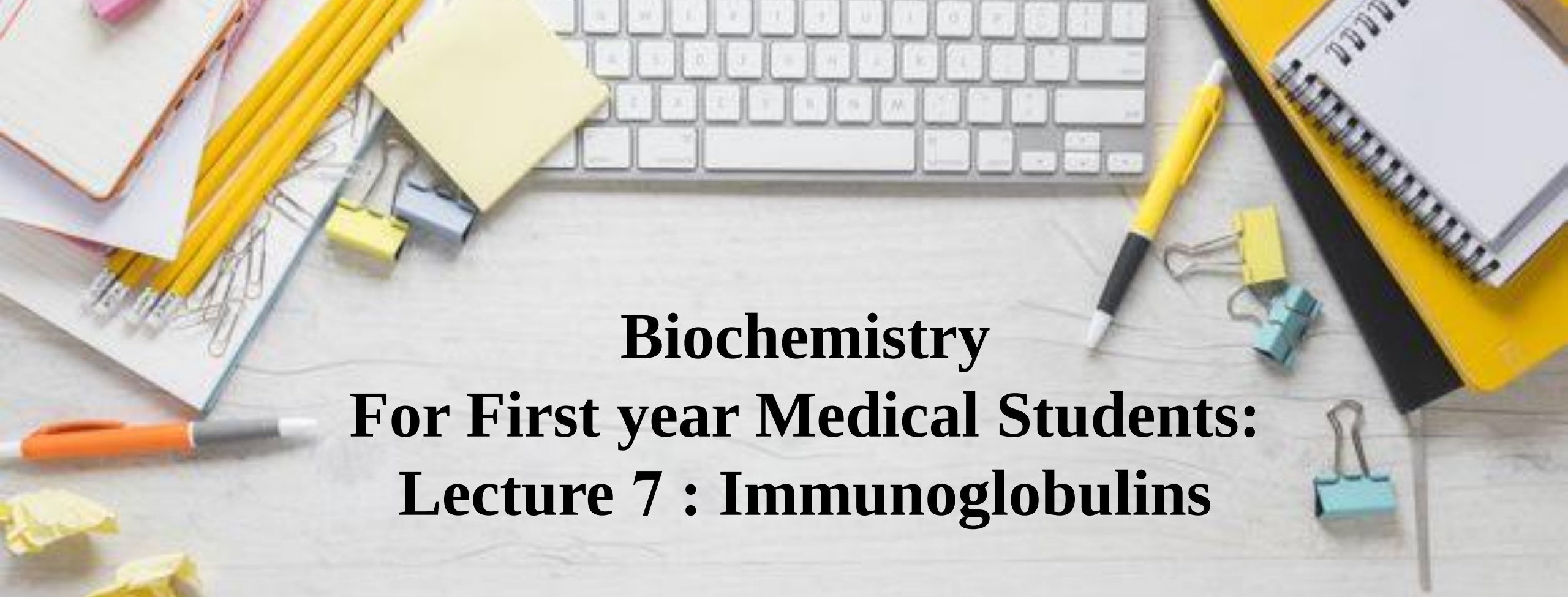

Biochemistry
For First year Medical Students:
Lecture 7 : Immunoglobulins

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Immunoglobulins

The main objectives of this lecture :

- Define Immunoglobins
- List the types & functions of Ig
- Correlate clinically.

Immunoglobulins (Igs):

are glycoprotein molecules also called antibodies (Abs) , that are produced in response to foreign substances entering the living body- antigens (Ags) or immunogens (viruses, bacteria, or toxins), binding to them and forming antigen-antibody complexes resulting in Ag elimination and protection of the body of the host).

Igs are produced by the lymphocytes and are found in fraction of blood called gamma globulin. Igs binding to Ags basically help to inactivate, weaken or enhance phagocytosis of Ags.

Structure:

All immunoglobulins have the same basic structure and consist of :

two identical 'light' and **two identical 'heavy' polypeptide chains**, held together by **disulphide bridges** (Figure1).

