# Immunoglobulin

Antibodies are globulin proteins (immunoglobulins) that react specifically with the antigen that stimulated their production.

- 20% of the protein in blood plasma.
- Blood contains three types of globulins: alpha, beta, and gamma.
- Antibodies are gamma globulins.

**IMMUNOGLOBULIN STRUCTURE**

Immunoglobulins are glycoproteins made up of light (**L**) and heavy (**H**) polypeptide chains.

- The terms "light" and heavy";
  light chains - molecular weight - 25,000 Dalton,
  heavy chains- molecular weight - 50,000 to 70,000 Dalton.
- The simplest antibody molecule has a Y shape and consists of four polypeptide chains: two H chains and two L chains.
- The four chains are linked by disulfide bonds.
- An individual antibody molecule always consists of identical H chains and identical L chains.

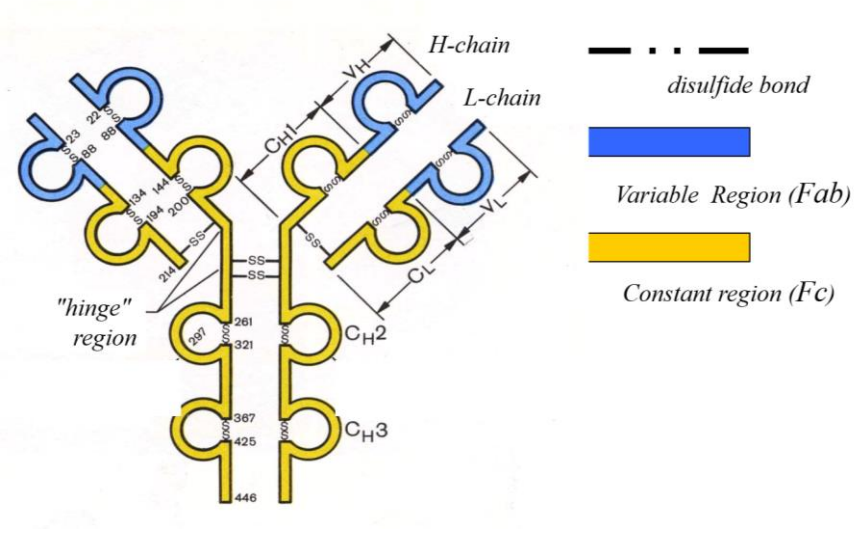


**Fig. Structure of Immunoglobulin (Ig)**

**L chains** belong to one of two types, k (kappa) or λ (lambda), on the basis of amino acid differences in their constant regions.

**H chains** are distinct for each of the five immunoglobulin classes and are designated γ (IgG), μ (IgM), α (IgA), ε (IgE), and δ (IgD).

- **L** and **H** chains are subdivided into variable and constant regions. The regions are composed of three-dimensionally folded, repeating segments called domains.
- An **L chain** consists of one variable (**VL**) and one constant (**CL**) domain.
- Most **H chains** consist of one variable (VH) and three constant (CH) domains.

- The variable regions of both L and H chains have three extremely variable ("hypervariable") amino acid sequences at the amino-terminal end that form the **antigen-binding site.**

There are **five classes of antibodies**: Ig G, Ig M, Ig A, Ig D, and Ig E.

**L chains** belong to one of two types, k (kappa) or λ (lambda), on the basis of amino acid differences in their constant regions. Both types occur in all classes of immunoglobulins.

**H chains** are distinct for each of the five immunoglobulin classes and are designated γ (IgG), μ (IgM), α ( IgA), ε ( IgE), and δ ( IgD).

**IMMUNOGLOBULIN STRUCTURE**

If an antibody molecule is treated with a proteolytic enzyme such as papain, peptide bonds in the "hinge" region are broken, producing two identical **Fab fragments,** and one **Fc fragment**.

The variable regions are responsible for antigen-binding, whereas the constant regions are responsible for various biologic functions, eg, complement activation and binding to cell surface receptors, placental transfer.

**IMMUNOGLOBULIN CLASSES**

**Ig G**

Each IgG molecule consists of two L chains and two H chains linked by disulfide bonds (molecular formula H2L2). Because it has two identical antigen-binding sites, it is said to be divalent.

- 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.
- It is therefore the most abundant immunoglobulin in newborn.
- IgG is one of the two immunoglobulins that can activate complement; IgM is the other.
- IgG is the immunoglobulin that opsonizes.

