ANTIBODY STRUCTURE & TYPES

E-MODULE

BY

DR. SEEMA MARWAHA

ZOOLOGY DEPTT.

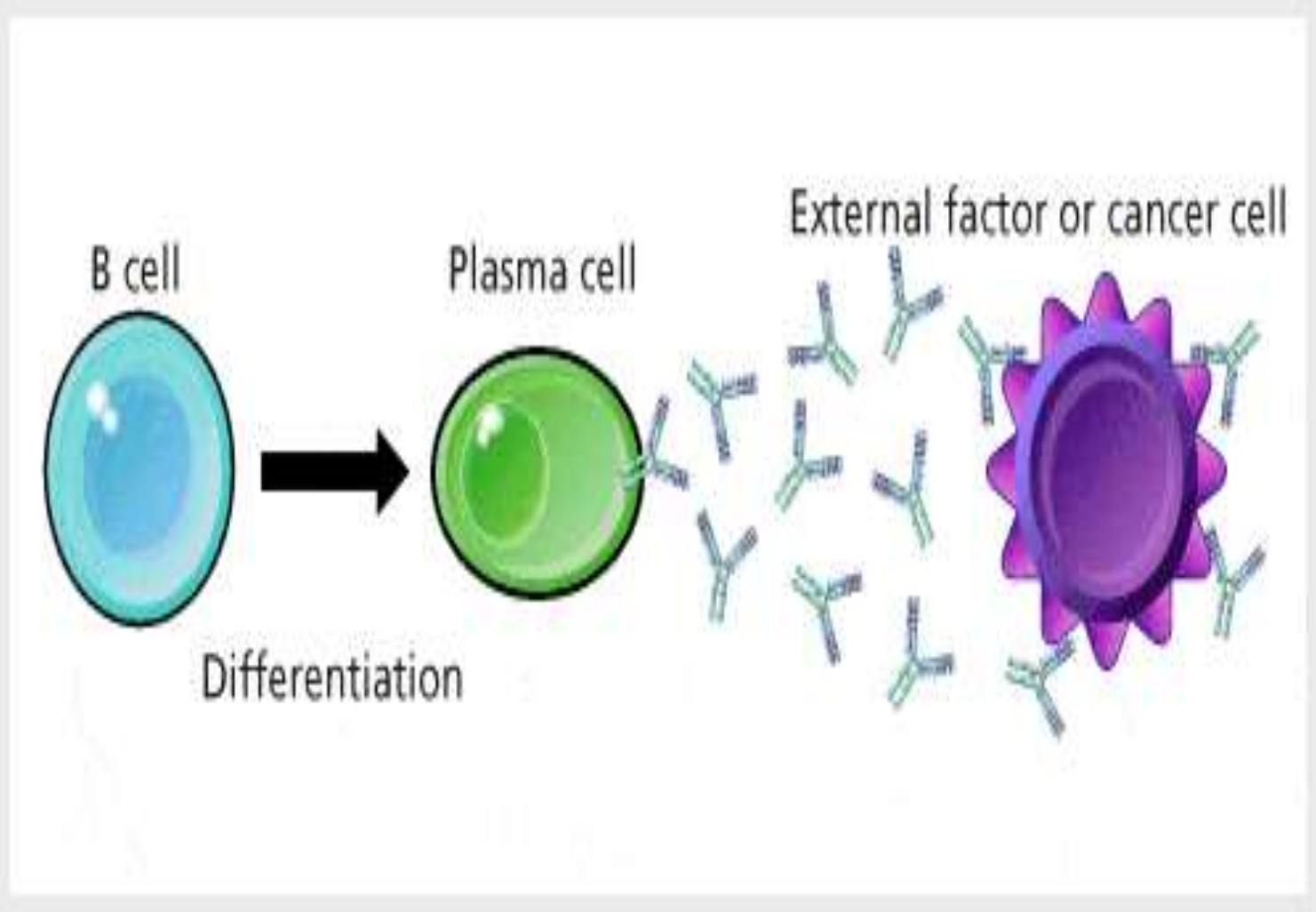
ANTIBODY

- **Antibody**, also called **immunoglobulin**, a protein produced by the immune system in response to the presence of a foreign substance, called an antigen.
- Antibodies recognize and bind to antigens in order to remove them from the body.

