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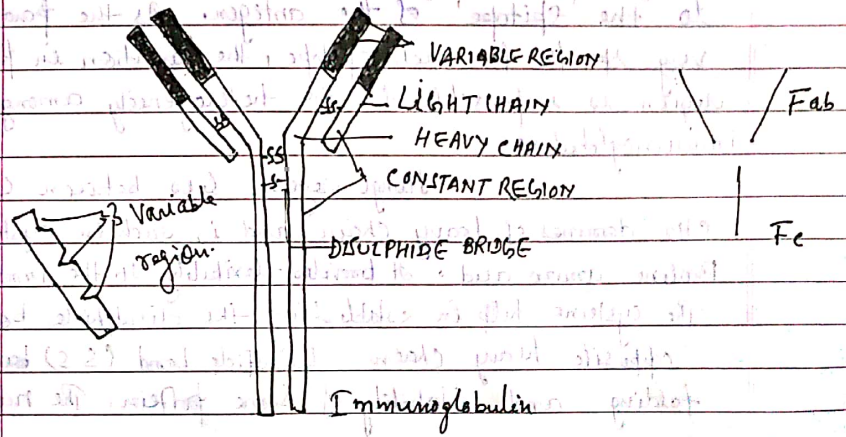
Antibody

Antibodies or Immunoglobulins are globular glycoproteins present in the serum and body fluids. Antibody is secreted by modified fate B lymphocyte i.e plasma cell and acts as an effectors of humoral immunity. The serum immunoglobulin antibodies produced in response to a particular antigen are heterogeneous. When an immunoglobulin binds with an antigen it is referred as antibody.

Structure of Immunoglobulin or Antibody.

Rodney Porter and Gerald Edleman (1950 - 60) were the first two firstly revealed the structure of immunoglobulin. Antibody molecules have a common structure of four polypeptide chain - Two short light chain(L) and two big heavy chain (H). Based on the molecular weight the polypeptides of short chain (MW 25,000) are known as light chain having 220 amino acid only. Heavy chains having have about 440 - 550 amino acid and mol. wt - 50,000 respectively. Both the chains contains several homologous units the domains with 110 amino acid residues. The four polypeptides are held together by covalent disulfide (S-S) bonds and gets Y shape.



At the junction of Light and heavy chain there is a flexible region called "Hinge region". The one end of both the chain (Co) are called Fc region as this region goes crystallisation during cold storage. The another region (NH_2) take part in antigen binding are called "Fab" or Fraction of binding antigen binding site.

Light chain — There are two types of light chain namely Kappa (K) and (λ) Lambda type. K type light chain dominate (60%) dominates over 'λ' type (40%) in the serum.

Each Light and heavy chain holds a constant domain towards carboxyl end. There is one constant region (CL) in light chain and 3 to 4 constant region in heavy chain. (CH_1, CH_2, CH_3 e.t.c).
The first 110 amino acid of the amino terminal region (NH_2) varies are called variable region V region, V_L in the light chain and V_H in heavy chain. Each variable domain contain 3 - 4 hypervariable sites which are known as complementarity determining region (CDRS). The hyper variable regions or 'paratope' is the complement to the 'epitope' of the antigen. As the paratope is very specific for each epitope, the variation in paratope region is responsible for the heterogeneity among the immunoglobulins.

Hinge region lies between CH_1 and CH_2 domines of heavy chain and is rich in cysteine and Proline amino acid. It provides flexibility to the immunoglobulin. The cysteine help in establishing the disulfide bond with opposite heavy chain. Disulfide bond (S-S) help in folding and stability of some protein. The number of

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hinge (S-S) bond depend upon the length of the hinge region. In addition to, inter disulfide bonds, each domain of light and heavy chains contain an intradisulfide bond

All immunoglobulin contain significant amount of carbohydrate in CH_2 region. The carbohydrate is of oligosaccharide type. It, however, does influence effector's function controlled by Fc fragments.

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Types of Antibodies :→

The antibodies are differentiated into five classes on the basis of their heavy chain. These are as follows —

① **IgG Antibody (Immunoglobulin G) →**

IgG is the most abundant class of antibody in serum, constitute about 80% of the total. It is a 160 KDa antibody made up of two γ heavy chains and two κ or two λ light chains. There are four subclasses, distinguished by differences in γ chain sequence and ~~numbered according~~. These are IgG_1, IgG_2, IgG_3 and IgG_4 and are encoded by different germ line C_H genes. There are difference in the size of the hinge region and the number and position of the interchain disulfide bond between the heavy chains. These changes in the amino acid differences between subclass of the IgG affects the biological activity of the molecules. IgG (IgG_1, IgG_3 & IgG_4) can easily cross the placenta and protect the foetus from infections. IgG antibody is found in milk upto 2 mths.

IgG_3 is the most effective complement activator followed by IgG_1 IgG_2. IgG_4 does not take part in activation.