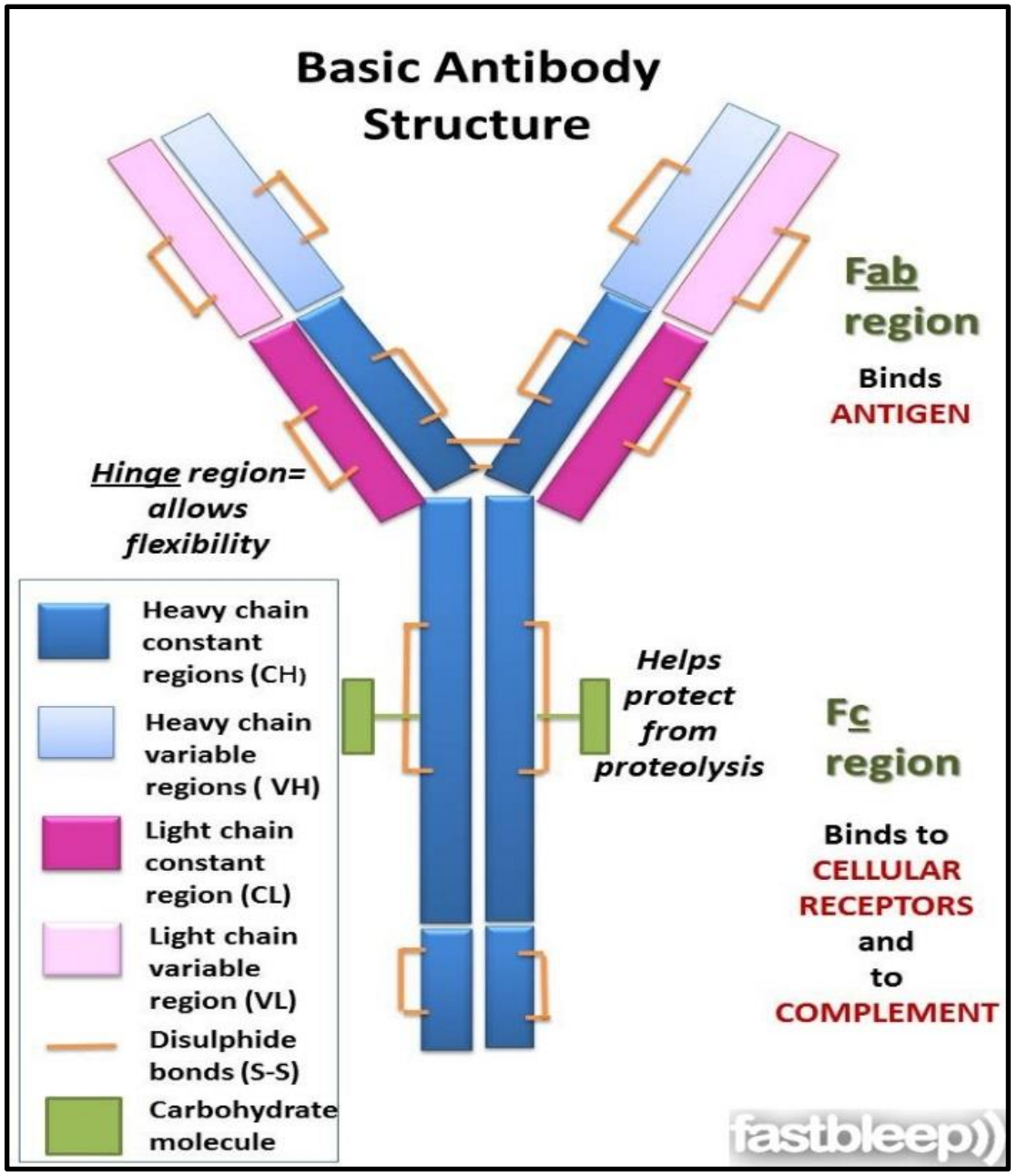
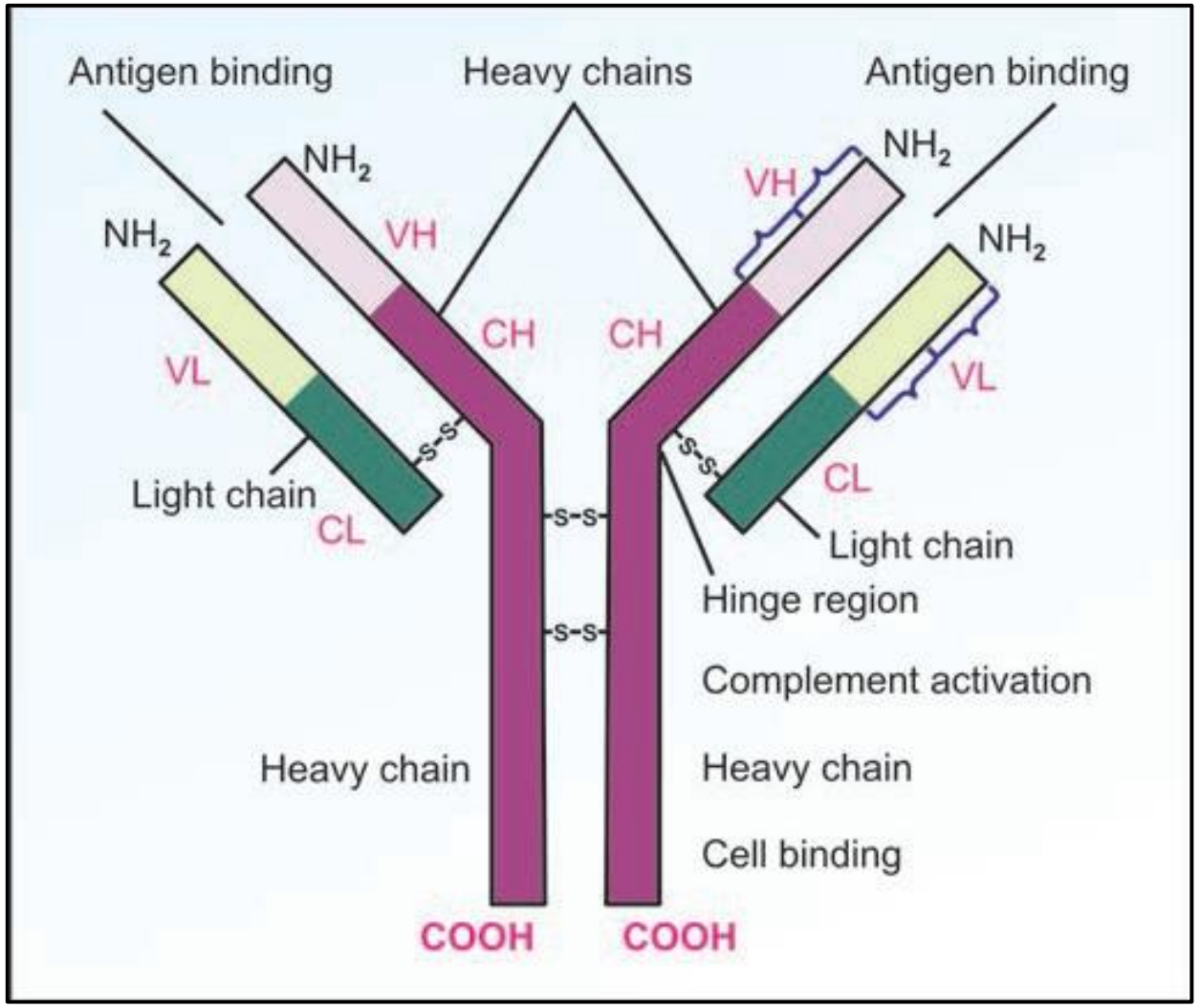


