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Lecture title: **Antibodies, types, and function**

Lecturer Affiliation:

Ammar M. Al-Aalim

Department of Microbiology, College of Veterinary Medicine, University of Mosul, Mosul, Iraq.

Summary:

1- Learning the Major types of Antibodies found in the body
2- The importance and function of antibodies
3- Pathways of its activation
4- The role it plays in the immune system stimulation
5- The cells that produce the antibodies

Antibodies are specific proteins produced by plasma cells as a result of the reaction between the B- B-lymphocyte and a specific antigen.

Plasma cells are found in bone marrow only and produce antibodies (proteins) in one case, which is the cancer.

Introduction:-

The injection of Ag in animal produce specific anti- serum which react selectively with Ag , this anti- serum contain protein which are responsible for this recognition and which said to posses an Ab function , this soluble protein belong to this class of protein called **Globulin.**

Owing to the migratory properties of or in electrophoresis field, they are called **δ globulin** because this are involve in immunity it is called **Immunoglobulin (Ig)** .

Functional duality of Ig:-

1- **Recognition function:-** means that Ab (Ig) have specifity for certain type of Ag or have ability to recognized specific Ag among hundred or thousands of Ag.

   Example:- Ab are able to discriminate between the chain of leucine and the chain of valine .

2- **Effecter function :-** Ig are capable of many other function that :-

   a- Complement Fixation (Complement Stimulation)

   b- Bind to certain cell called Cytophilia

   c- Placental transfer

   d- Catabolic function

Models for Ig study:-

The main difficulty in Ig study is their heterogeneity , this is because of Ag complexity and the function of immune system.

Ig isolation:- Ab are serum proteins their analysis by electrophoresis gives four main families of serum protein : albumin ,α, β and δ globulin.

Ab are mostly found in δ globulin and to little extent in B- globulin.

Ig are isolated on the basis of their net charge ,electrophoresis using a solid support (starch).

Ion exchange chromatography :-

Using resin DEAE cellulose , neutral PH and low ionic force ,only δ globulin not retained by the resin .

Gel filtration :- used to separate Ig .

Classification Criteria:- Ig classification according to their physico- chemical characters which is:-

1- Molecular weight .
2- Sedimentation coefficient (by ultra centerifugation).
3- Electrophoresis mobility.

And it antigens properties to five classes of Ig :- IgG , IgM , IgA , IgD and IgE.

Structure of Ig molecule :-

Generally it have Y shape except IgM and IgA , composed of 2 heavy H chain and 2 light chain have molecular weight 50000 dalton while the light chain 250000 dalton.

The heavy chain is connected to the light chain by disulphide bond (s ….s) , each H chain is connected together by same bond.

The H chain is composed of 440 aminoacids .

The L chain is composed of 220 aminoacids .

The immunoglobulin have two terminal , first one end by NH2 group and the other by CooH group .

There are 2 different zone in structure of Ig : constant zone (C zone) and variable zone (V zone).

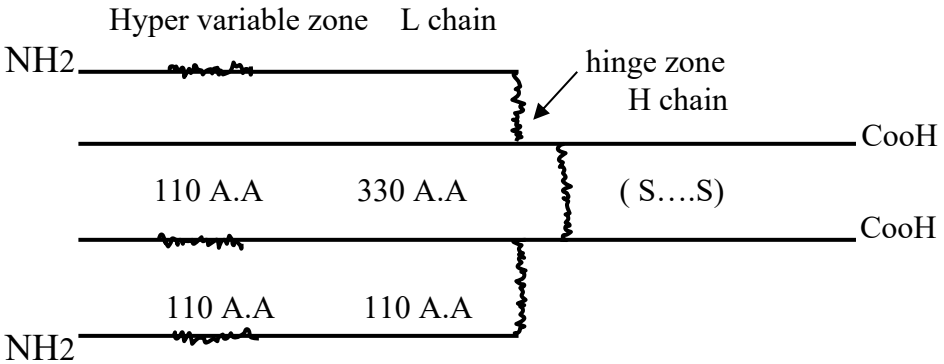
Constant zone:- composed of 330 amino acids of H chain (¾) and 110 amino acids of L chain (½) , the sequence of amino acids are stable in this area and controlled by genetic factor .

