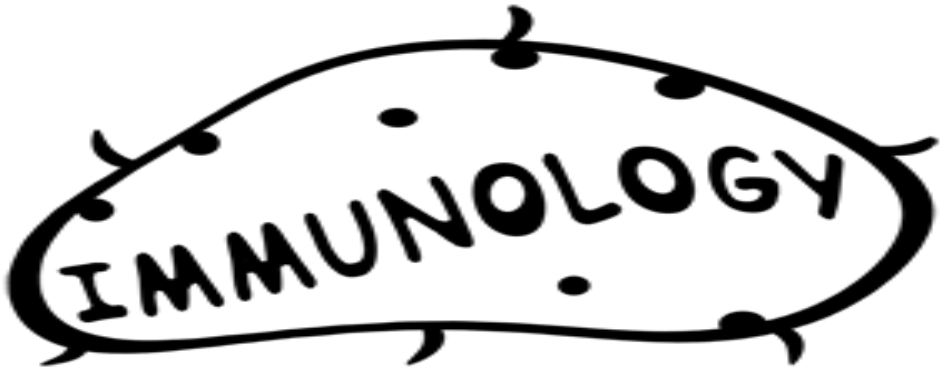
Foundation block

Antibody Mediated Immunity

lecture 4



Learning objectives: ملاحظة: الكلام الموجود في المستطيلات هو من شغل التيم

1. To describe B-cells as the mediators of humoral immunity, (antibody-mediated immunity)

2. To describe activation of B-cells which involve:

-Antigen recognition

-T-dependent & T-independent antigens

- Requirement for T-helper cells

3. To explain clonal selection, clonal expansion &

generation of plasma cells & memory cells

4. To describe primary & secondary immune responses

5. To describe the structure & function of Immunoglobulins

The Humoral Immune Response is the aspect of immunity that is mediated by secreted antibodies.

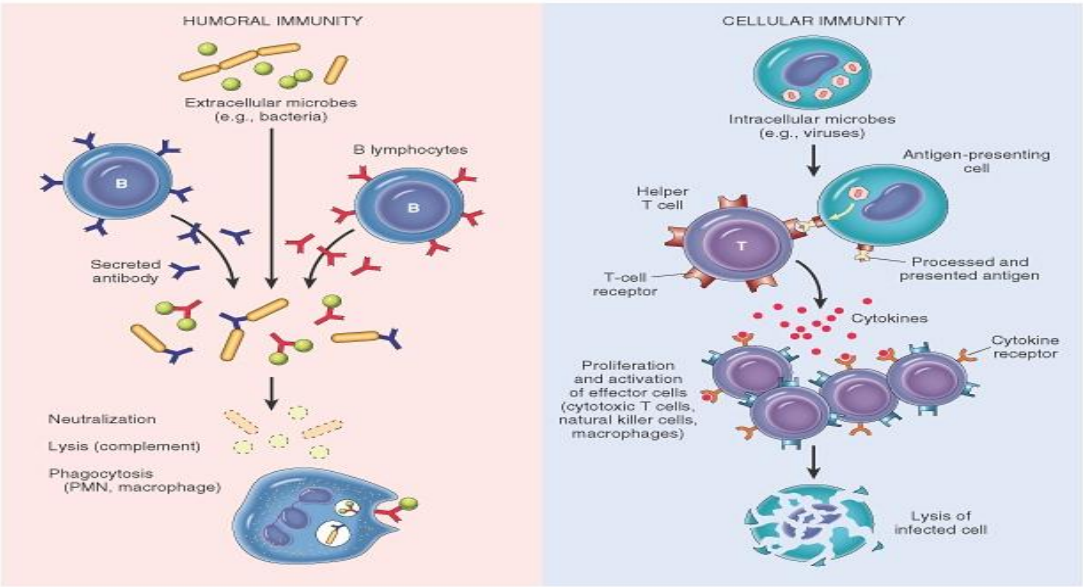
Recall: Adaptive immunity is divided into:

Humoral immunity	Cell Mediated Immunity
Humoral immunity mediated by antibodies (B cells)	Immune response in which antigen specific T cells dominate

Humoral immunity is so named because it involves substances found in the: humours or body fluids

Nature of antigen determine type of response either

EXTRACELLULA or INTERACELLUALR



Note: The bacteria or virus has antigen on its surface.