Figure: Immunoglobulin molecule:

NH_2 = amino terminal end;
COOH = carboxy terminal end;
Constant regions are shown as dark;

VH = variable heavy region;
VL = variable light chain;
CH = constant heavy region;
CL = constant light region.
Chains are connected by disulphide bridges, shown as –S-S bond.



- The **light chains** may be either of **two types**:

kappa or lambda.

- The **heavy chains** may be of **five types**:

alpha, gamma, delta, epsilon and mu.

The immunoglobulins are named after their heavy chain type, as IgA, IgG, IgD, IgE and IgM respectively Figure 2 and table-1).

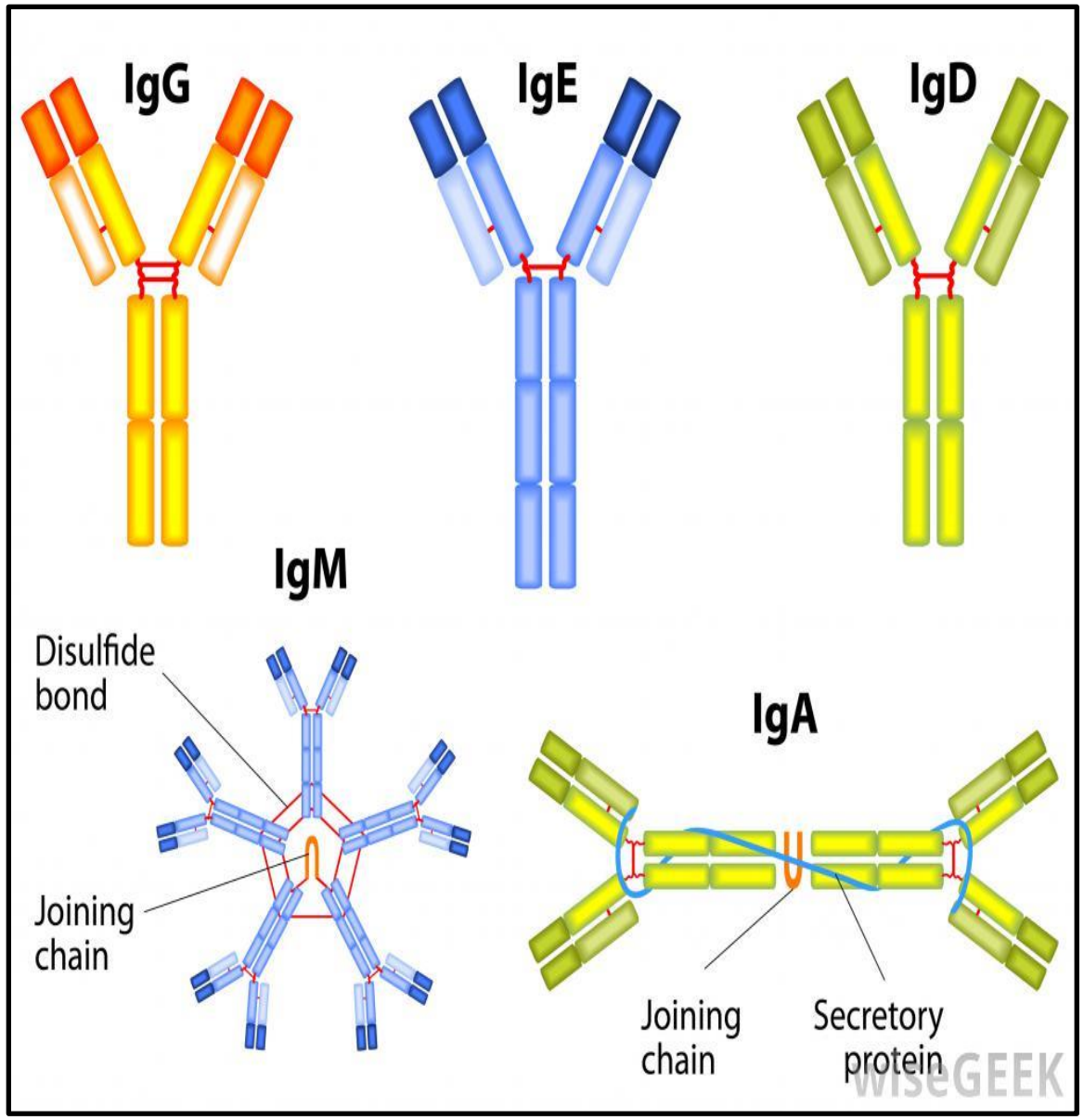


Figure 2: Types of Immunoglobulin.

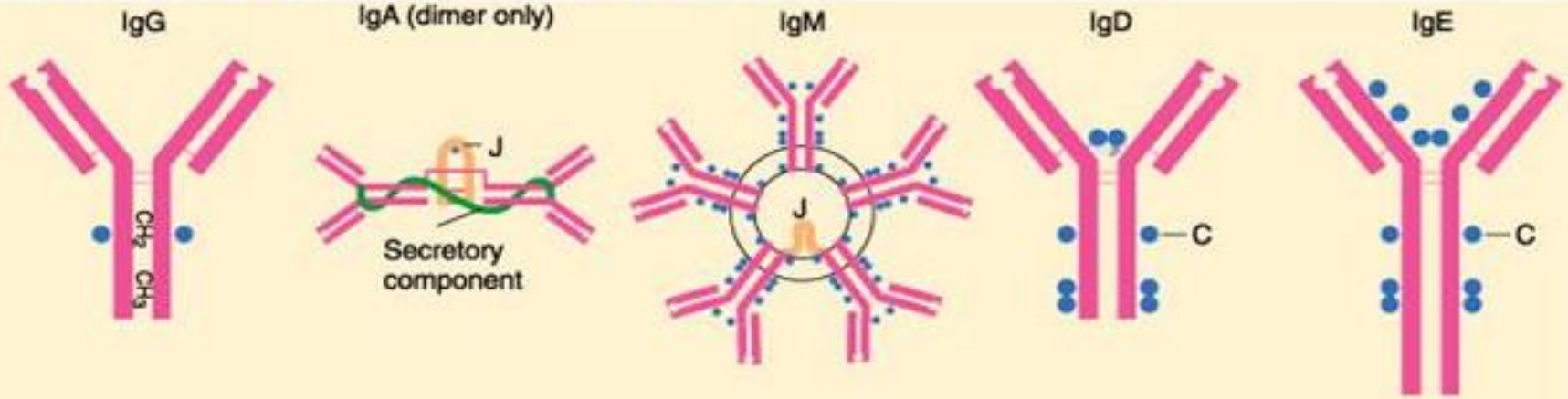
The molecules are characterized by two functional areas:

- The Fab, or variable end is the area that recognizes and binds to the antigen.
- The Fc end is responsible for interaction with other components of the immune system, e.g. complement and T-helper cells.
- **Based on differences in the amino acid sequences in the constant region of the heavy chains there are five classes of Igs (IgG, IgM ,IgA ,IgD and IgE).**

❖ **In each class of Ig small differences in the constant regions of the heavy chain occur, leading to subclasses of the Igs e.g. IgG1,IgG2,IgG3 etc.**

Table1: Classes of immunoglobulin			
Immunoglobulins	**Structure**	**Location**	**Action**
