II Semester- SC 2.5

Immunology

Unit II: Antigens and Immunoglobulins

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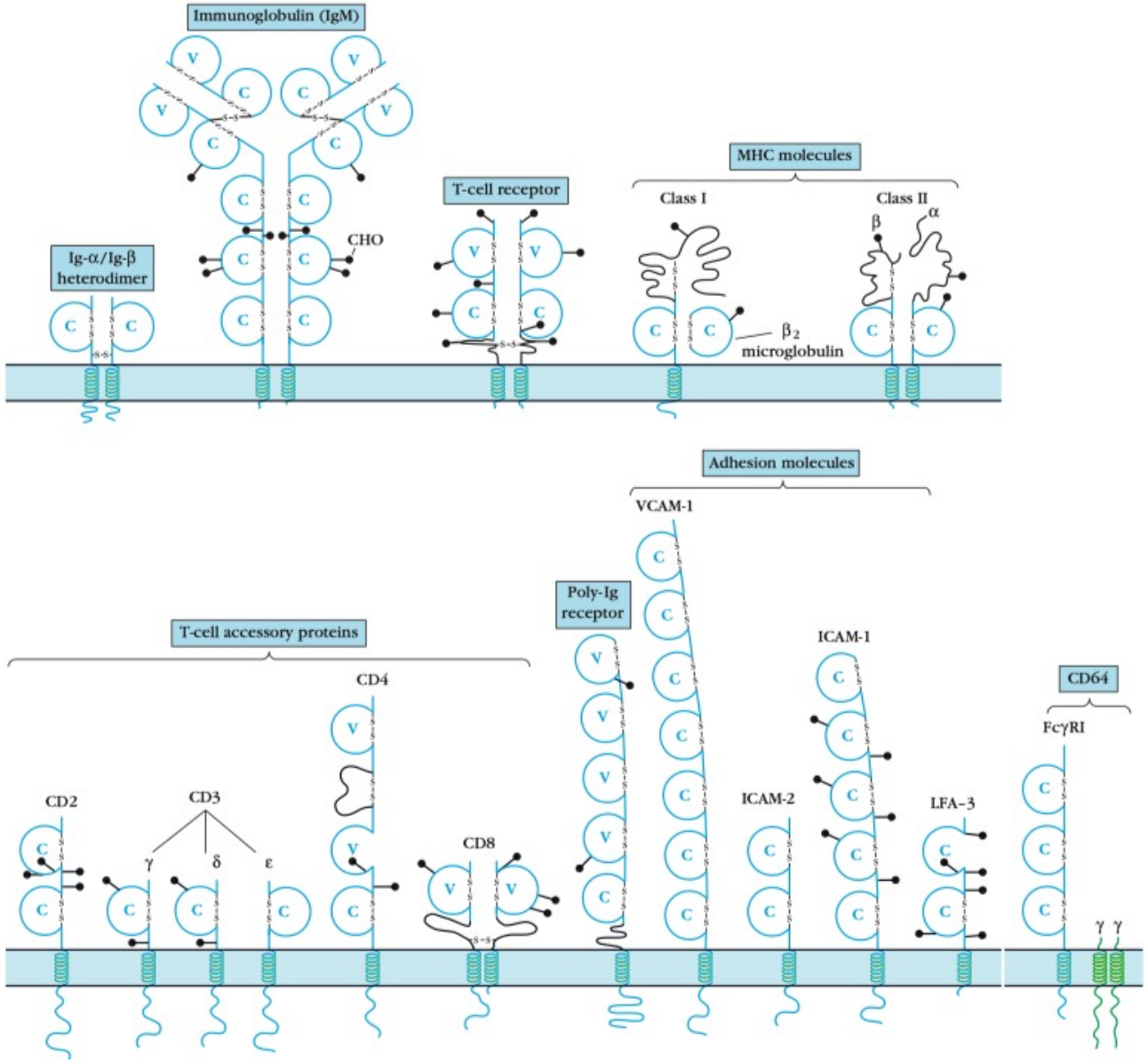
Contents