ANTIBODY

- Antibodies are produced by specialized white blood cells called B lymphocytes (or B cells)
- . When an antigen binds to the B-cell surface, it stimulates the B cell to divide and mature into a group of identical cells called a clone.
- The mature B cells, called plasma cells, secrete millions of antibodies into the bloodstream and lymphatic system.

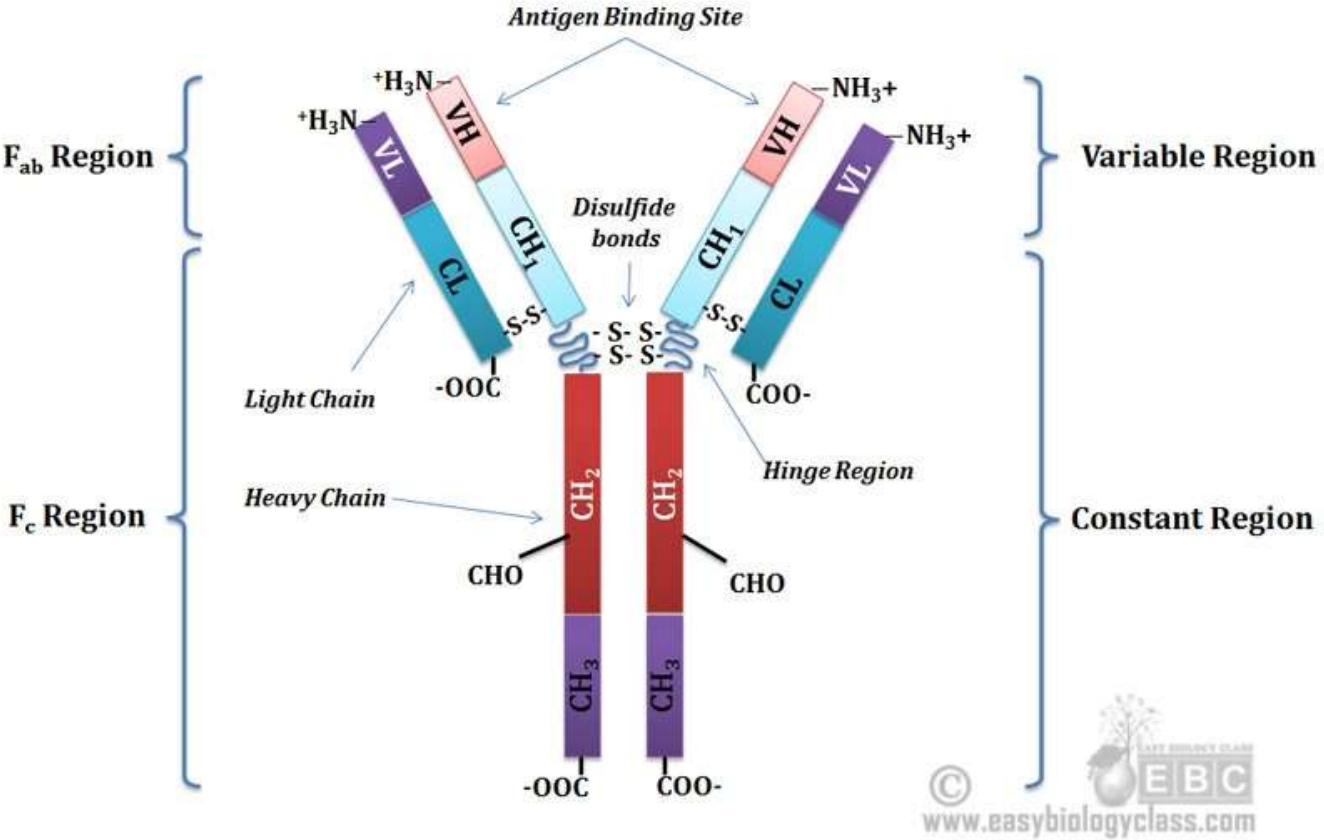
ANTIBODY FORMATION



STRUCTURE OF ANTIBODY

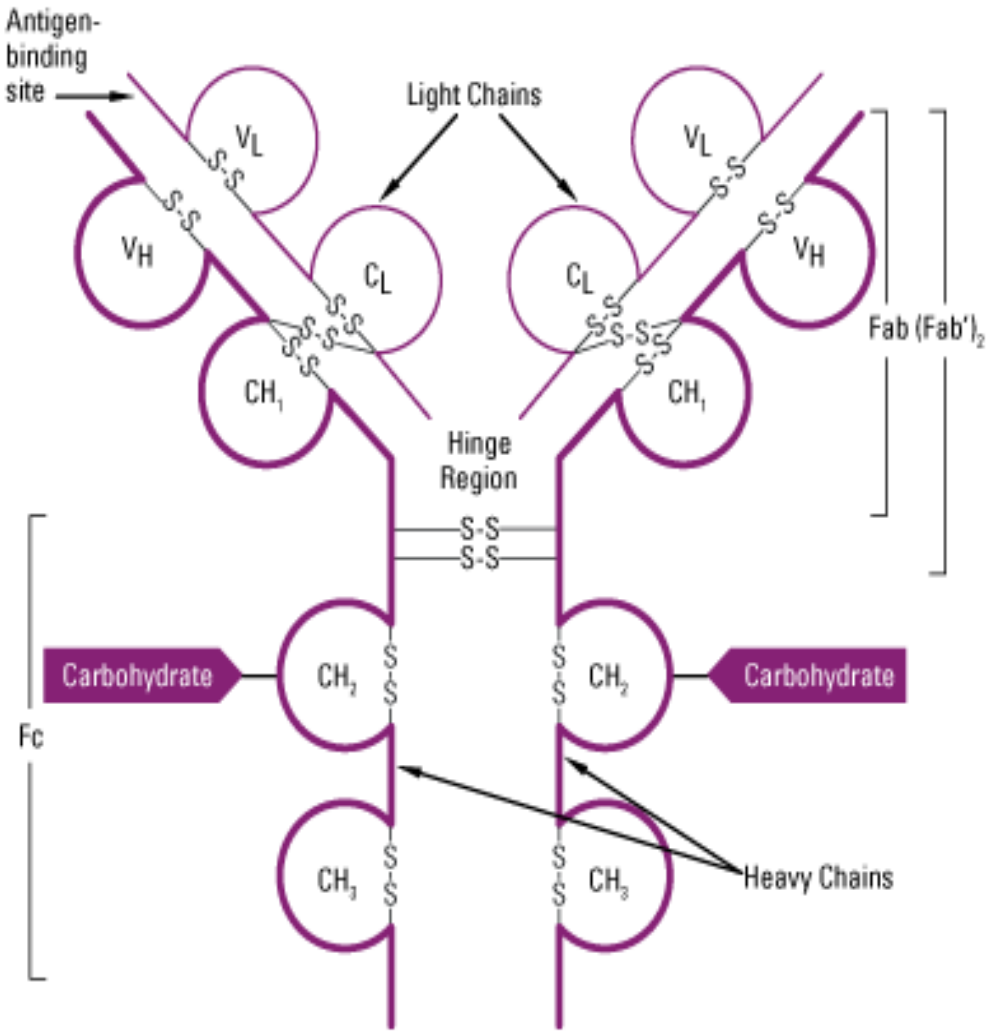
- The basic structure of these proteins consists of two pairs of polypeptide chains that form a flexible Y shape. The stem of the Y consists of two identical heavy chains and two light chains
- Within particular classes of antibodies the stem and the bottom of the arms are fairly similar and thus are called the constant region. The tips of the arms, however, are highly variable in sequence. It is these tips that bind antigen.
- Thus each antibody has two identical antigen-binding sites, one at the end of each arm, and the antigen-binding sites vary greatly among antibodies