IgG	**Monomer**	**ECF, can pass the placenta**	**Neutralizes toxins, Viruses activate complement**
IgA	**Dimer**	**ECF + (secretions (e.g, tears, saliva, mucus)**	**Antimicrobial**
IgM	**Pentamer**	**Mainly intravascular**	**IgM antibodies are associated with a primary immune response and are frequently used to diagnose acute exposure to an immunogen or pathogen.**
IgD	**Monomer**	**ECF+ cell membrane**	**Cell surface antigen receptors**
IgE	**Monomer**	**ECF**	**Antiallergenic, antiparasitic**

TABLE 15.2 Characteristics of the Immunoglobulin (Ig) Classes



	IgG	IgA (dimer only)	IgM	IgD	IgE
	Monomer	Dimer, Monomer	Pentamer	Monomer	Monomer
Number of Antigen Binding Sites	2	4 2	10	2	2
Molecular Weight	150,000	170,000–385,000	900,000	180,000	200,000
Percent of Total Antibody in Serum	80%	13%	6%	1%	0.002%
Average Life in Serum (Days)	23	6	5	3	2.5
Crosses Placenta?	Yes	No	No	No	No
Fixes Complement?	Yes	No	Yes	No	No
Fc Binds To	Phagocytes				Mast cells and basophils
Biological Function	Long-term immunity; memory antibodies	Secretory antibody; on mucous membranes	Produced at first response to antigen; can serve as B-cell receptor	Receptor on B cells	Antibody of allergy; worm infections

Electrophoresis of serum proteins:

Electrophoresis technique may be carried out to study a number of protein abnormalities. The normal pattern is shown in Figure3.