B. Immunoglobulins:

- Basic structure of immunoglobulin
- Types and functions of immunoglobulins

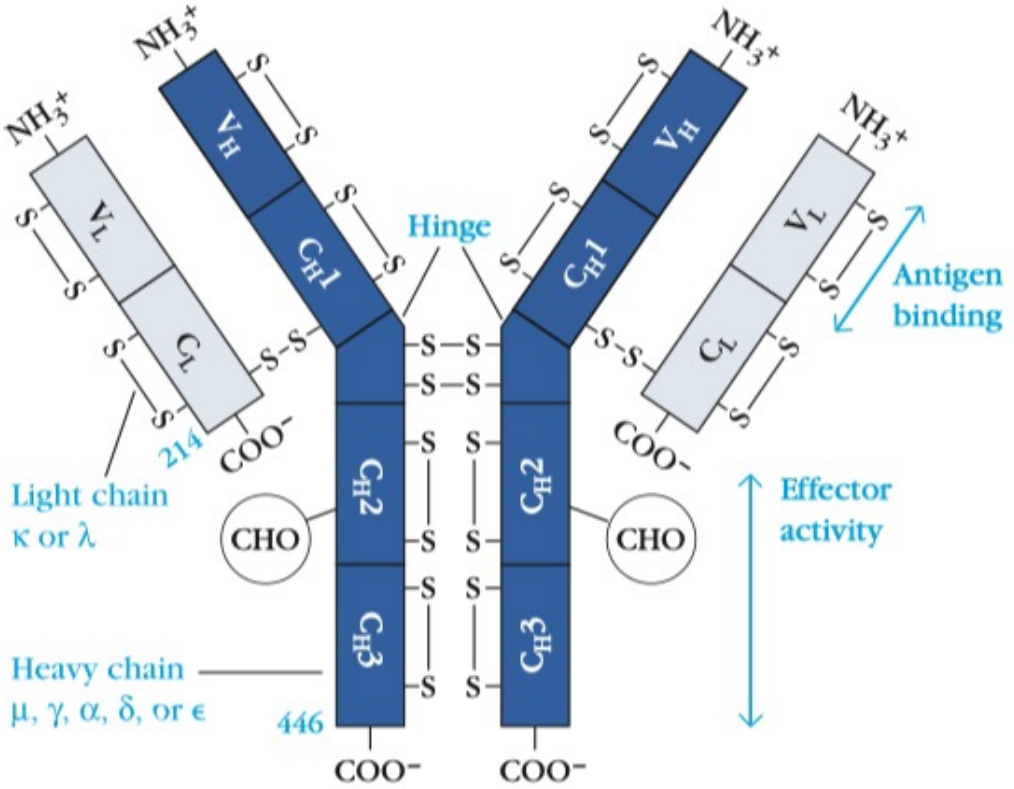
Introduction

- On stimulation with antigen, B cells secrete antibodies with antigen-binding sites identical to those on the B-cell membrane antigen receptor.
- Antibodies Are Made Up of Multiple Immunoglobulin Domains
- immunoglobulin superfamily
- BCR and TCR belong to immunoglobulin superfamily as they are coded by the same gene families and have similar structure
- Overlapping anti-parallel beta sheets

