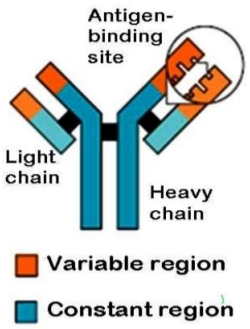
Introduction

• **Ab:**Proteins that recognize and bind to a particular antigen with very high specificity.
• Belong to a group of serum proteins called immunoglobulins (Igs).
• Ab is produced by B cells in response to a stimulation of Ag.
• Ab possesses a high degree of specificity and affinity
• Each antibody has at least two identical sites that bind antigen: Antigen binding sites.

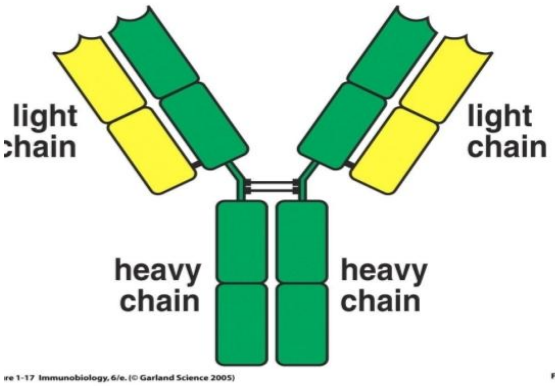
Antibodies Structure

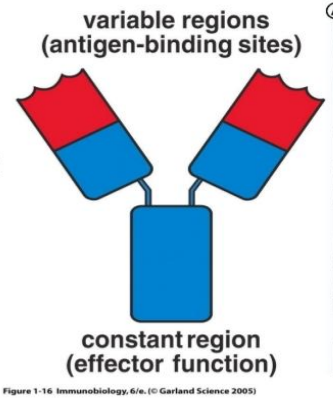
• Immunoglobulins are glycoproteins made up of Four polypeptide chains (IgG):
– Two light (L) polypeptide chains
– Two heavy (H) polypeptide chains
• The four chains are linked by disulfide bonds

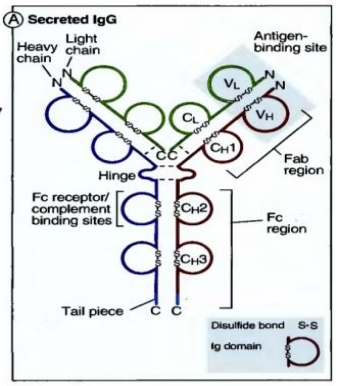


Variable (V) and Constant (C) Regions

• Each H-chain and each L-chain has V-region and C-region
1. V region: Terminal portion of L-chain and terminal portion of H-chain compose antigen binding site and located within the "Fab" fragment of antibody.It shows wide variation in amino acid sequences
2. C-region: lies in the carboxyl or terminal portion of the molecule. C-region shows an unvarying amino acid sequence and forms Fc fragments. It is responsible for biological functions.
• An antibody molecule is composed of two identical Ig heavy chains (H) and two identical light chains(L), each with a variable region (V) & constant region.



