



# **Immunoglobulins (Igs) Antibodies (Abs)**

**Lec.4.**

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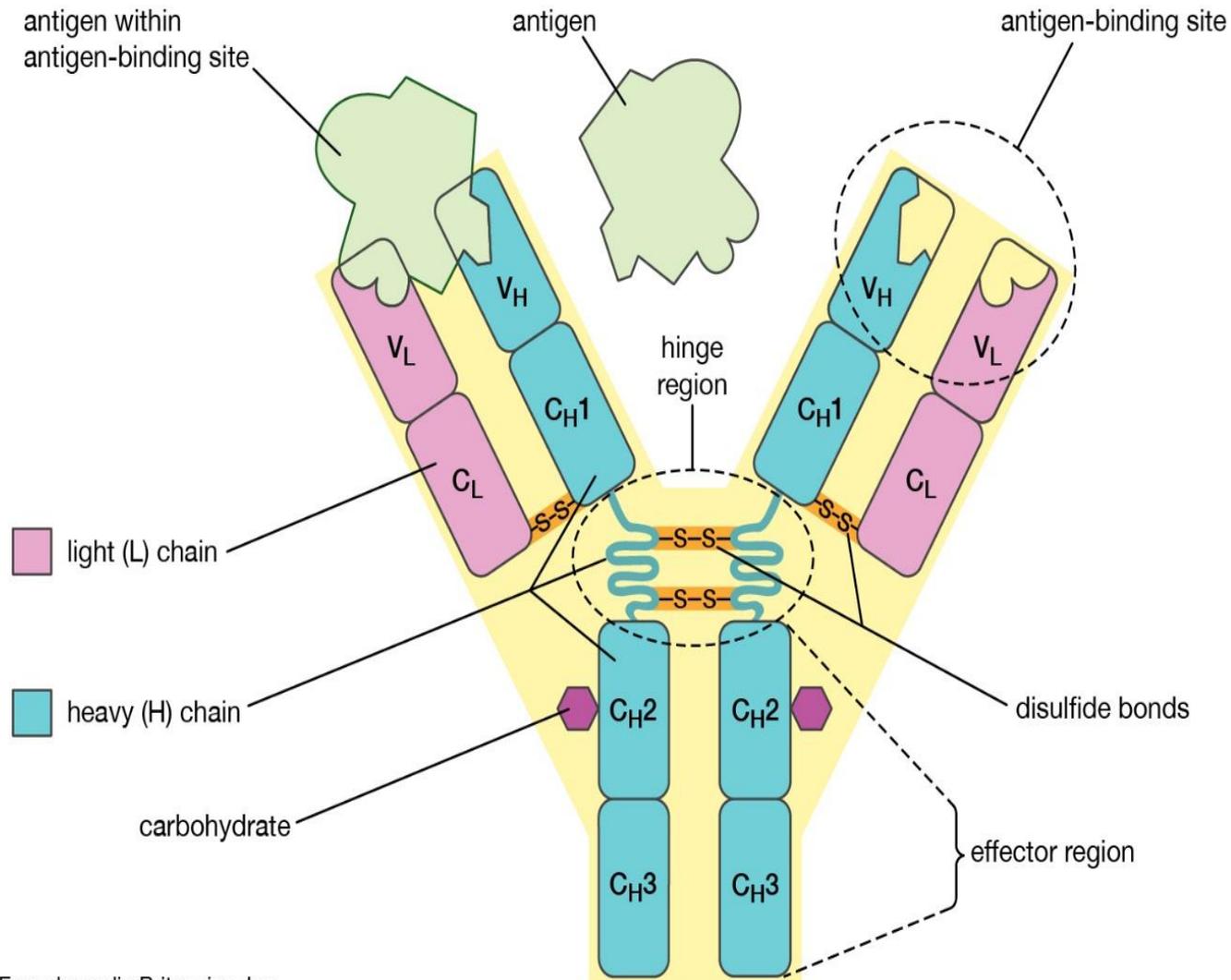
# Definition of Immunoglobulins (Igs)

- ▶ Immunoglobulins, also known as **antibodies**, are glycoprotein molecules produced by **plasma cells** (B-cell).
- ▶ They act as a critical part of the immune response by specifically **recognizing and binding to particular antigens**, such as bacteria or viruses, and **aiding in their destruction**.
- ▶ The antibody immune response is highly complex and exceedingly **specific**.
- ▶ The various immunoglobulin classes and subclasses (isotypes) differ in their biological features, structure, target specificity and distribution.