ANTIBODY STRUCTURE

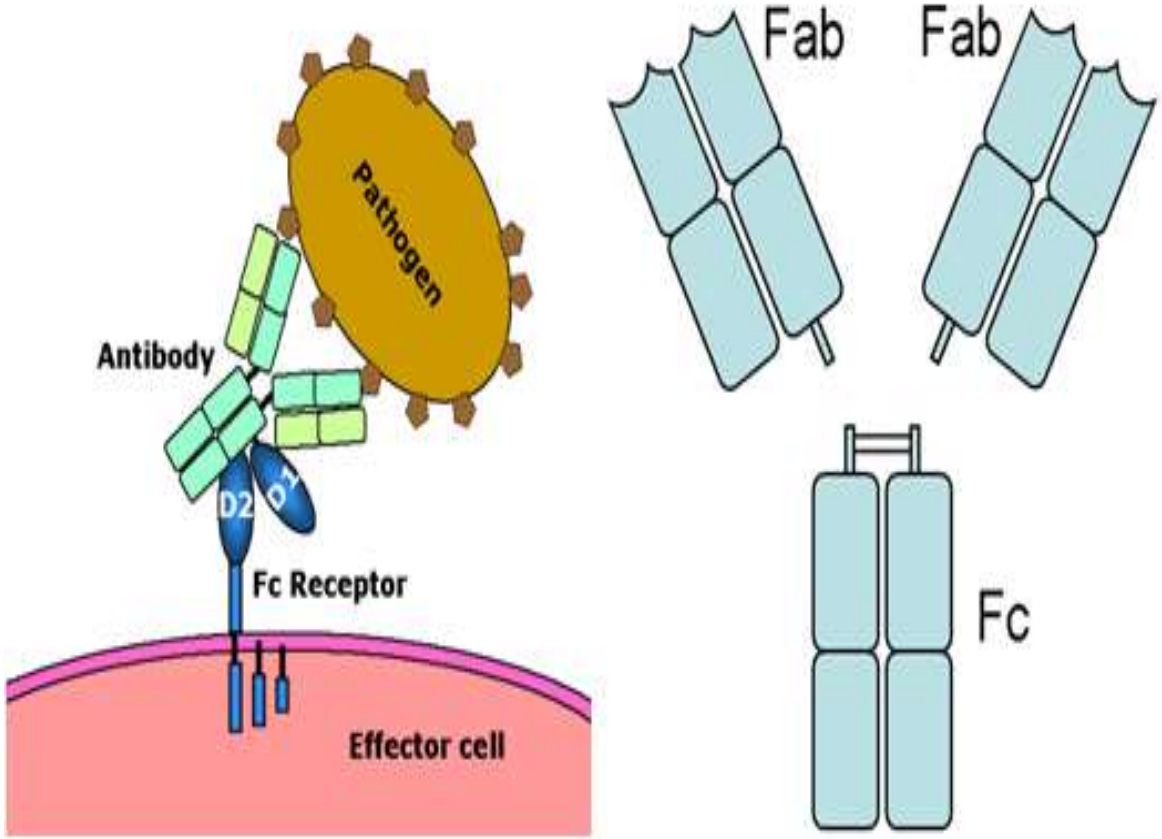


Variable (V) and Constant (C) Regions of an Antibody

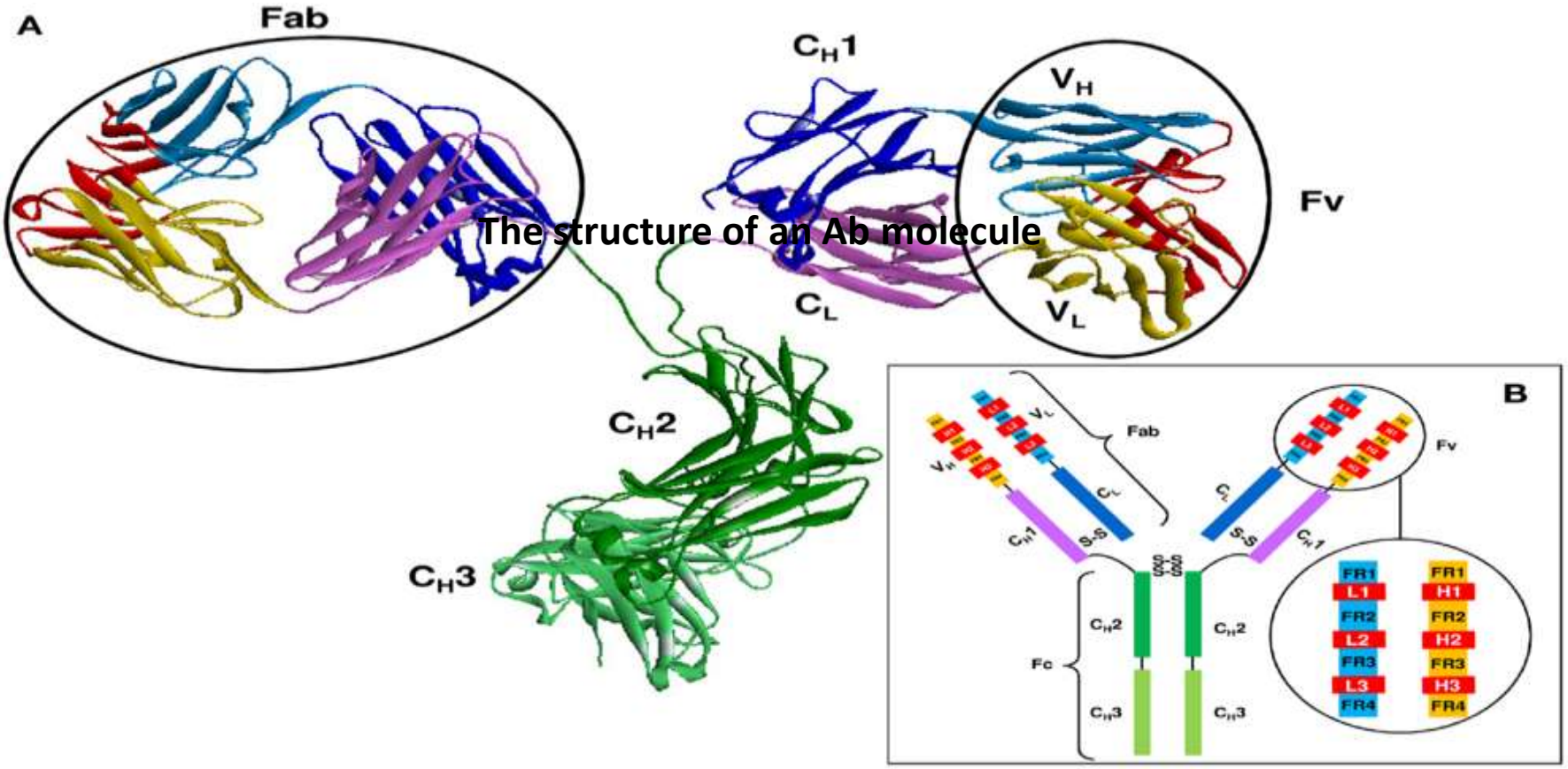
ANTIBODY DOMAIN STRUCTURE



Fc OF ANTIBODY



STRUCTURE OF ANTIBODY



The structure of an Ab molecule

STRUCTURE OF ANTIBODY

- Light Chain (L) consists polypeptides of about 22,000 Da and Heavy Chain (H) consists larger polypeptides of around 50,000 Da or more.
- There are five types of Ig **heavy chain** (in mammal) denoted by the Greek letters: α, δ, ε, γ, and μ. There are two types of Ig **light chain** (in mammal), which are called lambda (λ) and kappa (κ).

STRUCTURE OF ANTIBODY

- Each heavy and light chain in an immunoglobulin molecule contains an amino-terminal variable (V) region that consists of 100 to 110 amino acids and differ from one antibody to another.
- The remainder of each chain in the molecule – the constant (C) region exhibits limited variation that defines the two light chain subtypes and the five heavy chains subclasses. Some heavy chains (α, δ, γ) also contain a proline-rich hinge region.

STRUCTURE OF ANTIBODY

- The amino terminal portions, corresponding to the V regions, bind to antigen; effector functions are mediated by the carboxy-terminal domains.
- The ε and μ heavy chains, which lack a hinge region, contain an additional domain in the middle of the molecule.
- CHO denotes a carbohydrate group linked to the heavy chain.

ANTIBODY

- The association between an Ab and an Ag involves non-covalent interactions between the epitope – the binding site on the Ag, and the paratopes – the binding site on the Ab.
- The ability of Abs to bind virtually any non-self surface with exquisite specificity and high affinity is not only the key to immunity but has also made Abs an enormously valuable tool in experimental biology, biomedical research, diagnostics and therapy.

ANTIBODY STRUCTURE

- The six hypervariable loops within the variable domains of Abs, commonly termed as complementarity determining regions (CDRs), are widely assumed to be responsible for Ag recognition, while the constant domains are believed to mediate effector activation.

STRUCTURE OF ANTIBODY

. Within each variable domain lie six hypervariable loops , three in the light chain (L1, L2, and L3) and three in the heavy chain (H1, H2, and H3).

- The light and heavy variable domains fold in a manner that brings the hypervariable loops together to create the Ag binding site or paratope.
- Two additional domains of the heavy chain, CH2, and CH3, compose the Fc region which is responsible for mediating the biological activity of the Ab molecule.