If the bacteria or the virus is outside the cell (usually bacteria) then the cell will defend its self-using humoral immunity and in this case it is called (extracellular response).

But if it was inside the cell (usually virus) will defend using cellular immunity ((review the previous lecture)) and it's called (Intracellular response)

1. T-dependent:

-Antibody production by B-cells require T-helper cells (TH2)

-Macrophages recognize antigen & present it to T-helper cells

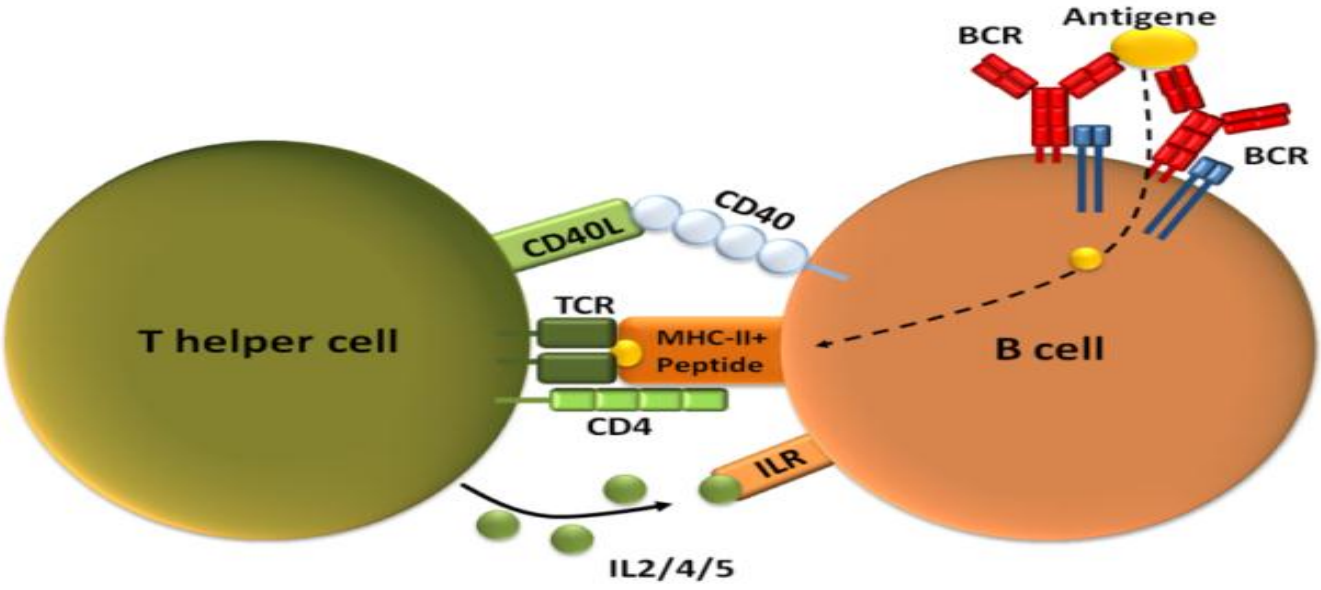
-T-helper cells stimulate B-cells specific for that antigen to become plasma cells

-T-dependent antigens are mainly proteins on viruses, bacteria & other foreign materials.