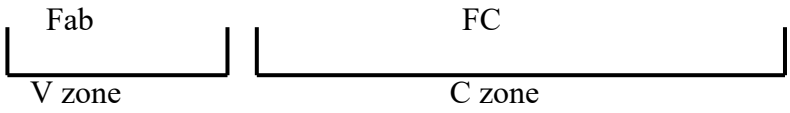
Variable Zone:- composed of 110 amino acids of both H and L chains , the sequence of amino acids in it are variable , it have very variable zone called **(Hyper variable zone)** the Ag is bind to this zone .

High Zone:- This part of Ig rich with amino acids (especially praline) to give it more elasticity , located between the disulphide bonds that connect H chain together and H chain to the L chain .

FC:- complement fixing fragment or crystalisable fragment , located on C zone of H chain and it is the effecter functions of Ig which is complement stimulation , placental transfer , catabolic function , protein A toxicity.

Fab:- Fragment Ag binding , located on V zone of both H and L chains. (NH2 end) **.**





The heavy chain is different from one class of immunoglobulin to another:-

1- δ ⟶ IgG.

2- M ⟶ IgM

3- α ⟶ IgA

4- δ ⟶ IgD

5- E ⟶ IgE

The light chain is divided in to :-

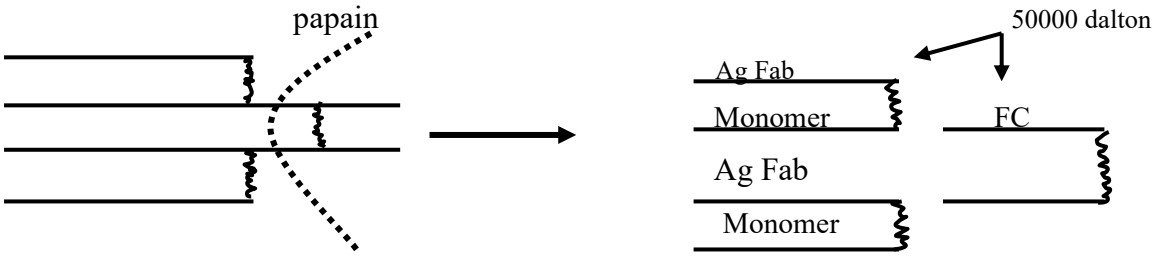
1- κ

2- λ

If the light chain is κ , the other light chain is also κ of if the light chain is λ ,the other light chain is also λ , but not both κ and λ .

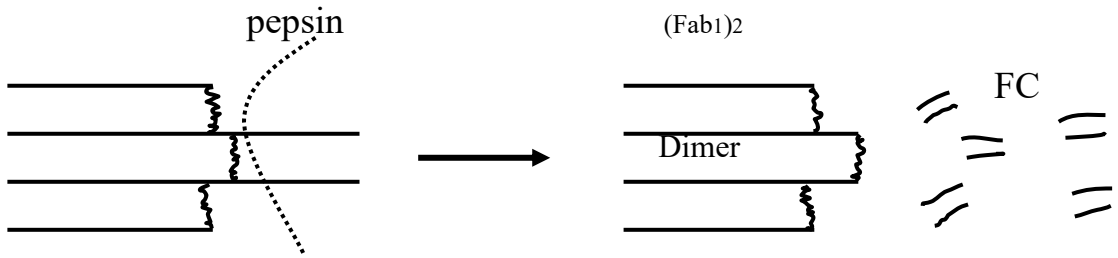
The effect of proteolytic enzyme on IgG molecule:-

1- **The Papain :-** will breakdown the molecule and it act just behind the hinge zone , so it will divide the molecule of IgG to three part or fraction , each have 50000 dalton molecular weight , the two identical parts fix the Ag (Fab) while the other part have same molecular weight but don't fix the Ag (FC) which composed of half part of heavy chain (H) only.



