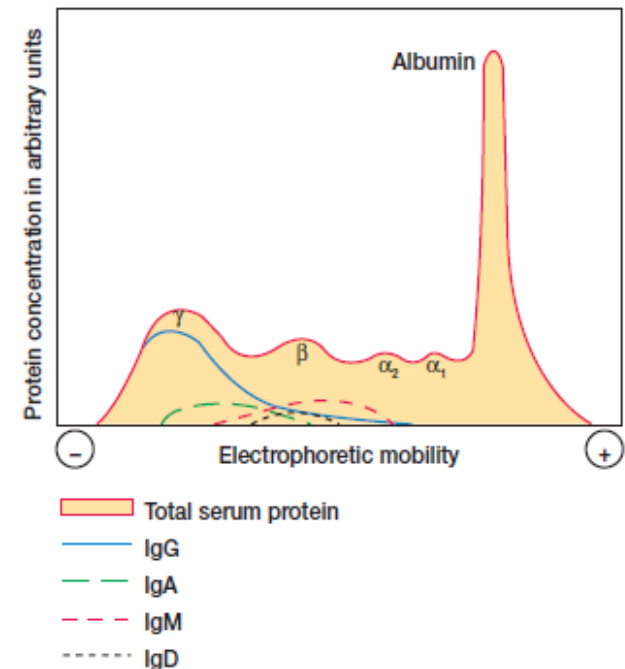


Antibodies structure & function

Microbiology V

Introduction

- An **antibody** or **immunoglobulin (Ig)** 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 present in the blood **serum**, tissue fluids, and mucosal surfaces of vertebrate animals.
- Serum glycoproteins are classified as:
 - albumin
 - alpha-1 globulin
 - alpha-2 globulin
 - beta globulin
 - **Gamma globulin**



Antibodies / Immunoglobulins

- The gamma globulin contains a heterogeneous class of **immunoglobulins**—
- **IgG, IgA, IgM, IgD and IgE.**
 - Most antibodies in serum are in the **IgG** class.
 - **IgE** class has low concentration in serum.
- These differ from each other in:
 - molecular size
 - structure
 - charge
 - amino acid composition
 - carbohydrate content.