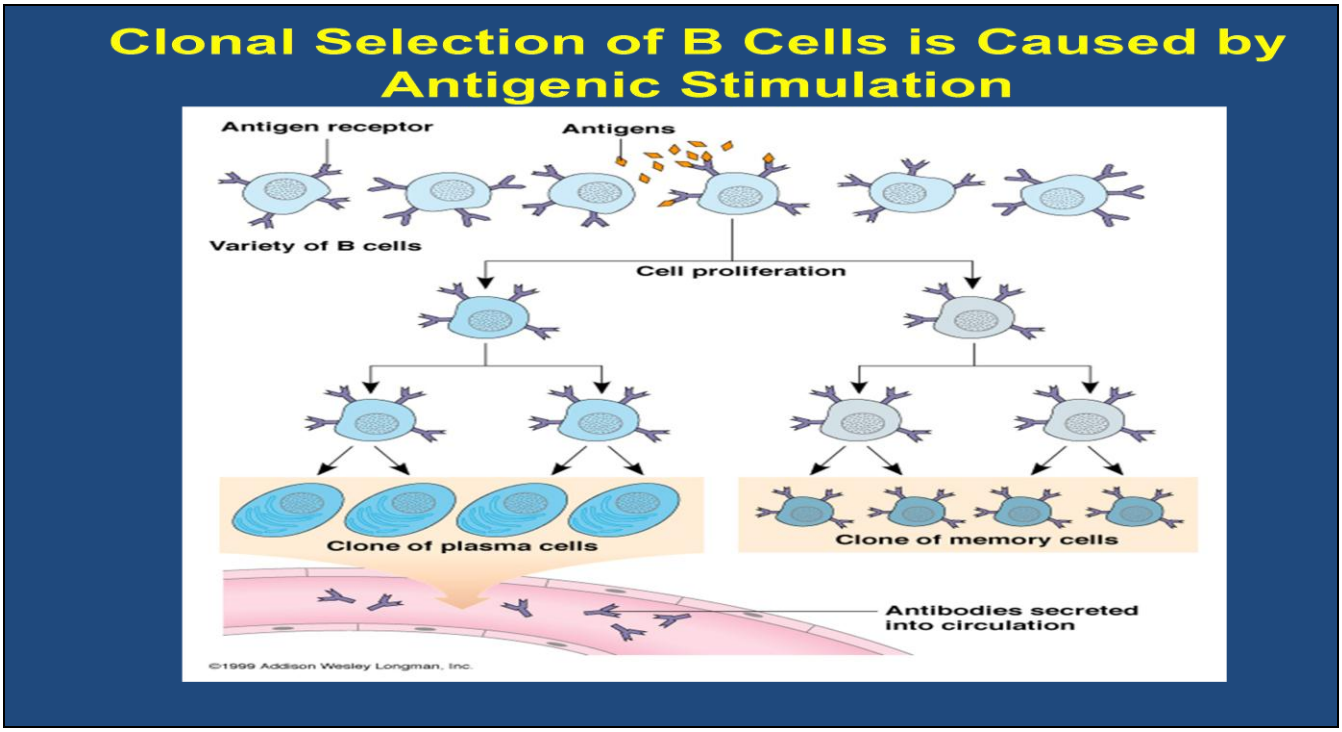
*** T-dependent → sometimes called "T-response"**

*** Proteins will trigger T-response .**

***Remember that B-cells are considered as antigen presenting cells.**



Primary & Secondary immune responses



Clonal selection

The selection and activation of specific B-lymphocytes and T-lymphocytes by the binding of epitopes (The surface portion of an antigen) to B-cell receptors or T-cell receptors with a corresponding fit.

Caused by antigenic stimulation

Clonal proliferation

The proliferation تكاثر of B-lymphocytes and T-lymphocytes activated by clonal selection in order to produce a clone of identical cells

It has two types of cells :

- **Clone of plasma cells** : produce antibodies.
- **Clone of memory cells** : remember a specific type of antigen in case it attacks again in the future.

2- T- independent antigens

-B-cells do not require T-helper cells to produce antibody.

-Antigens are mainly polysaccharides or lipopolysaccharides with repeating subunits (bacterial capsules).

-Immune responses are weak compared to T-dependent responses.

