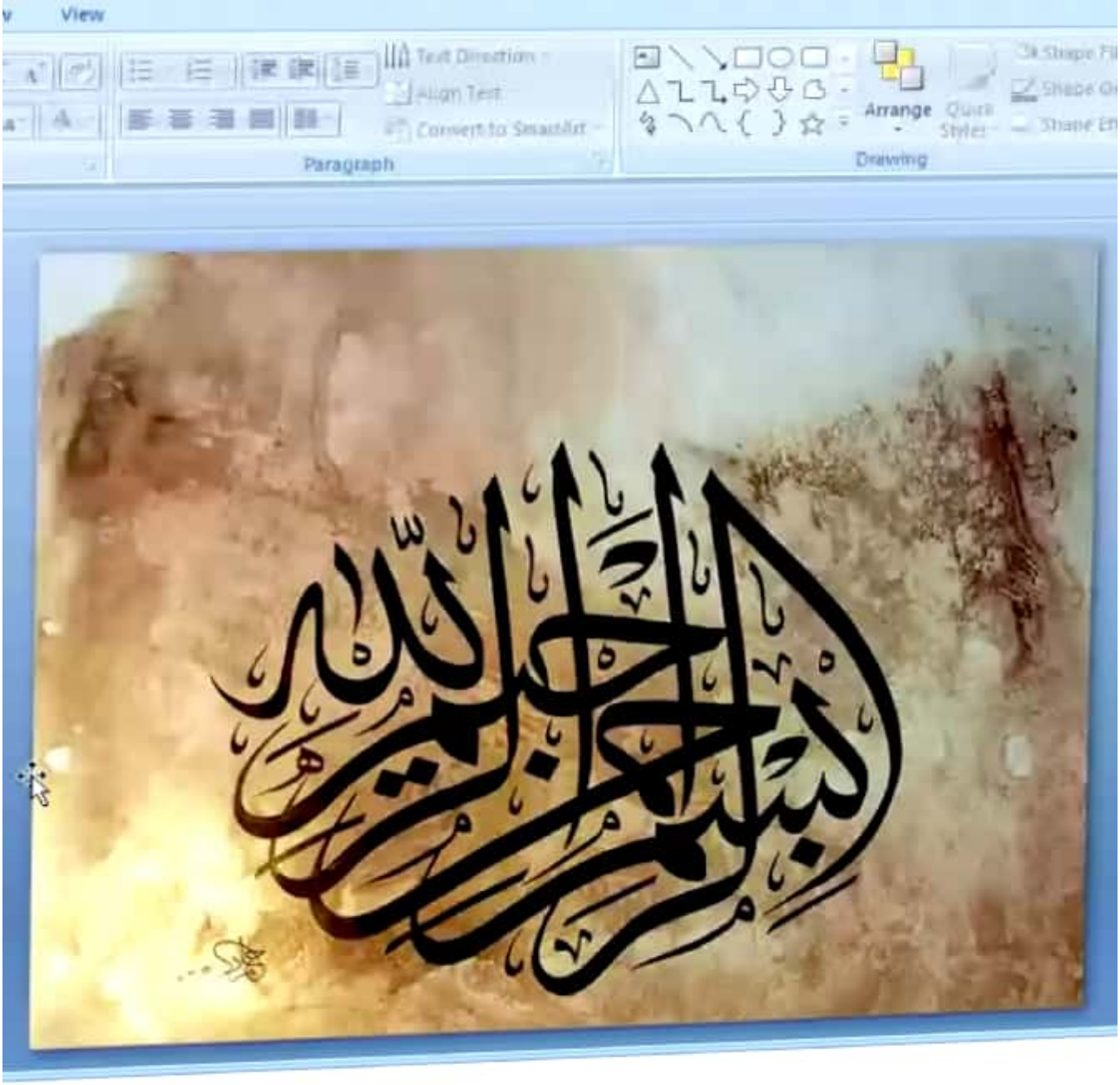

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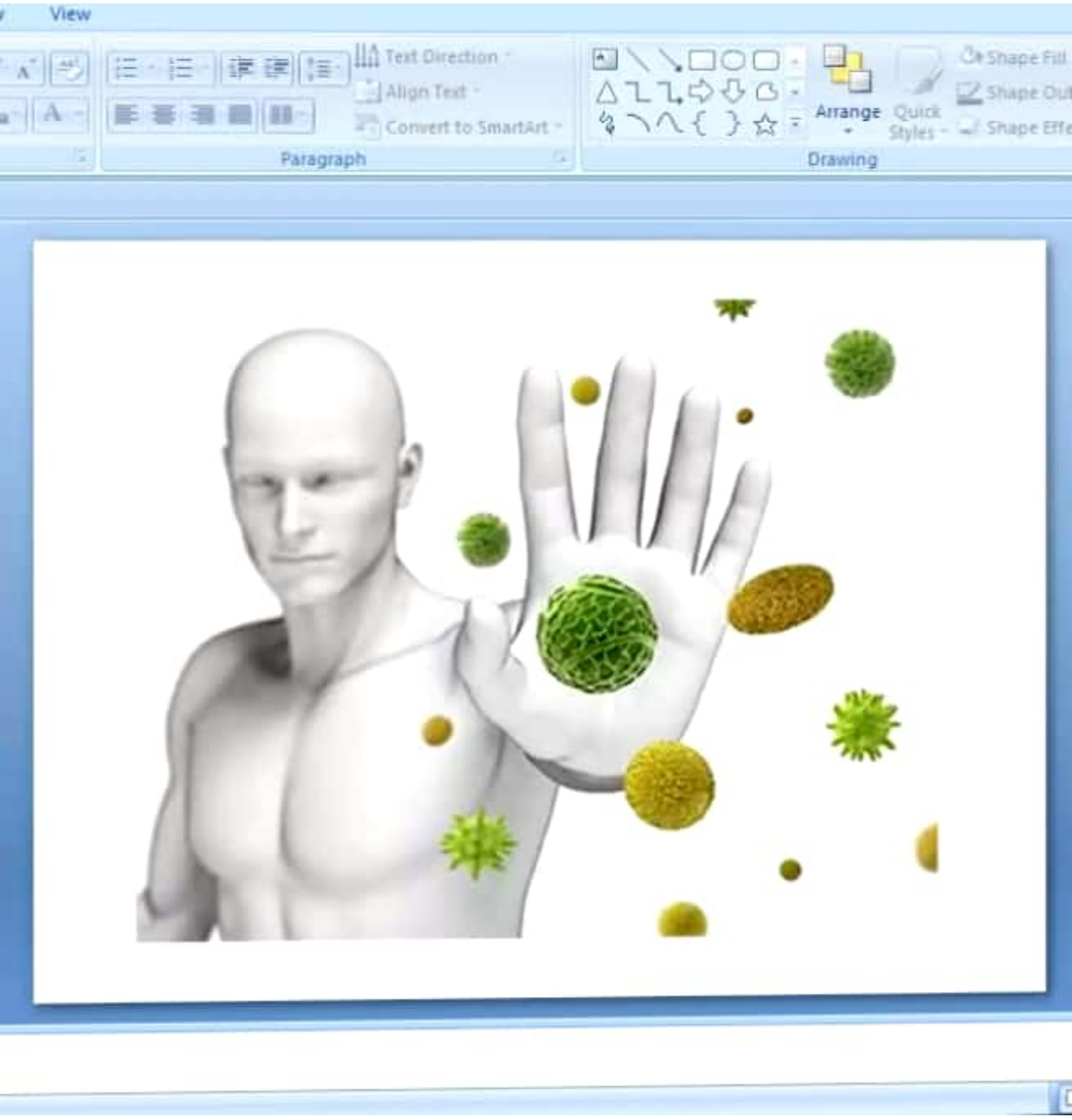

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Drawing

Immunoglobulin

By
DR .GULNAZ

Dr Gulnaz

You

Maha

Dr

Dr

S

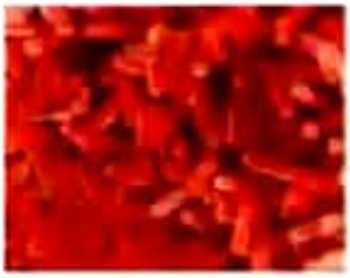
114 others

Objectives

- Define immune system
- Types of immunity
- Cells of immune system
- Definition of immunoglobulin
- Structure of immunoglobulin
- Classification of immunoglobulin
- Functions of each immunoglobulin.
- Disorders related to immunoglobulin.

What is immune system?

- The ability of body to resist the entry of disease causing organisms, like bacteria, virus & foreign particles, and destroy malfunctioning cells in the body.



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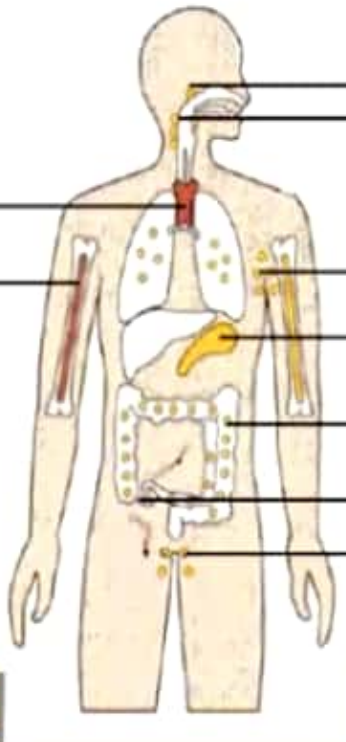
Immunity

- Immunity is Latin term 'IMMUNIS' means EXEMPT, referring to protection against foreign agents.
- So immune system is integrated body system of organs, tissues, cells& cell products that differentiate self from non self & neutralize pathogenic organisms.

Life is threat from everything in nature

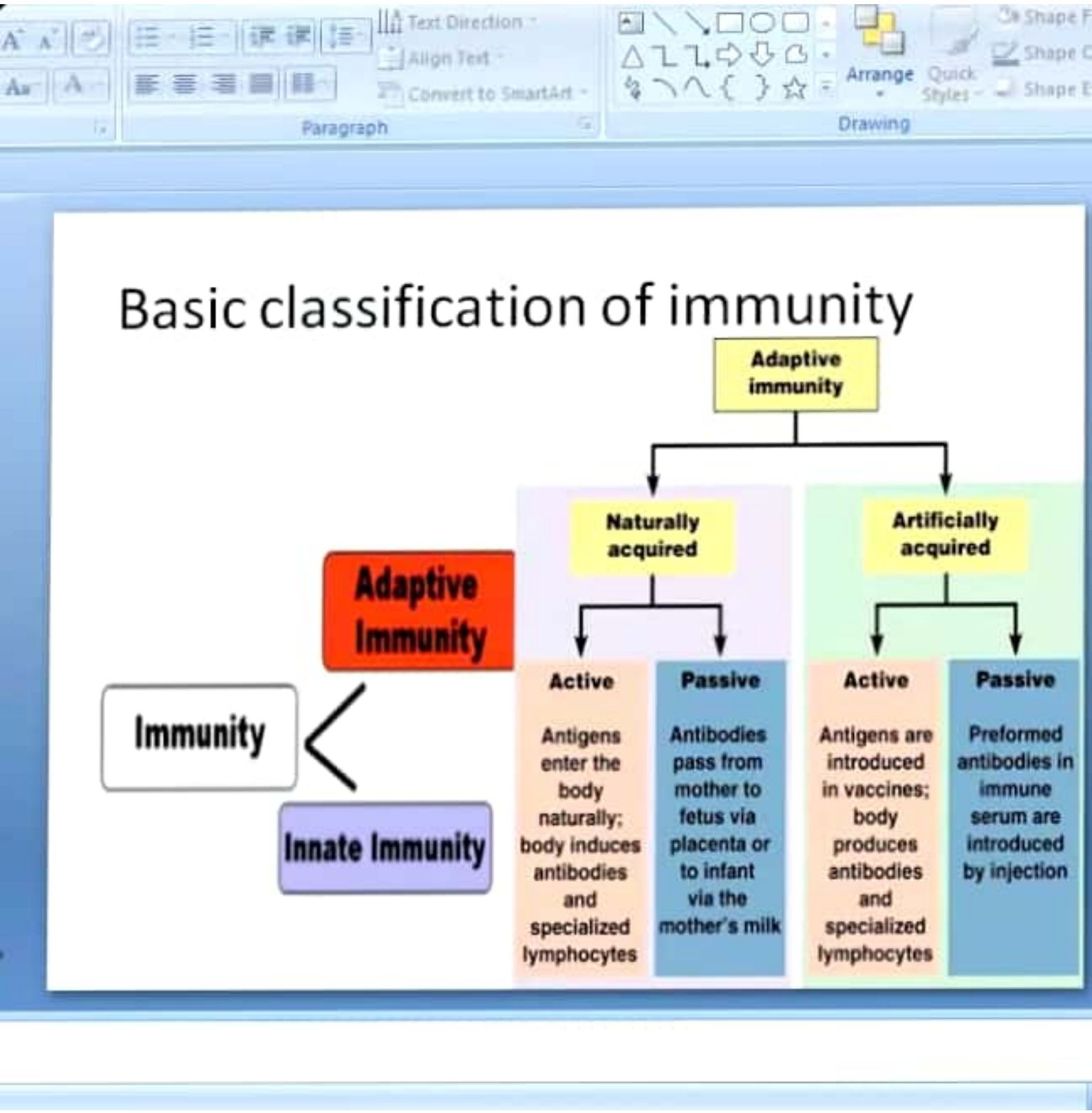
Lymphoid organs



Adenoids
Tonsils
Thymus
Bone Marrow
Lymph nodes
Spleen
Peyer's patches
Appendix
Lymph nodes

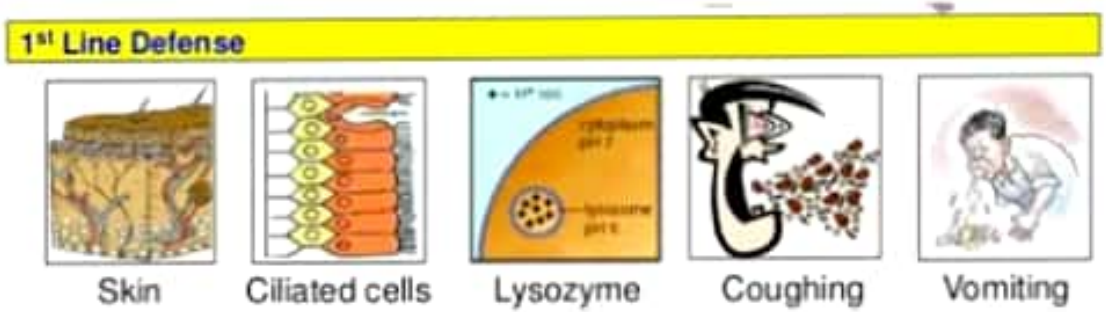
Primary Organs

Secondary Organs



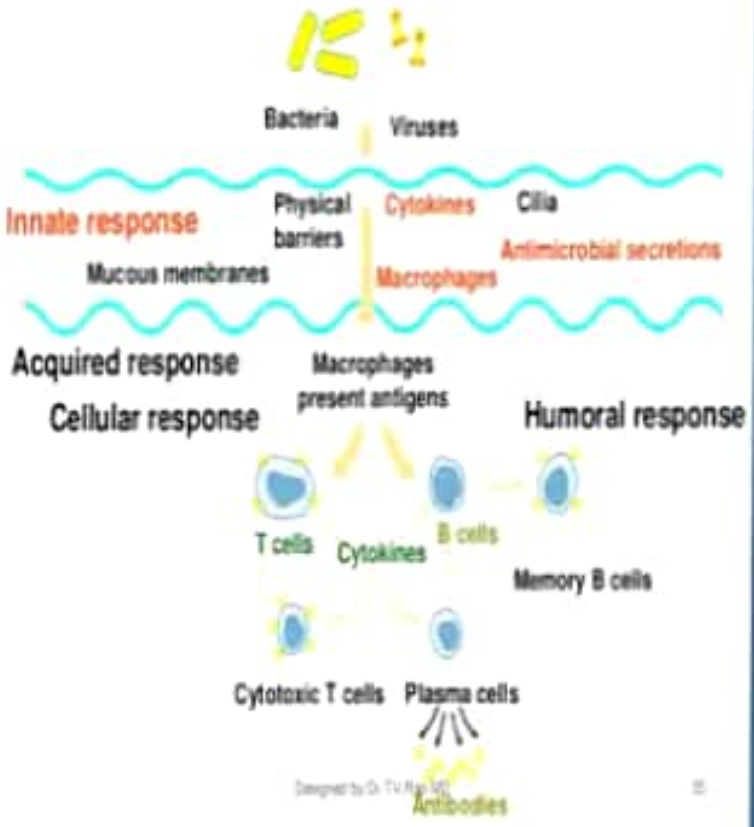
Innate immunity

- Natural or native immunity
- Inborn capacity of body to resist pathogens
- First line of defense against infection.
- Non specific recognition
- No immunologic memory.