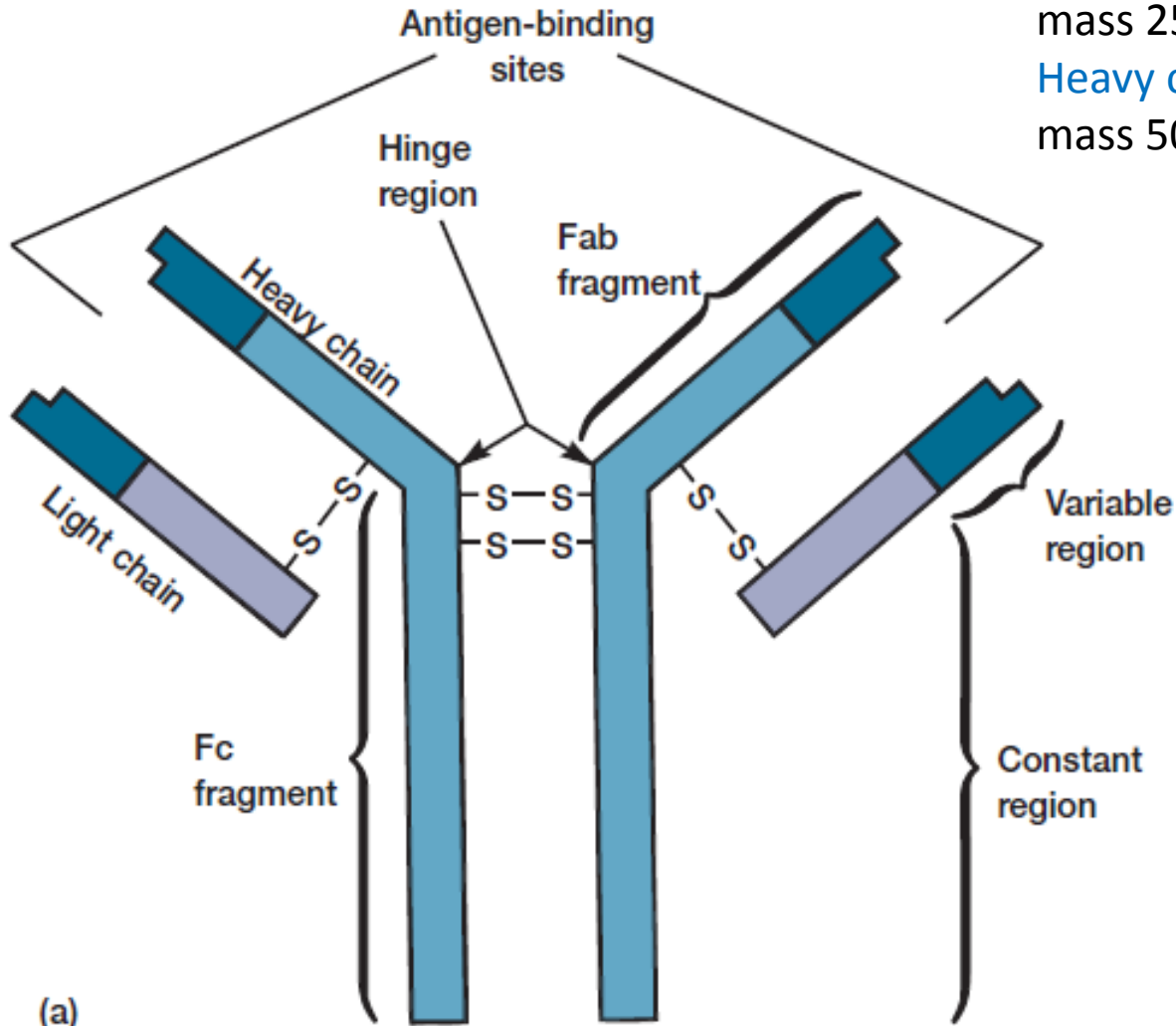
Immunoglobulin Structure

- Antibodies have more than one **antigen-binding site** or are **bivalent** .
 - Some bivalent antibody molecules can combine to form multimeric antibodies that have up to 10 combining sites.
 - **Structure:**
 - **Four polypeptide chains**
 - **2 light chains**
 - **2 heavy chains**
- } Connected by disulphide bonds S-S

Immunoglobulin structure

Light chain: 220 amino acids, mass 25 kDa.

Heavy chain: 440 amino acids, mass 50-70 kDa



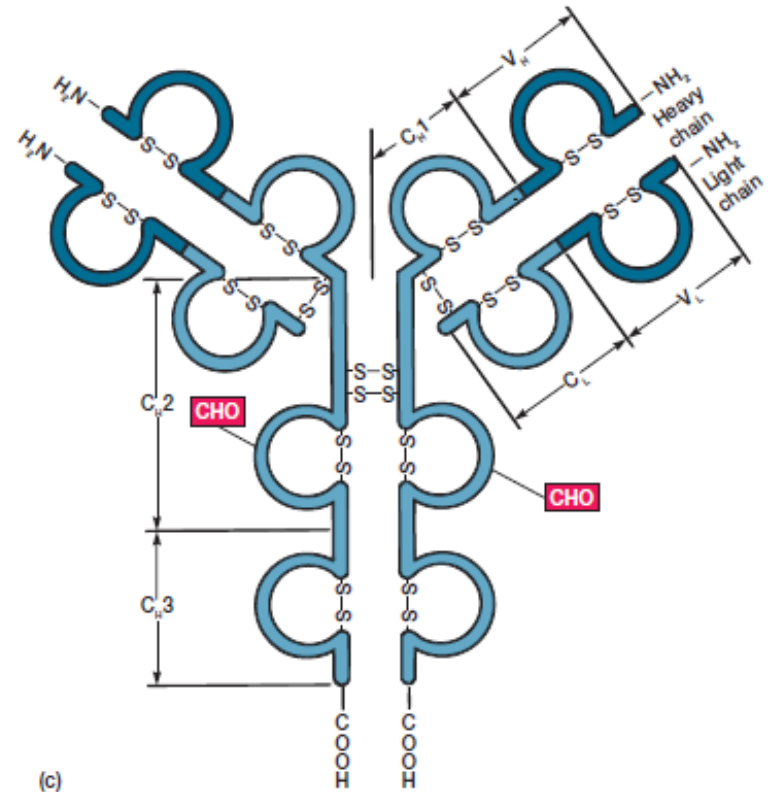
Light chain and heavy chain contain 2 regions:

Constant region: (CL and CH) – amino acids do not vary.