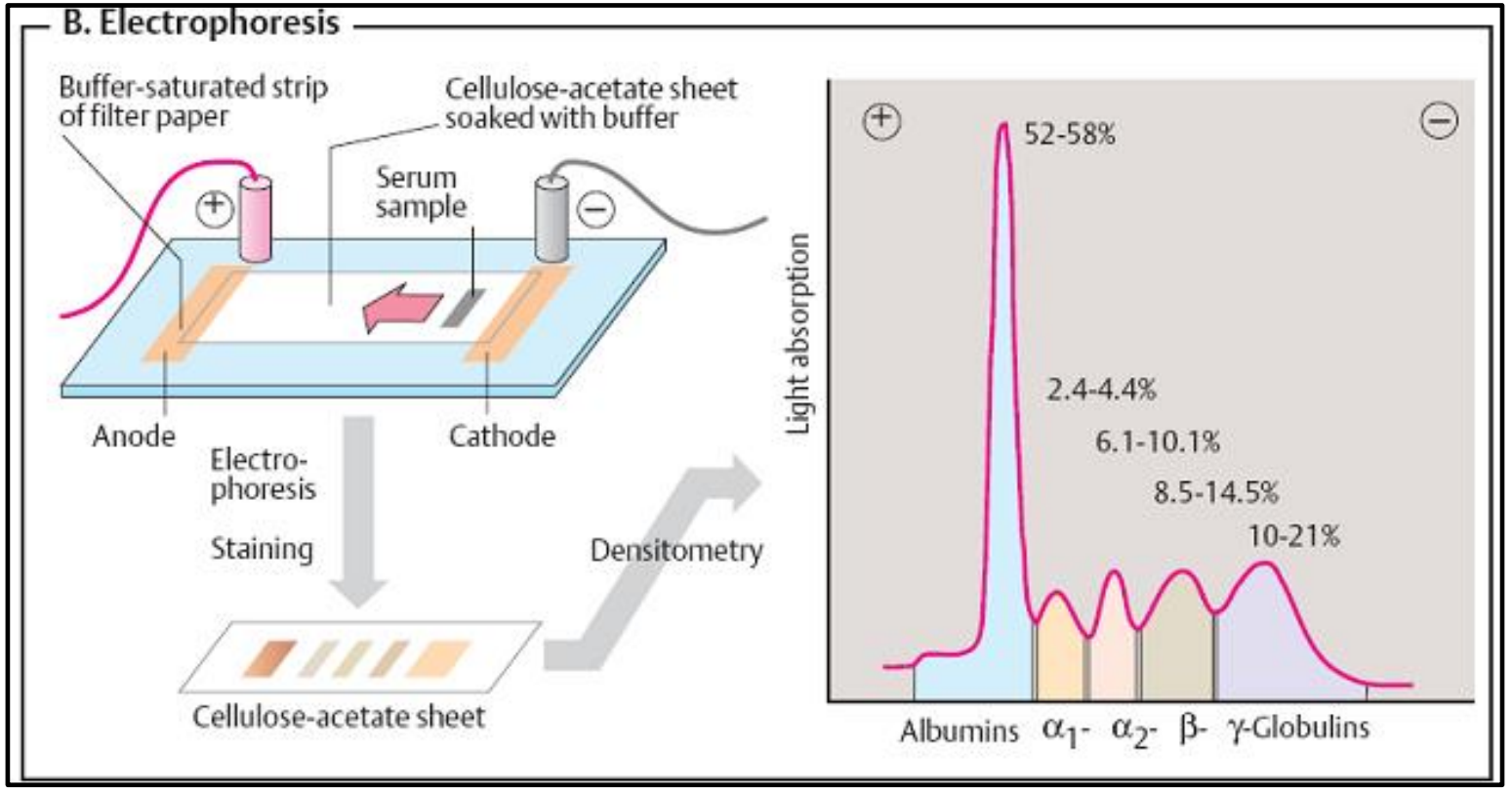
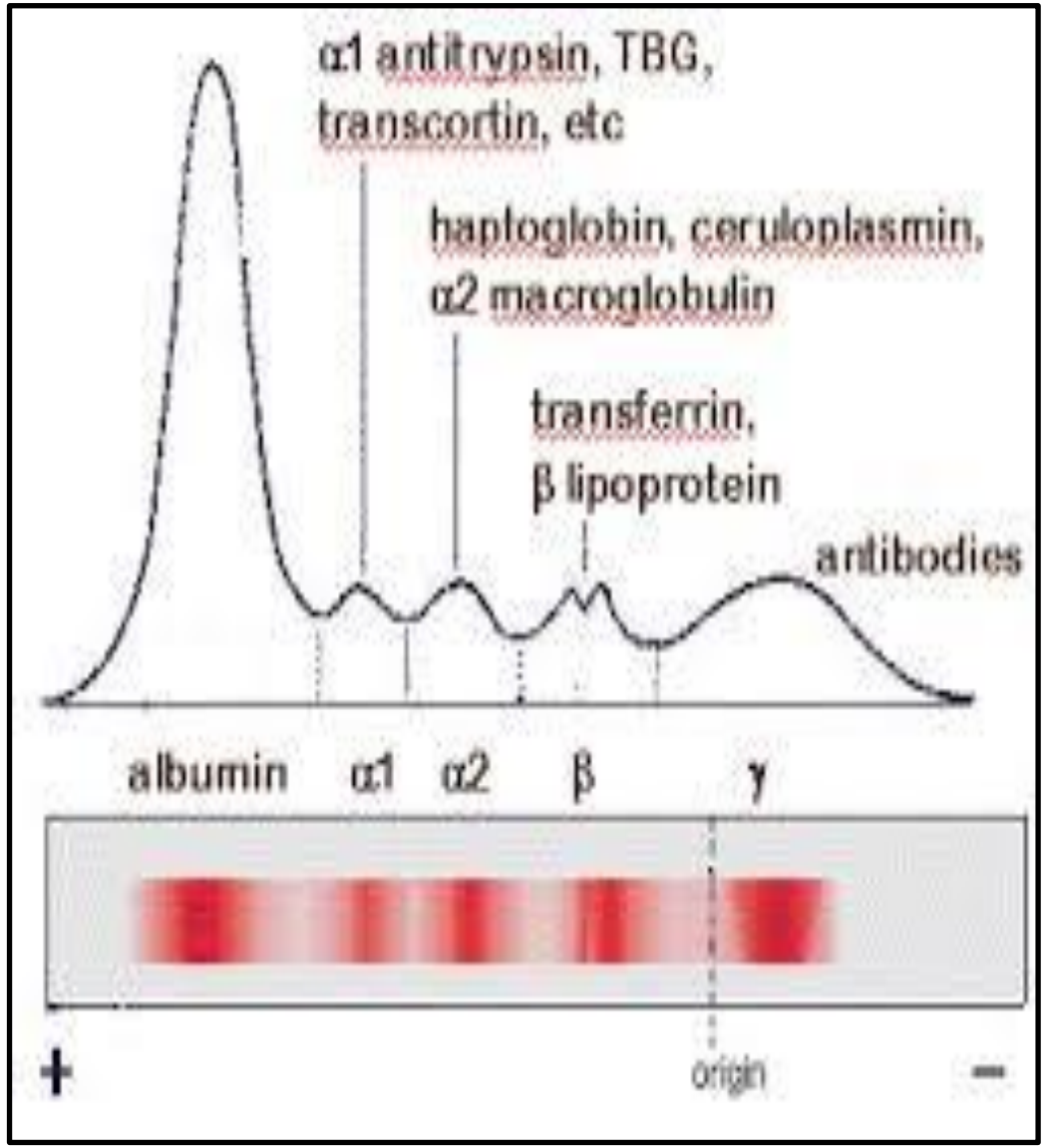