CLASSES OF ANTIBODY

- Antibodies are grouped into five classes according to their constant region. Each class is designated by a letter attached to an abbreviation of the word *immunoglobulin*: IgG, IgM, IgA, IgD, and IgE. The classes of antibody differ not only in their constant region but also in activity.

CLASSES OF ANTIBODY

The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	6%	80%	13%	0.002%	1%
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor

IgM

- IgM is the first antibody produced in response to a microbial attack by B cells.
- It is the largest antibody and is found in a pentameric form.
- It circulates in the blood and lymph and constitutes 6% of the total antibody content in the serum.
- It is involved in agglutination and opsonization.
- It has a large number of antigenic sites on its surface and therefore facilitates efficient activation of the immune system.

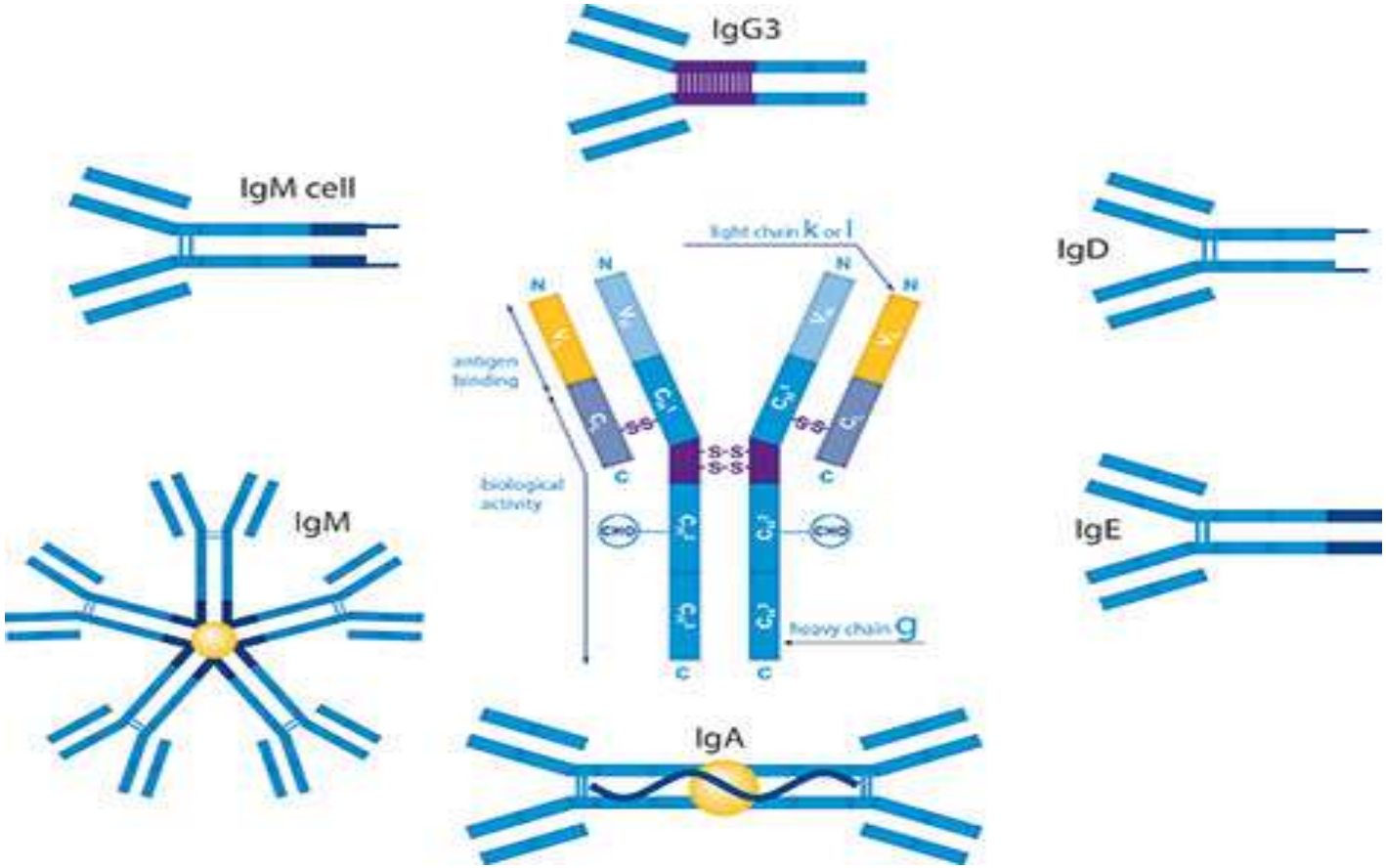
IgG

- Most abundant isotype in the plasma, and comprises 80% of the total antibody content in the serum. It detoxifies substances that are harmful and recognizes the antibody-antigen complex.
- It is transferred to the placenta through the foetus and protects the infant until it's birth.
- IgG is divided into four subclasses- IgG1, IgG2, IgG3, and IgG4. Among these, only IgG3 and IgG4 possess the ability to cross the placenta.
- The heavy chains of IgG have two antigen-binding sites and are of the sub-class gamma.
- It facilitates the process of phagocytosis and provides immunity to the developing foetus. It neutralizes the toxins and pathogens and offers protection to the body.

IgA

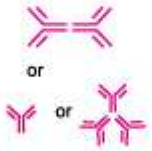