	T-dependent antigens	T- independent antigens
Require T-helper	Require	Do not Require
Immune responses	strong	weak
Antigens	Proteins on viruses, bacteria & other foreign materials.	Polysaccharides or lipopolysaccharides with repeating subunits (bacterial capsules).

Antibodies

Definition: **they are specific and bind to specific sites on the antigen and perform specific functions.**

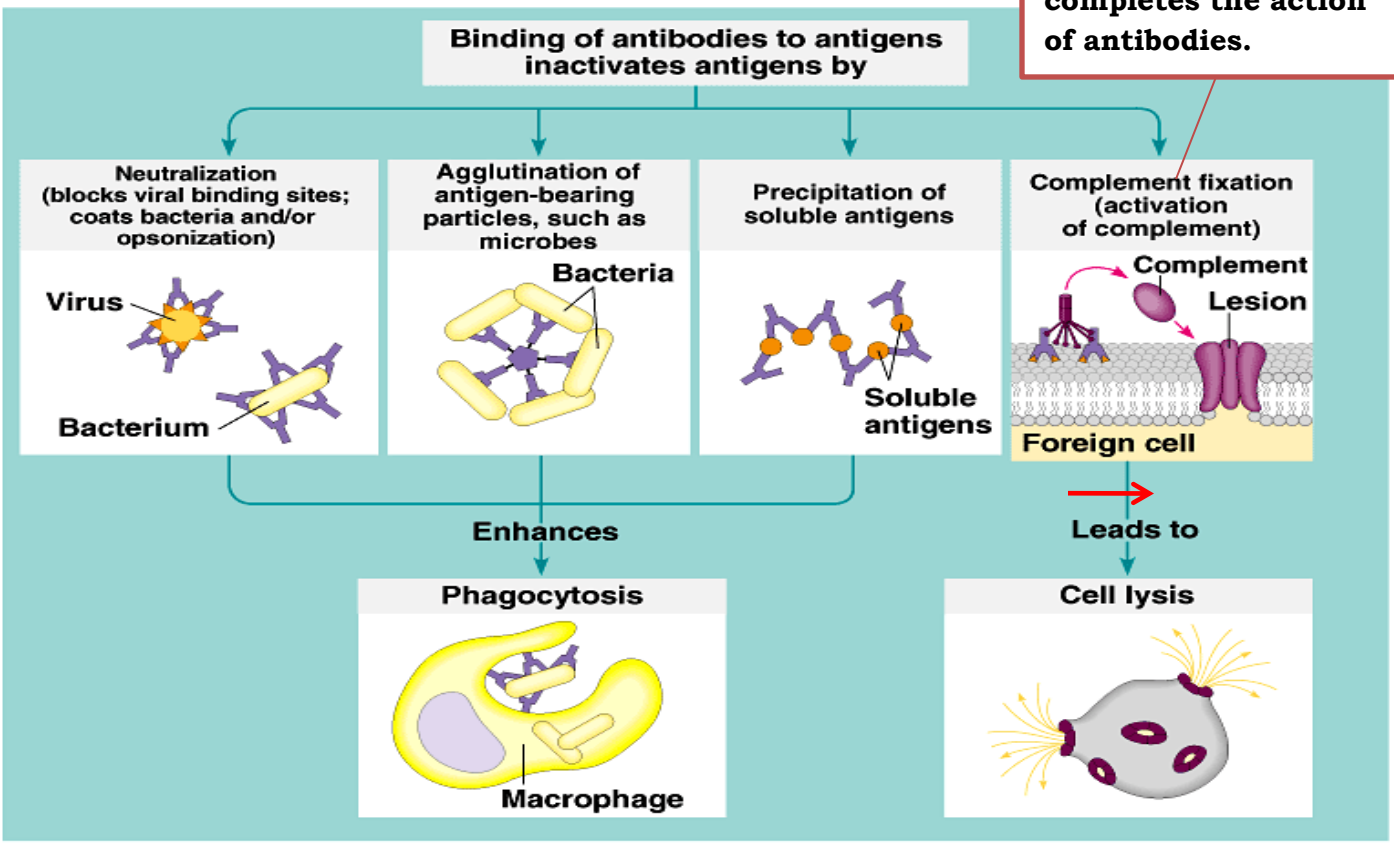
- **Antibodies are immunoglobulins with specific functions**
- **Antibodies bind to specific sites on antigen surfaces and perform protective functions by different mechanisms**