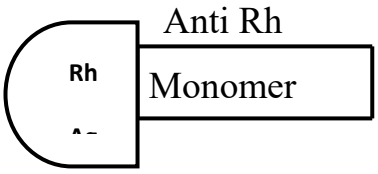
2- Pepsin :- it is strikes at a different point , it cleaves the Fc fragment from the remainder of the molecule , leaving the hinge zone intact it break the molecule

to (Fab1)2 which is large molecule (H and L chain) and to small fragment of FC.



The monomer can not produce agglutination while the diamer can produce agglutination because the part that responsible for Ag fixing is stable.

Example: in blood group (Rh) , if take Ag (Rh) and the Ab is anti Rh.



The binding occur between Ag (Rh) and the monomer (Ab) but the agglutination will not occur.

In some cases , a short Ab molecule directed against a deeply located membrane antigenic determinant can not produce agglutination , as the Fab arm are not long enough to connect Rh antigenic determinant on RBc , these Ab called **Incomplete Ab.**

An antihuman antibody (Immunoglobulin) is added which directed against incomplete Ab lead to agglutination.

Classes of Ig:-

1- **IgG:-** Have molecular weight 150000- 180000 dalton with sedimentation coefficient 7S , it is found in serum and in extravascular fluid like peritoneal and ascites fluid , this Ig is responsible for defensive mechanism against viral , parasitic and microbial infection.

It produce in high quantities, the concentration of IgG in serum is 1600 mg / dl this Ig is produced during the secondary immune response and found in different concentration in body fluid.IgG composed of 4 subunits.

2- **IgM:-** is responsible for the primary immune response, found in blood only (intravascular) with sedimentation coefficient 90S and the molecular weight of it is 900000 dalton so it is called macroglobulin composed of pentamer (5 subunits) of the basic 4 chain subunit held together by disulphide bonds with 7S and molecular weight 180000 dalton , the concentration of this Ig from 180-190 mg / dl.

This Ig produce during primary immune response , it is of limited defensive mechanism (capacity) . The function of IgM remain at least 3-4 day and then breakdown.

IgM is fixed the complement so it is effective agglutinating and cytolytic agent but it do not passing through placenta.

3- **IgA:-** present in intestinal secretion and bronchial secretion and nasal secretion , tears, saliva and colostrum .

It composed of 2 light chain and 2 heavy chain monomeric form is predominant in human serum , the dimmer 11S is the most common form in secretion in all species of animals .

Disulphide bond link 2 monomers of IgA to a J-chain refer as (secretory piece).

IgA provide new born with Abs which will protect him before the synthesis of his own Ig.

There are two types of IgA:-

1- serum IgA

2- secretary IGA

Why the IgA not digest by proteolytic enzymes?

Because presence of J- chain in structure of it, so prevent it lysis or digest while the other protein in colostrums digest by the proteolytic enzyme.

IgA not presence in so much concentration in serum as IgG.