Variable region: (VL and VH) – have different sequences. They form Ag – binding sites.

- The four chains are arranged in the form of a flexible **Y** with a **hinge** region.
- **Fc & Fab Fragments:**
- The stalk of the Y is termed the **crystallizable fragment (Fc)**
- It contains the site at which the **antibody** molecule can **bind to a cell**.
- The top of the Y consists of two **antigen-binding fragments (Fab)** that bind with compatible epitopes (or antigenic determinant sites).

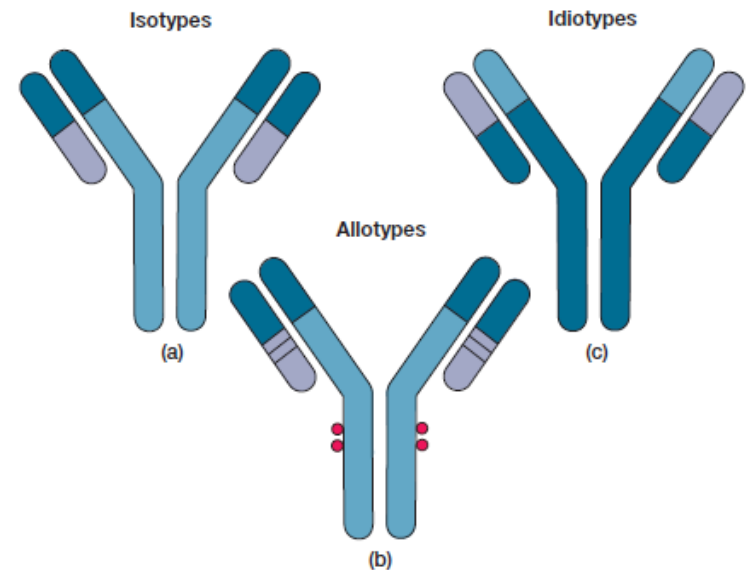
- **Fc fragments:** constant regions
- **Fab fragments:** constant and variable regions.
- Both the heavy and light chains contain several homologous units of about 100 to 110 amino acids.
- Each unit is called a **domain** has disulfide bonds forming a loop
- Interchain **disulfide bonds** also link heavy and light chains together.



- Light chain may be either of two distinct forms: called kappa and lambda.
- The **constant domains** of the **heavy chain** form the **constant (CH)** region.
- The amino acid sequence of this region determines the **classes of heavy chains**.
- gamma, alpha, mu, delta, and epsilon –
- IgG, IgA, IgM, IgD, and IgE classes
- Each immunoglobulin class differs in:
 - general properties,
 - half-life,
 - distribution in the body
 - interaction with other components of host's defensive systems.

Variants of Immunoglobulins

- **Isotypes:** variations in the **heavy chain constant regions (C_H)**
 - associated with the **different classes**
 - normally present in all **individuals**
- **Allotypes:** genetically controlled **allelic** forms of immunoglobulin molecules
 - **not present** in all individuals
- **Idiotypes:** individual **specific** immunoglobulin molecules
 - differ in the **hypervariable** region (V_L , V_C) of the **Fab** portion.