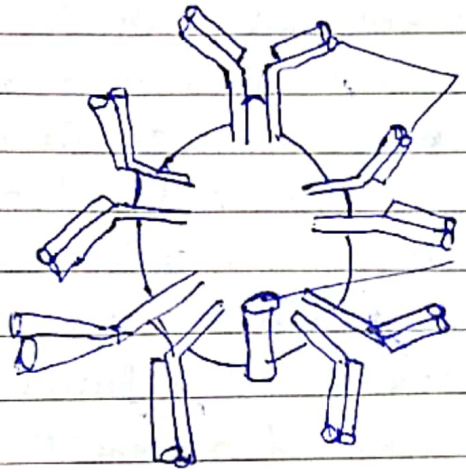
The IgG_1 and IgG_3 binds with the affinity with Fc receptors on phagocytic cells and thus cause opsonisation.

Igm (Immunoglobulin M) → Igm is a pentameric antibody having 900 KDa molecular weight. It is second highest in the plasma. It is generally composed of five monomers unit held together with by disulfide bond. The five subunits are arranged with their Fc regions in the center of the pentamers and the ten antigen binding sites on the periphery of the molecules. Each pentamer contains an additional Fc linked polypeptide called the J (joining) chain which binds the two monomers subunits forming pentameric antibody. Each subunit follows H_2L_2 model having two κ or λ Light chain and two μ heavy chain. Heavy chain of Igm posses 4 constant domain instead of a typical 3 constant domain and an additional 20 amino acid polypeptide on C terminal. It can bind with 10 antigen normally.

It is the first immunoglobulin class produced in a primary response to an antigen and it is the first immunoglobulin to be synthesized Igm is more efficient than IgG at activating Complement Activation requires two Fc region in close proximity and the pentameric structure of a single molecule of

IgM ~~fulfills~~ fulfills this requirement. Due to its higher valency it helps in opsonization for viral neutralization and for agglutination more efficiently.

Because of its large size IgM does not diffuse well so, can it found in very less amount in tissue fluid.



The presence of J chain allow IgM to bind to receptors on secretory cells. IgM plays an important accessory role as a secretory immunoglobulin. The IgM is frequently found in autoimmune disorder such as rheumatic arthritis.

Ques IgA (Immunoglobulin A.) !→

IgA constitutes only 10-15% of the total immunoglobulin in serum. IgA is a monomeric 360 KDa mol. wt antibody found in external secretion such as milk, saliva, tears and mucus of bronchial tract, urinogenital & digestive tract. In serum, IgA exists primarily as a monomer but polymeric forms such as dimer, trimers and even tetramere with a J chain and polypeptide chain called as seen.

secretory chain

The heavy chain of IgA contains two different kind of α chain having amino acid sequence variation, namely α_1 and α_2. One variant of α_2 lack disulphide bond between the heavy and light chain. The IgA naturally occur as dimeric which is most efficient to bind antigen. This dimeric form is called as IgA or SIgA antibody. It is quite resistant to proteolytic enzymes. IgA antibodies are poor activators of complement proteins but are good for neutralizing epithelial pathogens. They play important role in providing immunity to intestinal epithelial surface.

It acts as non-stick cover over the intestinal epithelial cells and thus preventing entry of large number of organisms and antigens to cross the epithelial cells and to reach inside. The microbial organism binds with IgA and thus they are unable to enter into the body. The SIgA antibody can cross link with antigens forming multiple epitopes. IgA binds to viral and bacterial surface antigen preventing adherence of antigen producing pathogens to mucosa membrane. Secretory IgA immunoglobulins provide effective protection against certain bacterial infections such as vibrio cholerae, Salmonella, gonorrhoeae etc. The secretion of SIgA is much more in breast milk which provide protection to new born babies as their immune system is not fully functional.

IgD (Immunoglobulin D):-

It is a 160 KDa molecules follows H2L2 model. It consists of two κ or λ Light chain and two δ of heavy chains. It constitutes only 0.2% of the total antibodies in the serum.

The heavy chain of IgD has only CH1 and CH3 domain only and it lacks interchain disulphide bond also. Hinged region is longer separating the two CH1 and CH3 domain. As such the IgD is very succeptible to proteolytic degradation and it has very short life span. IgD antibodies are active against insulin, Penicillin, diptheria, thyroid tissues and nuclear antigens. It also act as B-cell receptors. It is almost double in number in smoker than non smokers.

IgE (Immunoglobulin E):→ IgE lowest in Conc^{n} in serum immunoglobulins contains 2 κ and λ Light chain with two ε (epsilon) heavy chain. In IgE antibody the hinge region is absent and it is replaced by constant domain between CH1 and CH2 region. IgE antibody has four constant domain such as CH1, CH2, CH3 and

CH4 respectively.

The IgE takes active part in hypersensitive reactions and allergic manifestations. The heavy chain of IgE is susceptible to receptors on mast cells and basophil. The IgE antibody plays an important role in cell-mediated immunity with special reference to protozoans and helminthes infections. Binding of IgE to Fc receptors of basophil and mast cell facilitate crosslinkage of receptor-bound IgE molecules by antigen induce degranulation of basophil/mast cell. As a result, a variety of pharmacologically active mediators in the granules are released give allergic manifestations.