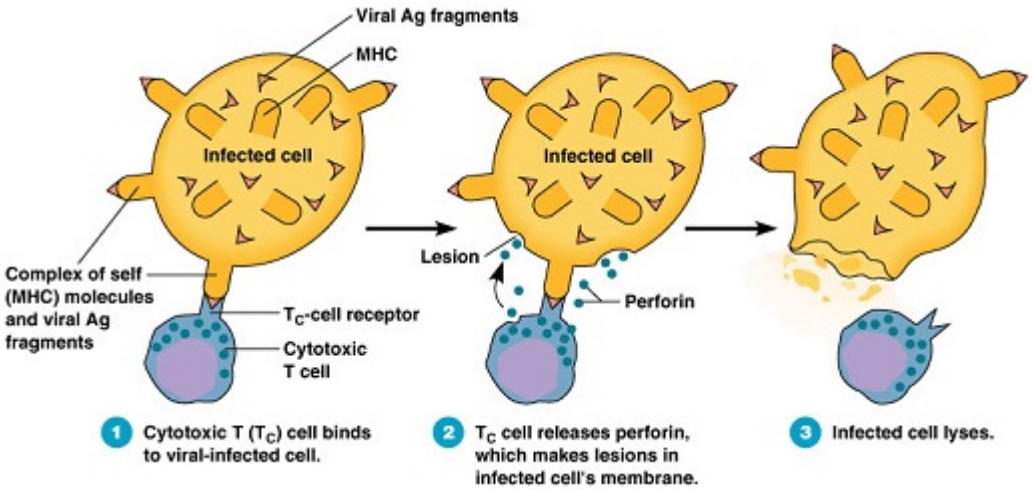
These cells play a central role in the immune response. Activated T_H cells influence the activity of other immune system cell through chemical agents such as cytokines and interleukins.

T helper cells can further be subdivided into 2 categories:T_{H1} and T_{H2} helper cells.

The distinction between T_{H1} and T_{H2} is based on their lymphokine profiles. T_{H2} cells have previously been to as T -helper cells because they provide lympohokines (IL-2 and IL-4) which activate T cells and B cells at the start of the immune response. T_{H1} cells play a role in allergic responses.

2) Cytotoxic T killer cells (T_C) or (NK cells) T clls: (T-cell activation endogenous antigen for cell-mediate immune system response)

These cells are used to destroy targeted cells on contact. Target cells can be cells infected with virus, tumor or cancer cells.



The T_C cells binds with MHC- antigen complex I on the cell's surface and the releases a protein called perforin. The perforin forms a pore in the membrane of the targeted cell, causing lysis. T_C cells continue their activity as long as the stimulating antigen persists; when it disappears, they undergo apoptosis (death).

The CD95 cytotoxic pathway

Binding of CD95L found on the T_c cell activates the enzymatic portion of the infected cell's CD95 to promote apoptosis.

Activation of cytotoxic T (T_c) cells is though to follow a T_H1 activation pathway. T_H1 cells secrete IL-2, which activates T_c cells. IL-2 triggers active T_c cell to divide, much like clonal selection of B cells forming more active T_c cells as well as memory T cells. Active T_c cells secrete IL-2, becoming self-stimulatory.

3) Delayed hypersensitivity T (T_D)

These cells may actually be T_H or T_C cells. They are associated with certain allergic reactions, such as poison ivy, or transplanted tissues rejection.

4) Suppressor T (T_S)

Not well understood - thought to turn off the immune response when an antigen is no longer present.

2. Role of T-Helper Cells (T-dependent exogenous antigens)

T_4 cells have receptor for major histo-compatibility complex II (MHC II) and antigen. CD4 binds to MHC II of B cell to induce antibody production

The form of T_4-cell receptors varies greatly. Each type of T_4-cell expresses just one type of receptor. Some T_4-cells have receptors that react with MHC and APC

Reactive T_4cells initiate an immune responses.

T_4-cells attach to B cell and produce interlukin 2 stimulating the transformation of B cells into plasma antibody producing cells.

3. Antigen Processing

a. Exogenous antigens are phagocytized by an APC, which then digests them to release antigenic determinants that are inserted into antigen-binding grooves of MHC II molecules. The MHC II antigenic determinant complexes are then displayed on the outside of the APC's cytoplasmic membrane.

b. T-independent antigens

The cross linking of repeating subunits to numerous BCRs on a B-cell stimulates the cell to proliferate becoming a plasma cell, and thus, produces antibodies without the help of T cell