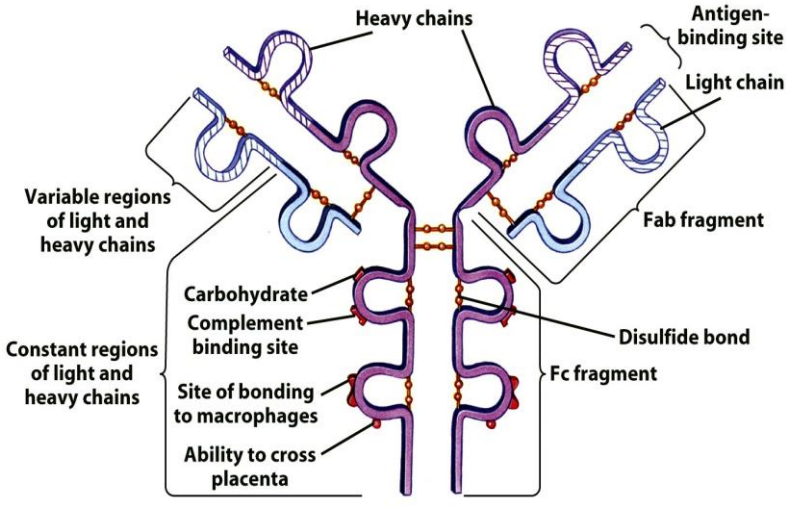


**Fig. Structure of Ig G**

**Ig A** is the immunoglobulin protecting the mucosal surfaces.

- **Ig A** is the main immunoglobulin in secretions such as colostrum, saliva, tears, and respiratory, intestinal, and genital tract secretions.
- It prevents attachment of microorganisms, eg, 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.

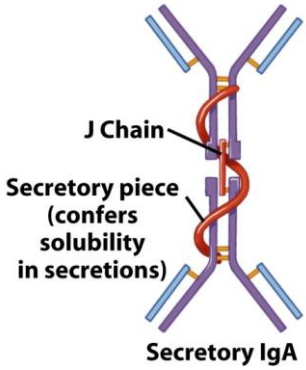


**Fig. Structure of Ig A**

**Ig M**

IgM is the main immunoglobulin produced early in the primary response.

- It is present as a monomer on the surface of all B cells, where it functions as an antigen-binding receptor.
- In serum, it is a pentamer composed of 5 H2L2 units plus one molecule of J (joining) chain. Because the pentamer has 10 antigen-binding sites, 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 can be produced by the fetus in certain infections. It has the highest avidity of the immunoglobulins; its interaction with antigens can involve all 10 of its binding sites.

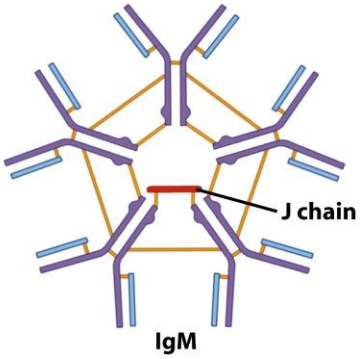


**Fig. Structure of Ig M**

**Ig E.** Ig E is medically important for two reasons:

(1) it mediates immediate (anaphylactic) hypersensitivity, and
(2) it participates in host defenses against certain parasites, eg, helminths (worms).

Although Ig E is present in trace amounts in normal serum (approximately 0.004%), persons with allergic reactivity have greatly increased amounts, and Ig E may appear in external secretions.
Ig E does not fix the complement and does not cross the placenta.

**Ig D.** 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.

| Ig | Major Functions |
|---|---|
| **Ig G** | 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. |
| **Ig A** | Secretory IgA prevents attachment of bacteria and viruses to mucous membranes Does not fix complement. |
| **Ig M** | Produced in the primary response to an antigen. Fixes complement. Does not cross the placenta. Antigen receptor on the surface of B cells. |
| **Ig D** | Uncertain. Found on the surface of many B cells as well as in serum. |
| **Ig E** | 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. |

**Monoclonal Antibodies**

- Immunotoxins: Mabs conjugated with a toxin to target cancer cells.
- Chimeric mabs: Genetically modified mice that produce Ab with a human constant region.
- Humanized mabs: Mabs that are mostly human, except for mouse antigen-binding.
- Fully human antibodies: Mabs produced from a human gene on a mouse.

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