

Antibody

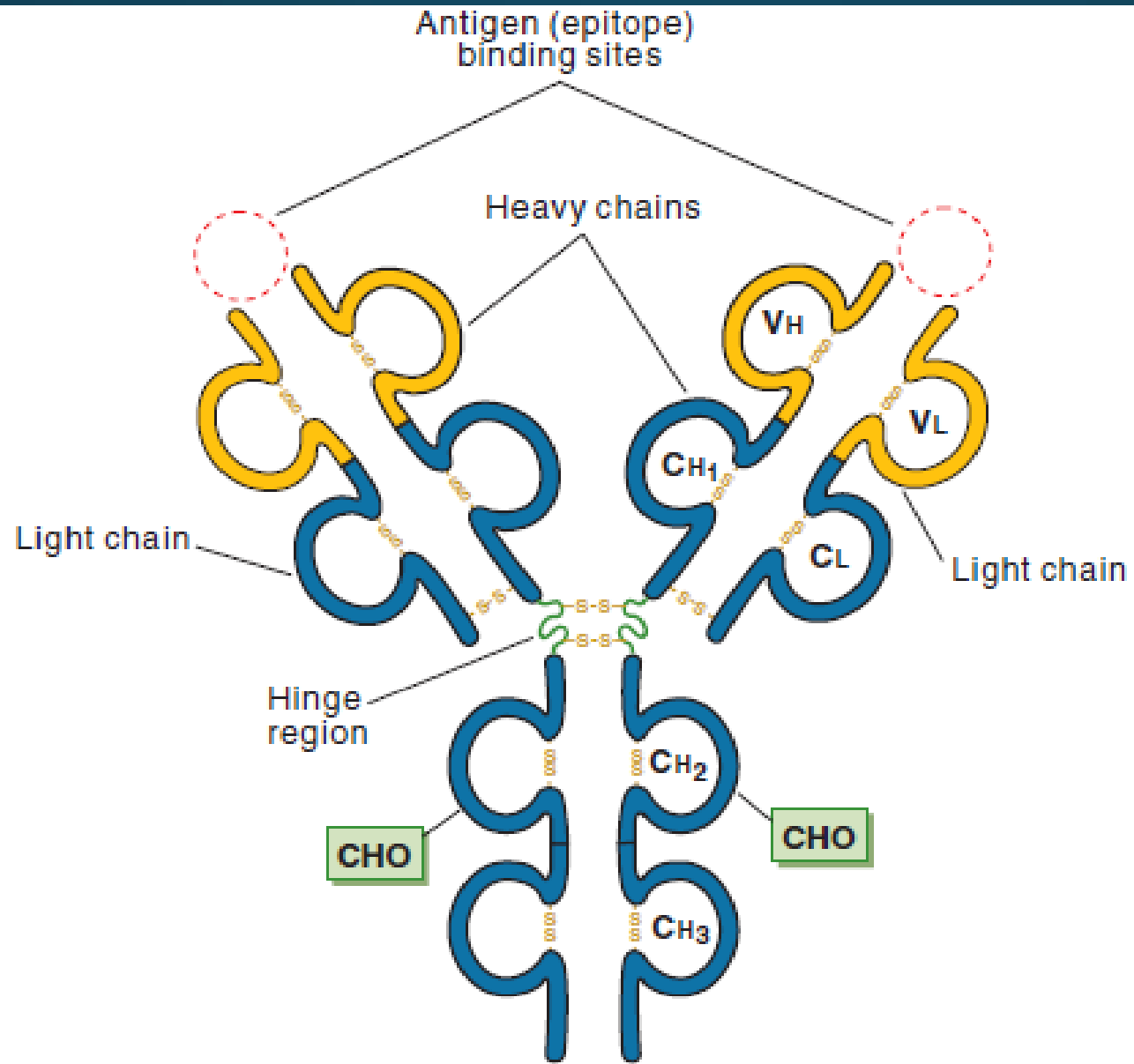
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Definition

- Antibodies are mucoproteins that are found mainly in the gamma-globulin fraction of serum on electrophoresis. When injected into animals, human immunoglobulin, being foreign, becomes antigenic. The resulting antihuman antibodies are grouped into five classes: IgG, IgA, IgM, IgE, IgD.

Structure

- The basic structural unit for each class is a four-chain protein with **two heavy (H)** and **two light (L) chain** polypeptides linked by disulphide bonds.
 - a. A differing, short amino acid sequence, specific for each of the **H chains**, permits differentiation into the five classes. These H-chain differences are called **isotypes** and are designated by the Greek letters gamma (γ), alpha (α), mu (μ), epsilon (ϵ), and delta (δ). Isotypes are genetic variations that all humans possess.
 - b. All five classes have an amino acid sequence in common on the **L chains**. Thus, they can be classified together as immunoglobulins. In addition, **two isotypes**, designated kappa (κ) and lambda (λ), exist for all five classes.