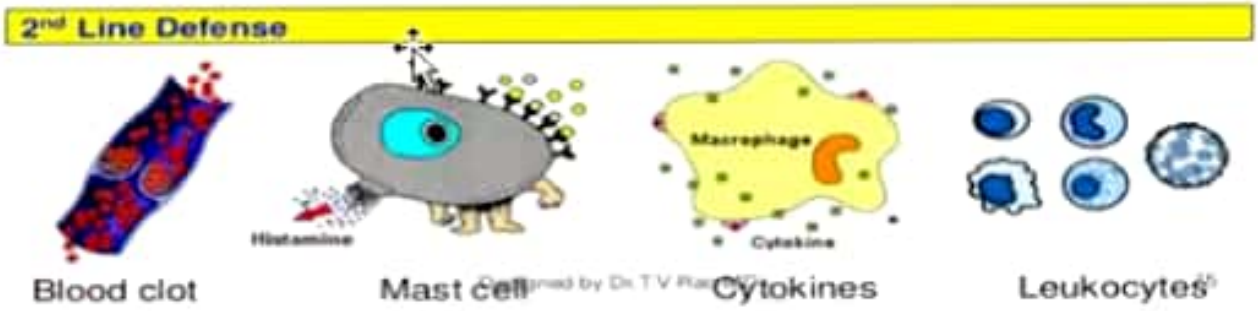
Innate immunity

- Barriers to infection in innate immunity are
- Physical barriers, skin & mucous secretions,cilia
- Chemical barriers
- Lysozymes secreted in skin & saliva
- Enzymes of GIT
- Phagocytic cells(neutrophils& machrophages), inflammatory cells,



Adaptive or acquired immunity

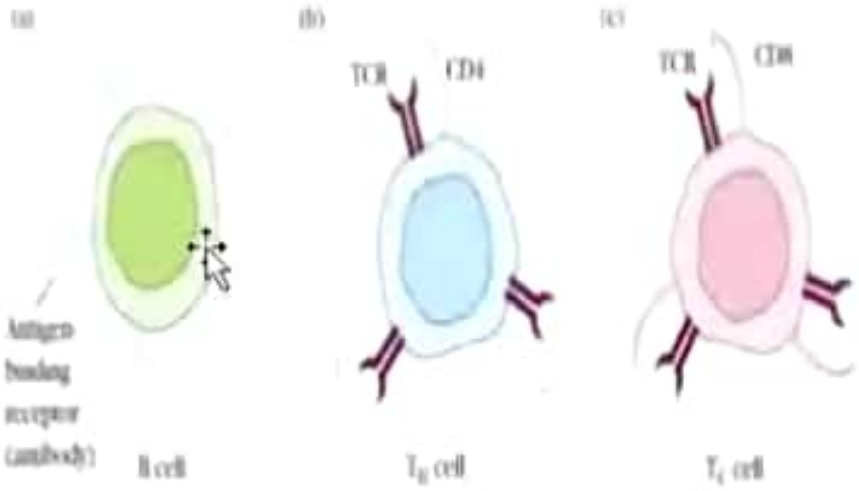
- 2nd line defense against infection
- Specific to foreign body like bacteria, viruses, toxins etc.(specific immunity)
- Response takes 7-10 days.
- Most powerful immune mechanisim.
- Development of immunologic memory

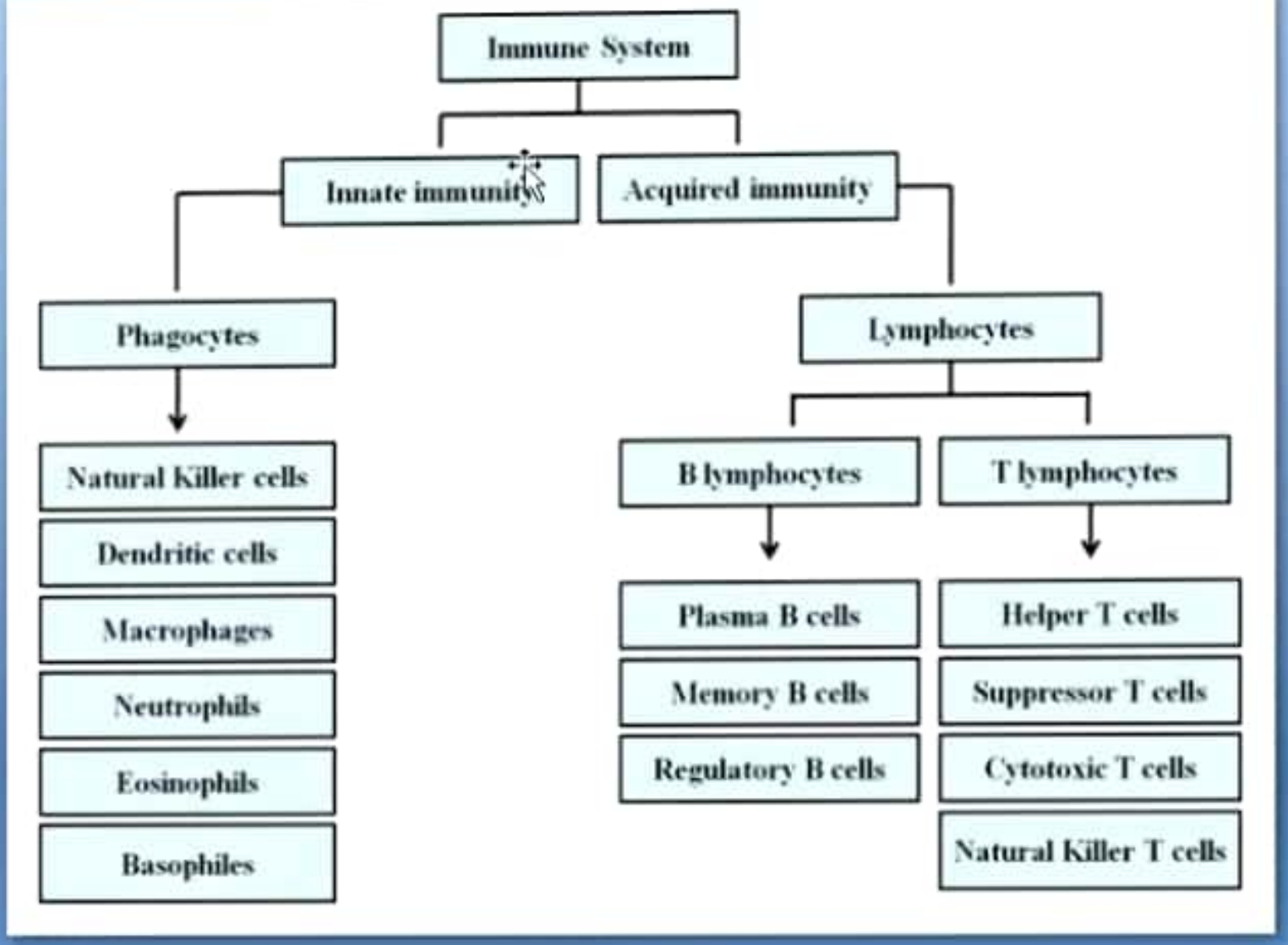


Cells of immune system

Adaptive immunity require two types of cells

- T- lymphocytes ⟶ Cellular immunity
- B- lymphocytes ⟶ Humoral immunity





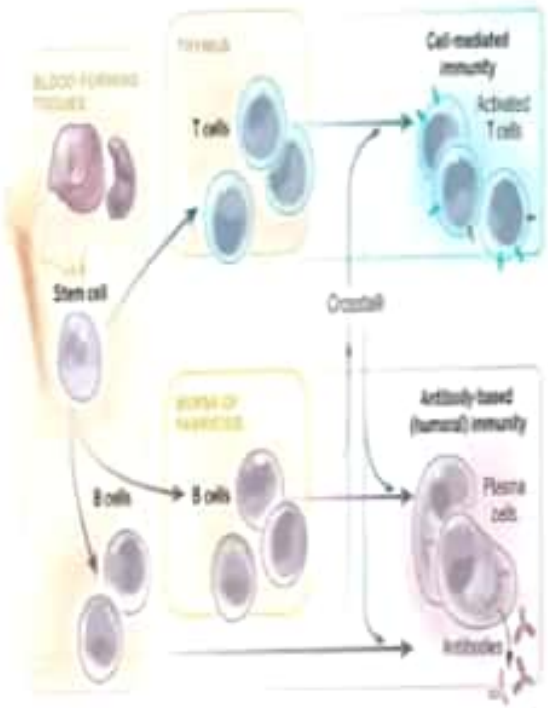
Adaptive immune defense

Specific defense requires

- B-lymphocytes (B-cells) and
- T-lymphocytes (T-cells).
- Both produced in bone marrow, however T lymphocytes mature in thymus , while B-cells mature in bone marrow.

- B cells produce antibodies that shaped like antigen receptors.

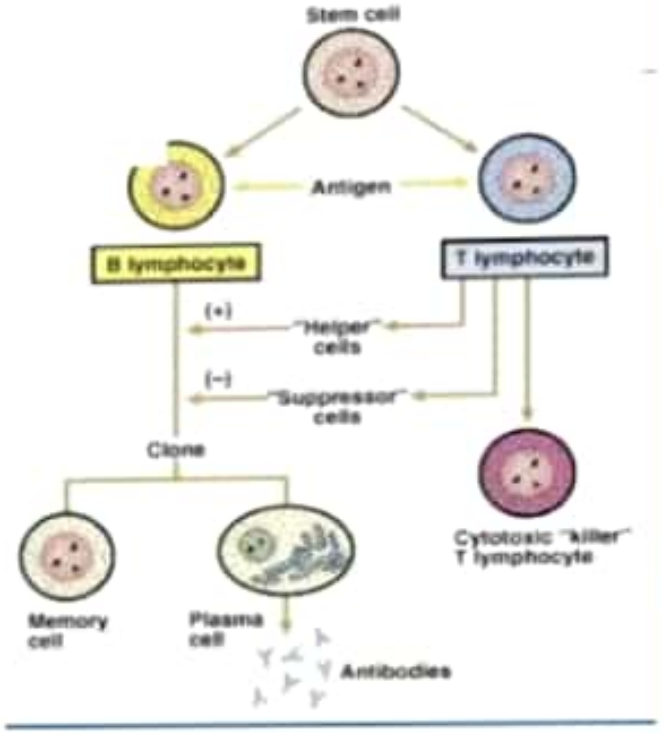
- T cells attack foreign antigen directly.

