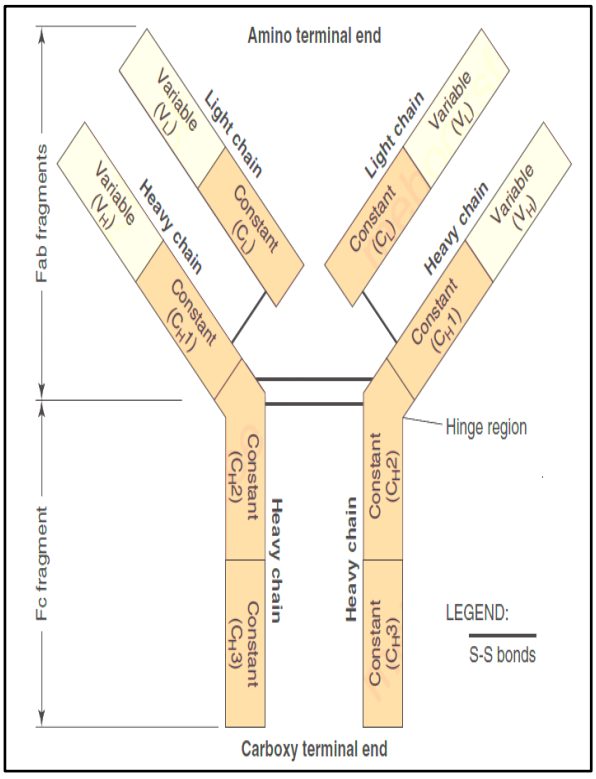
Antibodies

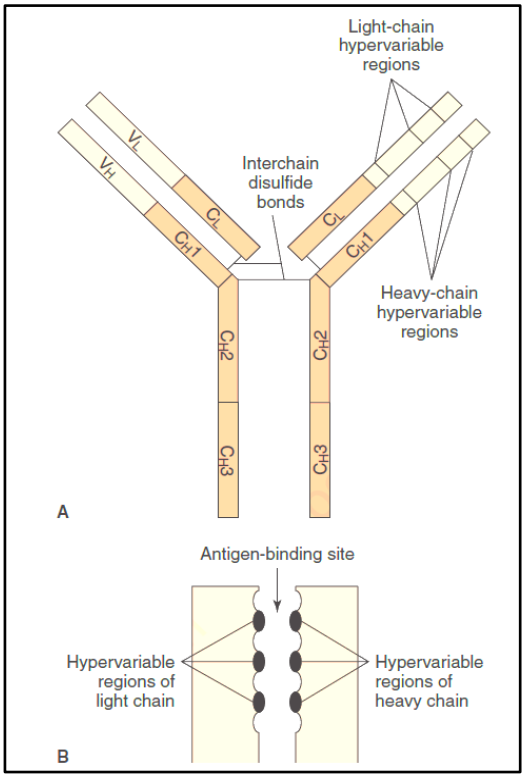
INTRODUCTION

Antibodies are globulin proteins (immunoglobulins [Ig]) that react specifically with the antigen that stimulated their production. They make up about 20% of the protein in blood plasma. Blood contains three types of globulins, alpha, beta, and gamma, based on their electrophoretic migration rate. **Antibodies are gamma globulins.** There are five classes of antibodies: IgG, IgM, IgA, IgD, and IgE. Antibodies are subdivided into these five classes based on differences in their **heavy chains**. The most important functions of antibodies are to **neutralize toxins and viruses**, to **opsonize microbes** so they are more easily phagocytosed, to **activate complement**, and to **prevent the attachment of microbes to mucosal surfaces**.

☒ Immunoglobulin structure

Immunoglobulins are glycoproteins made up of **light (L) and heavy (H) polypeptide chains**. The terms light and heavy refer to molecular weight; light chains have a molecular weight of about 25,000, whereas heavy chains have a molecular weight of 50,000 to 70,000. The simplest antibody molecule has a Y shape and consists of four polypeptide chains: two H chains and two L chains.





❖ **Immunoglobulin classes :**

IgM

IgM is the main immunoglobulin produced **early in the primary response**. It is present as **a monomer on the surface of virtually all B cells**, where it functions as an antigen- binding receptor, it is a **pentamer** composed of five H2L2 units plus one molecule of J (joining) chain , it is the most efficient immunoglobulin in agglutination, complement fixation (activation), and other antibody reactions and is important in defense against bacteria and viruses. It has the highest avidity of the immunoglobulins; its interaction with antigen can involve all 10 of its binding sites.

IgG

Each IgG molecule consists of two L chains and two H chains linked by disulfide bonds (molecular formula H2L2). There are four subclasses, IgG1–IgG4, **based on antigenic differences in the H chains and on the number and location of disulfide bonds**. IgG1 makes up most (65%) of the total IgG. **IgG2** antibody is directed against polysaccharide antigens and is an important host defense against **encapsulated bacteria**. IgG is the predominant antibody in the **secondary response** and constitutes an important defense against bacteria and viruses. IgG is the only antibody **to cross the placenta**; only its Fc portion binds to receptors on the surface of placental cells. IgG is the immunoglobulin that opsonizes. **It can opsonize (i.e., enhance phagocytosis)** because there are receptors for the γH chain on the surface of phagocytes.