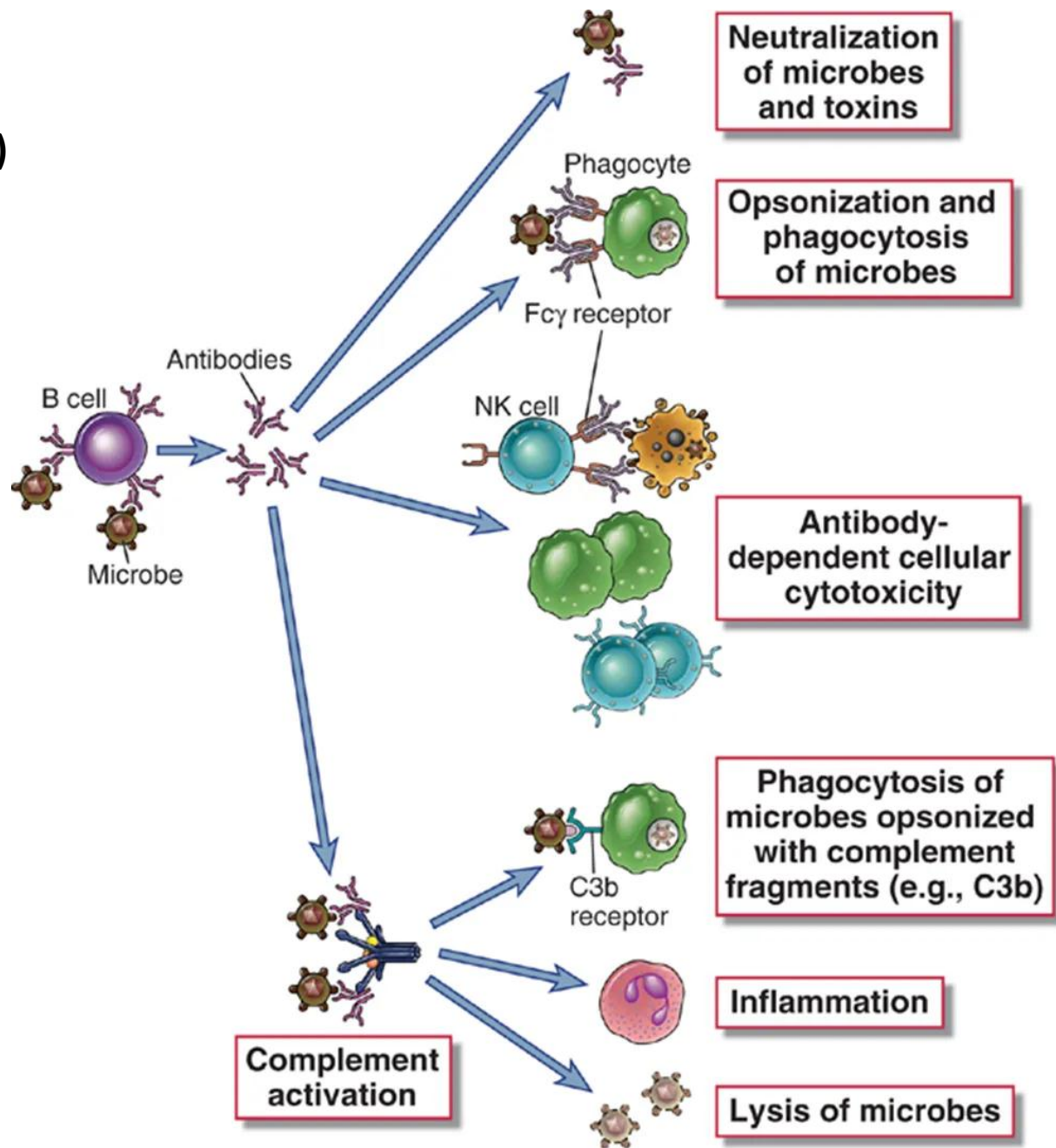


Immunoglobulin Function

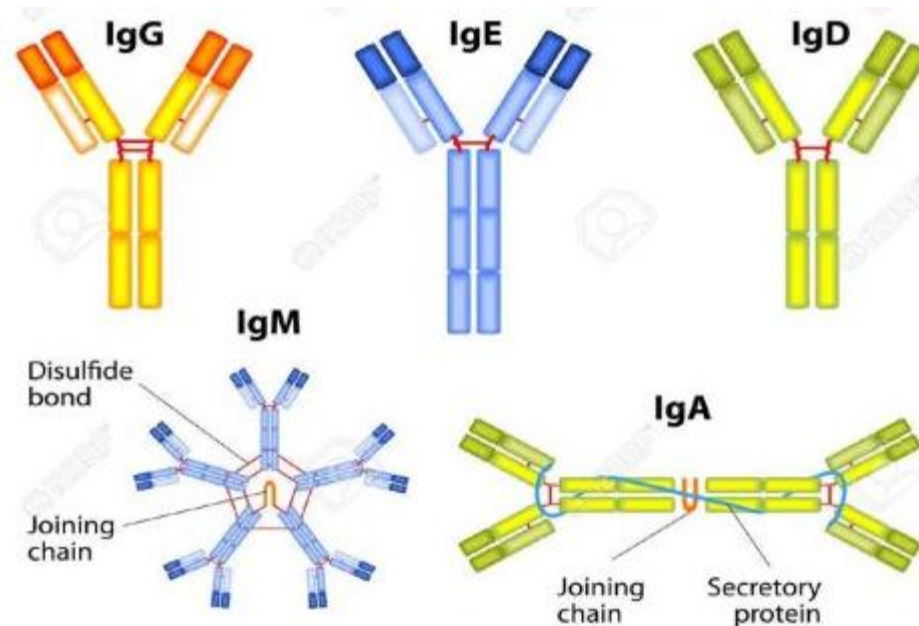
- Each end of the immunoglobulin molecule has a different role.
- **Fab region**: binds the antigen
- **Fc region**: binds to
 - host tissue
 - various cells of the immune system
 - some phagocytic cells
 - first component of complement system.
- Binding of an antibody with an antigen usually does not cause destruction of the antigen
- Antibody serves to **mark and identify** the target for immunologic attack
- Activate **nonspecific immune responses** that can destroy the target.

- For example, bacteria that are covered with antibodies -
- are better **targets for phagocytosis** by neutrophils and macrophages.
- The alteration of the surface of bacteria, viruses, and other particles so that they can be more readily **phagocytized** is termed **opsonization**.
- Immune destruction also is promoted by antibody-induced activation of the **classical complement system**.

Antibody function (immunoglobulins)