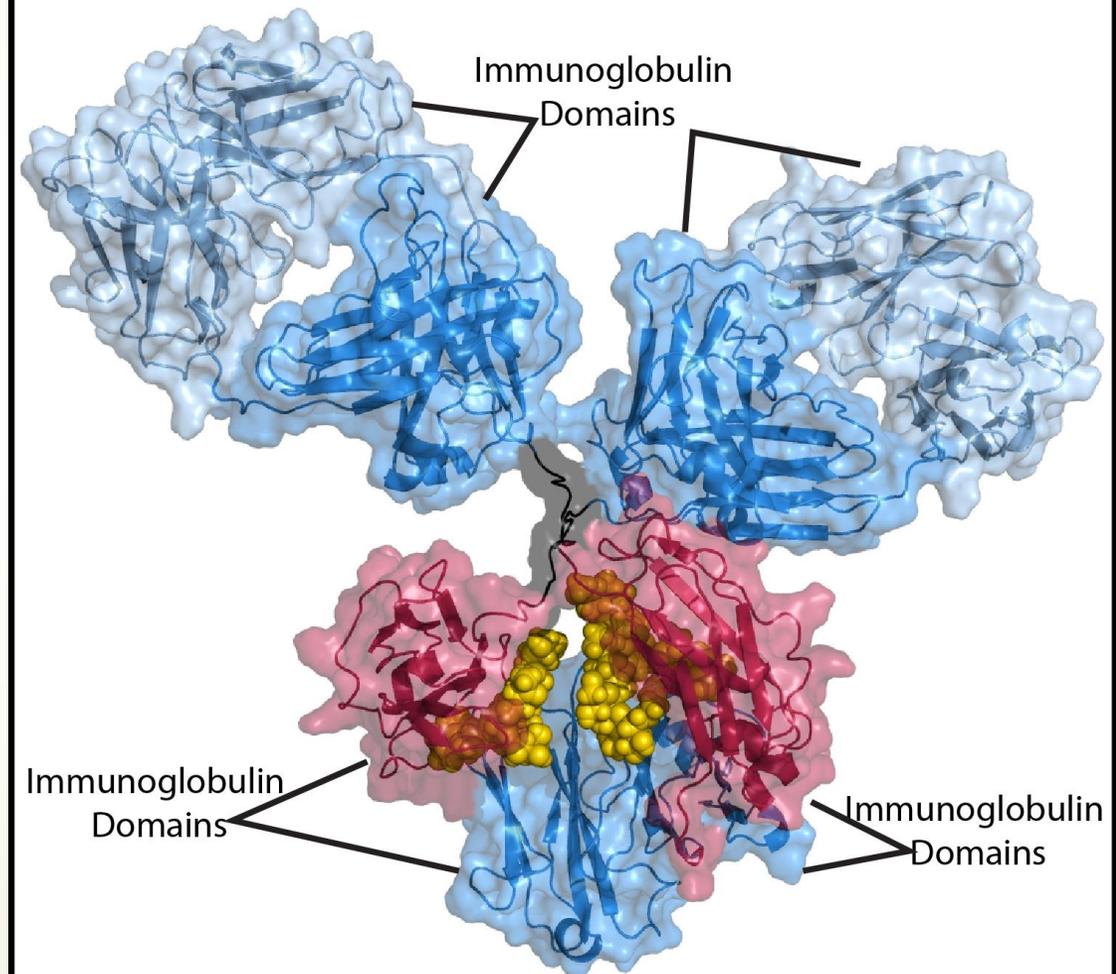
# The characteristics of antibodies.