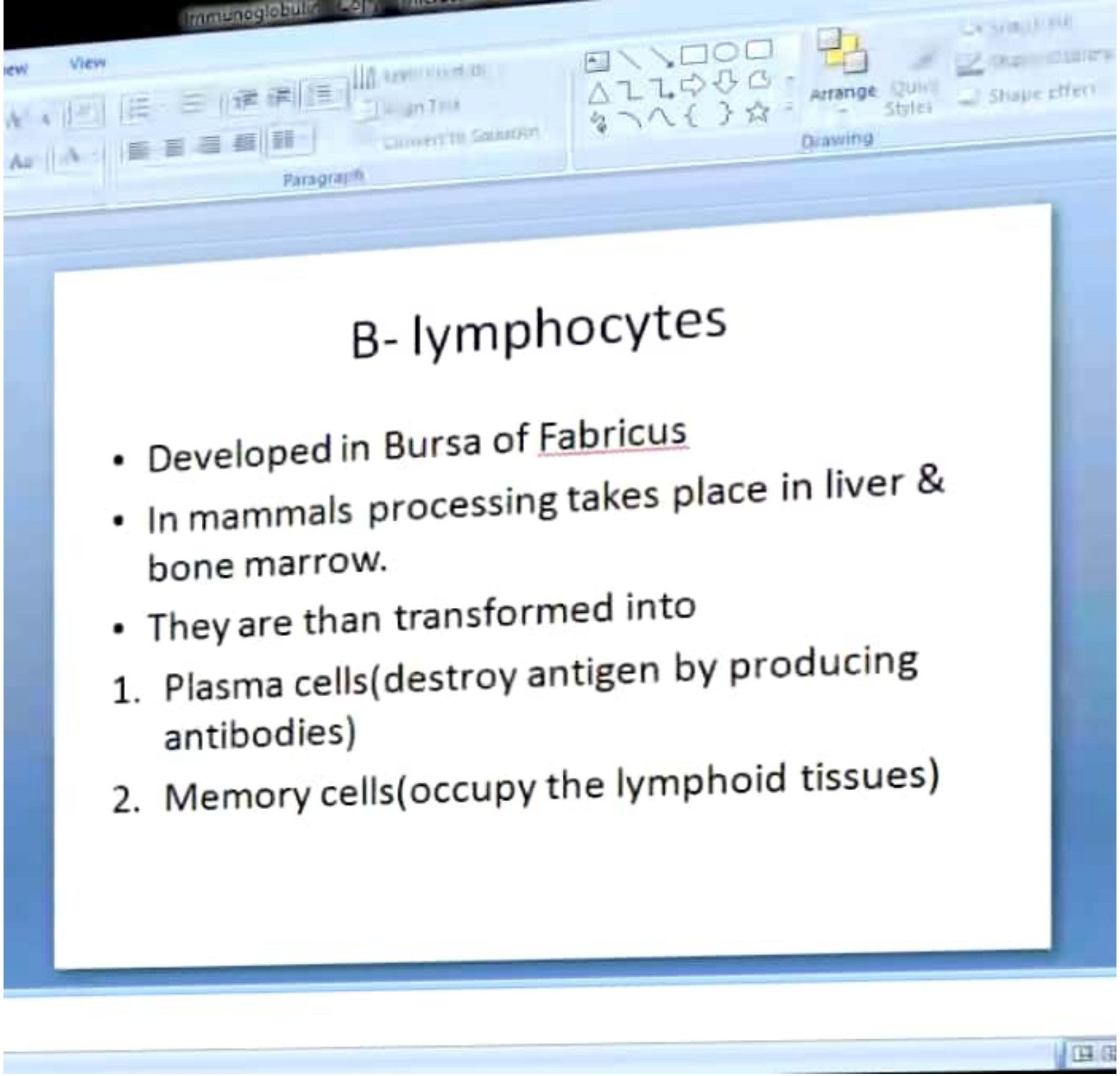


T- lymphocytes

- Four types

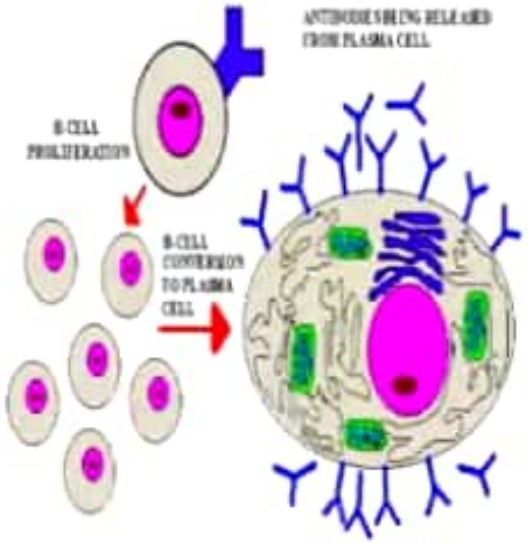
1. Helper-T cells (CD_4)
2. Cytotoxic –T cells or killer –T cells (CD_8)
3. Suppressor-T cells
4. Memory-T cells

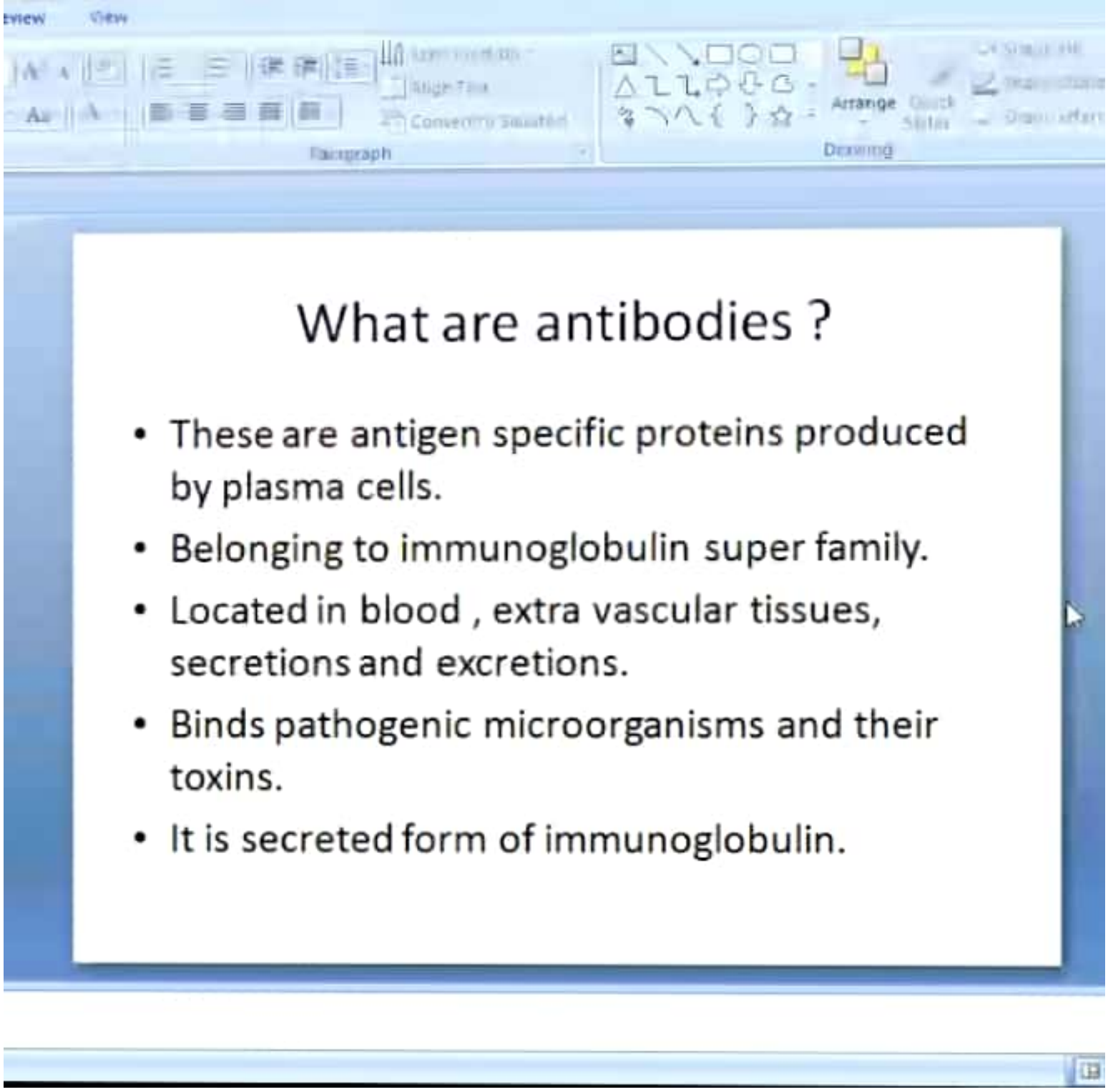




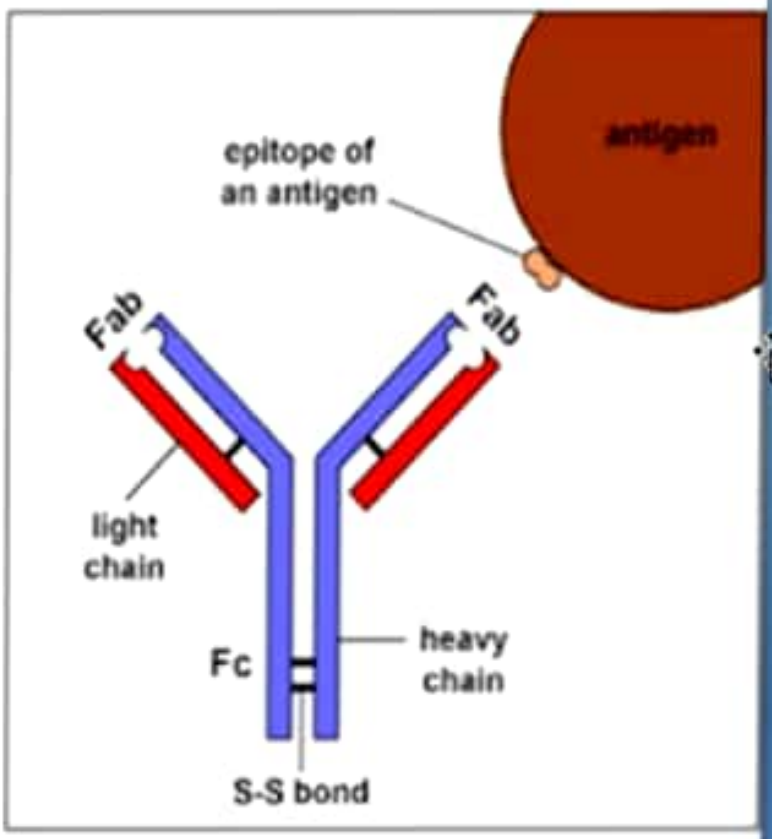
Humoral immunity

- Results in production of proteins called 'immunoglobulin's'' or ''antibodies''.
- Antigens are foreign substances which are harmful to body. They may be bacteria, viruses, etc.





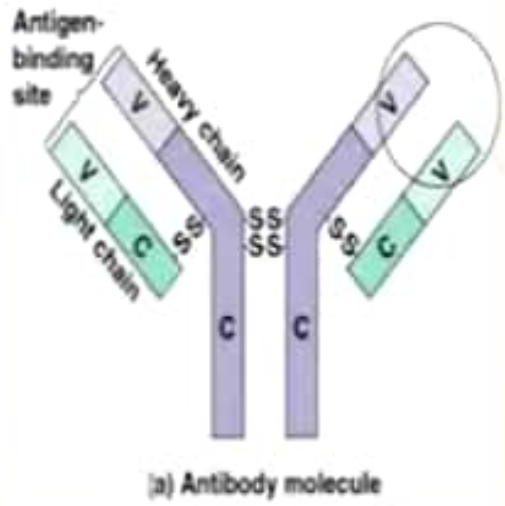
All antibodies are immunoglobulin but all immunoglobulin are not be antibodies.



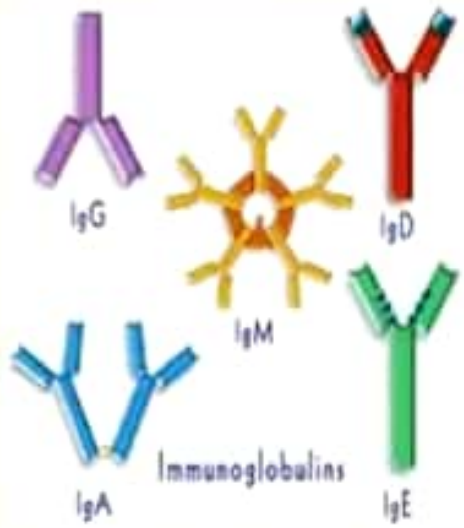
Definition of immunoglobulins

- Glycoprotein molecule produced by B cells or produced by plasma cells(antibodies),in response to immunogens(antigen)that provoke immune response.

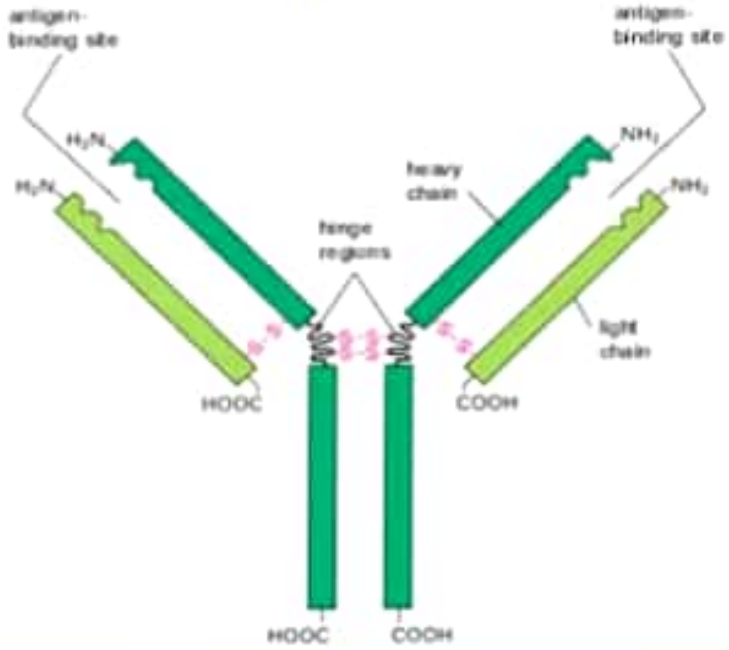
Immunoglobulins



(a) Antibody molecule

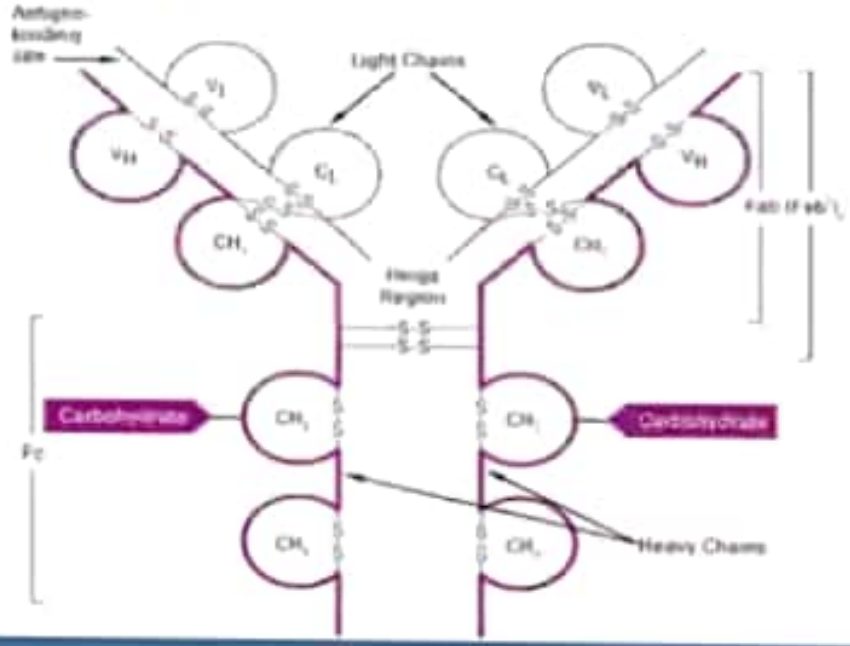


- They are composed of 82 to 96 percent polypeptide and 4 to 18 percent carbohydrate.
- They are gamma globulin
- Synthesized by plasma cells
- Constitute 25-30% of total plasma protein