Figure 3: Electrophoresis

Immunoglobulins are detected primarily in the **gamma globulin area** on electrophoresis.
Electrophoresis can show deficiency or excess of immunoglobulins and the presence of discrete bands **(paraproteins)**.
A quantitative measure of each protein class may be obtained by scanning the electrophoresis strip (Figure 4).



Measurement:

Immunoglobulins may be measured in a number of ways, the necessity for the request often being triggered by an observed increase in the ‘globulin’ fraction.

If an abnormality is detected, then the particular type of immunoglobulin, or light or heavy chains where these are produced alone, may be confirmed by immunofixation or quantitatively by other means.

Increased immunoglobulins:

Immunoglobulins may be increased non-specifically in a wide variety of infections and also in autoimmune disease. This increased synthesis comes from a number of cell lines, each producing its own specific immunoglobulin.

- The response is therefore said to be **'polyclonal'** and results in a diffuse increase in protein mass throughout the gamma globulin region on electrophoresis.
- In contrast, cells from a single clone **(monoclonal)** all make identical antibodies. As the cells multiply the immunoglobulin production becomes large enough to be observed on electrophoresis as a **single discrete band**. This may be an intact immunoglobulin or a fragment and is called a **paraprotein**.

Paraproteins:

Paraproteins are found in malignant conditions e.g. (multiple myeloma). The paraproteins may arise from any of the immunoglobulin classes.
Monoclonal light chains are produced in excess of heavy chains in 50% of cases of myeloma, and in 15% of cases only light chains are found. These light chains of Igs are small enough to spill into the urine where they are known as **Bence Jones protein**.

Deficiencies or absence of immunoglobulins:

Deficiencies or absence of immunoglobulins can occur as a result of infection, genetic abnormalities or the effects of therapy. If the situation is irreversible, replacement therapy has been used, either by addition of immunoglobulin-rich plasma or by the transplantation of bone-marrow-containing competent plasma cells.