- **Antibodies (in biology)** are **globulins (chemical structure)** and are therefore, also known as **immunoglobulins**
- They contain sugar residues and hence are **glycoproteins**
- They constitute **20-25%** of the total serum proteins
- When separated electrophoretically, most of them migrate in **gamma region**, hence they are also termed **gamma globulins**
- Most of them have molecular weight of **150,000-180,000** and sedimentation coefficient 7S-8S except for IgM. IgM has molecular weight of 900,000, sedimentation coefficient 19 S and termed **macroglobulin (M)**
- They are **thermolabile** and denatured on heating at 70°C for 1 hour
- **All antibodies are immunoglobulins** but NOT all immunoglobulins are antibodies
- All antibodies are made up of **light chain**(molecular weight 25,000) and **heavy chains** (molecular weight 50,000)

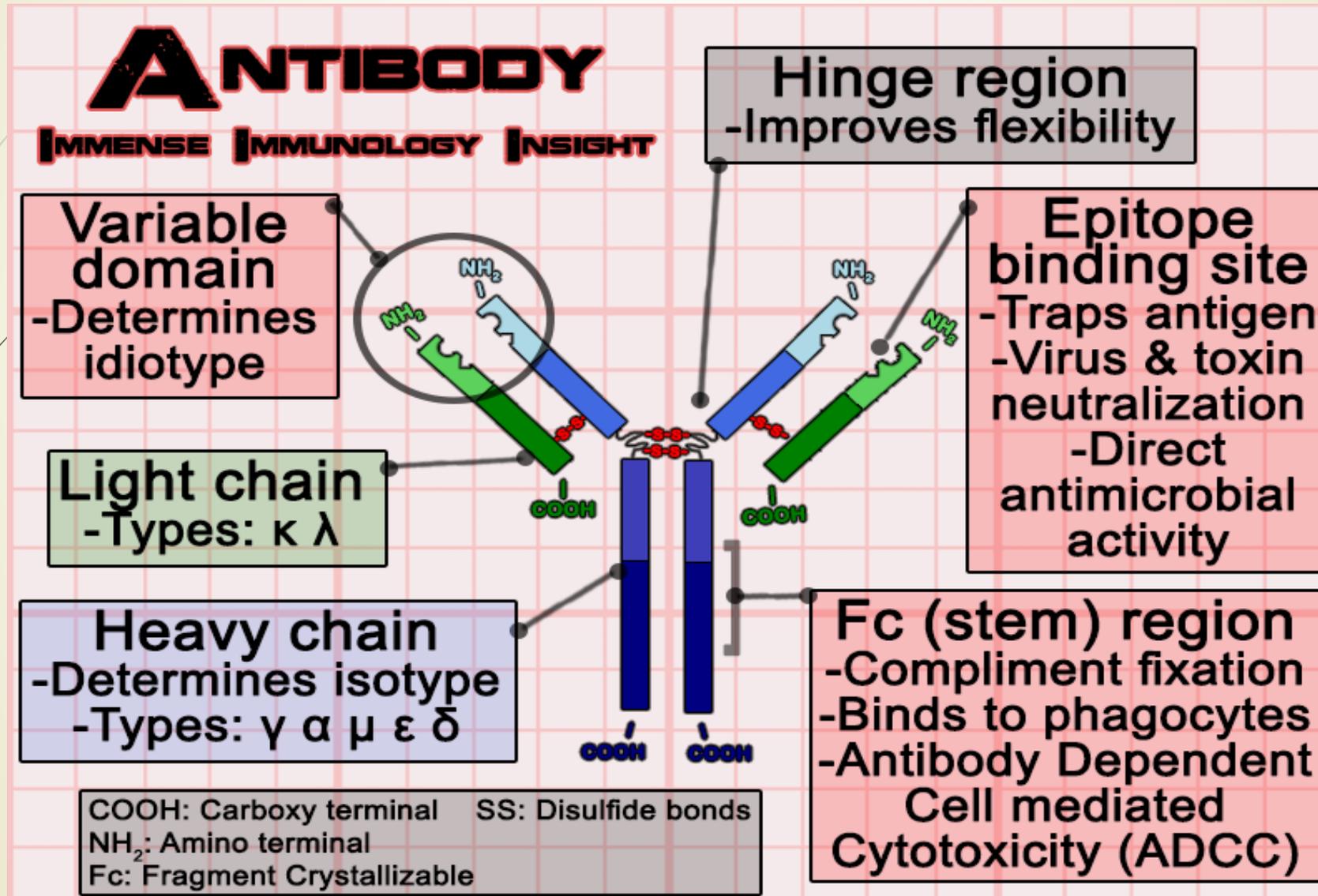
# Antibody structure



b: Crystal Structure of an IgG Antibody (1IGY)