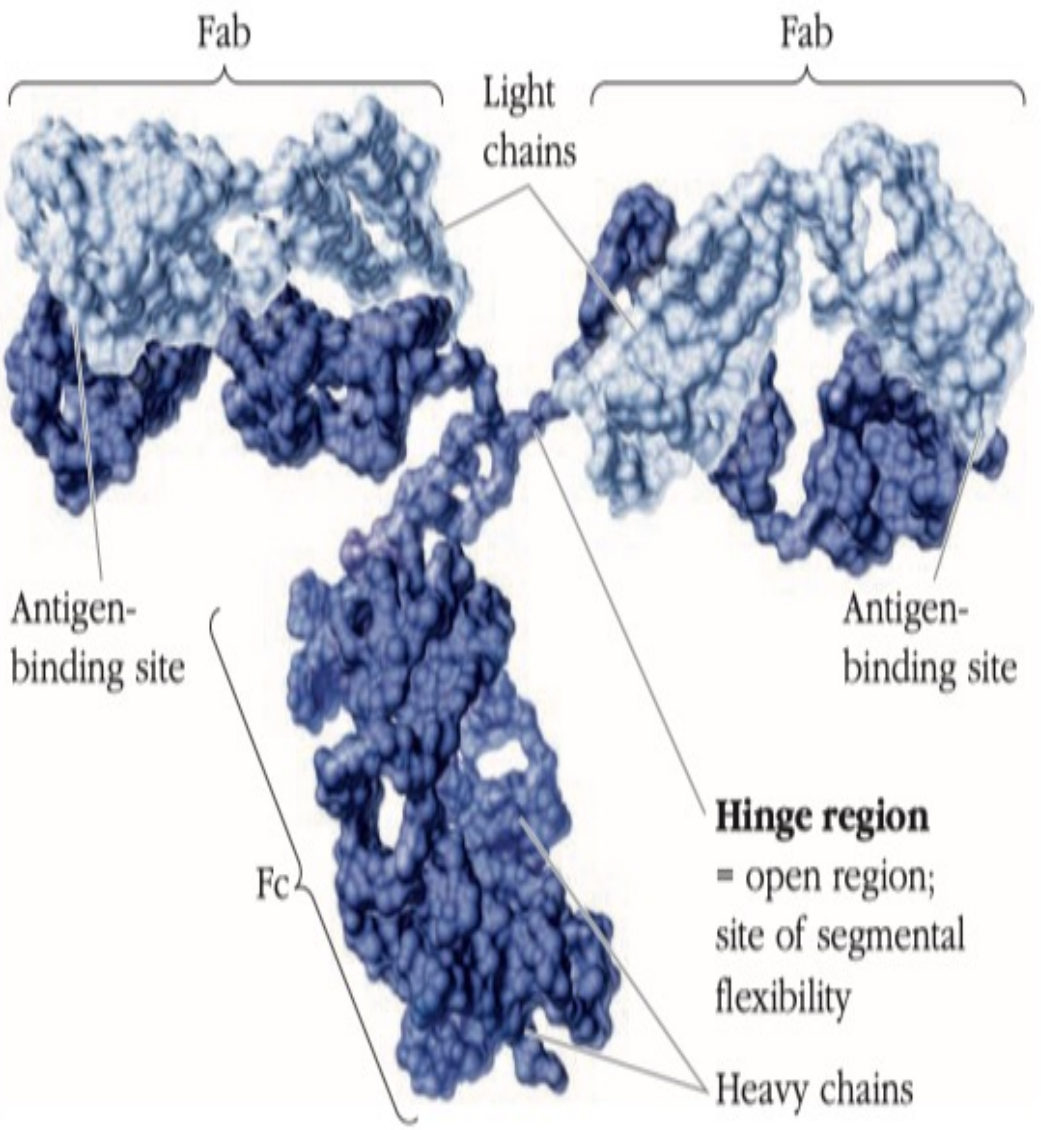

Immunoglobulin (IgM)
V
C
CHO
Ig-α/Ig-β
heterodimer
T-cell receptor
MHC molecules
Class I
Class II
β
α
β2
microglobulin
Adhesion molecules
VCAM-1
Poly-Ig
receptor
ICAM-1
ICAM-2
LFA-3
CD64
FcγRI
T-cell accessory proteins
CD2
CD3
γ
δ
ε
CD4
CD8