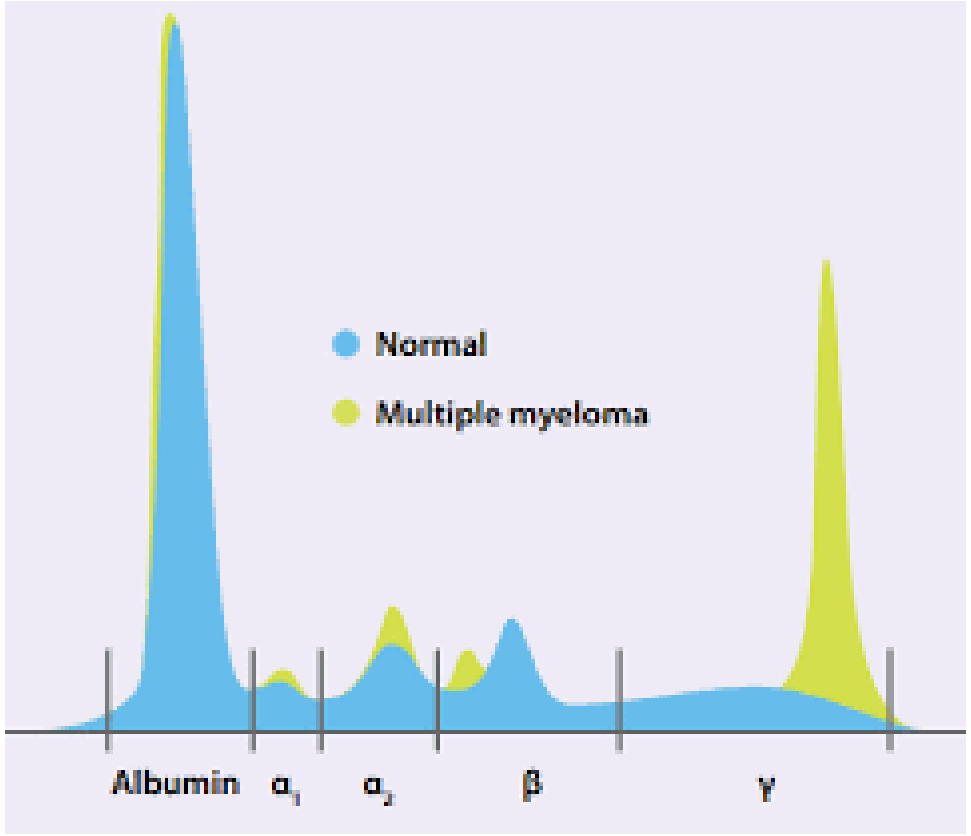


Figure: Normal SPE and monoclonal gammopathy electrophoresis (multiple Myeloma (paraproteins or M-spike)

SPEP

Polyclonal Gammopathy

Monoclonal Gammopathy

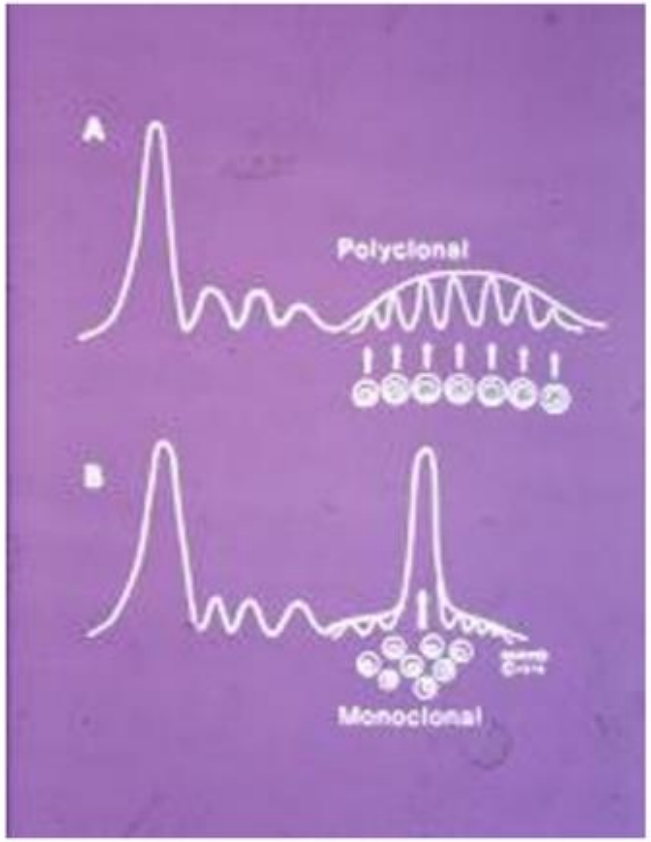


Figure: SPE bands for monoclonal gammopathy electrophoresis and polyclonal gammopathy.

