Humoral immunity

Humoral or **antibody mediated immunity** is directed primarily against:

1. **Exotoxin** mediated diseases such as tetanus and diphtheria

2. Infections in which virulence is related to **polysaccharide capsules**, e.g., pneumococcus

3. Certain **viral** infections

Exotoxin is a toxin released by a living bacterial cell into its surroundings.

Primary response

-- It is response on **first interaction** with antigen.

-- Body takes a **longer** time to respond (lag phase).

-- Lag period is typically from **7 to 10 days** but may be longer.

-- During this period a **small clone** of B cells specific to antigen is formed.

-- The serum antibody level continues to rise for **several weeks**, then declines to very **low levels**.

-- First antibodies to appear are **IgM** followed by **IgG** or **IgA**.

-- **IgM levels** drops **more quickly** as compared with other two.

Secondary response

-- **Second** encounter with the **same antigen** or closely related (or cross-reacting) one is called **secondary response**.

-- This time, the antibody response is **rapid** and lag phase is typically **only 3-5 days**.

-- Also, the level of antibody produced is **much higher**.

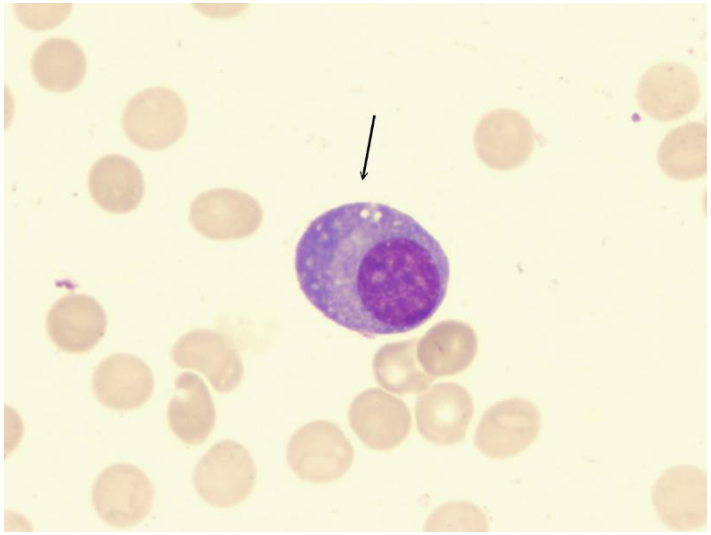
-- This is due to **memory cells** formed after first encounter.

Memory cell is a long-lived lymphocyte capable of responding to a particular antigen on its reintroduction, long after the exposure that prompted its production.

-- These memory cells **proliferate** to form a **large clone** of specific **B cells** including:

1. **Plasma cells** which mediate the **secondary** antibody response

2. **New memory cells**.



Plasma cells, also called plasma B cells, are white blood cells that originate in the bone marrow and secrete large quantities of proteins called antibodies in response to being presented specific substances called antigens.

-- Amount of **IgM** produced is **similar** to primary response, but **IgG/IgA** are produced in **much larger** quantities and they persist for longer periods.

-- The **first** dose of vaccines is **not very effective** because it evokes **only primary response.**

-- So **booster doses** are given to stimulate secondary response.

Booster dose: After initial immunization, a booster injection or booster dose is a re-exposure to the immunizing antigen.