# Functions of antibody region



# Classes of Immunoglobulin

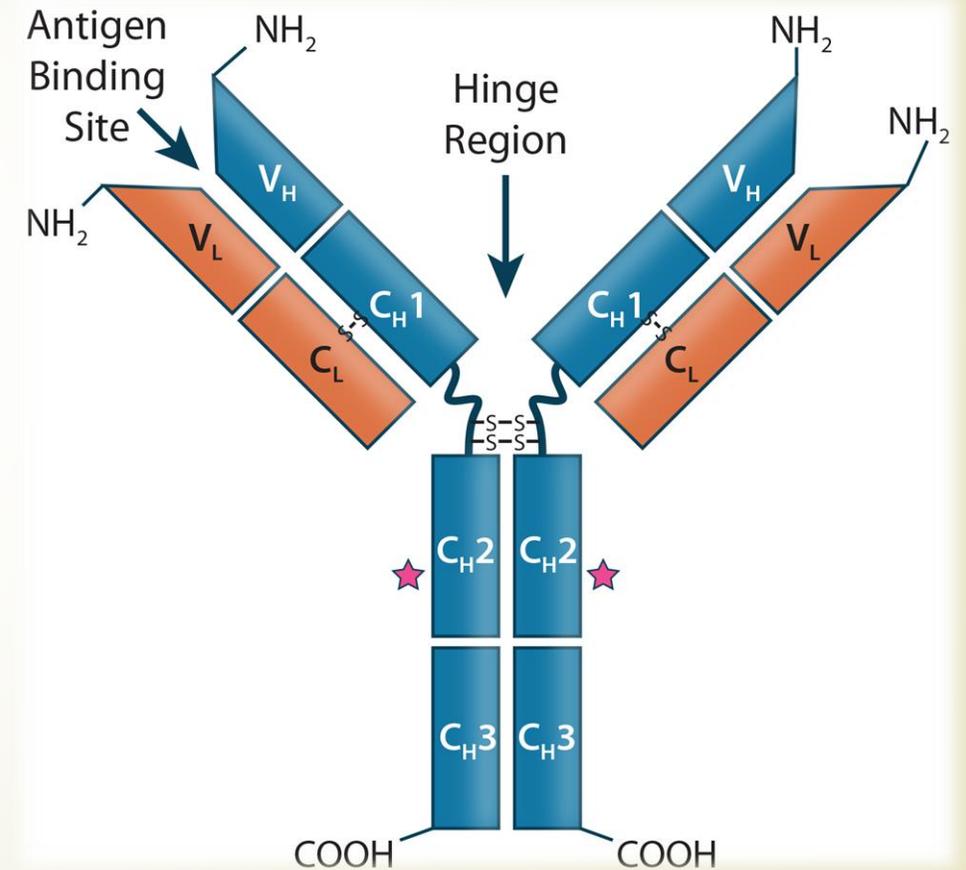
- There are five classes of immunoglobulins, according to their properties, They are:
- 1. Immunoglobulin G (IgG).
- 2. Immunoglobulin A (IgA).
- 3. Immunoglobulin M (IgM).
- 4. Immunoglobulin D (IgD).
- 5. Immunoglobulin E (IgE).