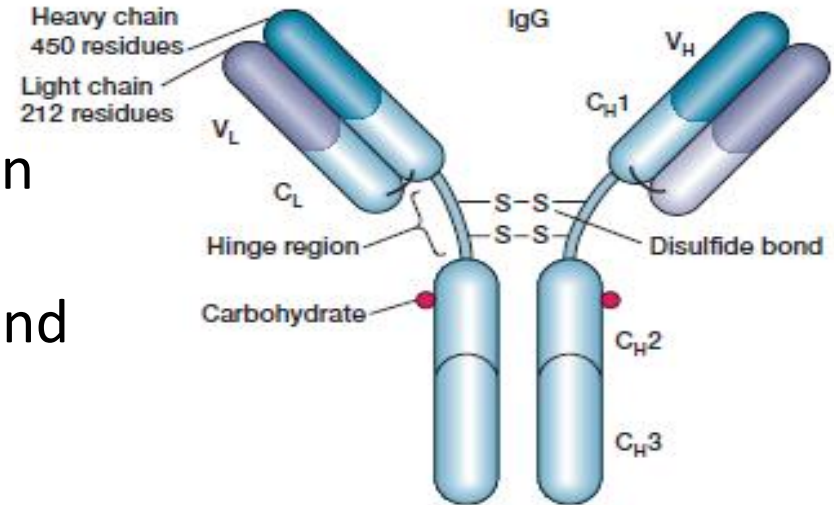


Immunoglobulin Classes: structure & function of IgG IgM IgA IgD IgE



IgG

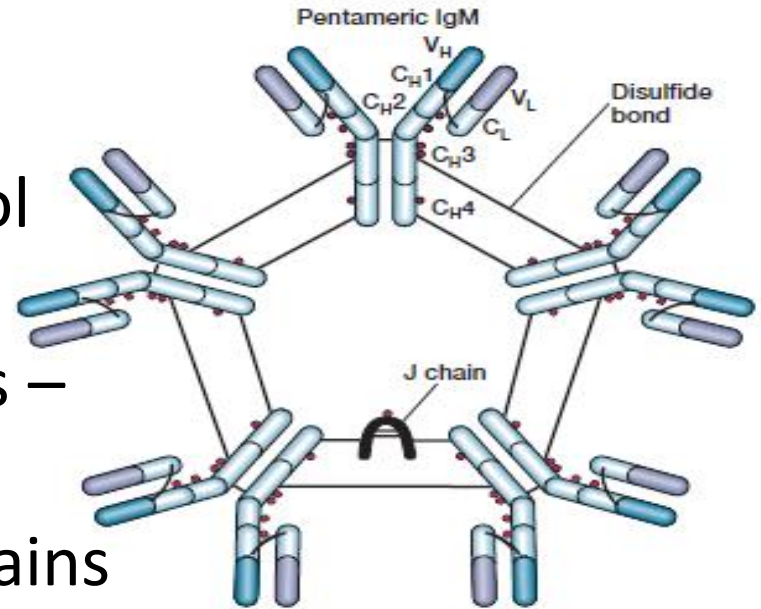
- Major immunoglobulin in human serum, 80%.
- IgG is present in **blood plasma** and **tissue fluids**.
- Half life of 23 days
- The IgG class acts against **bacteria** and **viruses** by **opsonizing** the invaders and **neutralizing toxins**.
- It **activates complement** by the classical pathway.
- IgG is the only immunoglobulin molecule able to cross the **placenta**
- provides **natural immunity** in utero and to the neonate at birth.
- Its **produced late** & appears after initial immune responses (IgM)



- There are **four** human **IgG subclasses**: IgG1, IgG2, IgG3 & IgG4
- 65% of the total serum IgG is **IgG1**, and 23% is IgG2
- **Anti-Rh(D)** antibodies are of the IgG1 or IgG3 subclass.
- IgG1 and IgG3 recognizes **specific antigens** -
- bind to **receptors** expressed on **monocytes** and **macrophages** – phagocytosis.
- These receptors are termed **Fc receptors**.
- The IgG4 antibodies function as **skin sensitizing immunoglobulins**.

IgM

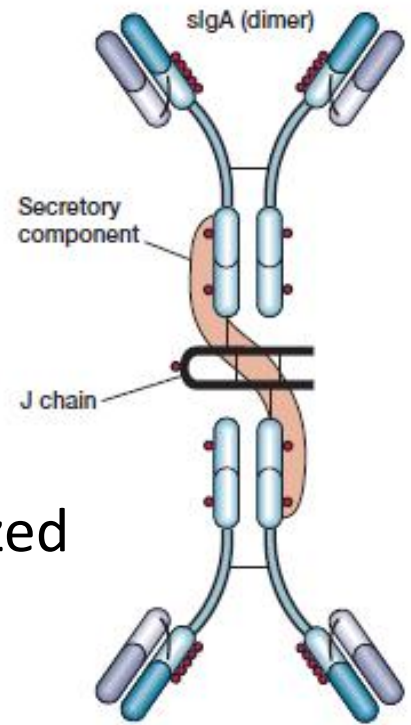
- 10% of the immunoglobulin pool
- Half life 5 days
- polymer of five monomeric units – pentamer
- Each composed of two heavy chains and two light chains
- monomers are arranged in a pinwheel array
- Fc ends in the center
- held together by disulfide bonds and a special **J** (joining) chain.



- IgM is the **first immunoglobulin** made during B-cell maturation
- Expressed as **membrane-bound antibody** on B cells.
- Secreted into serum during a **primary antibody response**
- Large & does not leave the bloodstream or cross the placenta.
- **IgM functions:**
 - Agglutinates bacteria
 - Activates **complement** by the classical pathway
 - **Enhances** the ingestion of pathogens by **phagocytic cells**
 - IgM are the **anti-A** and **anti-B isoheamagglutinins** produced
 - Its produced against – typhoid '**O**' **antigens**, **reagin** antibodies for syphilis.