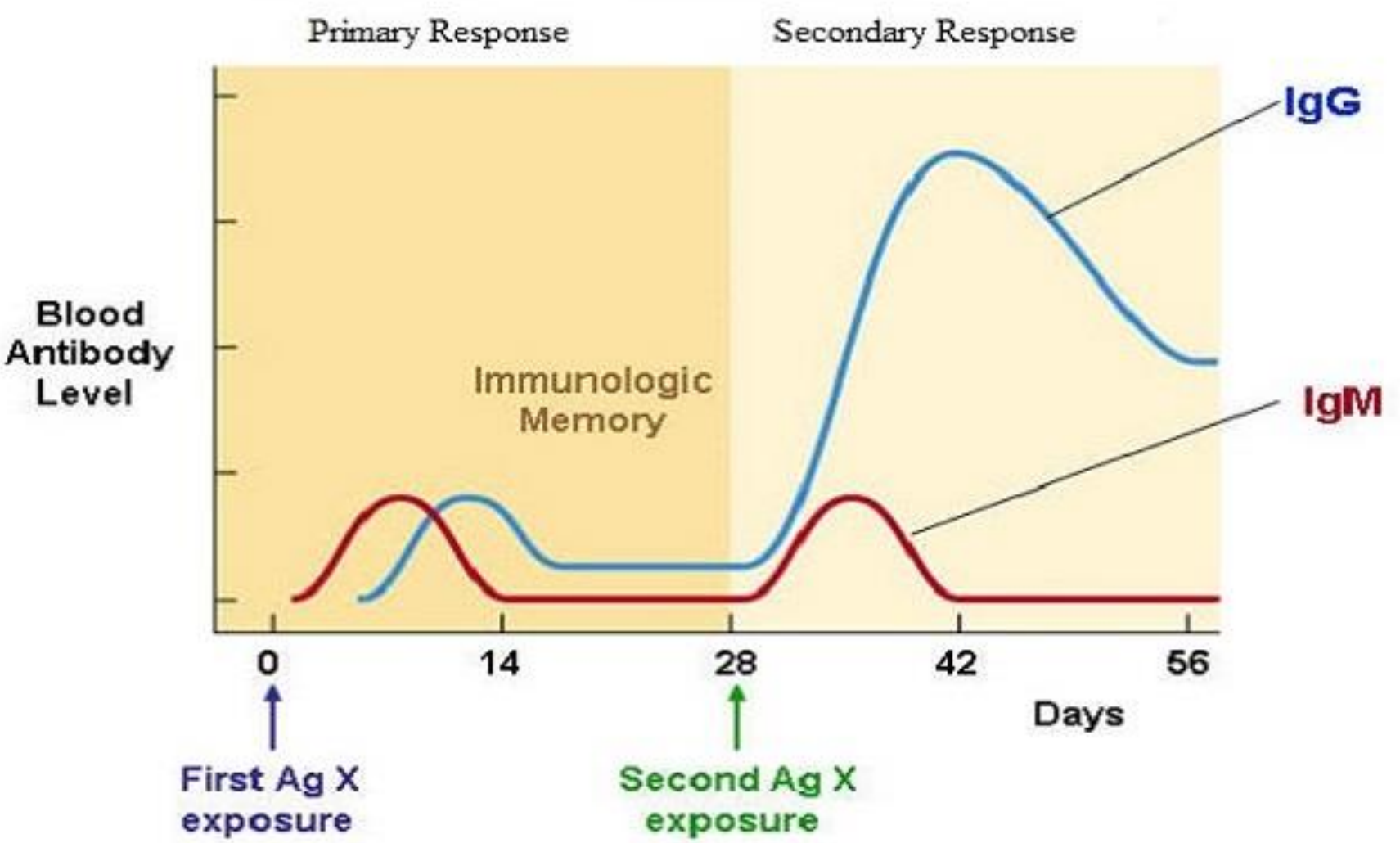


Fig. Immune Response and Secretion of antibodies

Humoral Immune Response

Primary and Secondary Immune Response

Attribute	Primary response	Secondary response
Antigen type	Both T dependent and T and T independent	Only T dependent
Responding cells	Naïve B or T cells	Memory B or T cells
Lag period	Longer (4- 7 days)	Shorter (1- 3 days)
Peak response	Occurs in 7- 10 days	Occurs in 3- 5 days
Magnitude	Low	High (100- 1000x)
Antibody isotype	IgM predominates	IgG predominates
Antibody affinity	Lower	Higher