# Comparative features of immunoglobulins

Property	IgG	IgA	IgM	IgD	IgE
<b>Light chain</b>	Kappa or lambda	Kappa or lambda	Kappa or lambda	Kappa or lambda	Kappa or lambda
<b>Heavy chain</b>	Gamma ( $\gamma$ )	Alpha ( $\alpha$ )	Mu ( $\mu$ )	Delta ( $\delta$ )	Epsilon ( $\epsilon$ )
<b>Serum concentration (mg/mL)</b>	12	2	1.2	0.03	0.0003
<b>Percentage</b>	75%	10% -15%	5% -10%	-	-
<b>Sedimentation coefficient</b>	7S	7S, 11S	19S	7S	8S
<b>Molecular weight</b>	150,000	160,000	900,000-1,000,000	180,000	190,000
<b>Half-life (day)</b>	23	6	5	3	2
<b>Placental transfer</b>	+ (IgG1, IgG3, IgG4)	-	-	-	-
<b>Presence in milk</b>	+	+	-	-	-
<b>Carbohydrate percentage (%)</b>	3	8	12	13	12
<b>Heat stability (56°C)</b>	+	-	+	+	-
<b>Location (mostly)</b>	Serum, extra-vascular	Transport across epithelium	Serum (intravascular)	B cell membrane	Serum, extra- vascular

# Immunoglobulin G (IgG)

- It is the major Ig in normal serum accounting for **70-80%** of the total immunoglobulins.
- It is equally distributed between the intravascular and extravascular compartments
- It is a monomer consisting two H and two L chains
- It is the **major immunoglobulin synthesized during secondary response**

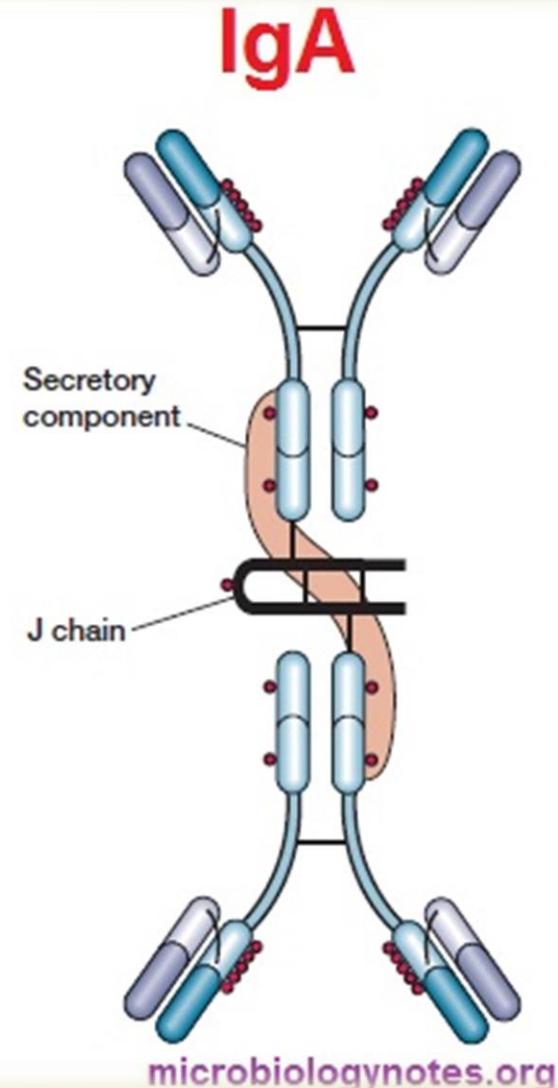


# Biological Activities of IgG

- ▶ In pregnant women, it has the ability to **cross the placenta and reach the fetal circulation** to provide a major line of defense (**naturally acquired passive immunity**) against infection in the newborn for the first few weeks
- ▶ **It neutralizes viruses, Toxin neutralization** in extravascular body spaces
- ▶ **Activate complement and enhances phagocytosis** by attach(phagocytic cells) and stimulates ingestion and killing of microorganisms
- ▶ It reacts with the target cell with the help of Fab portion and **mediates extracellular killing**
- ▶ It **participates in precipitation and complement fixation**, and in allergic reactions, e.g. Arthurs reaction and also in autoimmune diseases
- ▶ **IgG protects the body fluids**

