STRUCTURE OF IMMUNOGLOBULINS

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IMMUNOGLOBULIN

- **Immunoglobulin is a glycoprotein that is made in response to an antigen and can recognize and bind to the antigen that caused its production.**
- Antibodies are the globular proteins belonging to Immunoglobulin (Ig) family
- Are gamma globulins
- Synthesized by plasma cells
- Constitute 25-30% of total serum proteins
- Antibodies are present in serum, tissue fluids and mucosal surfaces.
- All antibodies are immunoglobulins, but all immunoglobulins may not be antibodies

CLASSIFICATION

- Based on structure and antigenic nature of H chain the immunoglobulins are classified into 5 classes:-

1. **Ig G- (gamma)**
2. **Ig A- (alpha)**
3. **Ig M- (mu)**
4. **Ig D- (delta)**
5. **Ig E - (epsilon)**

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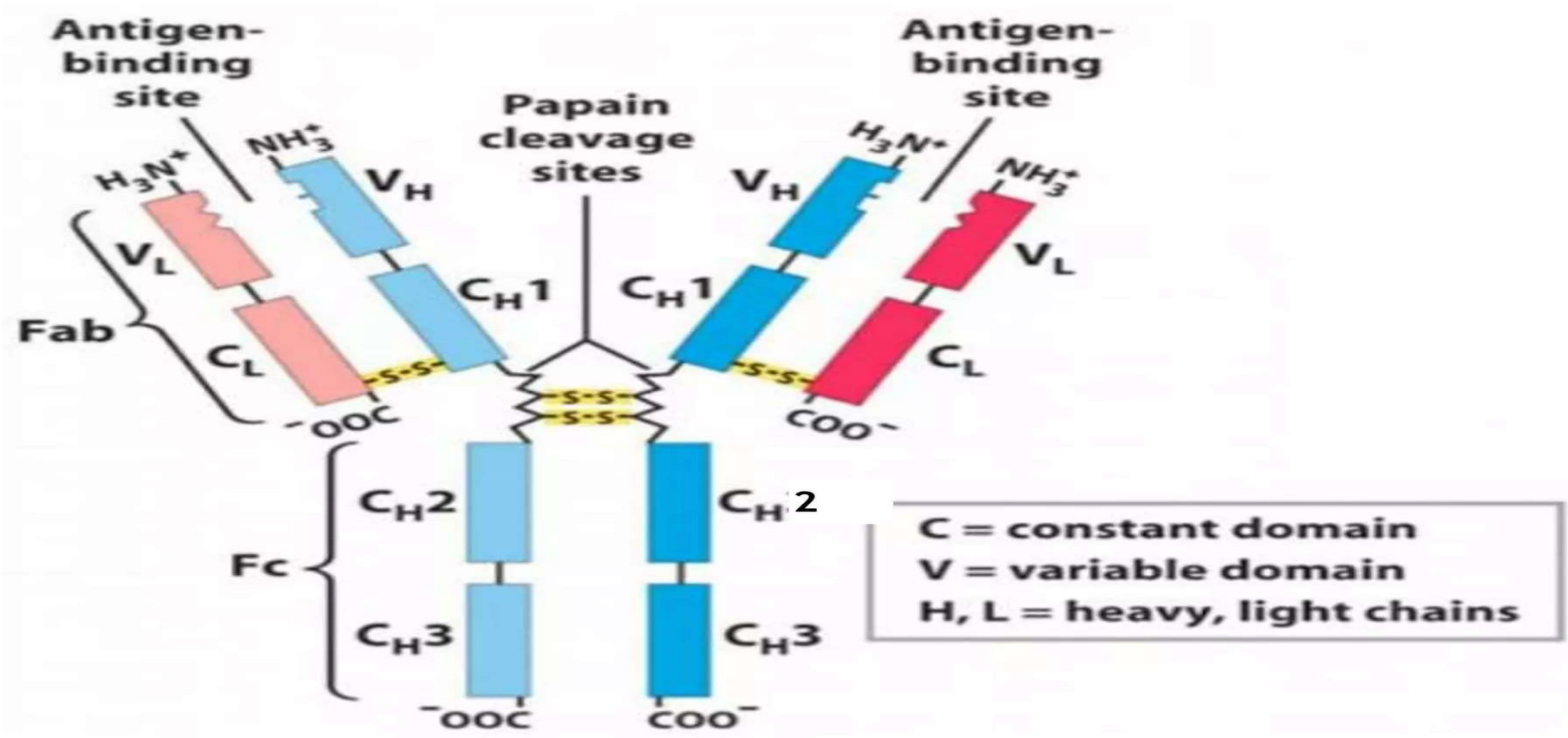