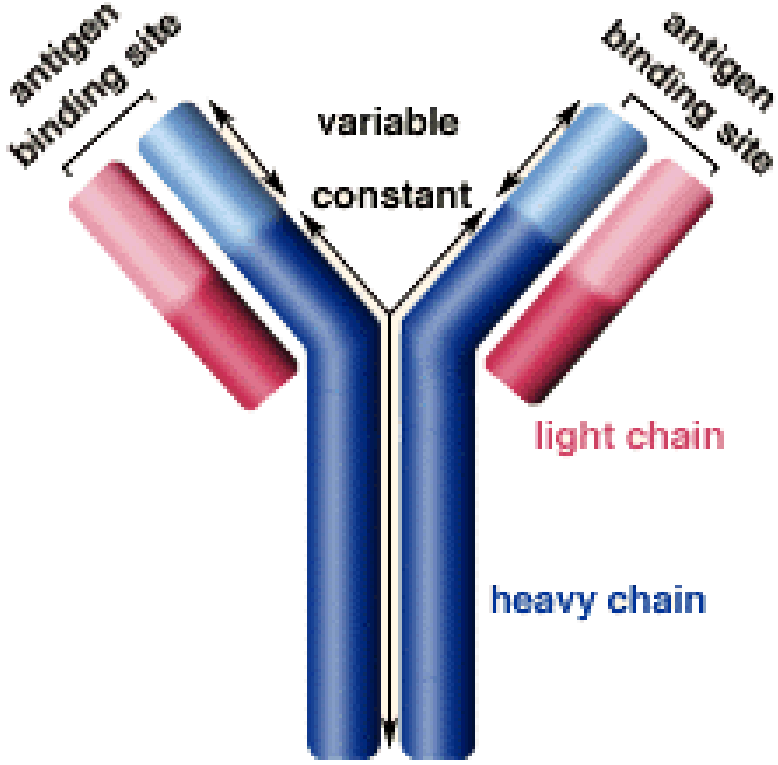
Affinity maturation

With each **succeeding** exposure to the antigen, antibody becomes **better suited** to bind.

This is due to **mutations** in DNA encoding for **antigen- binding site.**

These are called **super hypermutations**.

These mutations may result in replacement with **more suitable** amino acids.

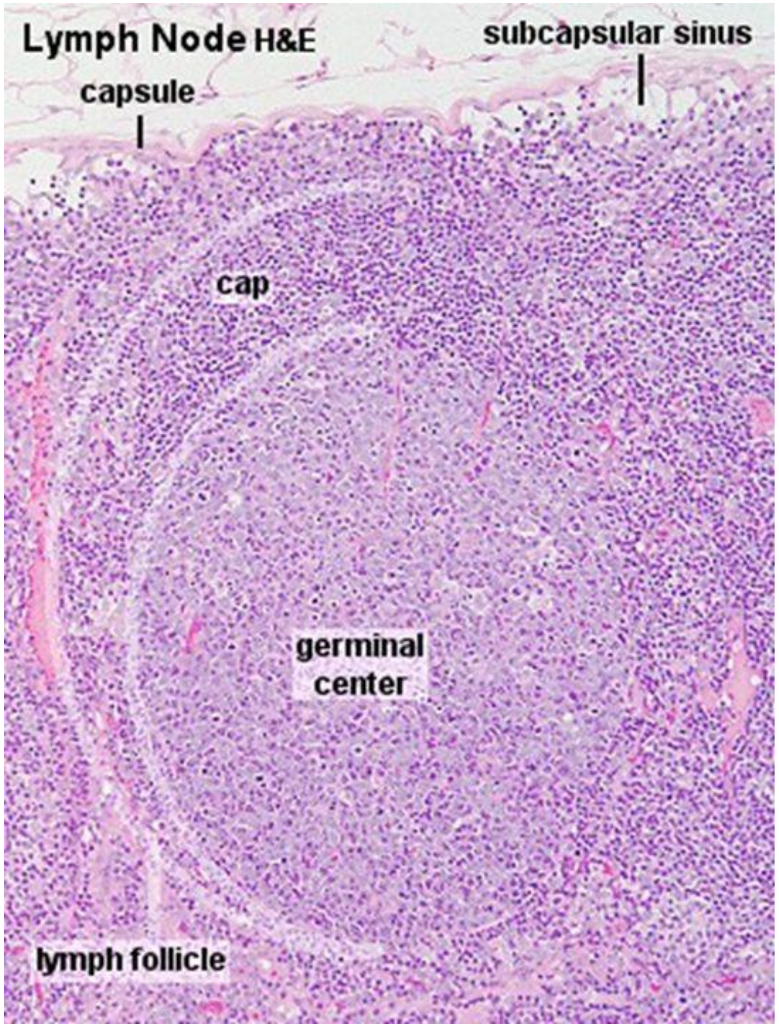


-- This process is called **affinity maturation.**

-- **Booster doses** also **improve** maturation of antibodies.

-- Affinity maturation occurs in the **germinal centers** of the **lymph follicles** in the spleen and lymph nodes.