There is a SPECIFIC antibody for any one given type of an antigen.

The interaction of antigens and antibodies occurs in order to clear antigens from the extra cellular fluid (ECF).

Protective functions of antibodies:

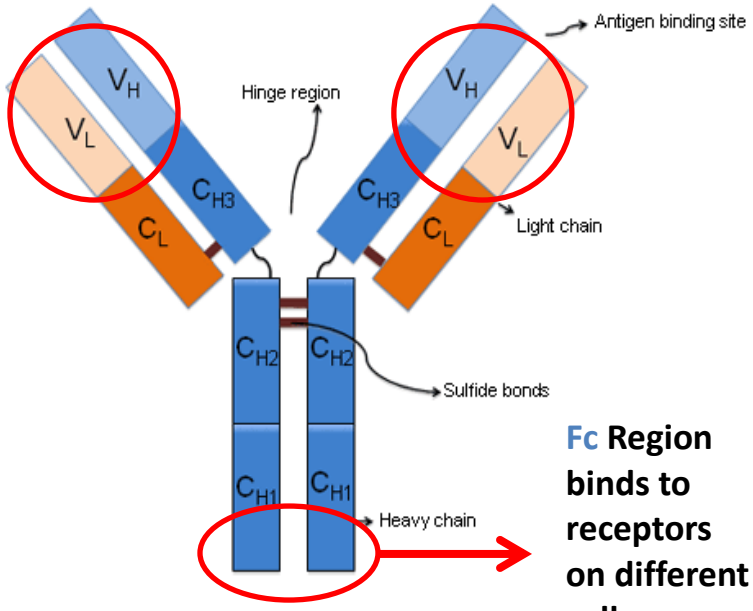
Complement: it completes the action of antibodies.



The diagram shows the interaction between innate and adaptive immunity and how they are not separated from each other.

Antibody structure and functions

1. **Made up of four polypeptides (amino acid chains).**
2. **Two longer and larger (heavy chains) and the other two shorter and smaller (light chains)**
3. **Have the shape of a letter "Y"**



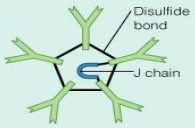
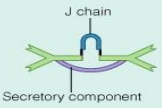
Fc Region binds to receptors on different cells

- **Variable region has the potential to bind with particular classes of antigens**
- **Once a raw antibody is stimulated to fit to a specific antigen, it can then react with ONLY that antigen**
- **This is known as SINGLE SPECIFICITY**
- **Can fit as precisely as a lock-and-key to an antigen**

The antigen binds only on the Variable region

- **The chains in blue are the heavy chains and they are identical in the same molecule; each chain is composed of 4 domains (tertiary structure of a protein).**
- **The chains in orange are the light chains and they are identical in the same molecule; each light chain is composed of 2 domains (globular proteins).**
- **Each chain whether it was heavy or light is composed of variable domains (V) and constant domains (C).For example, V_H: means variable heavy domain.**
- **In the heavy chain we have 3 constant domains and one variable.**
- **FC region is really important because the antibodies don't only get rid of antigens, but also attach themselves to the receptors of different cells and that will trigger certain biological activities in those cells.**
- **Remember we said before that adaptive immunity is specific and that is the reason behind the high specificity of antibodies.**