BASIC STRUCTURE EXPLANATION

- Composed of 4 polypeptide chains.
- Consists of 2 identical light chain (of 22000 Da) and 2 identical heavy chains (55000 Da)
- Linked by disulphide bonds and by non-covalent interaction
- Light chains similar in all immunoglobulins
- Light chains occur in 2 varieties (2 types of constant region sequences): kappa(κ) and lambda(λ)
- In a particular antibody either 2 lambda or 2 kappa chains are present but not 1 lambda and 1 kappa
- Light and Heavy chains are subdivided into variable and constant region.
- Each heavy and light chain contains amino terminal in variable region and carboxy terminal in constant region

- L-chain is composed of about 220 amino acids, around 100-110 amino acids are located at N-terminal (amino terminal) and the amino acid sequences varies among antibodies. This region of L-chain is known as variable region.
- H-chain consists of 110 amino acids located at N-terminal. This region is known as Variable region.
- Heavy chains are structurally and antigenically distinct for each class
- Each immunoglobulin peptide chain has intra chain disulphide bonds- form loops
- Light chain contains a single Variable domain (VL) and a single Constant domain (CL).
- Heavy chain contains one variable domain (VH) and 3 constant domains (CH1, CH2, CH3)
- Hinge region is the segment in heavy chain - between CH1, CH2

- **Fab region**-stands for **"Fragment antigen binding"** where antigen binding takes place.

  -Antigen binding is accomplished by amino-terminal region and effector functions by carboxyl terminal (C-terminal) region of antibody.

  -In an antibody molecule 2 Fab regions are found and they bind the antigens.

  -VL domain (L-chain) and VH domain (H-chain) form the antigen binding site.

- **Fc region-**it stands **"Fragment crystallizable"**

-It is so called because the well conserved amino acid sequence allows this fragment to crystallize.

-It allows interaction of immune complex with other phagocytic cells and complement.

-This region ensures that each antibody generates an appropriate immune response for a given antigen.

-This region also binds to several cell receptors such as Fc receptor.

-By doing this it mediates different physiological effects such as opsonization (modification of antigens by opsonin (which is a protein of innate and adaptive immune system) to make them more accessible to phagocytic cells and other immune cells), cell lysis and degranulation of mast cells.

DIGESTION WITH PROTEOLYTIC ENZYMES

- **Papain enzyme**- Peptide bonds in the hinge region are broken

  -Produces 3 fragments 2 identical fragments called Fab fragments – antigen binding activity.