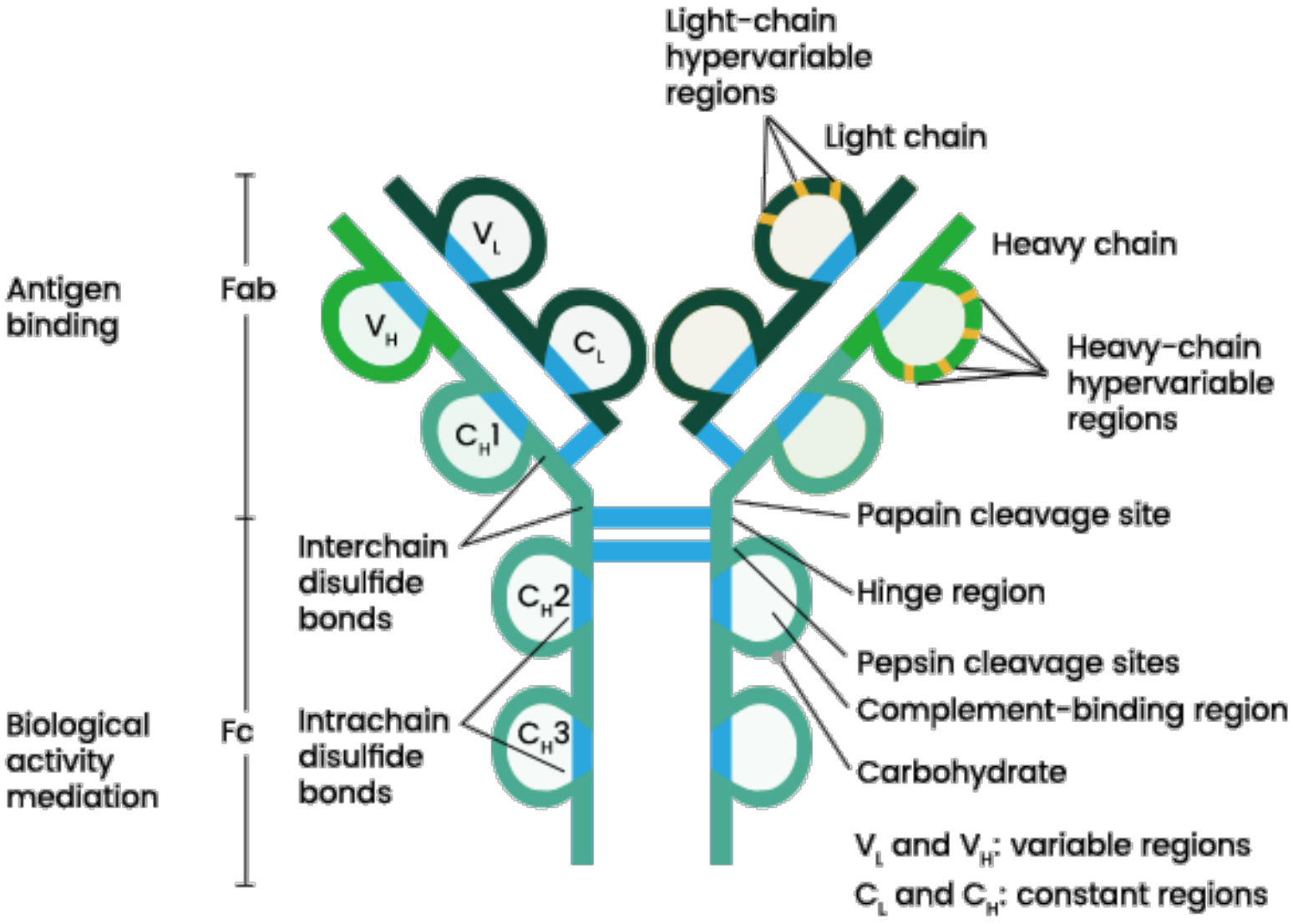
Structure of antibody

- All antibodies share a common structure of four polypeptide chains
- two identical light (L) chains and two identical heavy (H) chains.
- Each light chain is bound to its partner heavy chain by a disulfide bond between corresponding cysteine residues
- noncovalent interactions between the V_H and V_L domains and the C_H1 and C_L domains
- Multiple disulphide bridges link the two heavy chains together about halfway down their length, and the C-terminal parts of the two heavy chains also participate in noncovalent bonding interactions between corresponding domains.