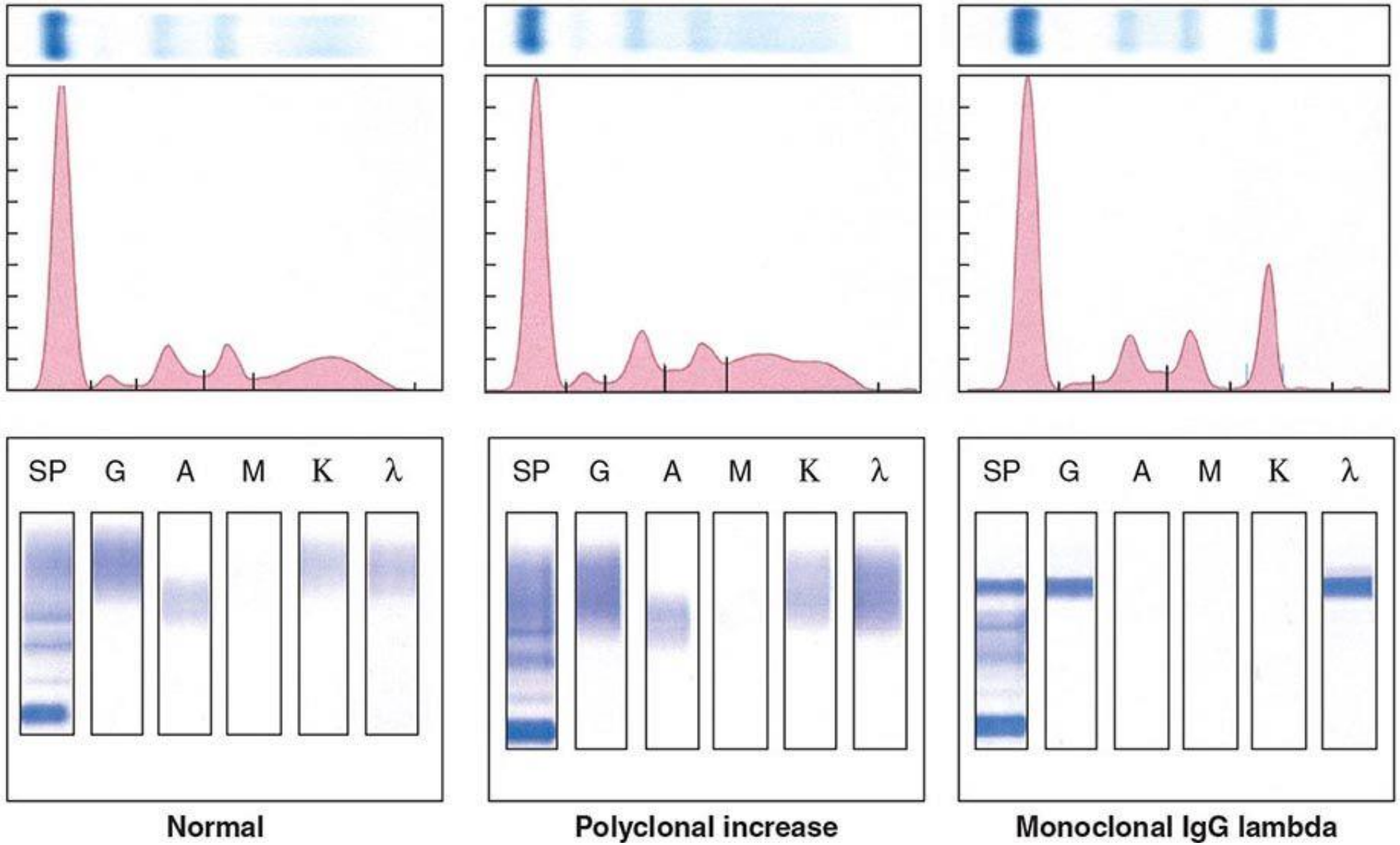


Figure: SPE , normal pattern , polyclonal and monoclonal Gammopathy.

Summary:

- **Immunoglobulins or Antibodies (Igs or Abs) are glycoprotein molecules produce by plasma cells. , in response to Antigens or immunogens entering the living (viruses, bacteria, or toxins), binding to them and forming antigen-antibody complexes resulting in Ag elimination and protection of the body.**
- **Based on differences in the amino acid sequences in the constant region of the heavy chains there are five classes of Igs (IgG, IgM ,IgA ,IgD and IgE).**
- **Serum Protein Electrophoresis is a technique that separate serum proteins into bands. The fraction of Igs band called gamma globulin or gamma band.**
- **Diseases associated with Igs called Gammopathy.**
- **One type of plasma cells produce one type of Ig this called Monoclonal Gammopathy. (in malignant conditions e.g, Multiple Myeloma)**
- **(Shape of gamma band in monoclonal Gammopathy is called Paraproteins – or M protein or M-spike**
- **Several types of plasma cells produce several types of Igs called polyclonal Gammopathy. (in nonmalignant conditions e.g, inflammation).**

Assessment and Evaluation:

After reading try to answer the following questions?

Q:Define Immunoglobulins?

Q: What are the types of Igs?

Q:Explain the chemical structure of Igs?

Q:Explain serum protein electrophoresis

Q:What is paraproteins?