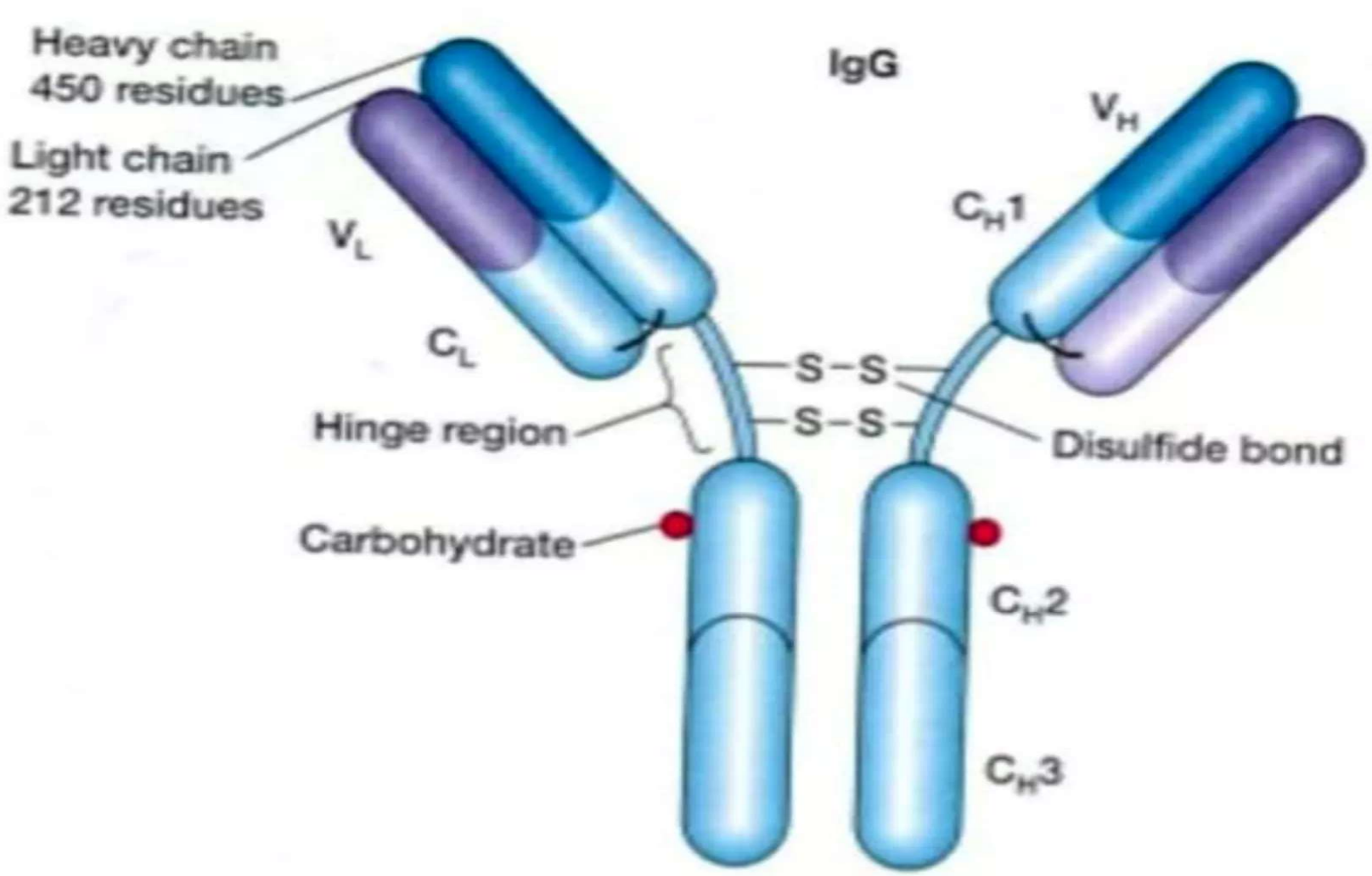
  -Other fragment called Fc fragment (Fraction crystallizable)

- **Pepsin digestion-** Produce a single fragment composed of two Fab like subunits F(ab) 2 binds antigen