- flexible hinge region: susceptible to proteolytic cleavage by the enzyme papain.
- Fab regions: antigen-binding region
- Fc region: constant region for all Abs of a given class and is easily crystallizable
- The Fab regions bind to the antigen, and the Fc region of the antigen-coupled antibody binds to Fc receptors on phagocytic or cytolytic cells, or to immune effector molecules.
- A family of Fc receptors exists; each Fc receptor is expressed on a different array of cells and binds to a different class of antibodies.




Light-chain hypervariable regions
Light chain
Heavy chain
Heavy-chain hypervariable regions
Antigen binding
Fab
V_L
V_H
C_L
C_H1
Papain cleavage site
Interchain disulfide bonds
Hinge region
C_H2
Pepsin cleavage sites
Complement-binding region
Biological activity mediation
Fc
Intrachain disulfide bonds
C_H3
Carbohydrate
V_L and V_H: variable regions
C_L and C_H: constant regions

Light chains

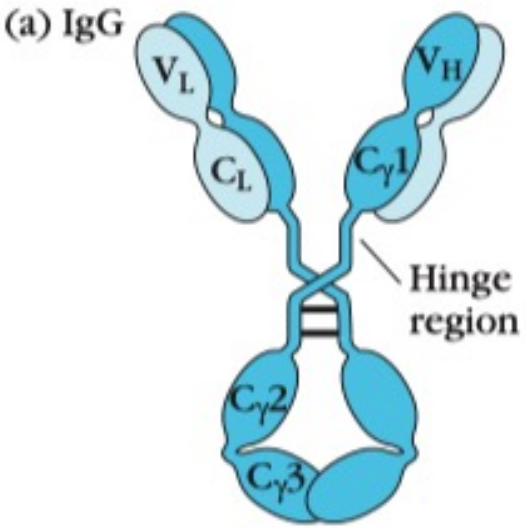
- The N-terminal half of light chains is thus referred to as the variable, or V_L , region of the light chain
- the less variable part of the sequence is termed the constant, or C_L , region
- The two major light chain constant region sequences are referred to as **κ** (kappa) or ƛ (lambda) chains
- ƛ chain constant region sequences could be further subdivided into four subtypes— ƛ 1, ƛ 2, ƛ 3, and ƛ 4
- even within the variable regions of the light chain, there are regions of hypervariability
- hypervariable regions could be shown to interact with the bound antigen, they were renamed the complementarity-determining regions, or CDRs.

Heavy chains

- 5 major classes of heavy chains
- **μ** (mu), **δ** (delta), **γ** (gamma), **ε** (epsilon), and **α** (alpha)
- Each different heavy-chain constant region is referred to as an isotype, and the isotype of the heavy chains of a given antibody molecule determines its class.
- IgM, IgD, IgG, IgE and IgA
- Minor differences in the amino acid sequences of groups of alpha and gamma heavy chains led to further subclassification of these heavy chains into sub-isotypes and their corresponding antibodies therefore into subclasses

