Antibodies

Antibodies are globulin proteins (immunoglobulins) that are synthesized in serum and tissue fluids, which react specifically with the antigen that stimulated their production Antibodies are one of the major plasma proteins, and against infection often referred to as "first line of defense". The most important function of antibodies is to confer protection against microbial pathogens. Antibodies confer protection in the following ways:

1. They prevent attachment of microbes to mucosal surfaces of the host.

2. They reduce virulence of microbes by neutralizing toxins and viruses.

3. They facilitate phagocytosis by opsonization of microbes.

4. They activate complement, leading to complement-mediated activities against microbes.

Immunoglobulins

There are five classes of immunoglobulins:

(i) immunoglobulin G (IgG),

(ii) immunoglobulin M (IgM),

(iii) immunoglobulin A(IgA),

(*iv*) immunoglobulin E (IgE),

(*v*) immunoglobulinD (IgD).

Structure of Immunoglobulins

Immunoglobulins show the following properties:

■ They are glycoproteins.

■ They are a complex structure of four polypeptide chains:

1.Two identical heavy (typically 55 kDa each) chains: Each heavy chain is made up of 420–440 amino acids. The two heavy chains are held together by one to five disulfide (S—S) bonds. Each heavy chain is bound to a light chain by a disulfide bond and by noncovalent bonds, such as salt linkages, hydrogen bonds, and hydrophobic bonds to form a heterodimer (H–L). Similar noncovalent interactions and disulfide bridges link the two identical heavy and light (H–L) chains to each other to form the basic four-chain (H–L)2 antibody structure.

2.Two identical light chains (25 kDa each). Each light chain is made up of 220–240 amino acids. Light chain is attached to the heavy chain by a disulfide bond. The light chains are structurally and chemically similar in all classes of immunoglobulins.This gives immunoglobulin an overall 'Y' or 'T' shape, which is the most widely recognized feature of immunoglobulin structure.

● The terms "heavy" and "light" refer to the molecular weights of the chains. The heavy chains have a molecular

weight of 50,000–70,000 Da, while light chains have a molecular weight of 25,000 Da. The heavy chains are longer, and light chains are shorter

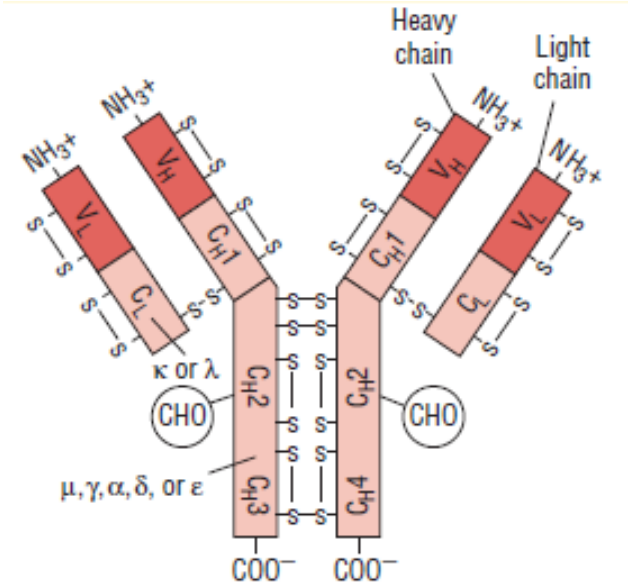


Diagram of monomer of the immunoglobulin

TABLE 13-1 Classes of immunoglobulins and their heavy chains and subclasses

Class	Heavy chain	Subclasses
IgG	Gamma	γ_1, γ_2, γ_3, γ_4
IgM	Mu	None
IgA	Alpha	α_1, α_2
IgE	Epsilon	None
IgD	Delta	None

Variable and constant regions

Each polypeptide chain of an immunoglobulin molecule containsan amino terminal part and a carboxy terminal part. The amino terminal part is called the variable region (V region) and the carboxy terminal part is called the constant region (C region).

Variable: The variable regions of both light and heavy chains consist of three highly variable regions known as hypervariable regions. The antigen combining sites Fab of the antibody molecule that consists of only 5–10 amino acids each are present in the hypervariable region of both the light and heavy chains. These antigen-binding sites are responsible for specific binding of antibodies with antigens.

Constant region: The carboxyl-terminal half of the molecule is called the constant (C) region. It consists of two basic amino acid sequences. The Fc fragment.