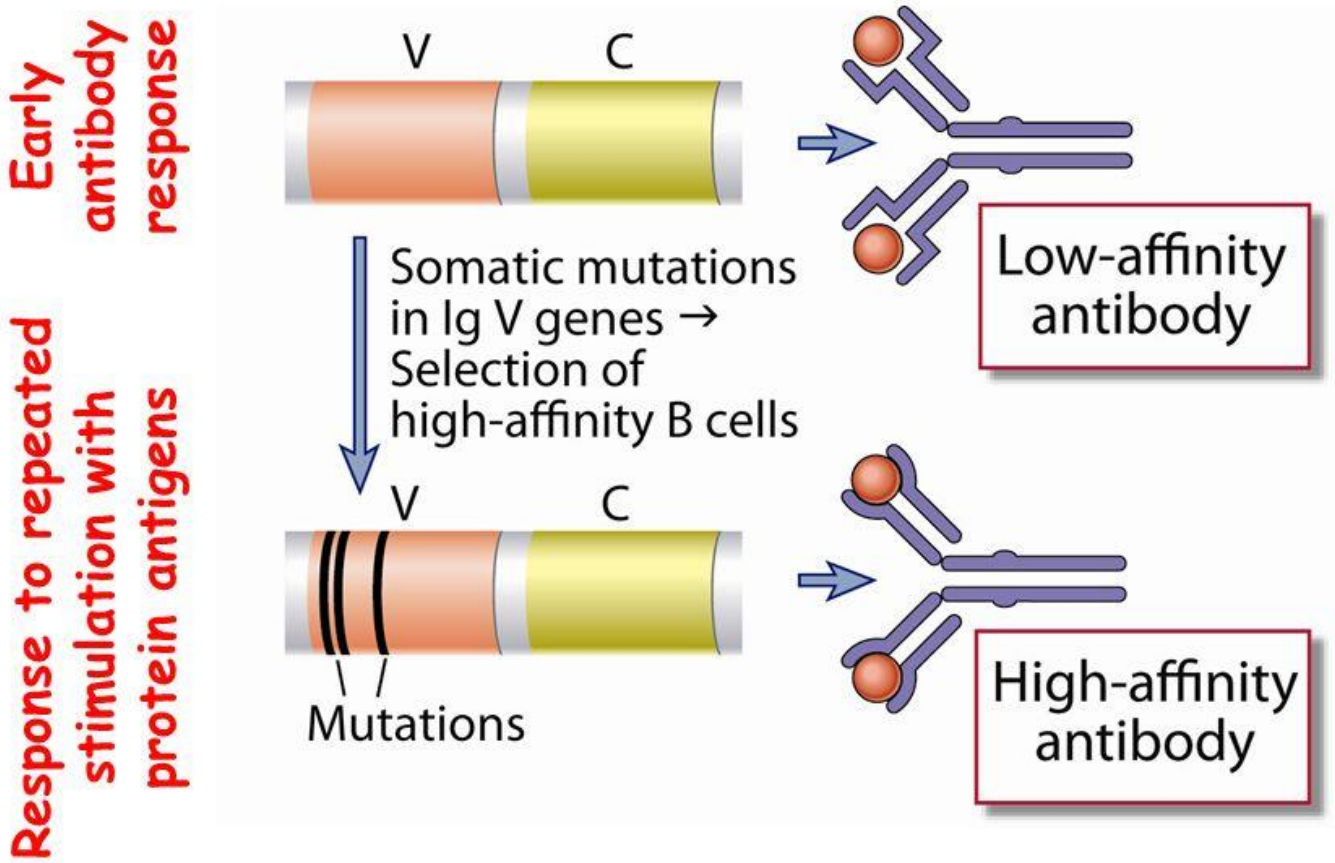
Lymphoid follicles are small masses of tissues that contain aggregations of inflammatory cells, mainly B cells with some T cells and dendritic cells.



- Lymph follicle:

- Mantle = cap (dark)
- Germinal center (light)

Affinity maturation of antibodies



Follicular dendritic cells

-- **Follicular dendritic cells (FDCs)** are cells of the immune system found in **primary and secondary lymph follicles** of the B cell areas of the lymphoid tissue.

Primary follicles: lymphoid follicles without a germinal centre.

Secondary follicles: lymphoid follicles with a germinal centre. These mostly contain B-cells.