TABLE 17.1 A Summary of Immunoglobulin Classes

Characteristics	IgG	IgM	IgA	IgD	IgE
					
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
Percentage of total serum antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood, lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Molecular weight	150,000	970,000	405,000	175,000	190,000
Half-life in serum	23 days	5 days	6 days	3 days	2 days
Complement fixation	Yes	Yes	No†	No	No
Placental transfer	Yes	No	No	No	No
Known functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

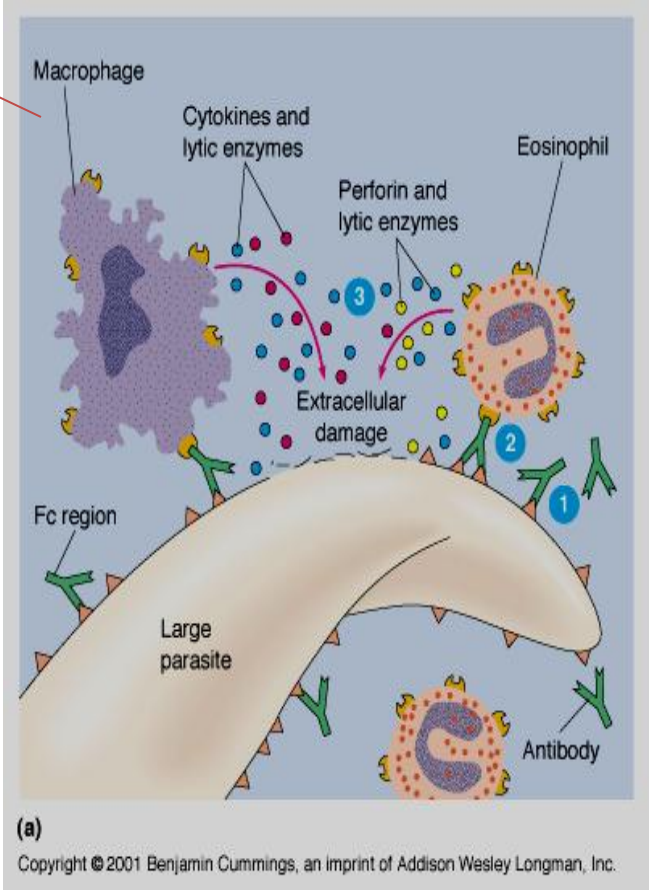
*Percentage in serum only; if mucous membranes and body secretions are included, percentage is much higher.
† May be yes via alternate pathway.

- **The most abundant type of immunoglobulin is IgG and it is the master in 2ry response.**
- **The immunoglobulins that use complement fixation are IgG ,IgM.**
- **The only immunoglobulin that can transfer from the mother to the fetus (through the placenta) is IgG**
- **IgE is the master immunoglobulin in secretions and it is important for allergic and parasitic infections.**
- **Both IgA and IgG have subclasses.**
- **Most of the cells have receptors for IgG, because IgG is widely scattered in the body.**
- **Immunoglobulins here are divided according to the type of heavy chain.**

For example, heavy gamma chain gives IgG, heavy alpha chain gives IgA, heavy delta chain gives IgD, heavy mu chain gives IgM, and heavy epsilon chain gives IgE.

Functions of Antibodies:

Use IgE because it is a parasite



Antibody dependent cell-mediated cytotoxicity

NK (natural killer cells) (lysing ability), Macrophage, neutrophils, and eosinophils have receptors for FC region of antibody

Antibodies coat infecting cell (large parasite usually) - FC facing outwards

Secretion of lytic enzymes to destroy parasite

الخطوات كالتالي :

اولاً : تقترب أحد الخلايا الدفاعية من البكتيريا الخلايا الدفاعية كالتالي:

Macrophage ,neutrophils, eosinophils and natural killer cells.

ثانياً : يقوم الانتيبدي بالارتباط بالخلية الدفاعية بواسطة **FC region**

ويرتبط بالخلية المتطفلة بـــ **Variable region**

ثالثاً: تتجمع مجموعات كبيرة من الانتيبدي وتحيط بالمتطفل إحاطة كاملة ثم تفرز أنزيمات محللة لتدمير الخلية المتطفلة أو الفيروس .