IgA

It prevents attachment of microorganisms (e.g., bacteria and viruses) to mucous membranes. Each secretory IgA molecule consists of two H2L2 units plus one molecule each of J (joining) chain and secretory component . The secretory component is a polypeptide synthesized by epithelial cells that provides for IgA passage to the mucosal surface. It also protects IgA from being degraded in the intestinal tract. **In serum, some IgA exists as monomeric H2L2. The IgA dimeric form is the most prevalent and is also called secretory IgA.**

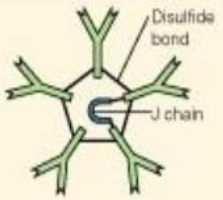
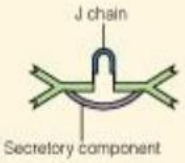
IgD

This immunoglobulin has no known antibody function but may function as an antigen receptor; it is present on the surface of many **B lymphocytes**. It is present in small amounts in serum.

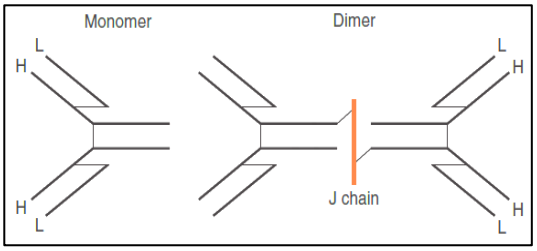
IgE

IgE is medically important for two reasons: **(1) it mediates immediate (anaphylactic) hypersensitivity ,** and (**2) it participates in host defenses against certain parasites (e.g., helminths [worms]).** The serum IgE level is usually increased in these infections. Because worms are too large to be ingested by phagocytes, they are killed by eosinophils that release worm-destroying enzymes. **IgE specific for worm proteins binds to receptors on eosinophils**, triggering the antibody-dependent cellular cytotoxicity (ADCC) response.

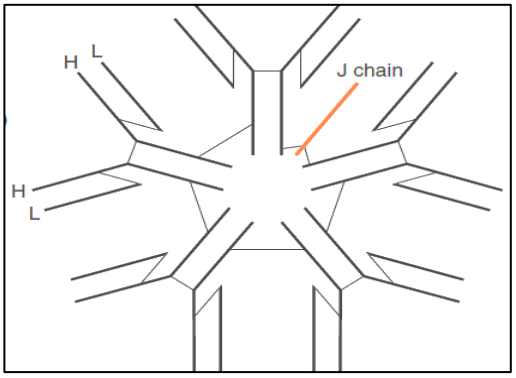
The Fc region of IgE binds to the surface of **mast cells and basophils**. Although IgE is present in trace amounts in normal serum (approximately 0.004%) persons with allergic reactivity have greatly increased amounts. **IgE does not fix complement and does not cross the placenta.**

Characteristics	IgG	IgM	IgA	IgD	IgE
					
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
Percentage of total serum antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Molecular weight	150,000	970,000	405,000	175,000	190,000
Half-life in serum	23 days	5 days	6 days	3 days	2 days
Complement fixation	Yes	Yes	No†	No	No
Placental transfer	Yes	No	No	No	No
Known functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

Immunoglobulin	Major Functions
IgG	Main antibody in the secondary response. Opsonizes bacteria, making them easier to phagocytize. Fixes complement, which enhances bacterial killing. Neutralizes bacterial toxins and viruses. Crosses the placenta.
IgA	Secretory IgA prevents attachment of bacteria and viruses to mucous membranes. Does not fix complement.
IgM	Produced in the primary response to an antigen. Fixes complement. Does not cross the placenta. Antigen receptor on the surface of B cells.
IgD	Uncertain. Found on the surface of many B cells as well as in serum.
IgE	Mediates immediate hypersensitivity by causing release of mediators from mast cells and basophils upon exposure to antigen (allergen). Defends against worm infections by causing release of enzymes from eosinophils. Does not fix complement. Main host defense against helminth infections.



Serum IgA Secretory IgA



IgM (pentamer)

ISOTYPES, ALLOTYPES& ,IDIOTYPES

Because immunoglobulins are proteins, they are antigenic, and that property allows them to be subdivided into isotypes, allotypes, and idiotypes.

Isotypes: Are defined by antigenic (amino acid) differences in their constant regions. **all isotypes are found in all normal humans**. For example, IgG and IgM are different isotypes, the constant region of their H chains (γ and μ) is different antigenically the five immunoglobulin classes—IgG, IgM, IgA, IgD, and IgE—are different isotypes; their H chains are antigenically different. The IgG isotype is subdivided into four subtypes, IgG1, IgG2, IgG3, and IgG4, based on antigenic differences of their heavy chains. Similarly, IgA1 and IgA2 are different isotypes.

Allotypes: On the other hand, are additional antigenic features of immunoglobulins that **vary among individuals**. They vary because the genes that code for the L and H chains are polymorphic, and individuals can have different alleles.

Idiotypes: Are the antigenic determinants formed by the specific amino acids in the hypervariable region. Each **idiotype is unique** for the immunoglobulin produced by a specific clone of antibody-producing cells.