# Immunoglobulins A (IgA)

- ▶ • It is the second most abundant immunoglobulin constituting **10-13%** of the total immunoglobulins
- ▶ • Secretory IgA present in the **seromucous secretions** such as saliva, tears, nasal fluids, sweat, and secretions of the lungs, genitourinary and gastrointestinal tract is the **dimer containing four H and four L chains**.
- ▶ It possesses a cysteine rich polypeptide chain called **J-chain (joining chain)** that joins two monomeric units of IgA
- ▶ • Also possesses an additional structural unit a glycine rich polypeptide called the **T (transport) or S (secretory component)** attached to the IgA molecule during transport across the cells, it protect IgA from digestion by proteolytic enzymes

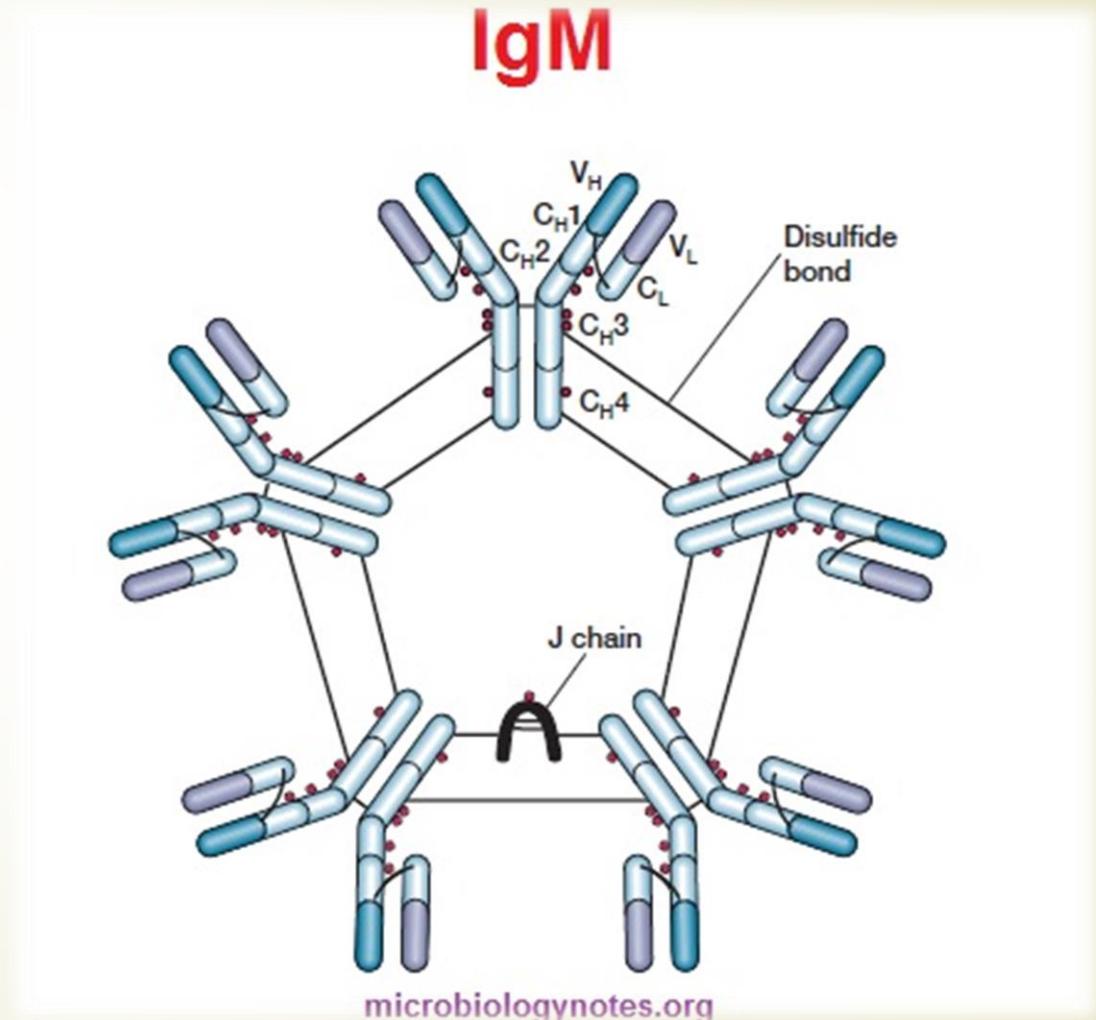


# Biological Activities of IgA

- ▶ **First line of defense in the resistance against infection.**
- ▶ **inhibiting bacterial and viral adhesion to epithelial cells** and preventing their entry into the body tissue
- ▶ The IgA in secretions ( secretory IgA) is **synthesized locally by plasma cells** concentrated in secretions and on mucous surfaces.
- ▶ It **plays important role in local immunity against respiratory, intestinal and urogenital pathogens**
- ▶ They also **activate complement by alternate pathway.**
- ▶ **promote phagocytosis and intracellular killing of microorganisms**
- ▶ **IgA protects the body surface**

# Immunoglobulins M (IgM)

- It is the **first Ab formed in every response**
- It constitutes **5-8%** of serum immunoglobulins
- It is a **pentamer containing 10 H and 10 L chains**
- **Five subunits of monomer joined together by J-chain** (joining chain)
- It is susceptible to mercaptoethanol serum treatment with mercaptoethanol selectively destroys IgM