- Usually found in liquids such as breast milk, serum, saliva, fluids of the intestine. IgA in breast milk protects an infant's gastrointestinal tract from microbial activity.
- It constitutes 13% of the total antibody content in the serum and is divided into 2 sub-classes- IgA1 and IgA2. Among these, IgA1 is highly found in the secretions and is also called the secretory immunoglobulin.
- It exists in both monomeric as well as dimeric forms.
- It provides the first line of defence against the pathogens and limits inflammation. It also activates the complement pathway and participates in the immune response.

TYPES OF ANTIBODY

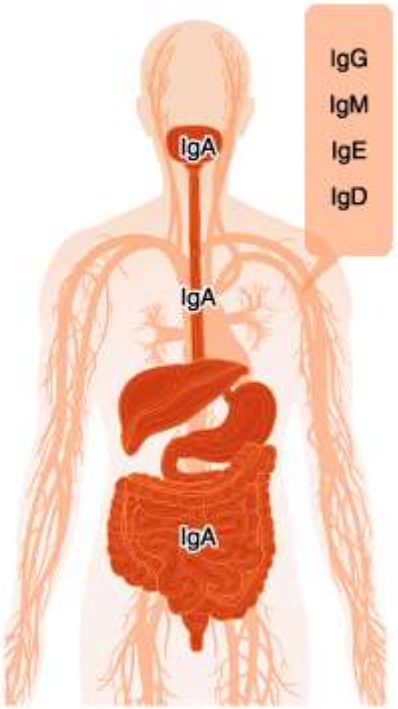


TYPES AND CHARAACTERISTICS

Types and characteristics of antibodies

IgG		• Highest opsonization and neutralization activities. • Classified into four subclasses (IgG1, IgG2, IgG3, and IgG4).
IgM		• Produced first upon antigen invasion. Increases transiently.
IgA		• Expressed in mucosal tissues. Forms dimers after secretion.
IgD		• Unknown function.
IgE		• Involved in allergy.

Distribution in the body



IgD

- It is involved in the production of the antibody by B cells.
- It is present as a monomer and weighs around 1,80,000 dalton.
- It comprises of less than 1% of the total antibody content in serum.
- It acts as a receptor on B cell surface and participates in B cell activation and differentiation.

IgE

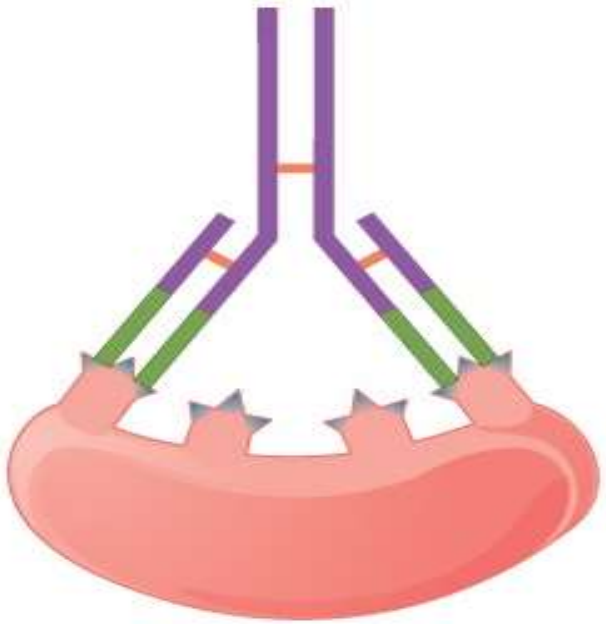
- IgE is present in the least amounts, around 0.02% of the antibody content in the serum.
- These are present in the linings of the respiratory and intestinal tracts and respond to allergic reactions.
- This is found as a monomer in the body and weighs about 200,000 Dalton