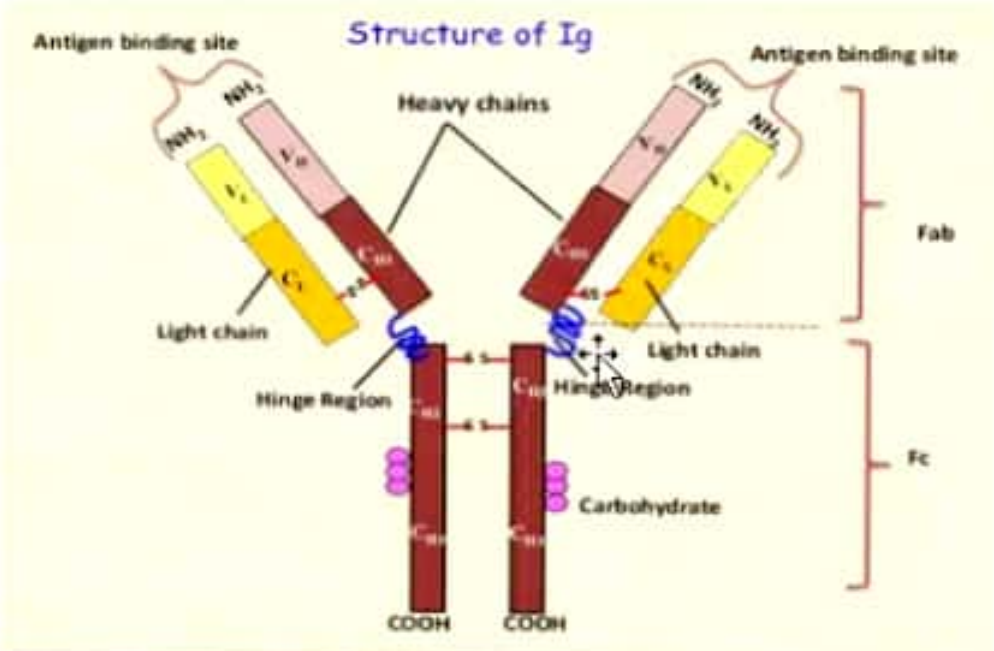


Structure of immunoglobulin

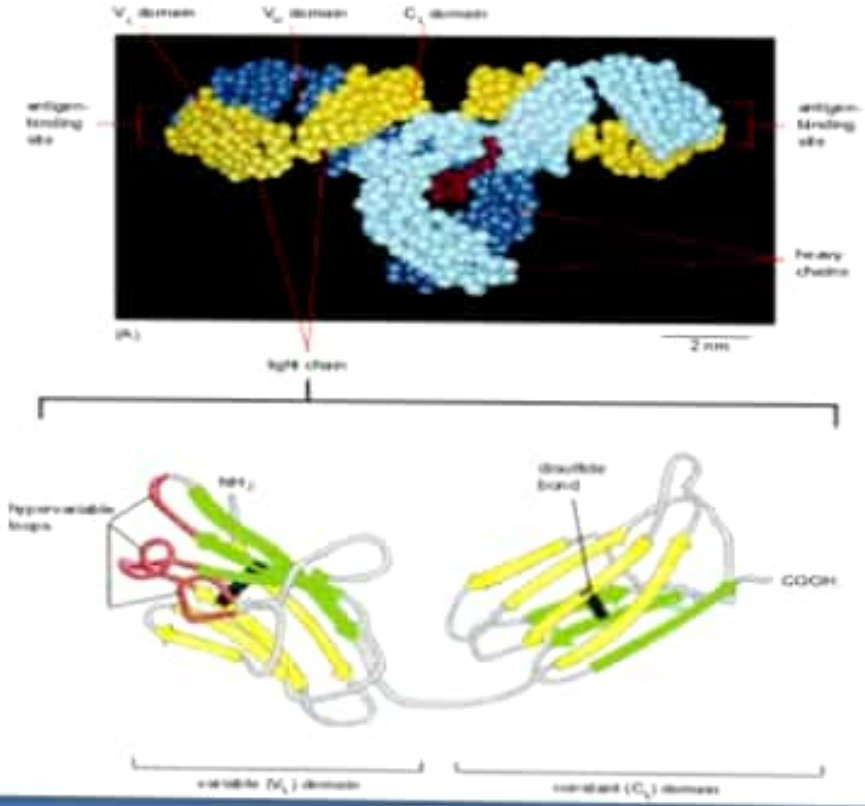
- All the immunoglobulin molecules basically consist of two identical heavy(H) chains and two identical light(L) chains held together by disulfide linkages and non covalent interactions.



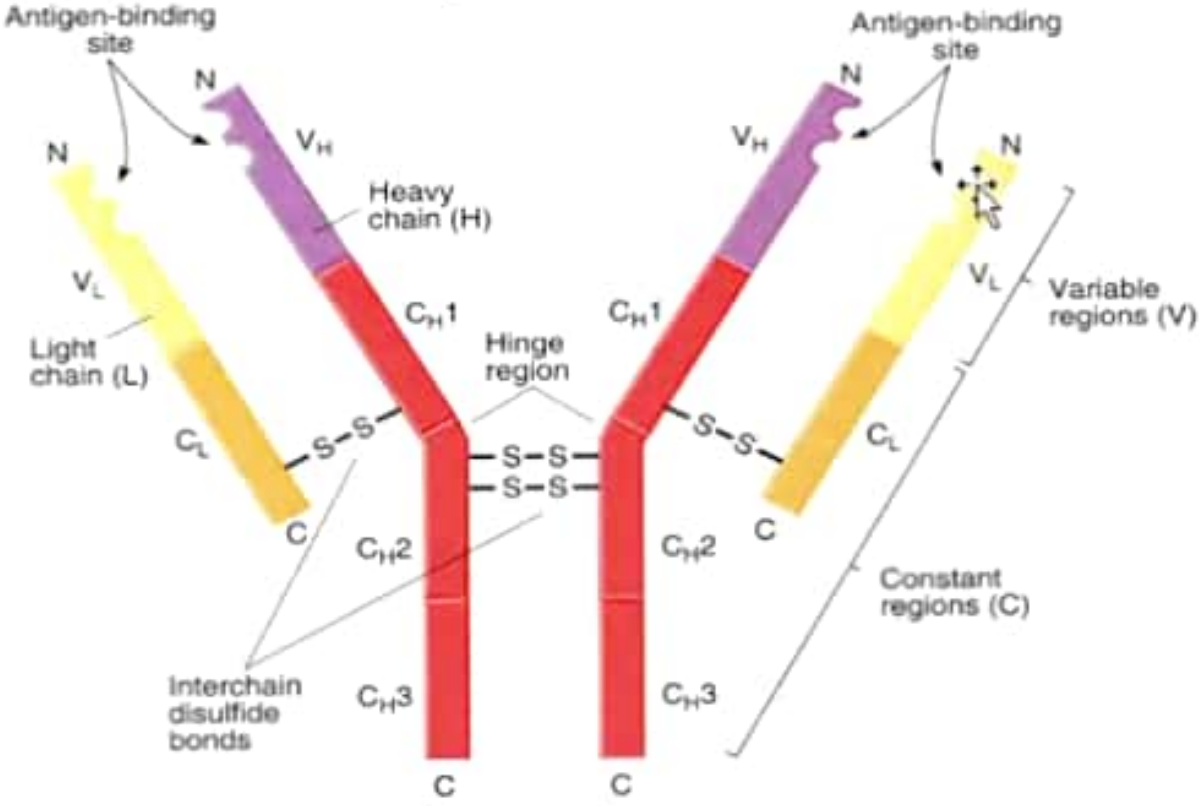
- Thus immunoglobulin is a Y-shaped tetramer(H_2L_2). Each heavy chain contains approximately 450 amino acids while each light chain has 212 amino acids. The heavy chain is linked to carbohydrates.



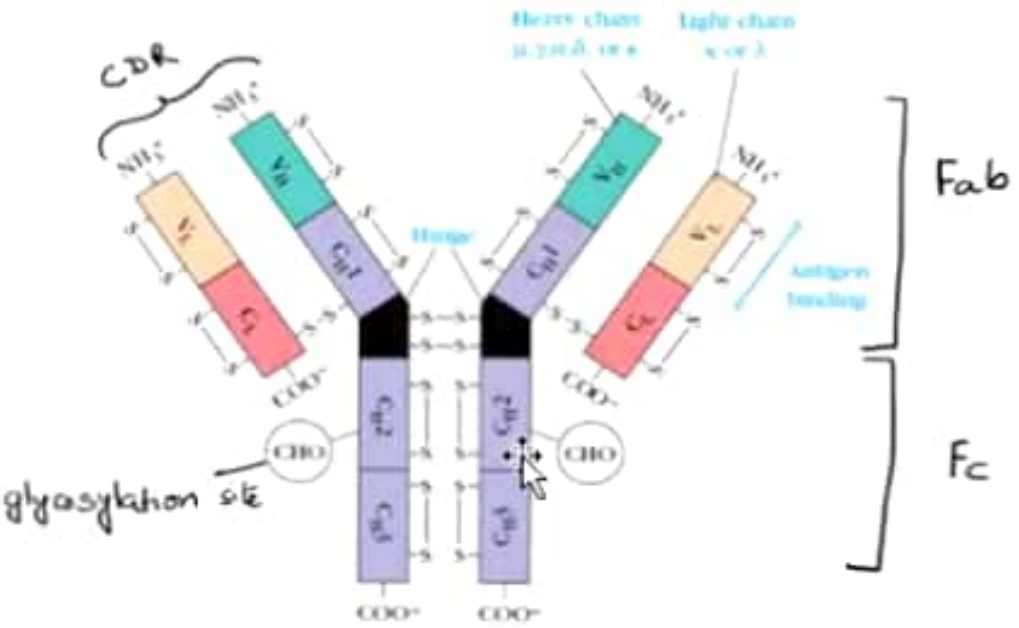
- Each chain contain two regions
- Constant
- Variable



- The amino terminal half of light chain is the variable(V_1)region,while the carboxy terminal half is the constant(C_1) region.



- In heavy chain, approximately one- quarter of amino terminal region is variable(V_H) while the remaining three quarters is constant(C_{H1}, C_{H2}, C_{H3}).



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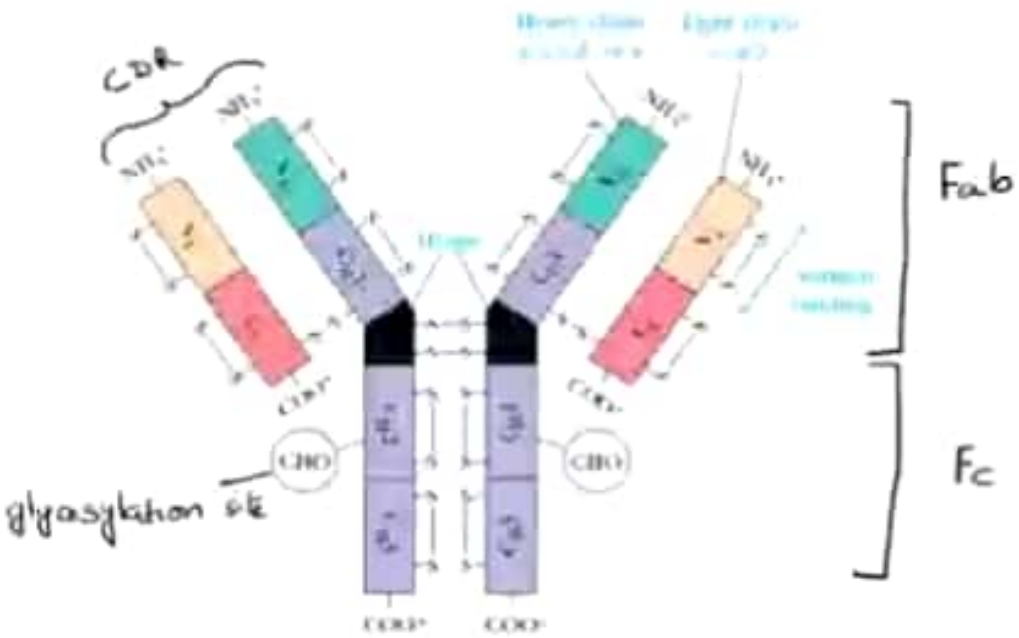
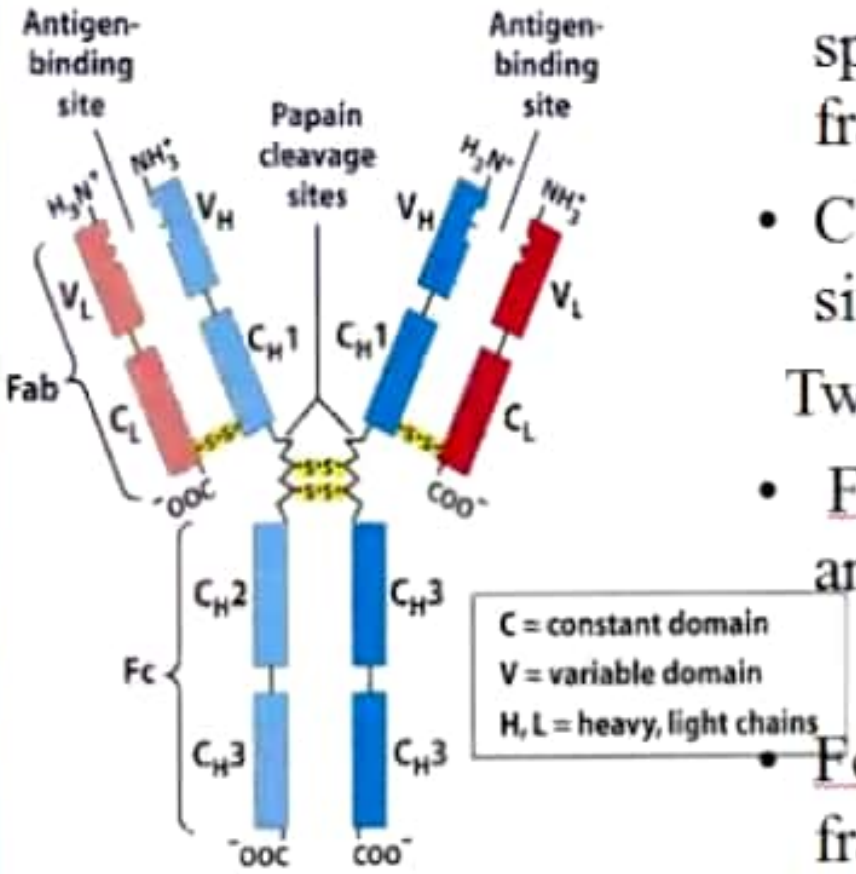




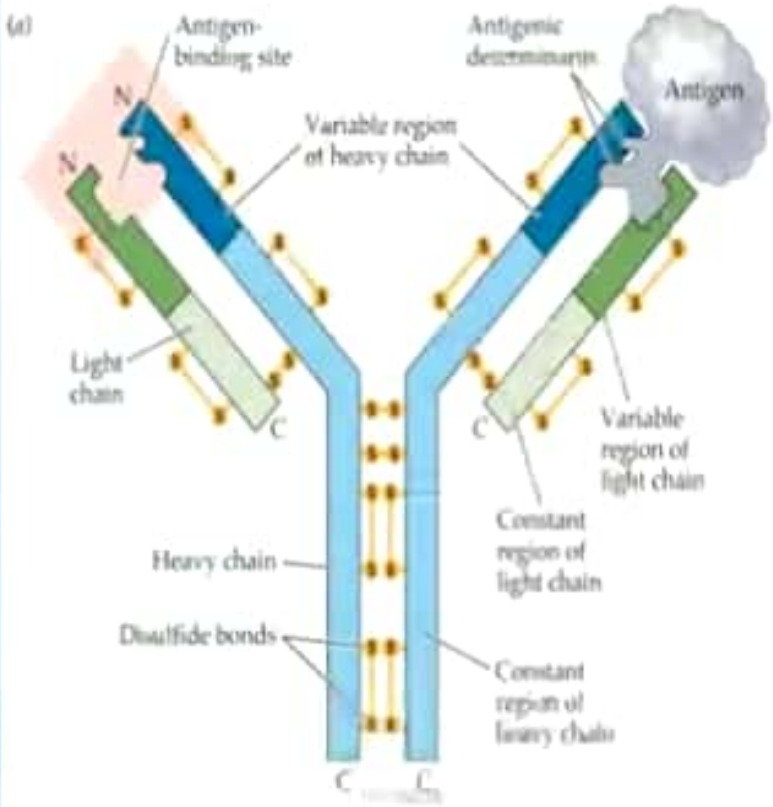
- Immunoglobulin can be split by Papain to their fragments.
- Cleavage occur at hinge site.