- **Initial encounter with antigen produce Primary immune response.**
- **Subsequent challenge with same antigen produce Secondary immune response**

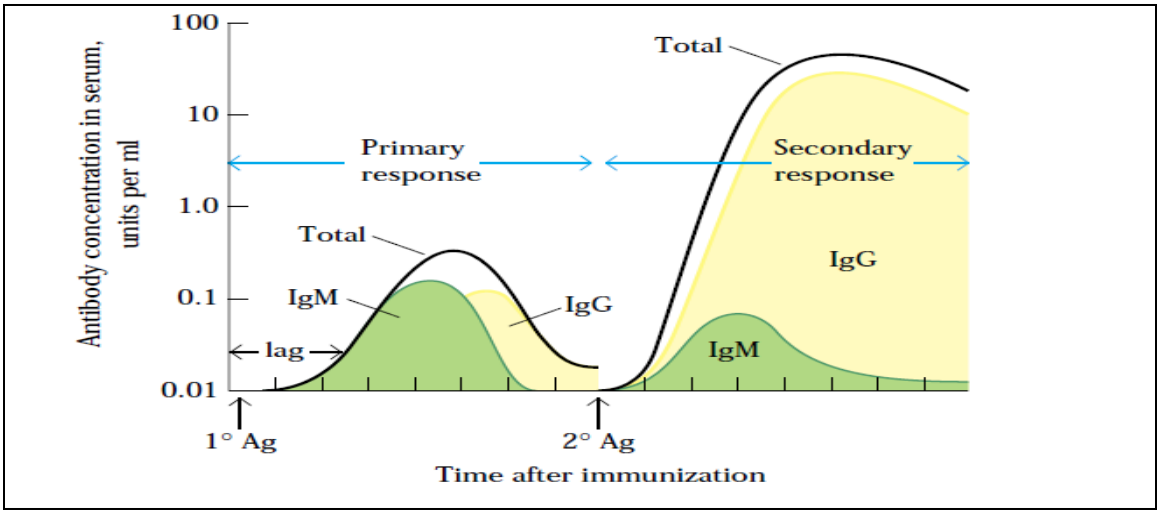
Primary immune response

Refers to the first encounter of your immune system with a virus or bacteria

Secondary immune response

Refers to the re-encounter of the same virus/bacteria with memory T cells and B cells.

Concentration & type of antibody in primary & secondary immune responses



	Primary Response :	Secondary Response:
Time	more time	less time swift(rapid)
Strength	weaker	stronger
mediated	IgM class of antibodies	IgG class of antibodies because of the memory cells

The time between application of a stimulus and the reaction

Comparison between primary & secondary responses

Property	Primary response	Secondary response
Responding B cell	Naive (virgin) B cell	Memory B cell
Lag period following antigen administration	Generally 4–7 days	Generally 1–3 days
Time of peak response	7–10 days	3–5 days
Magnitude of peak antibody response	Varies depending on antigen	Generally 100–1000 times higher than primary response
Isotype produced	IgM predominates early in the response	IgG predominates
Antigens	Thymus-dependent and thymus-independent	Thymus-dependent
Antibody affinity	Lower	Higher

Useful video about the complement system

http://www.youtube.com/watch?v=vbWYz9XDtLw&feature=youtube_gdata_player

Take Home Message:

- B cells can be activated by antigen to produce antibodies either with the assistance of helper T cells or directly by the antigen itself.
- Antibodies are made up of two heavy and two light amino acid chains and have a shape of letter “Y”.
- Different types of antibodies are located at various sites to provide protection by agglutination, precipitation, complement fixation etc.
- Secondary humoral immune response is swift and stronger immune response mediated by IgG class of antibodies because of the memory cells.

GOOD LUCK...

(لا تنسونا من صالح دعائكم)