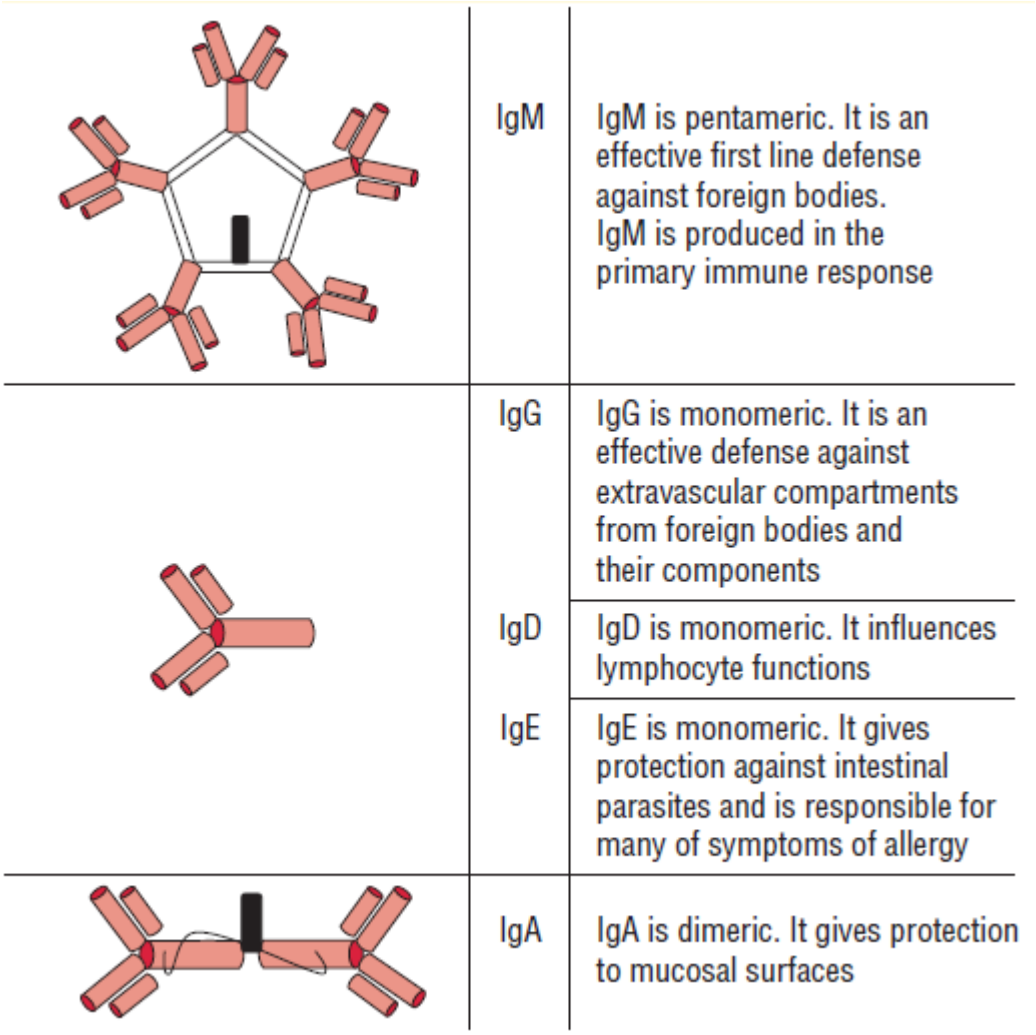
The constant region of the heavy chain has many biological functions.

1. It is responsible for activation of the complement,
2. binding to cell surface receptors,
3. placental transfer,
4. and many other biological activities.

The constant region of the light chain has no biological function.

Immunoglobulin Classes

The structure and biological functions of five classes of immunoglobulins (IgG, IgM, IgA, IgE, and IgD) are described below:



Schematic diagram of immunoglobulins and their functions.

Immunoglobulin G

IgG is a 7S immunoglobulin with a molecular weight of 150,000 Da. It has a half-life of 23 days—longest among all the Immunoglobulins IgG is the most abundant class of immunoglobulins in the serum, comprising

about 80% of the total serum immunoglobulin. There are four IgG subclasses IgG1, IgG2, IgG3, andIgG4—so numbered according to their decreasing concentrations in serum.

Immunoglobulin M

IgM constitutes about 5–8% of total serum immunoglobulins. It is distributed mainly intravascularly. It is a heavy molecule (19S) with a molecular weight varying from 900,000 to 1,000,000 Da (millionaire molecule). It has a half-life of 5 days IgM is basically a pentamer, composed of five immunoglobulin subunits (monomeric subunits, IgMs) and one molecule of J chain.

Immunoglobulin A

IgA is the second major serum immunoglobulin, comprising nearly 10–15% of serum immunoglobulin. It has a half-life of 6–8 days

IgA occurs in two forms: serum IgA and secretory IgA.

Serum IgA: It is present in the serum and is a monomeric 7S molecule with a molecular weight of 60,000 Da. It has a half-life of 6–8 days. It has two subclasses, IgA1 and IgA2

Secretory IgA: It is a dimer or tetramer and consists of a J-chain polypeptide and a polypeptide chain called secretory component, or SC,

Immunoglobulin E

IgE constitutes less than 1% of the total immunoglobulin pool. It is present in serum in a very low concentration (0.3 _g/mL). It is mostly found extravascularly in lining of the respiratory and intestinal tracts , with a molecular weight of 190,000 Da and half-life of 2–3 days.

Immunoglobulin D

IgD comprises less than 1% of serum immunoglobulins. It is a have a molecular weight of 180,000 Da. The half life of IgD is only 2–3 days.

IgG	IgM	IgA	IgD	IgE
Enhances phagocytosis	Especially effective against microorganisms and agglutinating antigens	Localized protection on mucosal surfaces	Serum function not known	Allergic reaction
Neutralizes toxins and viruses	First antibody produced in response to initial infection		Present on B cells; and function in initiation of immune response	Possibly lysis of parasitic worms
Protects fetus and newborn				

Role of immunoglobulins in human defense