Two fragments named

- Fab (fragment of antigen binding)

and

- Fc (crystallizable fragment or fragment for complement binding).

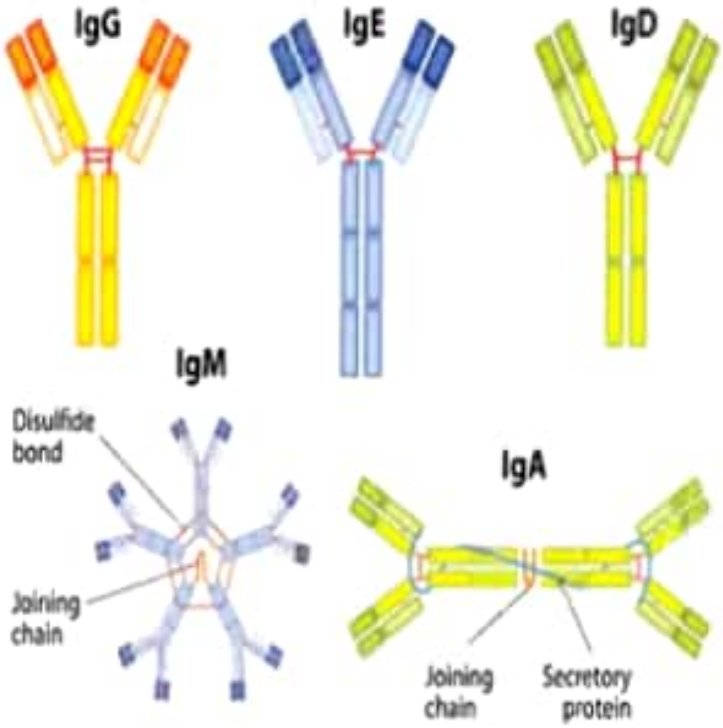


- The variable regions of both heavy and light chains forms antigen binding fragments(Fab), while constant region of heavy chain is responsible for various functions, e.g. complement activation and binding to cell surface receptors.

The constant region of light chain has no biological function.

Classification of immunoglobulins

- Immunoglobulin G (IgG)
- Immunoglobulin A (IgA)
- Immunoglobulin M (IgM)
- Immunoglobulin D (IgD)
- Immunoglobulin E (IgE)



View

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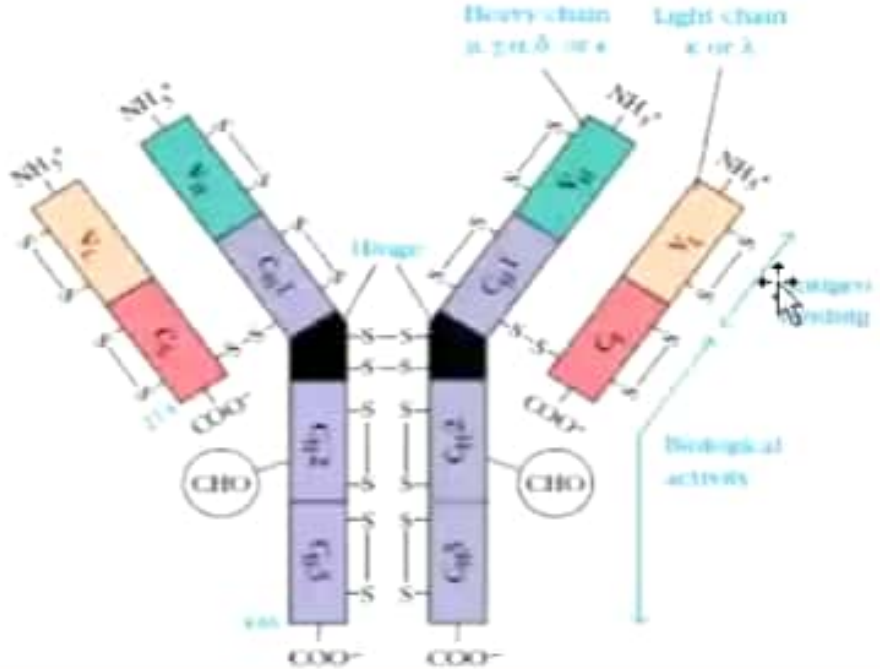
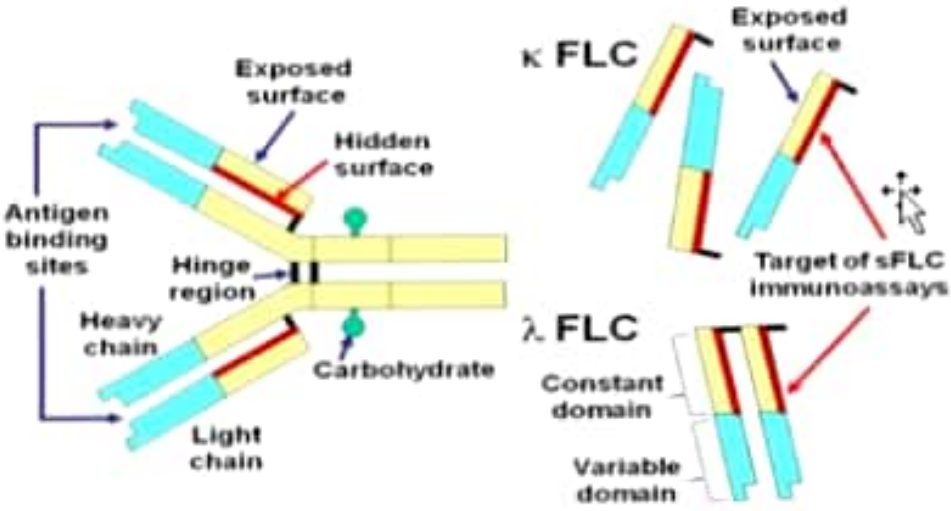
- Heavy chains in IgG, IgA, IgM, IgD and IgE are ϒ,α,μ,δ and ε respectively.
- The type of heavy chain determines the class and function of the given Ig.

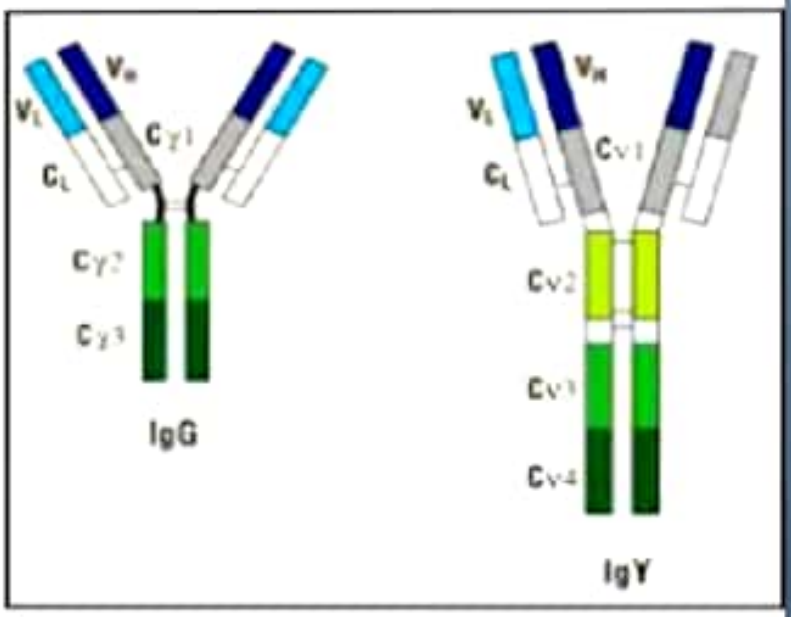


- Types of light chain are kappa(κ) and lambda(λ).
- Ig contains either two κ or two λ light chains.
- In humans κ chains are more common.



Immunoglobulin G

- Single Y-shaped monomeric molecule.
- Most abundant75-80%
- It contains less carbohydrate than other Ig and half life of 23 days, longer than other Ig.
- Triggers foreign cell destruction mediated by complement system.



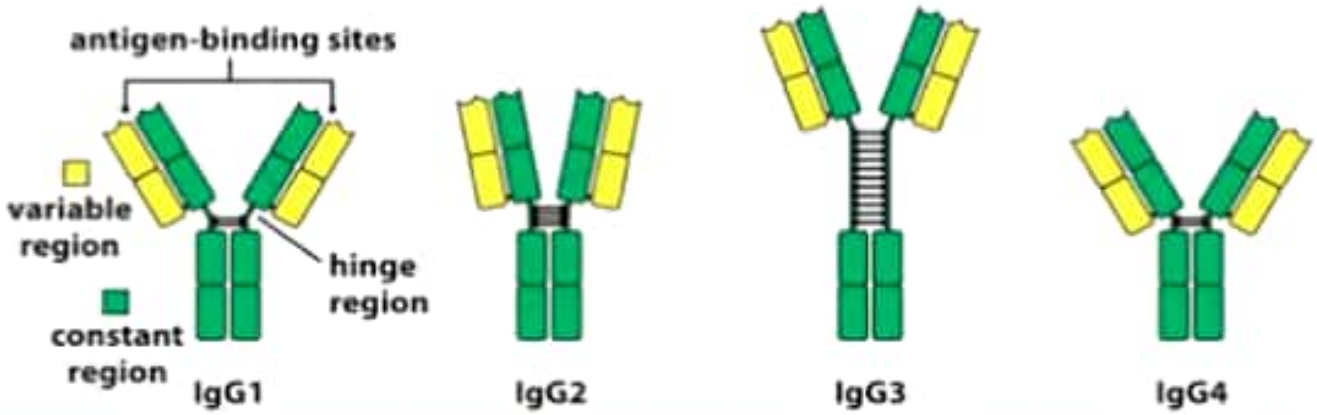
IgG

Four subclasses based on antigenic differences in H- chains and on number & location of disulfide bonds.

The capacity of a given individual to produce antibodies of one or another class is under genetic control.

Immunoglobulin G (IgG)

- Structure, Subclasses and Functions

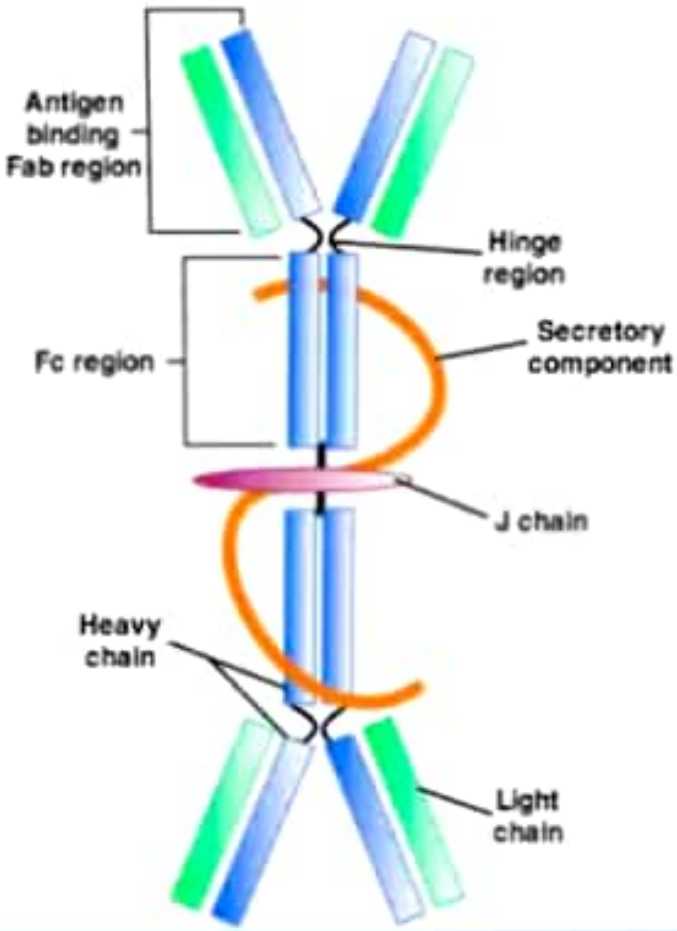


Functions of IgG

- Cross placenta and play an important role in protecting developing fetus.(IgG_1,IgG_3,IgG_4)
- Activates complement(IgG_3)
- Antibody dependent cell mediated cytotoxicity.
- Opsonization (IgG_1,IgG_3)
- Feedback inhibition of B-cell.

Immunoglobulin A(IgA)

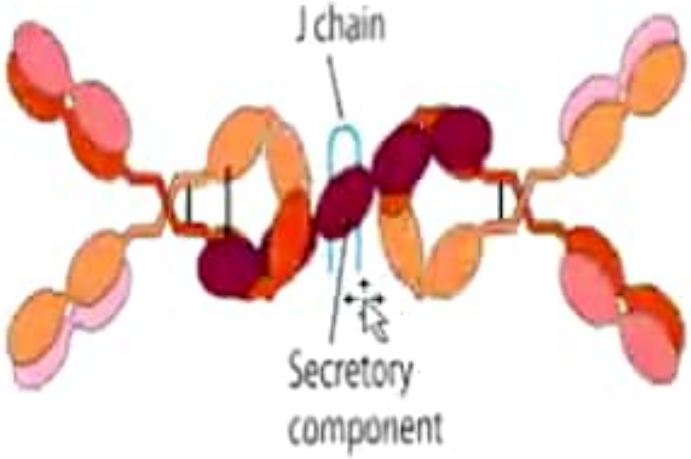
- Constitute 10-15% of total immunoglobulin.
- Occurs in two forms
- Secretory IgA
- Serum IgA
- Secretary IgA is dimeric molecule formed by two monomer units, joined together at their carboxy terminals by a protein termed J-chains.
- Half life is 6-8 days



Secretary IgA has a secretary component attached to dimer, transport protein (T-piece).