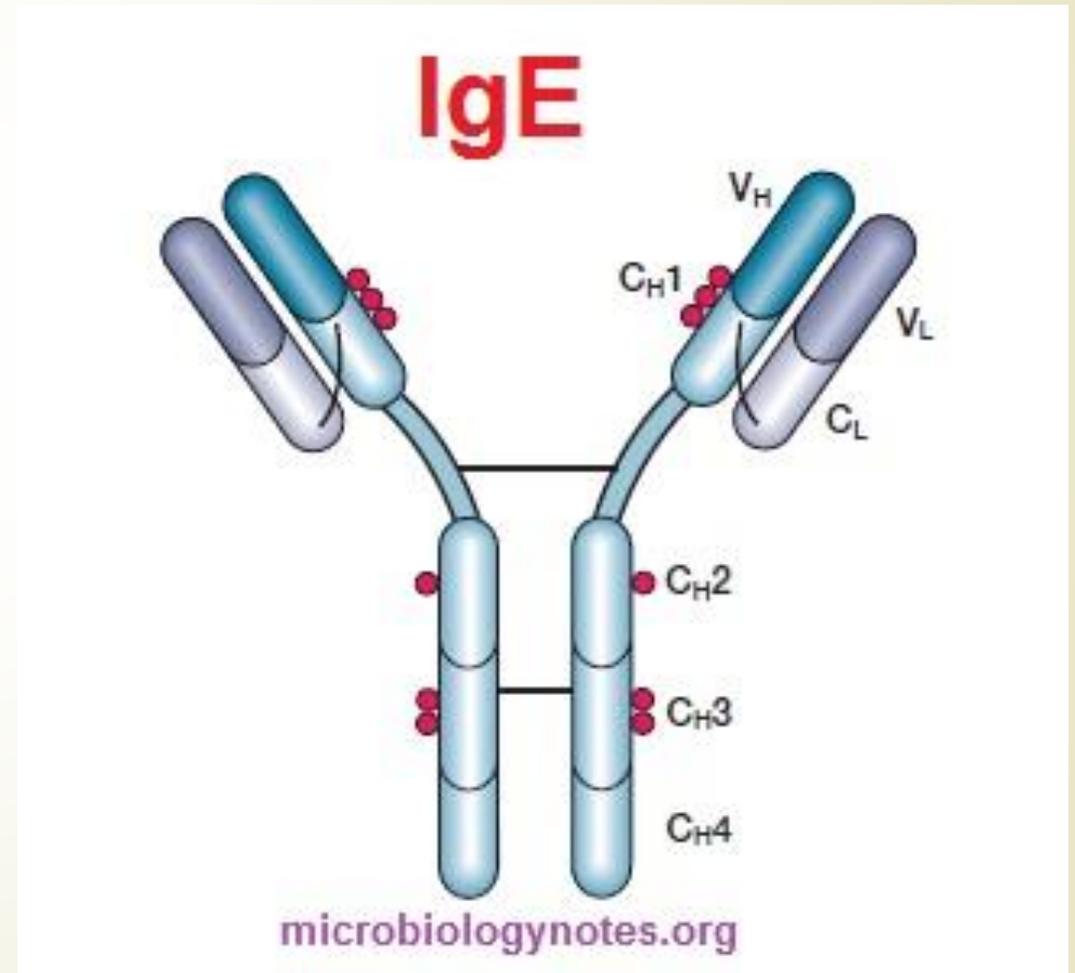


# Biological Activities of IgM

- It **activates complement**
- **neutralizes toxins and viruses**
- It is most **efficient in agglutination**, immune haemolysis, opsonization and bactericidal action
- Most of the IgM (80%) is intravascular in distribution, hence it offers **protection against bacteremia and septicemia**
- As it is **not transported across the placenta**, its detection in fetus or newborn indicates intrauterine infection, which is useful in the diagnosis of congenital infection
- • It **fixes complement by classical pathway**
- • As it is a **short-lived immunoglobulin** that disappears rapidly, its demonstration in serum **indicates recent infection**
- • **Monomeric IgM appears on the surface of unstimulated B lymphocytes** and acts as recognition receptor for antigens
- **IgM protects the blood stream**

# Immunoglobulins E (IgE)

- ▶ It occurs in very low concentration 0.02% of the total antibodies but the level is greatly elevated in atopic conditions such **as asthma, hay fever and eczema**
- ▶ It is structurally similar to IgG- monomer contains two H and two L chains
- ▶ **IgE are larger than IgG.**
- ▶ It responds quickly to the receptor of the mast cells and basophils.
- ▶ Mast cell and basophils are spread cells that take part in allergic reaction.
- ▶ Molecular weight is about 2 lakh KD.



# Biological Activities of **IgE, IgD**

- It is **extravascular in distribution** and has affinity for the surface tissue cells, particularly mast cells and basophils.
- It **causes degranulation of mast cells and basophils**, releasing pharmacologically active substances, **Histamines**.
- it is **responsible for Type- I hypersensitivity reaction**.
- It also plays an important role in **immunity against helminthic parasites**