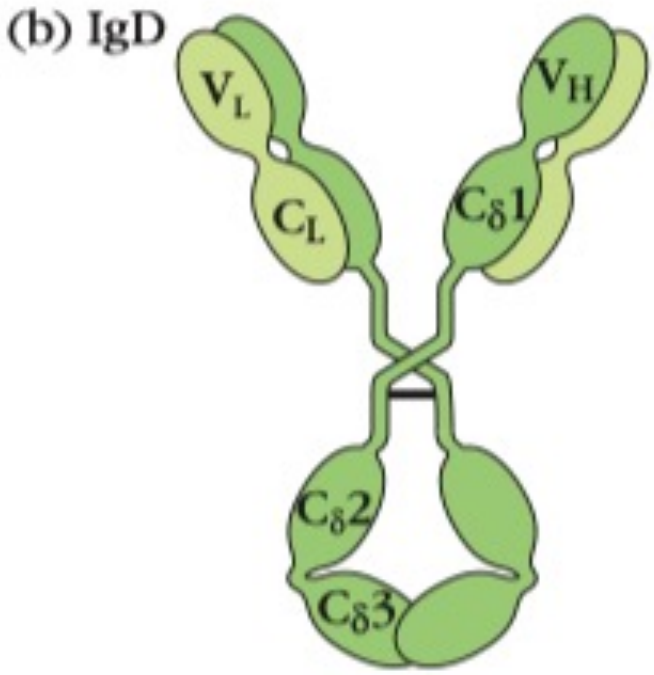
IgG

- **γ** (gamma) heavy chain
- Most abundant isotype in the plasma and comprises 80% of the total antibody content in the serum. It is transferred to the placenta through the foetus and protects the infant until its 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.
- gG protects against bacteria, viruses, neutralises bacterial toxins, triggers complement protein systems and binds antigens to enhance the effectiveness of phagocytosis.



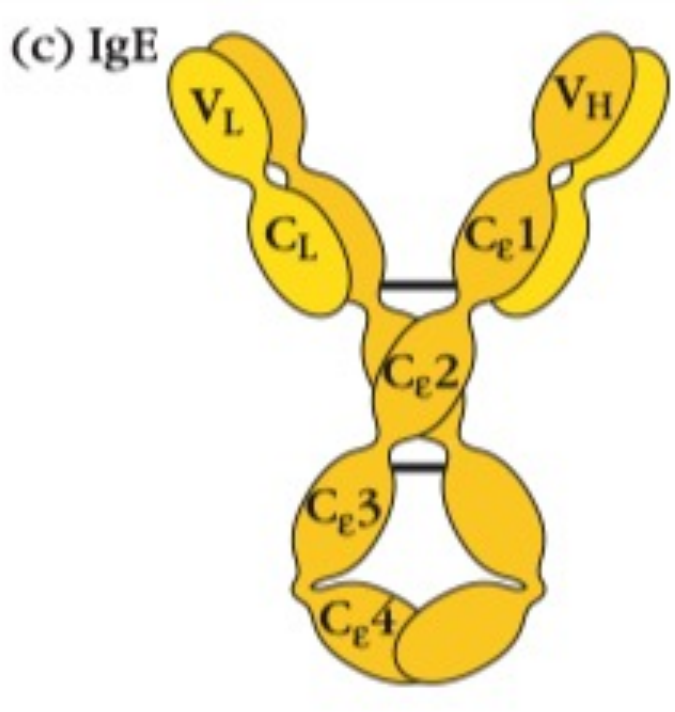
IgD

- **δ** (delta) heavy chain
- It is present as a monomer and weighs around 180 KDa
- It comprises 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.