-- **Follicular dendritic cells** capture **antigen-antibody complexes** on their surface via **Fc receptors**.

Fc receptors: Those regions which attach to Fc part of an antibody

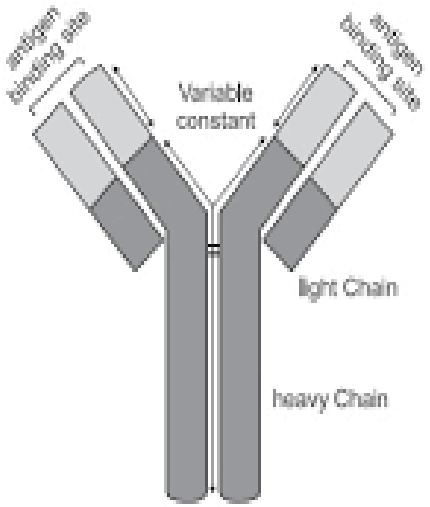
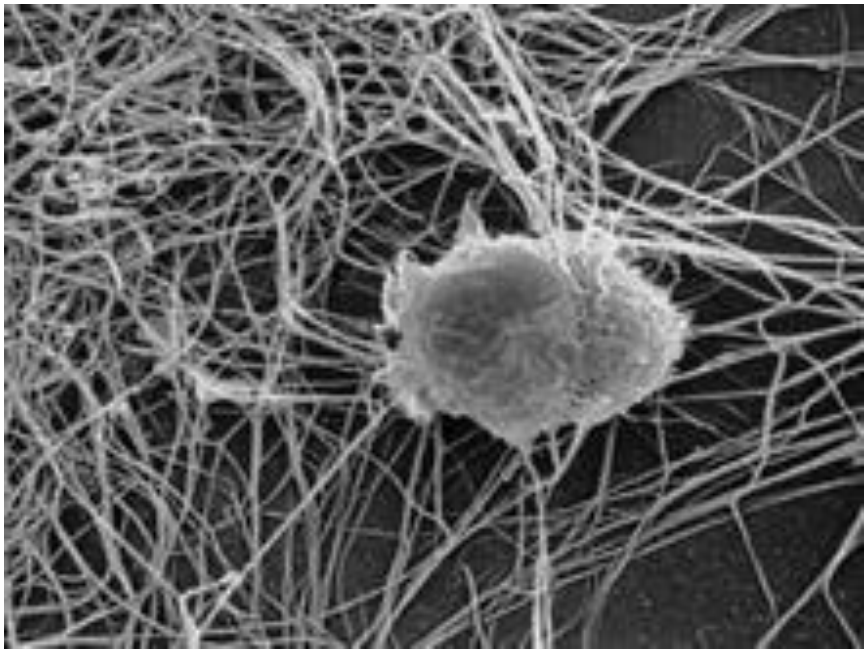