- **They raise in infections and responsible for allergic symptoms.**
- **IgE Mediates reaginic hypersensitivity**
- **Immunoglobulin D (IgD)**
  - • It occurs in low concentration accounts for less than 1 % of the total immunoglobulins
  - • It is **structurally similar to IgG monomer** containing two H and two L chains
  - function as **antigen receptor on the surface of B lymphocytes for recognition of antigens** and **activation lymphocyte** to produce antibodies

# Monoclonal antibody

- ▶ A monoclonal antibody (mAb or moAb) **are laboratory-produced molecules** engineered to serve as substitute antibodies made by **cloning a unique white blood cell**
- ▶ **Monoclonal antibodies** can have **monovalent affinity**, binding only **to the same epitope** In contrast, **polyclonal antibodies** bind to **multiple epitopes** and are usually made by several different antibody secreting plasma cell lineages
- ▶ Monoclonal antibodies using as immunotherapy for **cancer cells** by the following ways:
  - **Flagging cancer cells**
  - **Blocking cell growth, or Preventing blood vessel growth**
  - **Blocking immune system inhibitors**
- ▶ **Anti-SARS-CoV-2 Monoclonal Antibodies** target **the spike protein of virus** which benefit in treating SARS-CoV-2 infection, these drugs include:
  - Bamlanivimab 700 mg plus etesevimab 1,400 mg administered as an intravenous (IV) infusion
  - Casirivimab 600 mg plus imdevimab 600 mg administered as an IV infusion
  - Sotrovimab 500 mg administered as an IV infusion
- ▶ When using anti-SARS-CoV-2 mAbs, treatment **should be started as soon as possible** after the patient receives a positive result on a SARS-CoV-2 antigen test or nucleic acid amplification test and **within 10 days of symptom onset**.



**Thank you**