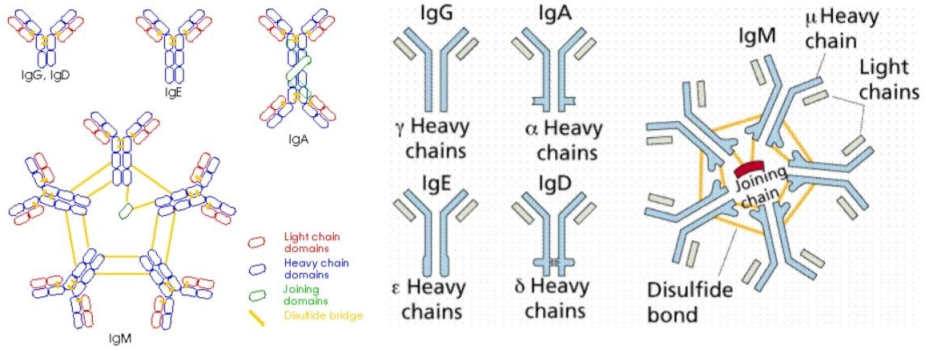


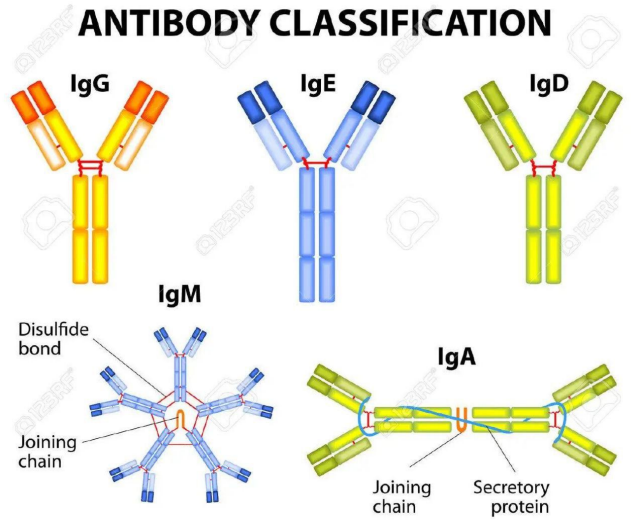


- **Five classes of Antibodies:**

1. IgG
2. IgM
3. IgA
4. IgD
5. IgE

H-chains are distinct for each of the five Immunoglobulins

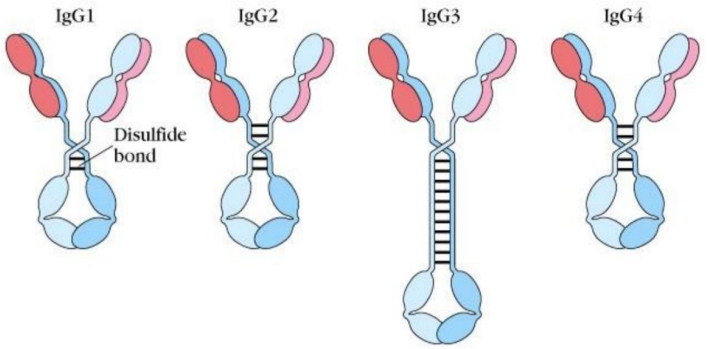




1. IgG

• Structure: Monomer
• Percentage serum antibodies: 80%
• Location: Blood, lymph, intestine
• Half-life in serum: 23 days
• Complement Fixation: Yes
• Placental Transfer: Yes
• Known Functions: Enhances phagocytosis, neutralizes toxins and viruses, protects fetus and newborn.

Four subclasses: IgG1, IgG2, IgG3, IgG4



2. IgM

• Structure: Pentamer
• Percentage serum antibodies: 5-10%
• Location: Blood, lymph, B cell surface (monomer)
• Half-life in serum: 5 days
• Complement Fixation: Yes
• Placental Transfer: No
• Known Functions: First antibodies produced during an infection. Effective against microbes and agglutinating antigens.

3. IgA

• Structure: Dimer
• Percentage serum antibodies: 10-15%
• Location: Secretions (tears, saliva, intestine, milk), blood and lymph.
• Half-life in serum: 6 days
• Complement Fixation: No
• Placental Transfer: No

• Two subclasses : IgA1, IgA2
• Known Functions: Localized protection of mucosal surfaces. Provides immunity to infant digestive tract