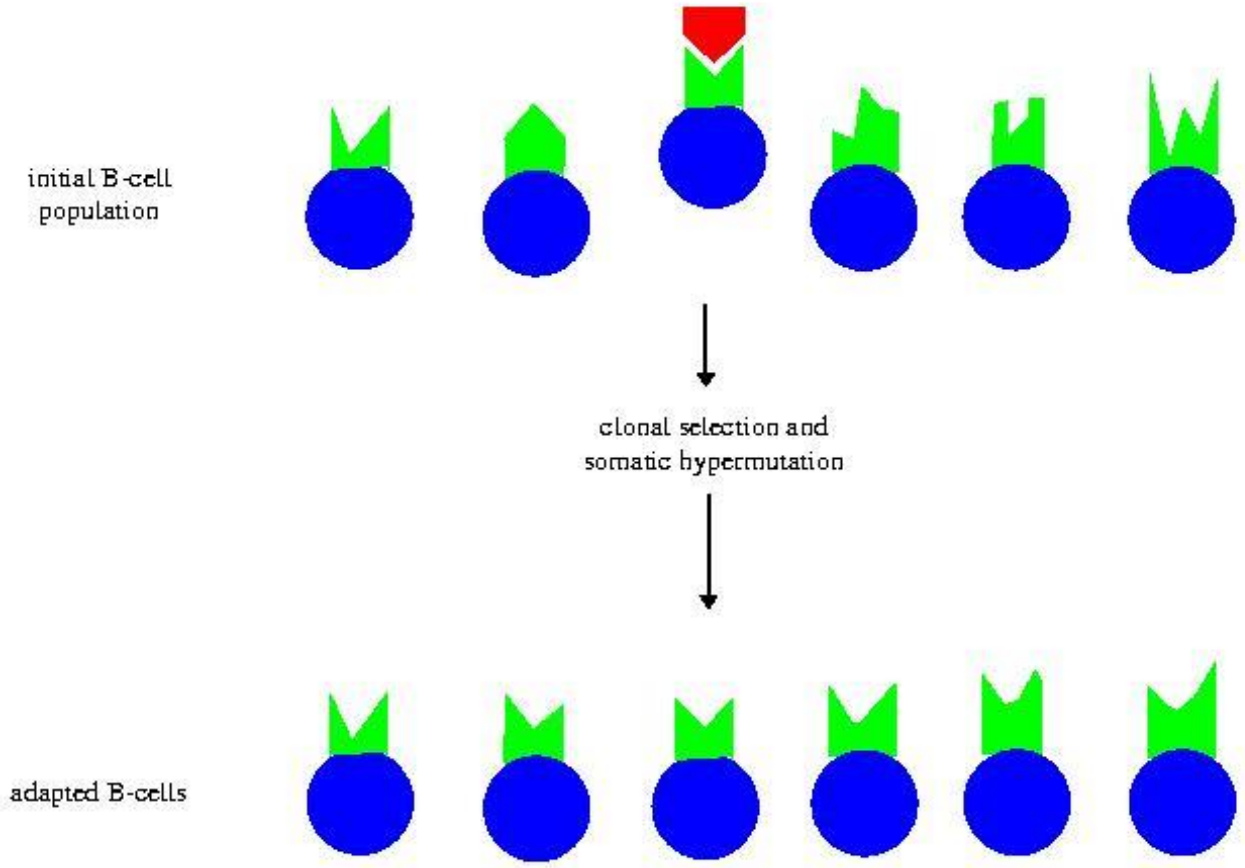
Fig. 10. 6 Antibody Structure



-- The **complexes** interact with an **activated B cell** bearing the Ig that best fits the antigen.

-- This activated B cell is **stimulated** to form a clone of many B cells capable of synthesizing the **improved antibody.**

AFFINITY MATURATION II



Response to multiple antigens administered simultaneously

-- On administration of **more than one antigen**, the host reacts by producing **antibodies to all of them**.

-- So **combined immunization** is widely used.

Example is **DTP vaccine** which covers **diphtheria, tetanus** and **pertussis**.

Another example is **MMR vaccine** for **measles, mumps** and **rubella**.

Functions of antibodies

---- **Opsonization** refers to the coating of antigen with antibody that results in enhanced uptake of the antigen.

--- **Neutralization** prevents adherence of bacteria, viruses and toxins.

--- **Complement activation** facilitates immunity, enhances uptake, and kills susceptible bacteria.