  -Fc fragment is not recovered- digested to small numerous peptide

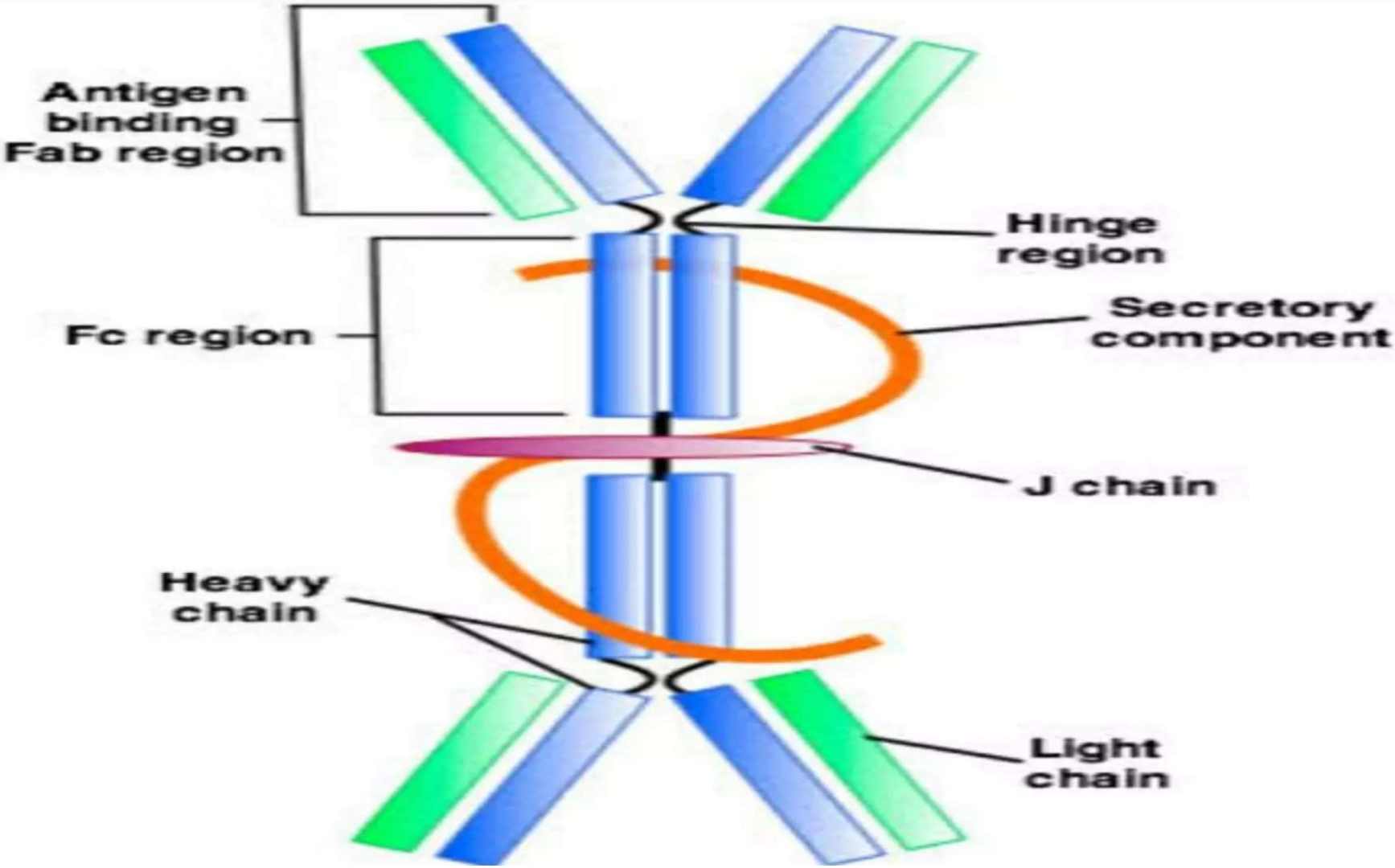
IMMUNOGLOBULIN G (IG G)