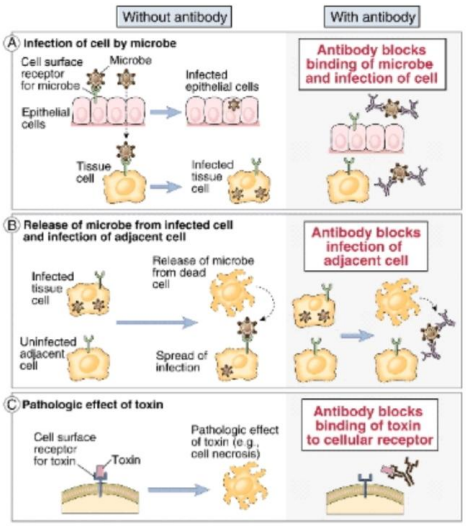
4. IgD
• Structure: Monomer
• Percentage serum antibodies: 0.2%
• Location: B-cell surface, blood, and lymph
• Half-life in serum: 3 days
• Complement Fixation: No
• Placental Transfer: No
• Known Functions: In serum function is unknown. On the B cell surface, initiate immune response.

5. IgE
• Structure: Monomer
• Percentage serum antibodies: 0.002%
• Location: Bound to mast cells and basophils throughout the body,Blood.
• Half-life in serum: 2 days
• Complement Fixation: No
• Placental Transfer: No
• Known Functions: Allergic reactions. Possibly lysis of worms.

Antibodies Functions
• Neutralization: Bind antigen- neutralize toxins, virus particles
• Opsonization
• Complement activation- IgG,M
• ADCC
• Mast cells activation
• Transcytosis- movement across epithelial cells

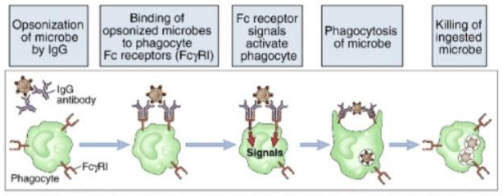
1. Neutralization
• The first step in a microbial infection involves attachment of the organism to the outside surface of the human body, either some part of the skin or the mucosal surfaces

• High-affinity antibodies that bind to the microbial ligand and prevent the microbe's attachment to human epithelium stop the infection before it starts
• Antibodies thus bind and inactivate foreign antigenic entities directly.



2. Opsonization

• Many bacteria are coated with polysaccharide → slippery and hard to endocytose
• But IgG can bind polysaccharide
• Macrophage can specifically bind IgG via FCγ receptor

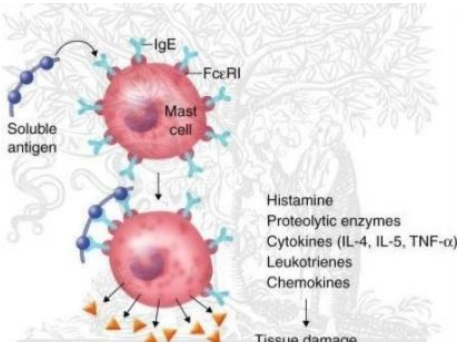


3. Complement Activation

• Classical: IgM or 2 adjacent IgG's binds to C1Q on bacterial surface results in cascade that can cause bacterial lysis
• Alternative: antibody binding attracts C3B →phagocytosis and opsonization

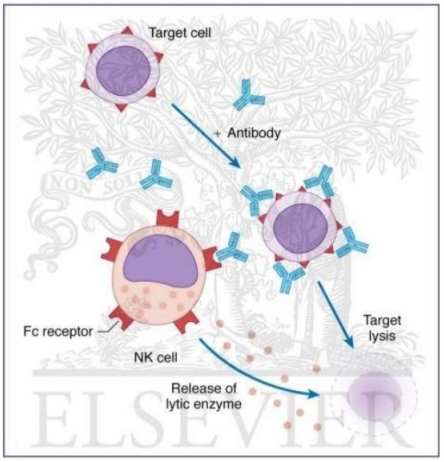
4. Mast Cell Activation

• IgE exists in serum at very low concentration (ng/ml)
• IgE binds to FC-ε receptors on Mast, Basophil, and Langerhan cells
• Antigen cross links bound antibodies →degranulation and release of histamine, heparin, proteases, chemotaxins which attracts WBC's
• This induce Phospholipase activity → mucus production, sneezing and other allergic symptoms



