

Lecture Outline**B cell immunity****Jan 24, 2001**

Humoral immunity is mediated by antibodies. Humoral immunity can be transferred from an immune individual to a non-immune individual with serum known as passive immunization.

I. Steps to get B cell activation. B cell activation occur in 2° lymphoid tissue.

1. B cell receptor binds antigen to trigger endocytic uptake of both BCR and antigen.
 2. B cell binds nearby T cell and they form conjugate.
 3. Costimulation for B cells when CD40 on B cells binds CD40 ligand on T cells.
- Costimulation can also be in the form of IL-4 from Th cells. Drives B cell into B cell cycle.

II. Characteristics of activated B cells

1. Express more cell adhesion molecules (**CAMs**) that help the B cells bind to other cells.
2. **Clonal proliferation.** B cells when activated go through a rapidly dividing stage.
3. **Isotype switching.** During early immune responses, primarily IgM is made initially but with continued activation and in the presence of cytokines B cells can isotype switch to IgG, IgA, IgE.
4. After activation B cells differentiate into memory cells and **plasma cells.**

Plasma cells are the only stage of B cells capable of secreting antibodies.

III. Antibody Isotypes During Infections.**Isotype switching**

After B cell activation during the proliferation and differentiation stages the B cells can switch which antibody isotype is expressed and secreted.

Antibodies of different isotypes provide different effector functions. If the immune system is exposed to the pathogen for a longer period of time or repeated exposures the immune system will respond by making more effective antibody isotypes. Higher affinity and able to provide more effector functions. The order of isotype switching is somewhat sequential. **IgM---IgG1---IgE---IgA.** This changing of heavy chain expression is done by genetic recombination at the DNA level and is irreversible.

IgM vs IgG

Clinical evaluation of antibody responses are measured to characterize an infection.

High IgM Low IgG = recent exposure

High/low IgG Low IgM = past exposure

IV. Functions of antibodies.

1. **Neutralization:** blocks a molecule on the pathogen surface that is essential for adherence of the pathogen or entry into host cells. Antibodies can block the active sites of toxins.

2. **Opsonization:** When specific antibody binds to the surface of a pathogen, the Fc region of the antibody can bind to Fc receptors on the surface of macrophages and neutrophils which facilitate trigger phagocytosis. Enhancement of phagocytosis is known as **opsonization.**
A substance which enhances phagocytosis is known as an **opsonin.** Antibodies can act as opsonins.

3. **Antibody-dependent cell-mediated cytotoxicity (ADCC):** Antibody can enable cells of the innate immune system to kill pathogens by ADCC. Killing of target cells or pathogens can occur when the Fc portion of antibody bound to the target binds to the Fc receptors of a cell which has cytotoxic capability. Cells which can participate in ADCC include NK cells, macrophages, monocytes, neutrophils, and eosinophils. If the target is too large to be phagocytized, the cells degranulate and damage the target by releasing proteolytic enzymes at the immune cell/target cell interface.

4. **Complement Activation** classical pathway of complement, leading to lysis of the pathogen. Which isotype is produced often controls the effector functions of abs. Some isotypes are better at some functions than others.