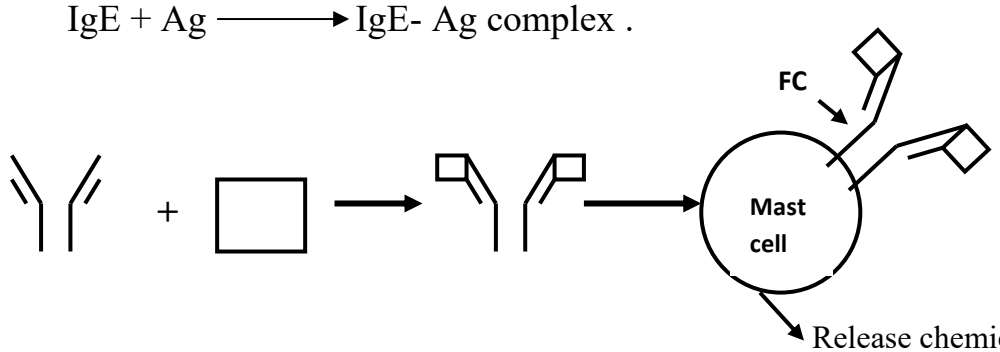
4- **IgD:-** immunological function is unknown, it is found in serum and in the lymphocyte (on the surface of B- lymphocyte with IgM) and in chronic lymphatic leukemia.

Operate as antigen receptor and control of lymphocytic activation and suppression.

5- **IgE:-** important in immunopathology , is responsible for immediate type of hypersensitivity reaction . anaphylactic shock , asthma , hay fever , urticaria .

IgE bind to basophil, mast cell and blood platelets this binding triggers the release of several mediators .

IgE + Ag ⟶ IgE- Ag complex .



Release chemical mediators:-

1- histamine

2- serotonin

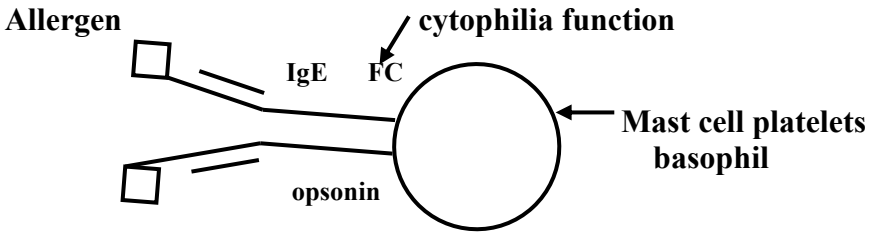
3- SRS anaphylaxis
4- Brady kinin
5- Heparin

Because the Ag cause allergy , so it called **Allergin**

Allergy :- is reversible process , mean it does not cause death of mast cell (degranulation).

IgE increase in parasitic infection with eosenophil .

IgE act as opsonin which fix the ag by FC fragment on macrophage leade to phagocytosis



IgE called regain because induce allergy or hypersensitivity .

In parasitic infestation there is increase in IgE level in the blood.

Neutrophilia:- increase in the percentage of neutrophil in the blood due to pyogenic infection , when this cells die will give us the pus.

Lymphocytosis:- increase in the percentage of lymphocyte in the blood due to virus and some bacterial infection.

Eosinophilia:- increase number of eosinophil in allergy status and parasitic infection.

If we have a case of allergy , who we can desensitize it ?

With the certain level of IgE antibody , we can not prevent presence of allergen in atmosphere but we can prevent production of Ab of IgE type , either by production

of Ab of other type of Ig then IgE for example production of IgG than IgE, IgG when conjugated to allergen .It will not induce case of allergy . Or by induce specific immunological tolerance mean immunoparalysis or immunoun responsiveness , the body keep the capacity to respond to all other Ag but unresponsive to this allergen. Repeated injection of very small doses or very large doses of allergen (pollen) we will get a specific immunological tolerance.

Ig	IgG	IgA	IgM	IgD	IgE
M.W	150000	6600	900000	180000	200000
Additional subunits	------	J chain Secretary piece	J chain Secretary piece	------	------
Concentration mg / dl	1600	130	180	0.002	0.2
Half life in day	23	6.5	3	------	2
Placental transfer	cross	------	------	------	------
Presence in secretion	------	+	------	------	------
In milk	+	+	------	------	------
Activation of complement	+	------	++	------	------
Binding to cell and macrophage	+	------	------	------	------
agglutination	++	++	++	------	------
Anti viral activity	+	+	+	------	------
antibacterial	+	+	+	------	------
allergy	------	------	------	------	+