- Most abundant class in serum
- Constitutes 80% total immunoglobulin
- Present in blood, plasma and tissue fluids
- Contains less carbohydrate than other immunoglobulins
- It has a half life of 23 days: the longest of all of the immunoglobulin isotypes
- Crosses placenta and provide natural immunity to foetus and neonate at birth
- Acts against bacteria and viruses by opsonizing
- Neutralize toxin
- Activate complement by classical pathway
- Catabolism of IgG is unique in that it varies with its serum concentration


IgG
Heavy chain
450 residues
Light chain
212 residues
V_L
C_L
V_H
C_H1
S–S
S–S
Hinge region
Disulfide bond
Carbohydrate
C_H2
C_H3

IMMUNOGLOBULIN A (IG A)

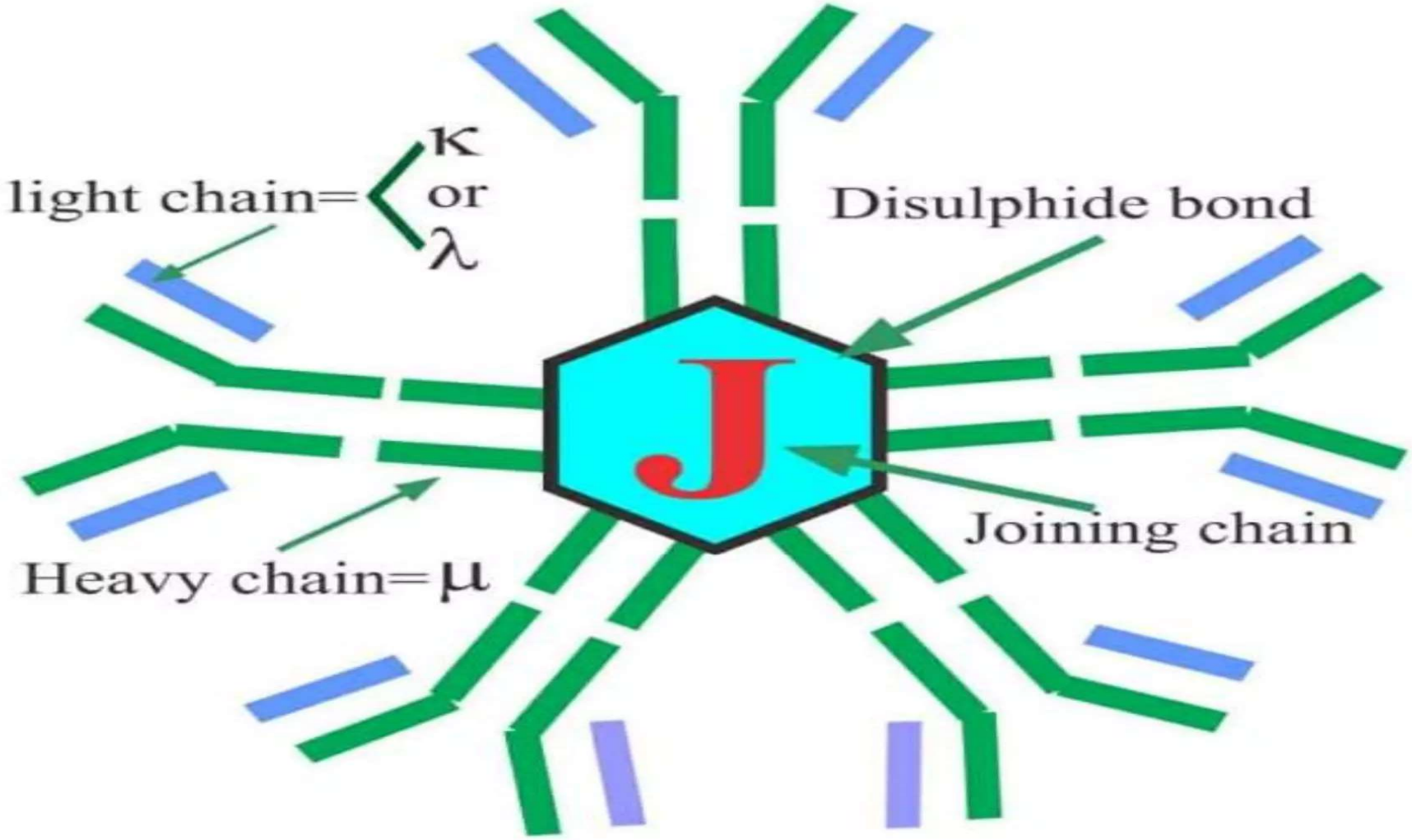
- Constitutes 10-15 % of total immunoglobulins
- Present in milk, saliva, tears, mucous of respiratory tract, digestive tract and genitourinary tract.
- In serum exist as monomer
- In external secretions exist as dimer called secretory Immunoglobulin.
- Has ‘J’ chain and secretory piece.
- Half life: 6-8 days