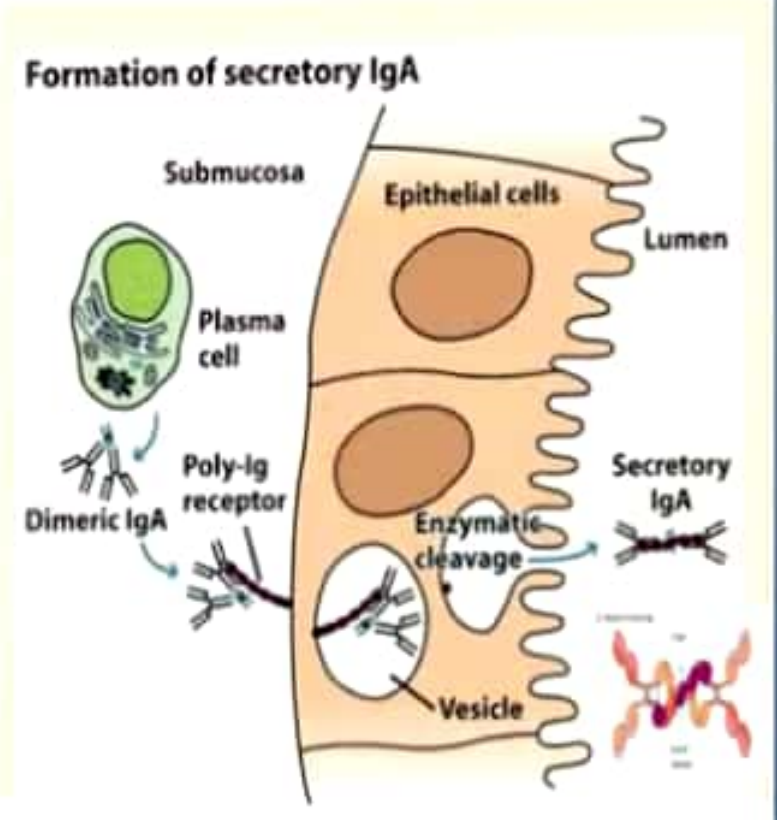
- It provides passage for IgA to the mucosal surfaces and
- protects it from degradation.

(a) Structure of secretory IgA

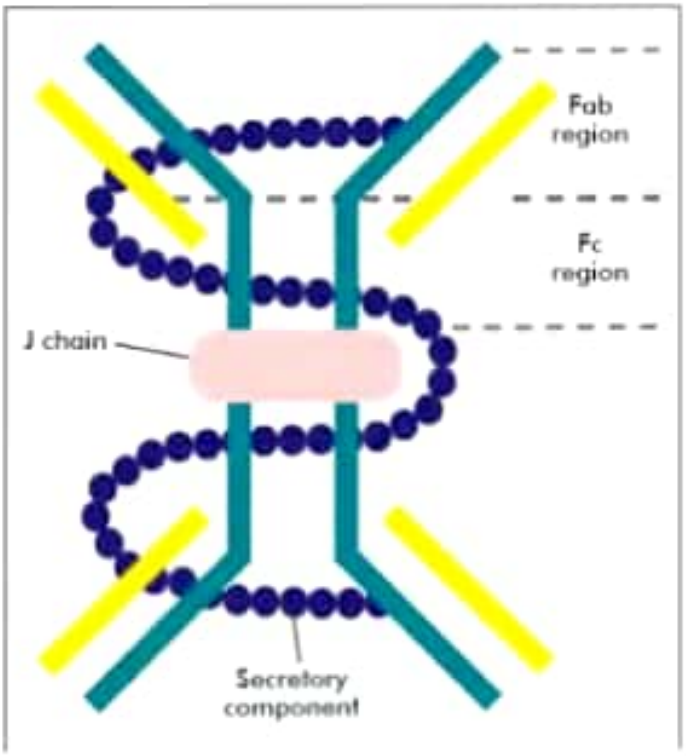


Formation of IgA

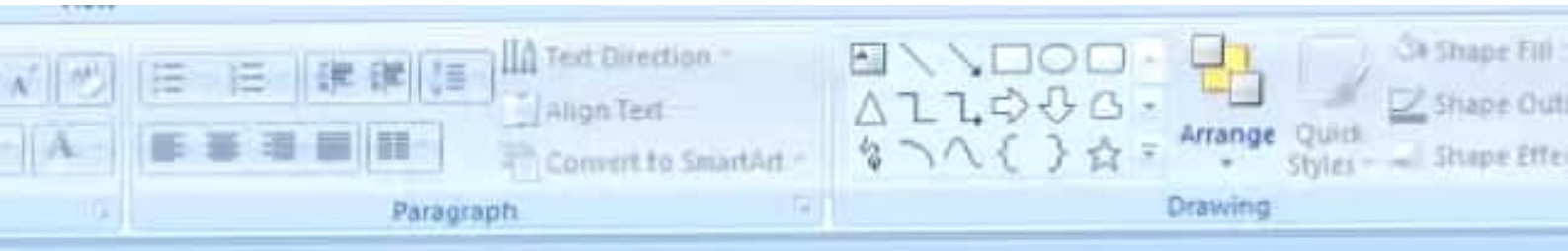
- Dimeric IgA binds to the receptor on the surface of epithelial cells, endocytosed and transported across the cell to luminal surface.
- After reaching the surface the poly-IgA receptor cleaved and become secretary component.



Secretary IgA is found in secretions such as saliva, tears, sweat, colostrums, prostatic secretions, nasal, bronchial secretions and walls of the intestine.



Serum IgA exists as monomeric form.
It is found in internal secretions such as synovial, amniotic, pleural and CSF.

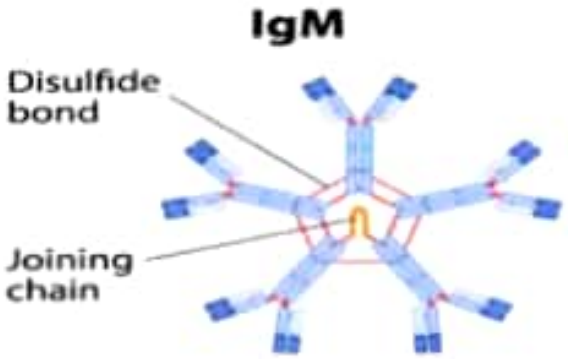


Functions

- Provide first line of defense against infections.
- Secretary IgA binds to micro organism and prevent their attachment to mucosal surfaces of respiratory and digestive tract, and prevent the access of foreign particles to the circulation.
- Provides defense against salmonella, Vibrio cholera, N-gonorrhoea and influenza etc.
- Protects newborn during first months of life.
- Promotes phagocytosis and intracellular killing of bacteria.
- Activates complement system.

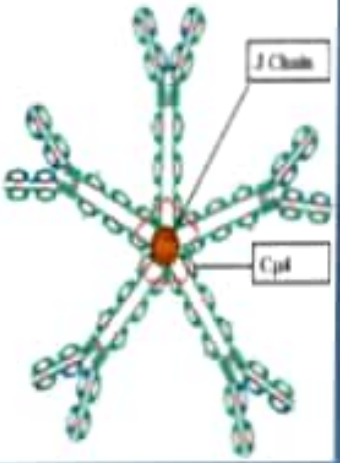
Immunoglobulin M(IgM)

- Accounts for 5-10% of total serum proteins.
- Polymer of 5 monomeric units.
- Held together by disulfide bonds and J chains.
- Largest immunoglobulin with mol-wt of 900,000-10,00,000.
- J chain is a small glycopeptide with an unusually high content of aspartic acid and glutamic acid .

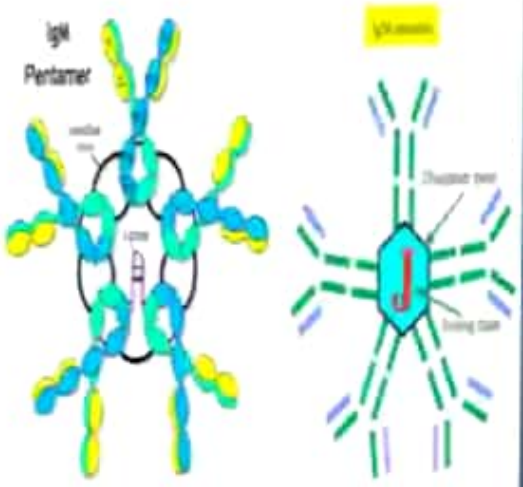


IgM

- Structure
  - Pentamer (19S)
  - Extra domain (C_{H4})
  - J chain



- Most of IgM is present intravascullarly(80%)
- Low concentration in intracellular tissue fluids.
- Can not cross placenta.
- First Ig made by fetus and B cells.
- Presence of IgM in newborn indicate congenital infection.



Dr Gulnaz

You

Dr

Dr

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Shandana

S

116 others

- First immunoglobulin to be produced in response to antigen. Its presence indicates recent infection.

- It agglutinates bacteria.
- Activates complement system.
- Causes opsonization and immune hemolysis.
- Protects against blood invasion by microorganisms.

- The natural blood group antibodies, anti-A and anti-B are IgM.

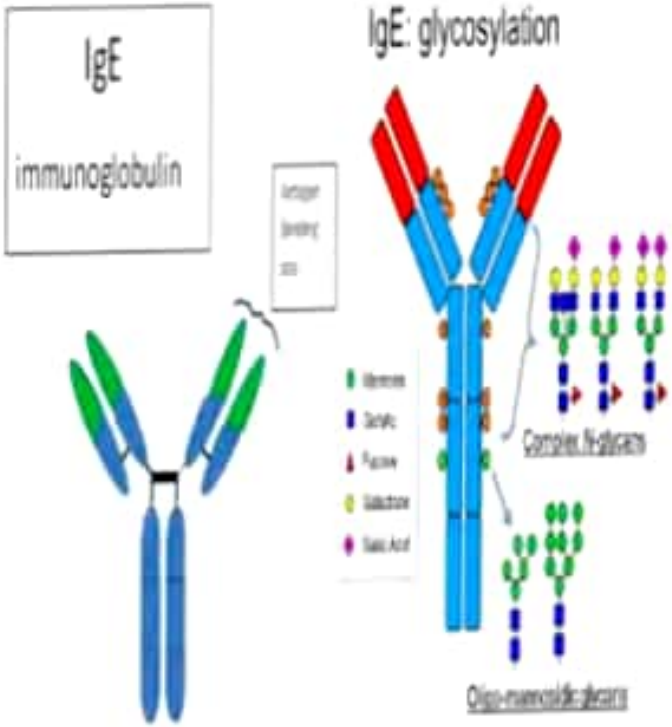
- First immunoglobulin to be produced in response to antigen. Its presence indicates recent infection.

- It agglutinates bacteria.
- Activates complement system.
- Causes opsonization and immune hemolysis.
- Protects against blood invasion by microorganisms.

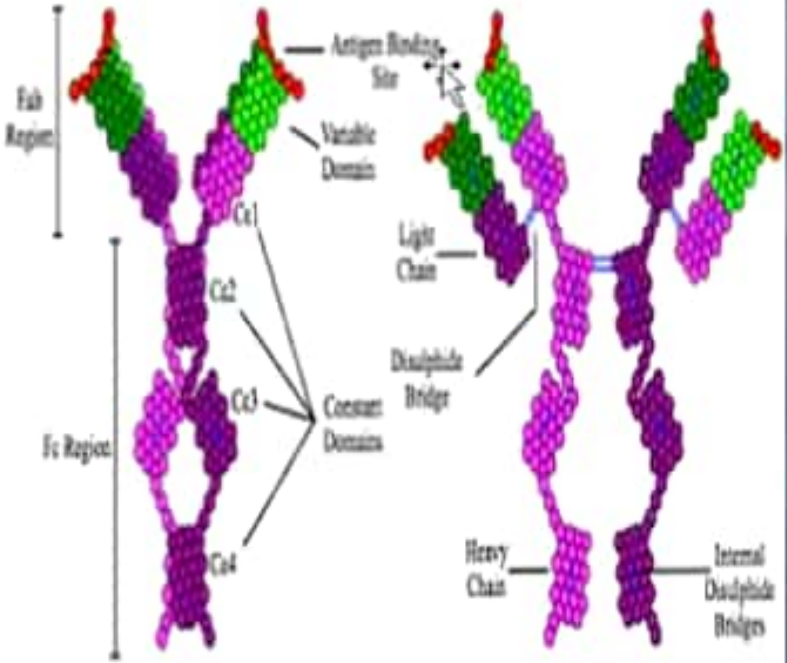
- The natural blood group antibodies, anti-A and anti-B are IgM.

Immunoglobulin E (IgE)

- Structurally similar to IgG.
- Has four constant region domains.
- Molecular wt 190,000
- Half life two days.
- Heat labile.
- Mostly present extracellularly.
- Does not cross placenta.

