Immunoglobulins (Antibodies): Classes, Functions and Levels

What are Immunoglobulins?

Immunoglobulins are simply proteins that act as antibodies! These proteins are produced by a type of blood cells known as B cells in response to an immunogen. Their role is to identify and neutralize antigens

Immunoglobulins are among the most abundant proteins in the blood since they comprise about 20% of total plasma proteins.

They derive their name from the fact that when the serum that has got antibodies is subjected to a process of electrophoresis, five main peaks of proteins are identified. These are based on their differential ability to migrate in an electric field.

Antibodies are generally drawn as a ‘Y’ shaped structure and when they are in this conformation the heavy chain can be thought of as being ‘inside’ the light chain.

The five classes or isotypes of immunoglobulins are: IgA,IgE,IgD,IgG and IgM

Structure of Immunoglobulins

An immunoglobulin has:

- 2 heavy chains
- 2 light chains
- chains that are linked together by disulfide bonds
- An amino-terminal variable known as (V) region
- A carboxyl-terminal constant known as (C) region

Normal Ranges of immunoglobulins:

- IgA = 50-350 mg/dL
- IgD = <6 mg/dL
- IgE = <25 ?g/dL
- IgG = 800-1500 mg/dL
- IgM = 45-150 mg/dL

In this article, we are specifically looking at the causes of elevated immunoglobulin levels

Immunoglobulin A:

Immunoglobulin A exists in three forms which are:

A monomer, a dimer, and dimer plus a secretory piece.

The dimer form is transported across respiratory and intestinal mucosal barriers into the lumen by the secretory piece which is the receptor for immunoglobulin A Fc portion on the epithelium of the mucosa.

There exist two subclasses of IgA?1 and ?2.

Properties of immunoglobulin A

This immunoglobulin is found in high concentration in serum

It exists mainly as a dimer with a half-life of 6 days.

Functions of IgA

IgA Protects mucosal tissues, tears, saliva, and colostrum by blocking bacteria, viruses, and toxins from binding to host cells.

Immunoglobulin A is **increased** in lymphoproliferative disorders such as;

- Berger's nephropathy,
- Chronic infections,

- Autoimmune disorders,
- Liver disease.

Immunoglobulin A is **decreased** in:

- Nephrotic syndrome,
- Protein-losing enteropathy,
- Congenital deficiency,
- Lymphocytic leukemia,
- Ataxia-telangiectasia,
- Chronic sinopulmonary disease.

Immunoglobulin E:

Properties of immunoglobulin E

Immunoglobulin E has four C domains with a molecular weight of 188000d.

It is unstable at 56 degrees and is called a **reagin**.

There is a very low serum concentration of immunoglobulin E because its Fc region binds avidly to mast cells and basophils.

Function of immunoglobulin E

This immunoglobulin binds to circulating basophils and tissue-bound mast cells via a receptor on their surface. The binding of an antigen to these IgE sensitized cells trigger the release of vasoactive amines mainly histamines. This results in atopic disease characterized by a local reaction known as hives and a systemic reaction known as anaphylaxis.

This immunoglobulin does not cross placenta nor fix complement via a conventional pathway.

Immunoglobulin E levels are **elevated** in conditions such as;

- Allergic_disorders,
- Parasitic_infections,
- Immunologic disorders,
- IgE myeloma,
- Acquired Immunodeficiency syndrome (AIDS),
- Pemphigoid.

IgE is decreased in:

- Hypogammaglobulinemia,
- Neoplasm (breast, bronchial, cervical cancers),
- Ataxia-telangiectasia.

Immunoglobulin G:

Of all the immunoglobulins, immunoglobulin G has the highest concentration in serum with a half-life of 18-25 days.

Functions of IgG

1. Complement fixation that eventually causes cell lysis.
2. Mediates placental passage of maternal antibody to the fetus in the womb.
3. It also adheres to cells that possess a receptor for Pc fragment from IgG (Fcy)

It is **elevated** in the following conditions:

- Chronic granulomatous infections,
- Infectious diseases,
- Inflammation,
- Myeloma,
- liver disease.

IgG is **decreased** in:

- Congenital or acquired deficiency,
- Lymphocytic_leukemia,
- Drug use such as phenytoin and methylprednisolone,
- Nephrotic syndrome,
- Protein-losing enteropathy.

Immunoglobulin M

Immunoglobulin M exists in two structural forms. A monomer form is synthesized by B cells and retained also on the membrane of B cells. It serves as the B cell receptor specific for a single antigenic epitope.

Secreted immunoglobulin M exists as a pentamer. This simply means that it exists as five monomeric IgM molecules that are joined together by a J chain.

The pentamer is secreted following antigen and cytokine activation of plasma cells, with hypervariable regions on the pentamer same as those on the membrane-bound monomeric receptors.

IgM has four constant domains on the H and L chains, therefore, its pentamer form has the highest molecular weight of the immunoglobulins.

Functions.

It’s the first antibody to appear after the antigenic stimulus and fixes the complement avidly.

Immunoglobulin M is **elevated** in;

- Infectious diseases such as brucellosis and malaria,
- Waldenström’s macroglobulinemia,

- liver disease.
- congenital deficiency,
- lymphocytic leukemia,
- nephrotic syndrome.

Remember!

Only immunoglobulins M and G are able to fix complement.

Only immunoglobulin G crosses the placenta.

Immunoglobulin M has the highest number of antigen binding sites – 10 sites.

immunoglobulin G has the highest concentration in serum -80%.

immunoglobulin E has the lowest concentration in serum.