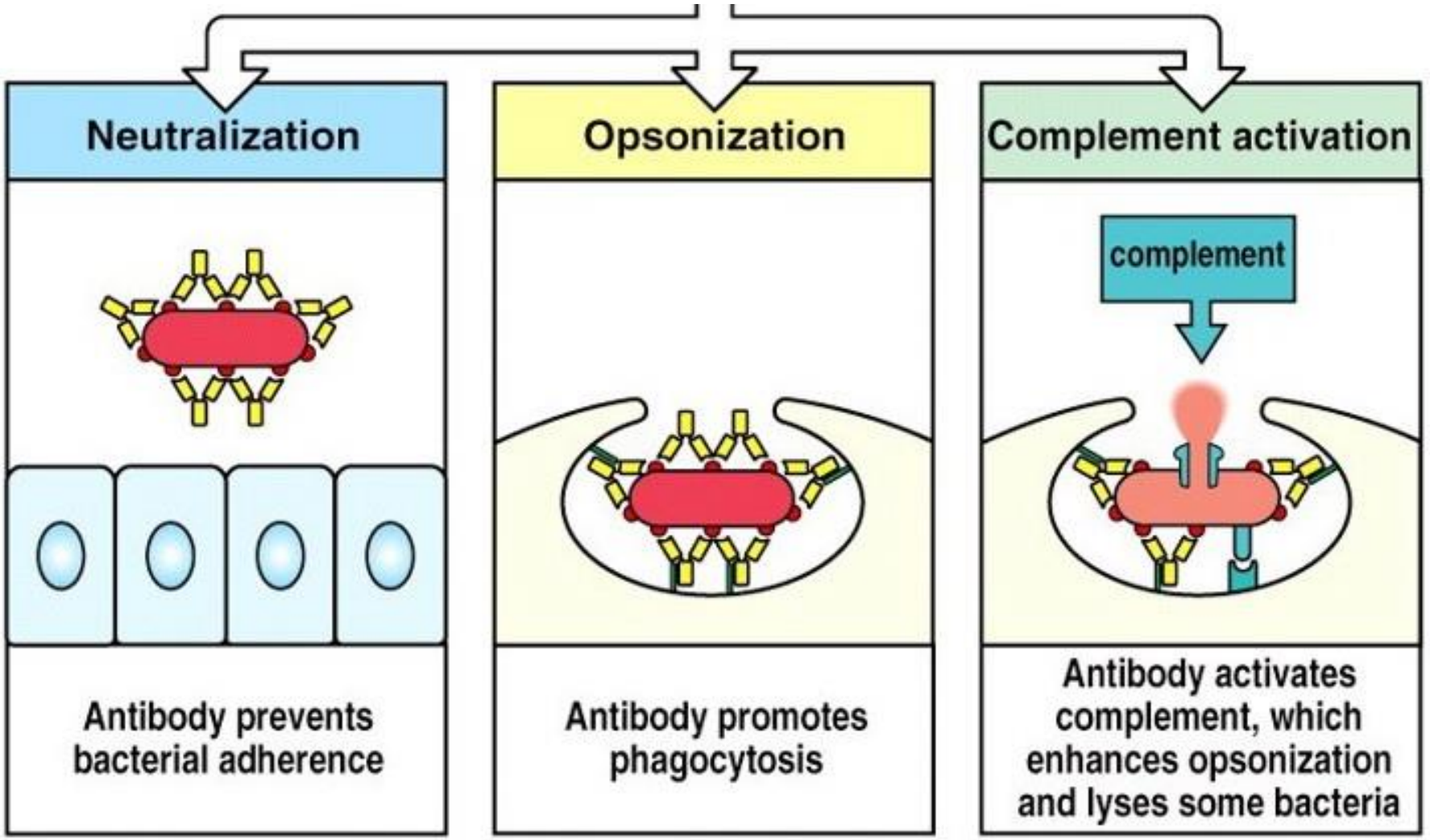


Figure 9-1 Immunobiology, 6/e. (© Garland Science 2005)

Antibodies in the fetus

-- Fetal antibodies are **primarily IgG** acquired by **transfer of maternal IgG** across the **placenta.**

-- Fetus **can make** some antibodies if infection occurs, such as in congenital syphilis

-- Newborn infants **can make Igs** to certain protein antigens.

For example, vaccine containing Hepatitis B surface antigen is **effective** in newborns.

Cell-mediated immunity

-- In **intracellular** and **viral infections**, **cell-mediated immunity** is primarily important.

-- It plays major role in **resistance** and **recovery**.

-- It is also important in **defense** against **fungi, parasites and cancer.**

-- It is also responsible for **rejection of organ transplants.**

-- Its **suppression** by drugs or diseases such as AIDS results in **overwhelming** (heavy) infections or tumors.

Its main constituents are:

1. **Macrophages**
2. **Helper T cells**
3. **Natural Killer cells**
4. **Cytotoxic T cells**

Cytokines play a major role in **communication** between cells.

-- Some viruses such as **measle**s and **cytomegaloviruses** can **suppress** CMI against other microbes.

-- **Measles virus** infection can make tuberculin test **negative** and cause reactivation of dormant (resting) organisms.

-- It is suggested that its attachment to macrophages **suppress production of IL-2,** a cytokine.

-- In CMI, primary and secondary response patterns are **similar to humoral immunity**.

-- In persons having **competent CMI**, opportunistic pathogens **rarely or never** cause disease.

-- Spread of **viruses** and **tumor cells** is also restricted.

Recommended book

Immunology by Riott and Brostoff

Coffee thrown from a bottle at -30C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