5. ADCC: Antibody-Dependent Cell Mediated Cytotoxicity

• IgG binds target cell (virally infected or tumorigenic)
• FC-γR on NK (non B, non T, natural killers) bind IgG
• Crosslinking of receptors →perforin/protease release by NK



6. Transport/transcytosis

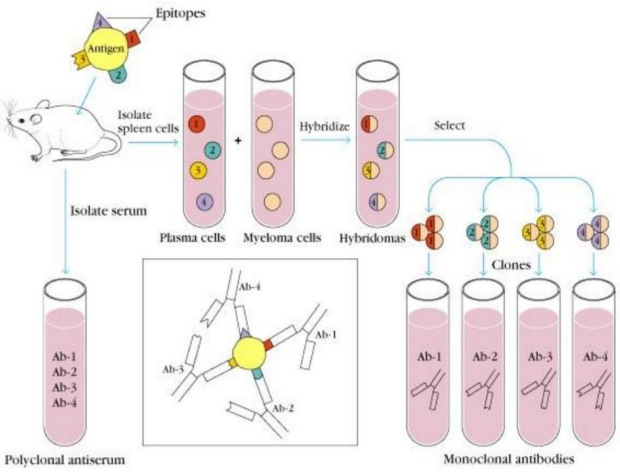
• Submucosal lymphoid follicles secretes IgA (trachea, for example)
• Epithelial M cells phagocytose/pinocytose foreign particles in lumen transport digested antigens into follicle and stimulate antibody production
• Placental transport: active transport of IgG across placenta give protection for baby up to six months

Artificial Antibodies

• Antibodies made artificially
• Two types:
1. Polyclonal Ab:
– A mixture Ab with different specificities and affinities
– Generate in a natural response or artificial immunization
2. Monoclonal Ab:
– Ab produced by single clone (or one hybridoma clone) and having a single specificity

Monoclonal Ab Applications

• Diagnostic Tests
– mAbs are capable to detect tiny amounts (pg/mL) of molecules
– Ex. Pregnancy hormones
• Diagnostic Imaging
– mAbs that recognize tumor antigens are radiolabeled with iodine I-131
• Immunotoxins
– mAbs conjugated with toxins
• mAbs To Clear Pathogens
• mAbs for treatment (thrombotic diseases, cancer..)



Artificial antibodies

POLYCLONAL.	MONOCLONAL.
Derived from different B Lymphocytes cell lines	Derived from a single B cell clone
Batch to Batch variation affecting Ab reactivity & titre	mAb offer Reproducible, Predictable & Potentially inexhaustible supply of Ab with exquisite specificity
NOT Powerful tools for clinical diagnostic tests	Enable the development of secure immunoassay systems.

Done by:Dr.mohammed farhoud

A patient is treated with humanized monoclonal antibody against his tumor cells. This antibody molecule is genetically engineered such that the mouse portion that determines antigen specificity is transcribed and translated with the remainder of the antibody molecule derived from human. The portion from the mouse antibody would be found in which of the following?

a. μ chain only.
b. allotype.
c. variable region.
d. kappa chain.
e. isotype.

The sibling of a child with strep throat is tested for antistreptococcal antibodies and found to have none (neither IgM nor IgG). Which of the following is one possible interpretation of these results?

a. The sibling has a memory response.
b. The sibling had previous exposure to the bacteria.
c. The sibling was tested during the latent period.
d. The sibling recovered quickly from the infection, already clearing the bacteria.

A 2-year-old child with a sore throat is tested for antistreptococcal antibody to see if the infection is due to this bacterium. The child is found to have only IgG antibodies to this organism with no detectable IgM. This indicates which of the following?

a. remote, not a current, infection with streptococcus.
b. passive transfer of maternal IgG across the placenta.
c. an immunodeficiency disease in which only IgM is lacking.
d. overwhelming infection with streptococcus.

Ans:C/C/A