Antigen
binding
Fab region
Hinge
region
Fc region
Secretory
component
J chain
Heavy
chain
Light
chain

- Provides local immunity.
- Secretory Ig A binds to surface antigens of microorganism and prevent its attachment and invasion of the mucosal surfaces of respiratory and digestive tract- immune elimination.
- Secretory IgA provides important line of defense against *Salmonella*, *Vibrio cholerae*, *N. gonorrhoeae*, influenza virus and poliovirus.
- Secretory IgA present in breast milk protects newborn during first months of life.
- Promotes phagocytosis and intracellular killing of microorganisms

IMMUNOGLOBULIN M(IG M)

- Accounts for 5-10% of total serum proteins
- Polymer of five monomeric units (pentamer)
- Held together by disulfide bonds and 'J' chain
- Mol. Wt. of 900,00010,00,000 (millionaire molecule)
- Half life: 5 days
- Most of IgM (80%) present intravascularly
- Present in low concentration in intercellular tissue fluids
- Cannot cross placenta
- Presence of IgM antibody in serum of newborn indicate congenital infection.
- Earliest immunoglobulin to be synthesized by foetus (20 weeks)


light chain= κ or λ
Disulphide bond
J
Joining chain
Heavy chain= μ

- First immunoglobulin to be produced in primary response to antigen
- Relatively short-lived hence it's demonstration in the serum indicates recent infection
- Monomeric IgM appears on the surface of unstimulated B lymphocytes and act as receptors for antigens
- Functions

  - It agglutinates bacteria
  - Activates complement by classical pathway
  - Causes opsonization and immune hemolysis
  - Believed to be responsible for protection against blood invasion by microorganisms

IMMUNOGLOBULIN E (IG E)

- Structure is similar to Ig G
- Has 4 constant region domains.
- Mol. Wt. 1,90,000
- Half life: 2 days
- Heat labile (inactivated at 56°C in 1 hour)
- Normal serum concentration 0.3 ug/ml
- Mostly present extra cellularly
- Does not cross placenta

- Produced in the lining of respiratory and intestinal tract
- Known as reagin antibody
- Does not activate complement nor agglutinate antigens
- Binds to the Fc receptors on the membranes of blood basophils and tissue mast cells
- Mediates immediate hypersensitivity reaction and P.K. reaction
- Responsible for symptoms of anaphylactic shock, hay fever and asthma.
- Play a role in immunity against helminthic parasites

IMMUNOGLOBULIN D (IG D)

- Structure is similar to IgG
- Serum concentration 30 micrograms per ml
- Constitutes 0.2% of total immunoglobulins
- Half life: 3 days
- IgD together with IgM is major membrane bound immunoglobulin on unstimulated B lymphocytes-acts as recognition receptors for antigens

ROLE OF DIFFERENT IMMUNOGLOBULIN CLASSES

- IgG: Protects the body fluids
- IgA: Protects the body surfaces
- IgM: Protects the blood stream
- IgE: Mediates type I hypersensitivity
- IgD: Role not known