IgA

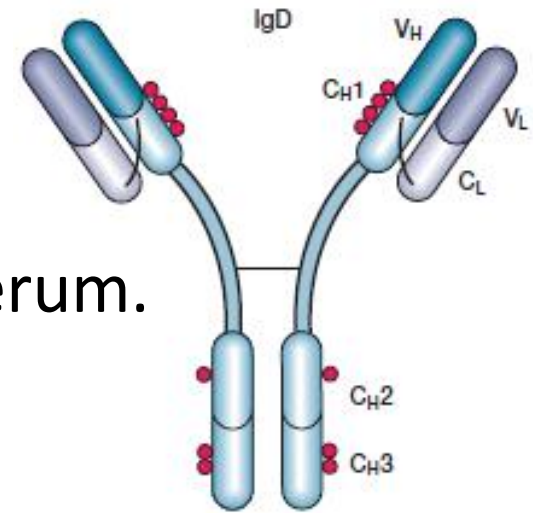
- 15% of the immunoglobulin pool.
- Half life 6 days
- Serum IgA is present as a monomer of two heavy and two light chains
- Mostly occurs in mucous secretions as a polymerized dimer held together by a J chain
- **Secretory IgA (sIgA)**
- It has special features associated with secretory mucosal surfaces.
- Primary immunoglobulin of mucosal associated lymphoid tissue
- Secretory IgA - found in saliva, tears, and colostrum.
- It protects surface tissues against infectious microorganisms by the formation of an immune barrier



- In colostrum sIgA helps protect nursing newborns.
- In the **intestine** it attaches to viruses, bacteria, and protozoan parasites such as *Entamoeba histolytica*.
- This prevents pathogen adherence to mucosal surfaces and invasion of host tissues – **immune exclusion**.
- the antigen-sIgA complexes are excreted through the adjacent epithelium into the gut lumen.
- This rids the body of locally formed immune complexes and decreases their access to the circulatory system.
- Secretory IgA also plays a role in the alternative complement pathway

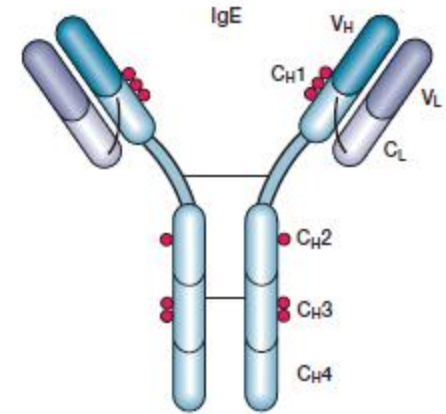
IgD

- In trace amounts – 3mg/100ml blood serum.
- It is intravascular.
- Half life 3 days.
- Its monomer structure similar to IgG.
- Do not fix complement
- Cannot cross the placenta
- Abundant in combination with IgM – surface of B cells
- Bind antigens & signal the B cell to start antibody production


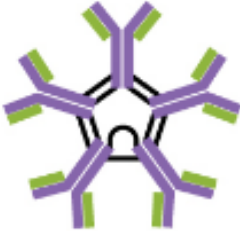


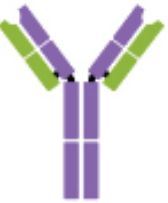


• IgE

- Small percent of the total immunoglobulin pool.
- It is extravascular. Half life 2-4 days.
- It causes anaphylactic reactions
- IgE molecules have four constant region domains
- C1, C2, C3, and C4 on their heavy chains.
- It binds to special Fc receptors on mast cells and basophils.
- Cells **degranulate** when two IgE molecules on the surface are **cross-linked** by binding to the same antigen.
- Releases histamine and other pharmacological mediators of anaphylaxis.
- It also stimulates **eosinophils** and gut **hypermotility** which aid in the elimination of **helminthic parasites**.
- Though IgE is present in small amounts –it has very potent biological capabilities



The Five Immunoglobulin (Ig) Classes

Properties	IgG monomer	IgM pentamer	Secretory IgA dimer	IgD monomer	IgE monomer
Structure					
Heavy chains	γ	μ	α	δ	ϵ
Number of antigen-binding sites	2	10	4	2	2
Molecular weight (Daltons)	150,000	900,000	385,000	180,000	200,000
Percentage of total antibody in serum	80%	6%	13% (monomer)	<1%	<1%
Crosses placenta	yes	no	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to	phagocytes				mast cells and basophils
Function	Neutralization, agglutination, complement activation, opsonization, and antibody-dependent cell-mediated cytotoxicity.	Neutralization, agglutination, and complement activation. The monomer form serves as the B-cell receptor.	Neutralization and trapping of pathogens in mucus.	B-cell receptor.	Activation of basophils and mast cells against parasites and allergens.

Thank you