AFFINITY/AVIDITY

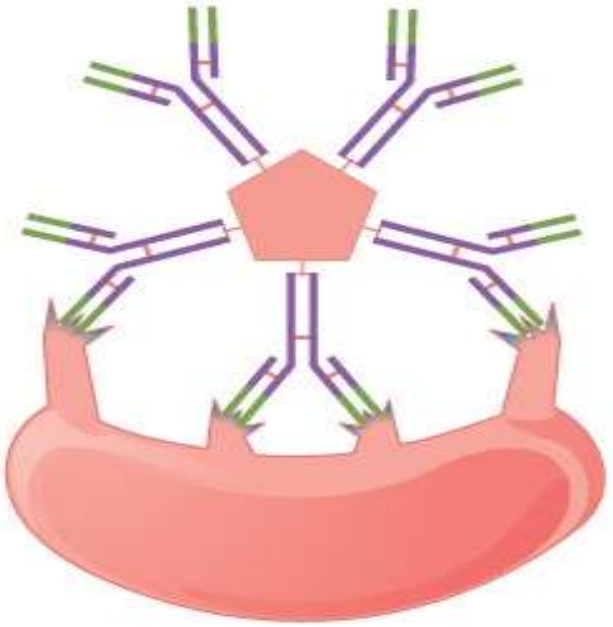
- Affinity refers to the attraction that a specific antibody possesses to its corresponding antigen. A high degree of specificity equates to bonding of that antibody to a specific antigenic epitope. Naturally occurring ABO antibodies possess a high degree of specificity to their antigenic counterparts.
- Avidity refers to the strength that an antigen-antibody immune complex possesses at that epitope. Naturally occurring ABO antibodies have a high degree of avidity, resulting in a powerful paratope-epitope bond.

AFFINITY AND AVIDITY

(a) Affinity versus avidity



Affinity refers to the strength of a single antibody–antigen interaction. Each IgG antigen binding site typically has high affinity for its target.

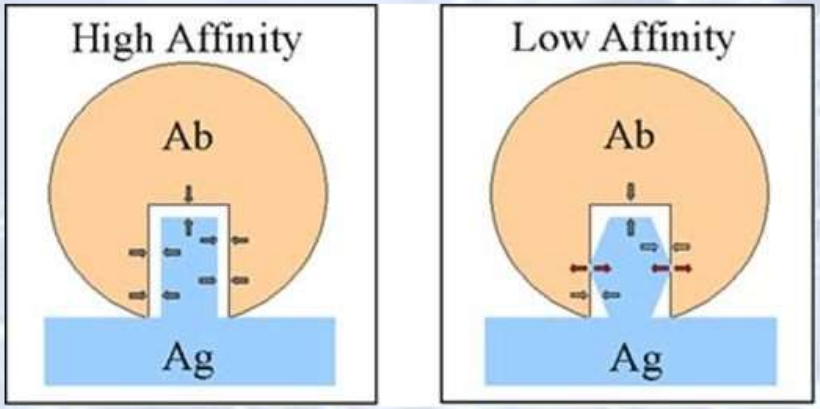


Avidity refers to the strength of all interactions combined. IgM typically has low affinity antigen binding sites, but there are ten of them, so avidity is high.

HIGH/LOW AFFINITY

AFFINITY AND AVIDITY

A. Affinity - Antibody affinity is the strength of the reaction between a single antigenic determinant and a single combining site on the antibody. It is the sum of the attractive and repulsive forces operating between the antigenic determinant and the combining site of the antibody as illustrated



REFERENCES

- Kuby Immunology
  By J.Kindt, A. Goldsby, A.Osborne
- The Elements of Immunology
  By Fahim Halim Khan
- Textbook of Zoology
  By P.S Dhami,J.K Dhami
- Google