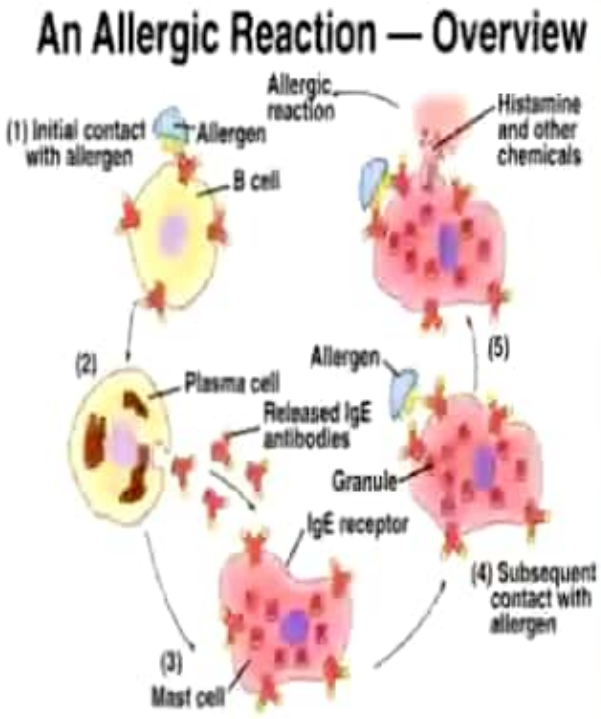


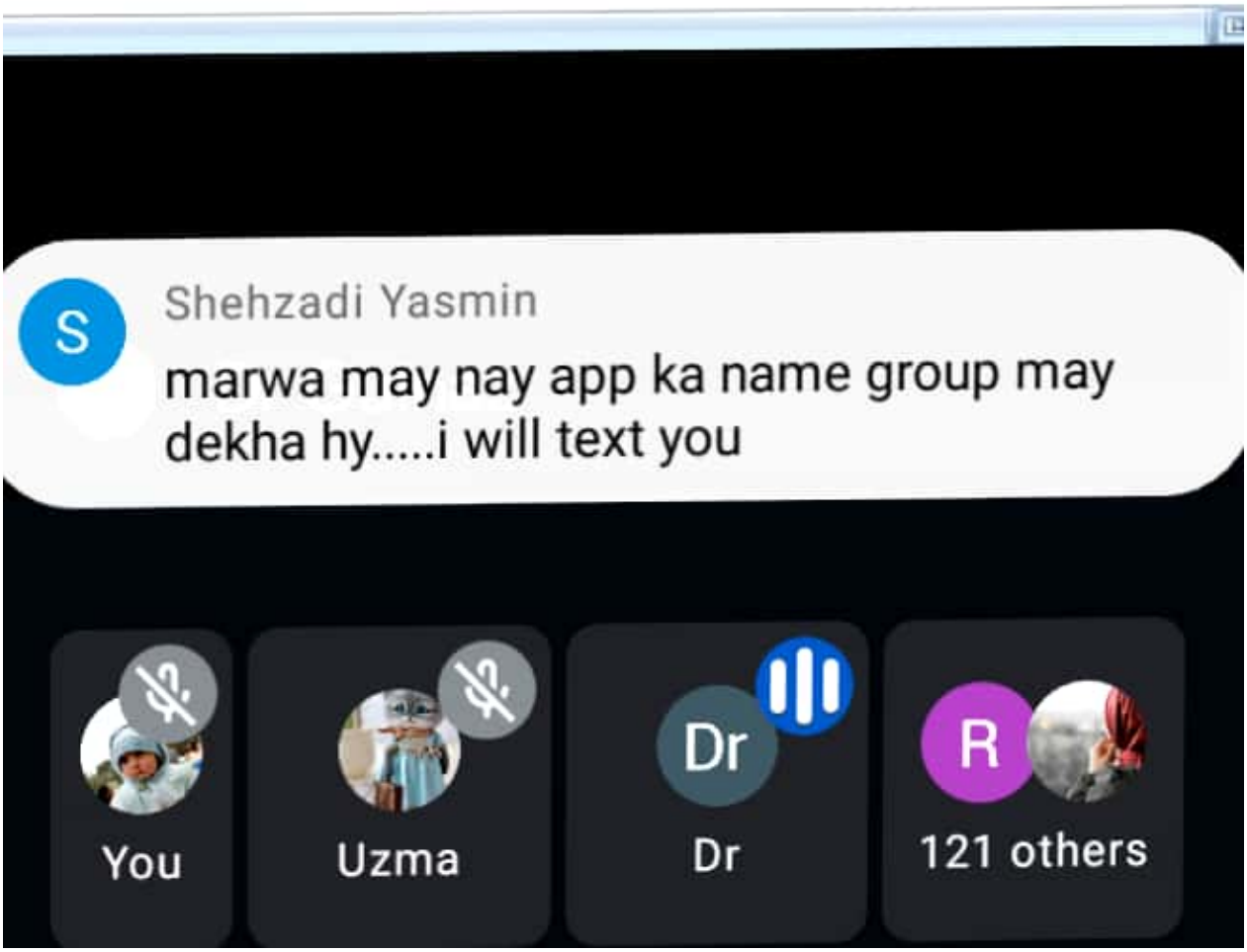
- IgE antibodies bind allergens through the Fab protein.
- Binding of IgE antibodies to tissue cells like mast cells occur at Fc portion.



Upon combination with allergens IgE triggers the release from mast cells the histamine which is responsible for the characteristic wheal and flare skin reactions evoked by the exposure of the skin of allergic individuals to allergens.

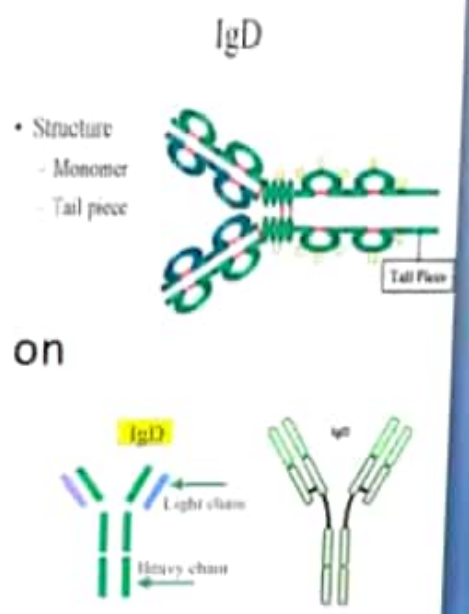
It protects against parasite such as halminthes, shistosomiasis by causing release of enzymes from eosinophil.





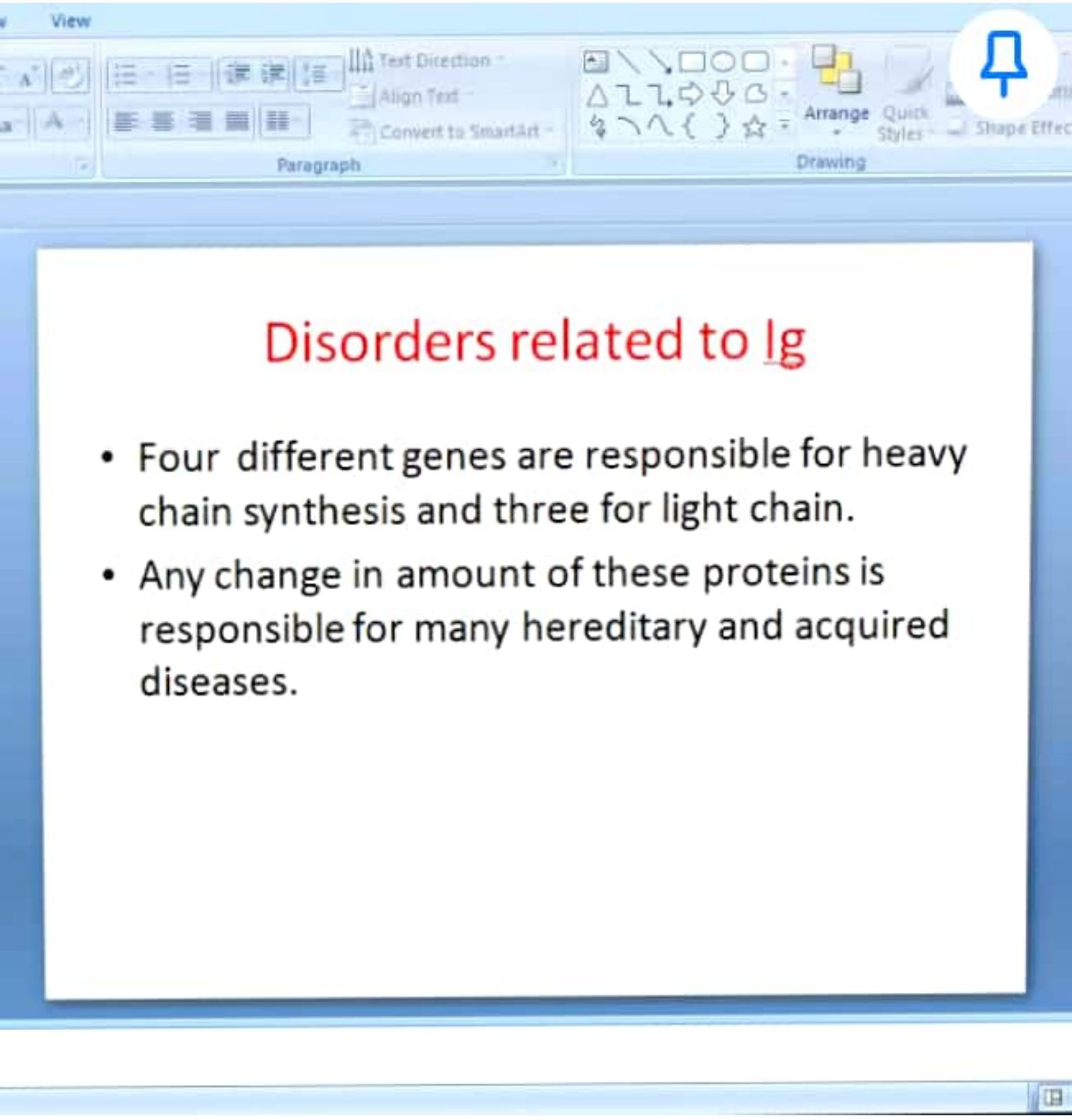
Immunoglobulin D (IgD)

- Structure similar to IgG.
- Constitute 0.2% of total immunoglobulin.
- Half life is 3 days.
- IgD along with IgM is the predominant immunoglobulin on the surface of human B lymphocytes and it has been suggested that IgD may be involved in differentiation of these cells.



IRAJ IKRAM joined

You | Eman | Dr | 121 others



MULTIPLE MYELOMA

- Plasma cell cancer
- Constitute 1% of all cancers.

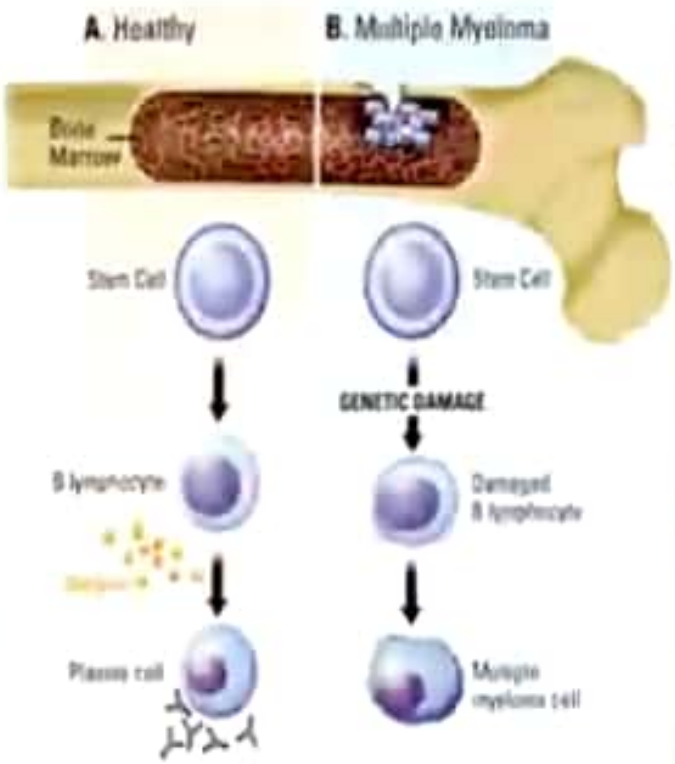
- Cause:

Overproduction of immunoglobulin , Sp IgG and IgA.

In some cases IgM & IgD.

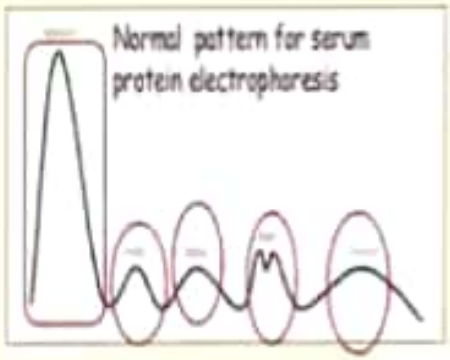
Mechanism of disease

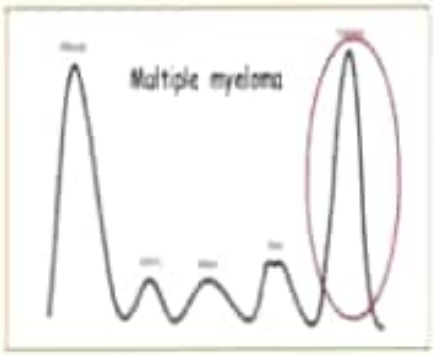
- Plasma cells infiltrated the bone marrow & produce abnormal & excessive amount of Ig(myloma proteins).
- Plasma cells also produce excessive & abnormal amount of cytokines, which plays an important role in bone destruction.

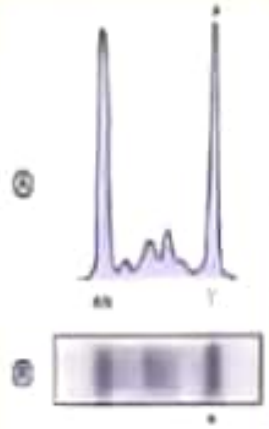


Diagnostic criteria

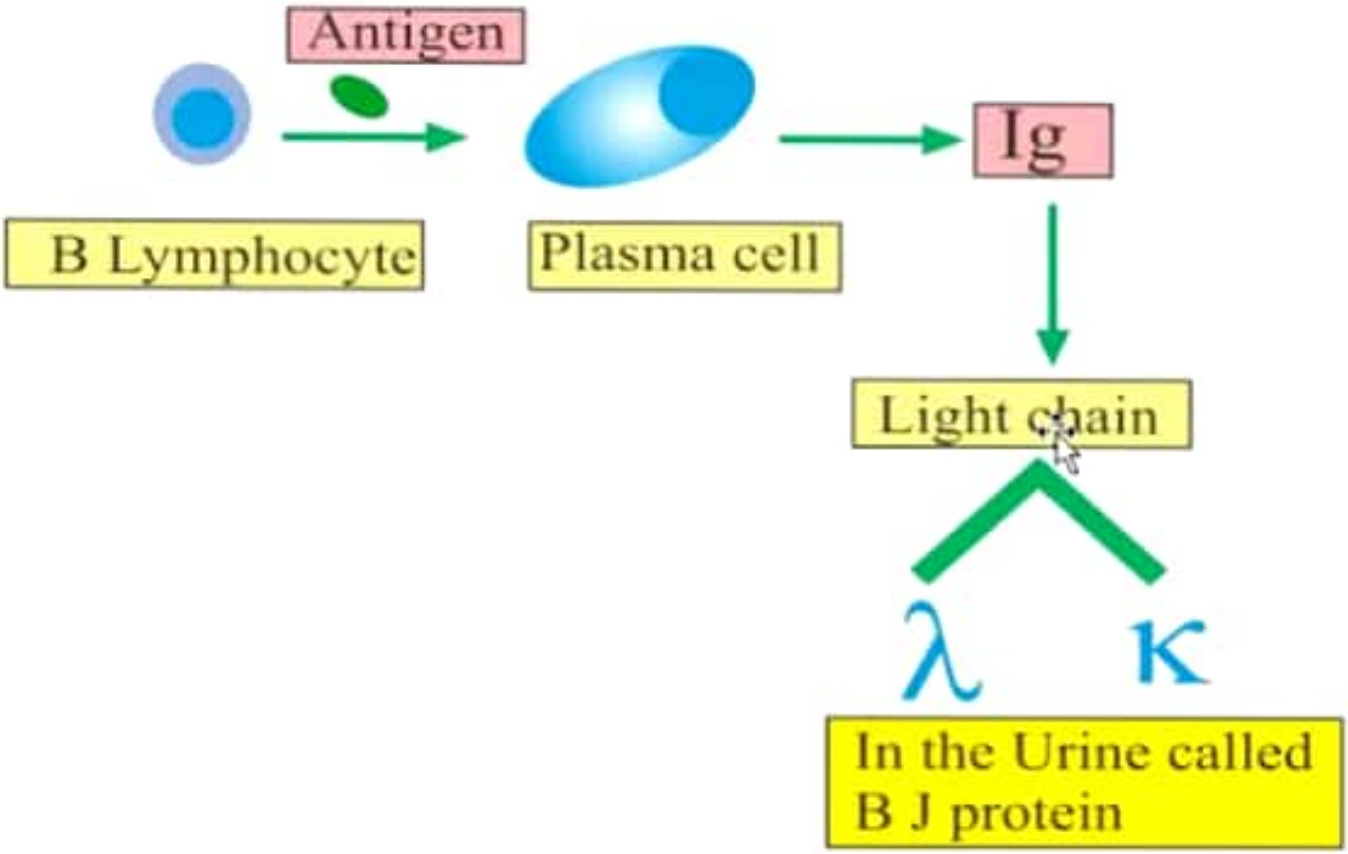
There is M-band
b/w
β and γ-globulin
band due to decrease
synthesis of normal
globulin.