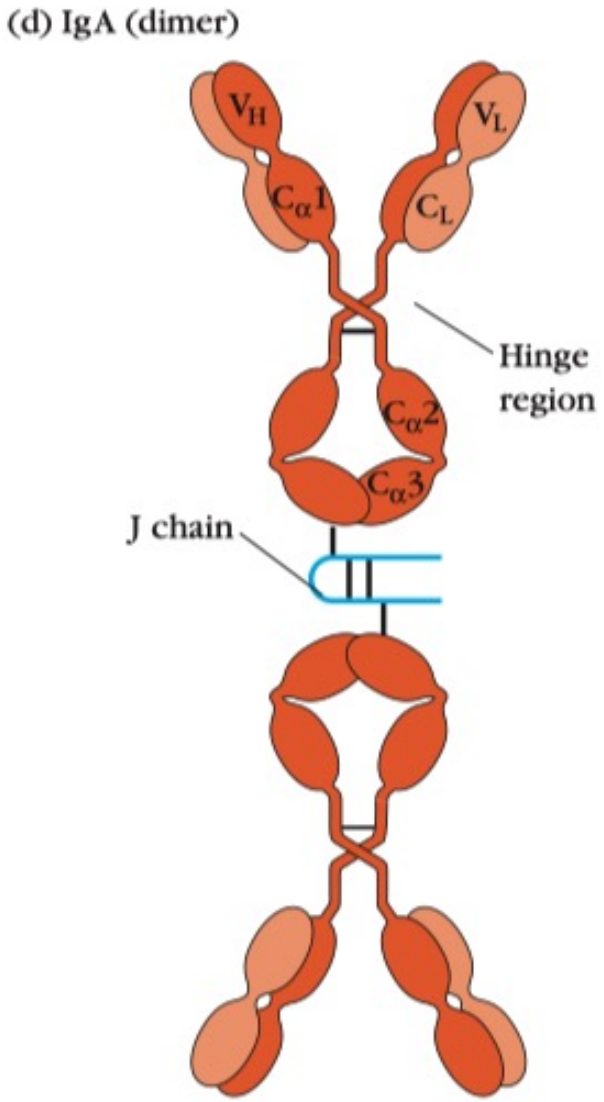
IgE

- ε (epsilon) heavy chain
- 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 200KDa
- IgE bind to mast cells and basophils which participate in the immune response.



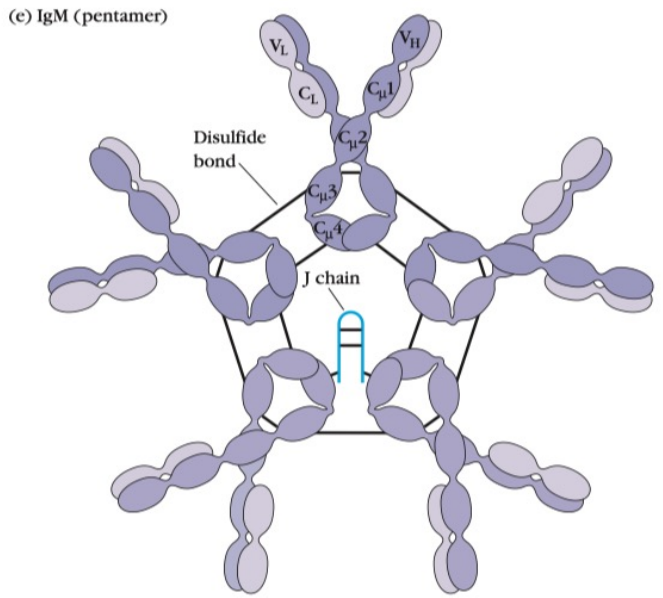
IgA

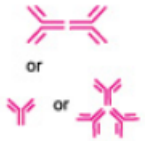
- **α** (alpha) heavy chain
- Usually found in liquids such as breast milk, serum, saliva, fluids of the intestine. IgA in breast milk protects an infant's gastrointestinal tract from microbial activity.
- It constitutes 13% of the total antibody content in the serum and is divided into 2 sub-classes- 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.



IgM

- **μ** (mu) heavy chain
- 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	IgM	IgA	IgE	IgD
					
Heavy chain	γ (gamma)	μ (mu)	α (alpha)	ε (epsilon)	δ (delta)
MW	150 kDa	900 kDa	385 kDa	200 kDa	180 kDa
Number of antigen binding sites	2	10	4	2	2
% of total antibody in serum	80%	6%	13%	0.002%	1%
Fixes complement	YES	YES	NO	NO	NO
Distribution	Intravascular and extravascular	Mainly intravascular	Intravascular and secretions	Basophils and mast cells (in saliva and nasal secretions)	Lymphocyte surface
Function	Main blood antibody, neutralizes toxins, opsonization	Primary response, fixes complement. Monomer serves as B-cell receptor	Secreted into mucus, tears and saliva	Antibody of allergy and anti-parasitic activity	B cell receptor