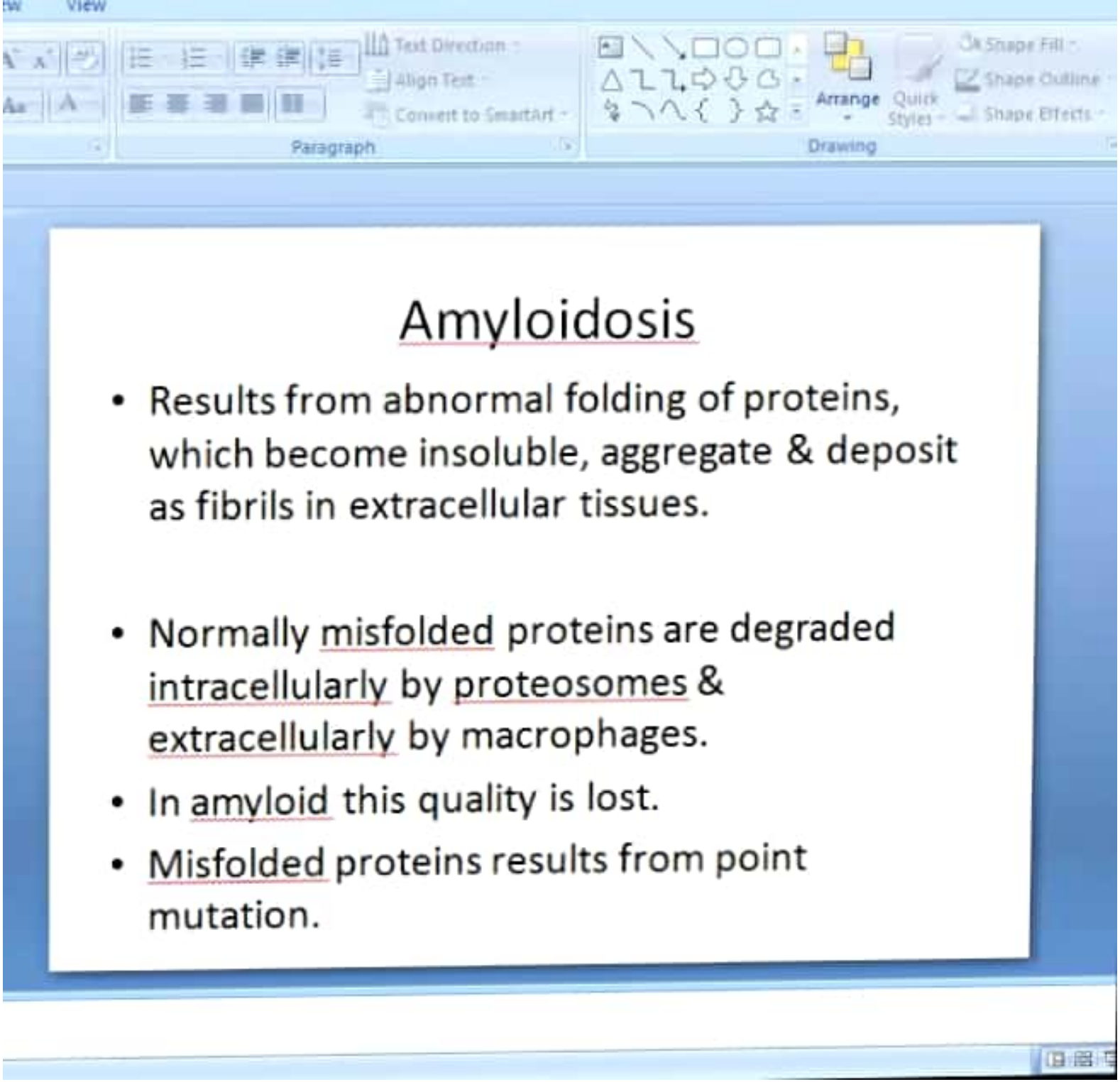




B.J. Proteins



- Found in multiple myloma patients.
- Precipitated on heating urine from 45-60^{0}C and re dissolve on heating above 80^{0}C.



Classification of Amyloidosis

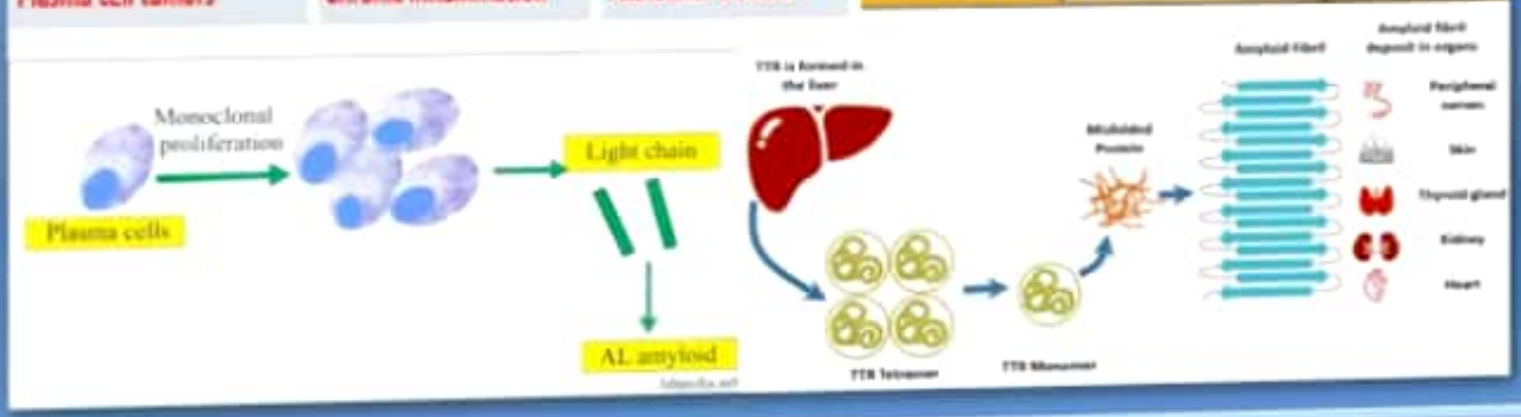
- Primary amyloidosis.
- Amyloidosis associated with multiple myloma.
- Secondary associated with inflammatory or infectious disease(serum amyloid a or SAA protein)
- Amyloidosis associated with aging.
- Familial amyloidosis.

BIO CHEMICAL FORMS

MAJOR

AL protein	AA protein	β Amyloid protein(Aβ)
Complete Ig light chains/amino terminal fragment of light chains/both Secreted by monoclonal population of plasma cells Plasma cell tumors	Non Immunoglobulin Derived from SAA protein which is synthesized from liver Acute phase protein Chronic inflammation	Derived from proteolysis of Amyloid precursor protein transmembrane glycoprotein Alzheimer disease

TYPE	SOURCE of AMYLOID	ORGANS INVOLVED
AL (Primary) Amyloidosis	Bone Marrow (Light chains produced by plasma cells)	Kidneys, Heart, Liver, GI system, Nervous system
AA (Secondary) Amyloidosis	Circulating inflammatory protein (Serum amyloid A)	Kidneys, Liver
TTR (Familial) Amyloidosis	Unstable, mutant transthyretin produced in the liver	Nervous system, Heart
SSA (Senile systemic) Amyloidosis	Wild-type (normal) transthyretin	Heart



In-call messages

what is BJ protein??

m

mansha imran 4 min

Yes

Sumayya Rehman 4 min

Bence Jones Proteins

Z

Zohra Bibi Roll No 12 4 min

Light chains proteins in multiple myeloma patients

You 4 min

why or how they are produced?

You 2 min

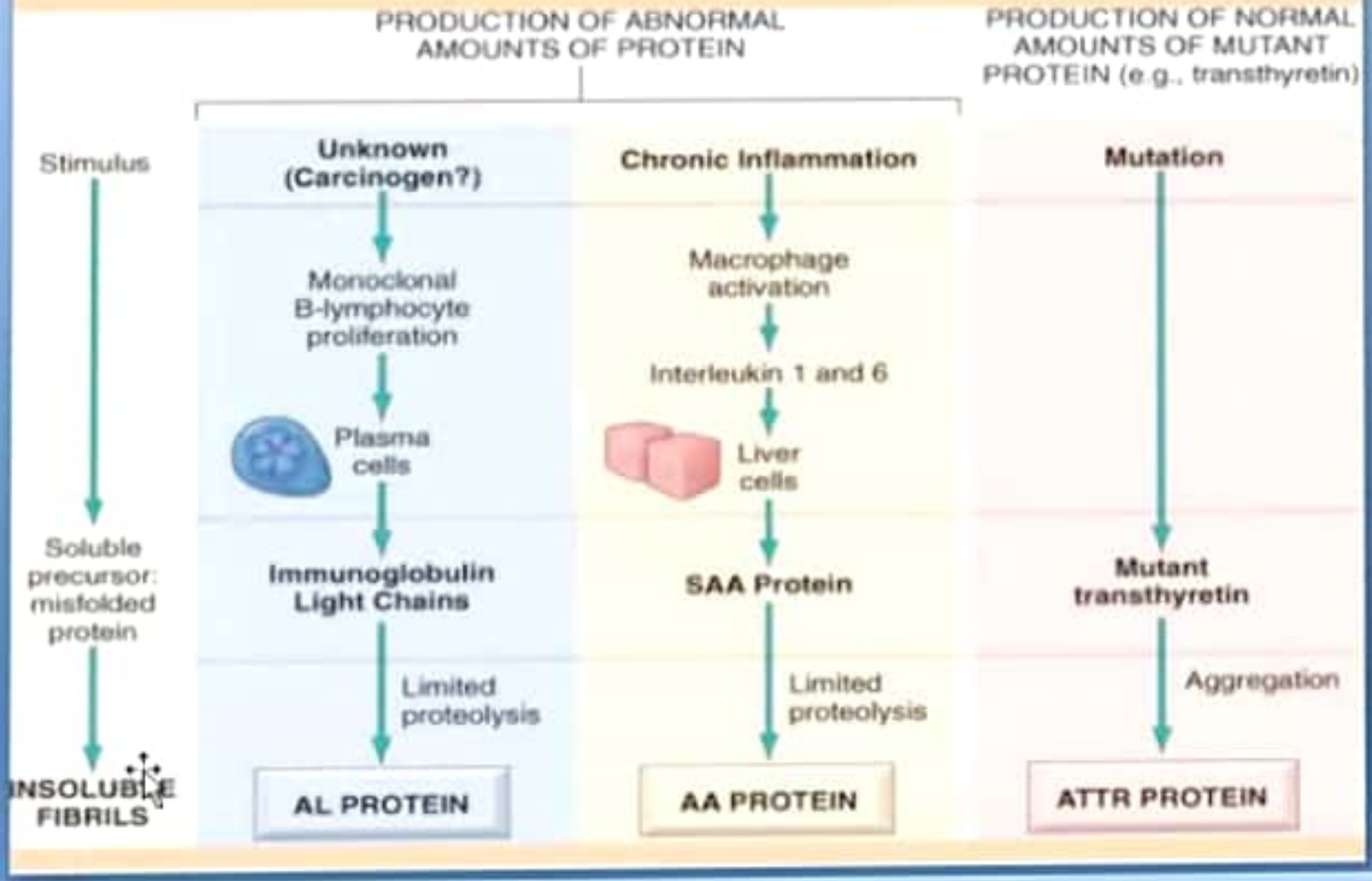
thanks summaye and zohra

Sumayya Rehman 1 min

too many light chains are made by ribosome, they enter the blood and due to small size, they are able to filter into the urine and precipitate at specific temperatures (this is how we identify them) so its also called light chain disease

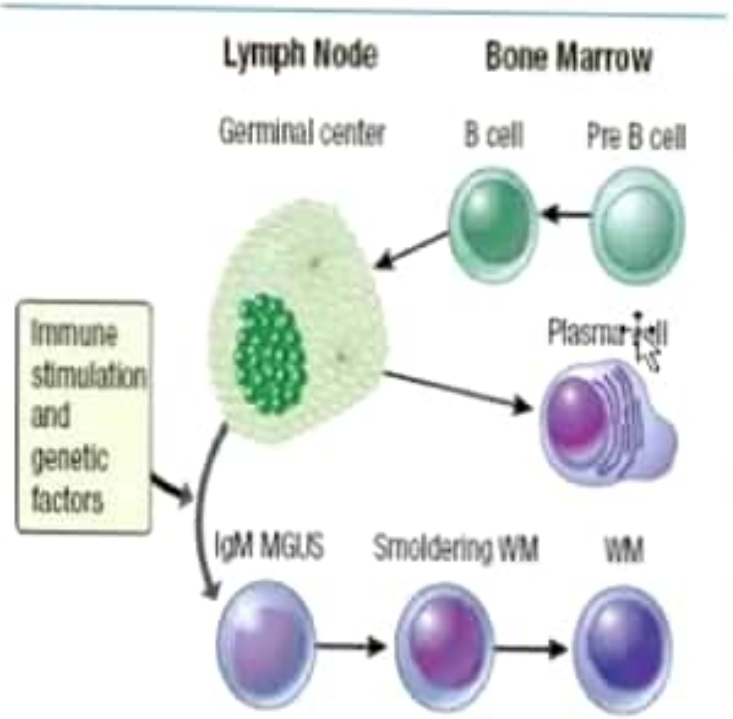
Send message

PATHOGENESIS OF AMYLOIDOSIS



Waldenstrom's Macroglobinemia

Malignant disease of lymphoid elements characterized by high serum concentration of IgM.



- Cryoglobinemia
- Cryoglobulin is serum IgM protein that ppts at temp lower than body temp.
- Pt develops peripheral thrombosis in cold weather.