Domains

1. Both H and L chains are divided into constant region domains, designated CH and CL, and variable region domains designated VH and VL.
 - a. The amino acid sequence in the constant regions of both the H and L chains is similar for all antibody molecules within each class.
 - b. The amino acid sequence of the variable regions on both H and L chains varies with the epitope toward which the particular antibody is directed.
2. Amino acids that show marked differences between antibodies of different specificities form a hypervariable region within each variable region.

3. The hypervariable regions of both the H and L chains associate to form two epitope-binding regions known as the antibody **idiotype**.
4. A hinge region also exists between the CH₁ and CH₂ domains, permitting flexibility in the movement of the two antigen-binding sites.

Properties of Antibodies

Immunoglobulin G

1. Structural properties

a. IgG is composed of two L chains and two H chains.

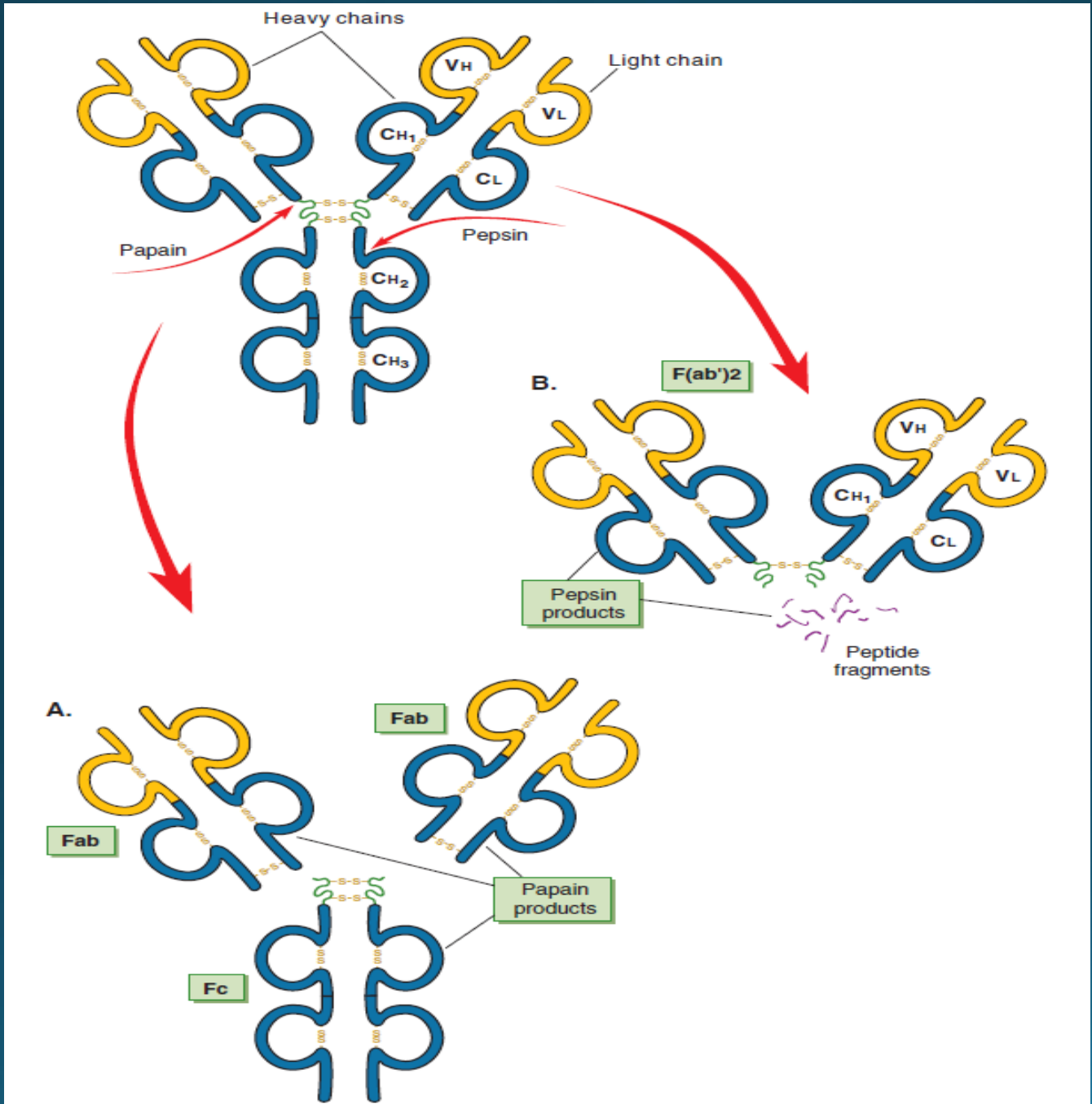
b. Enzymatic cleavage

(1) Papain splits IgG into three fragments.

(a) Two of these fragments, Fab (fragment, antigen binding) are similar, with each containing only one of the reactive sites for the epitope. Because Fab is monovalent, it can bind to but cannot enter into lattice formation and precipitate or agglutinate antigen.

(b) A third fragment (Fc, crystallizable) activates complement, controls catabolism of IgG, fixes IgG to tissues or cells via an Fc receptor, and mediates placental transfer of antibody.

(2) Pepsin splits behind the disulfide bond, joining the two H chains, permitting the two Fab fragments to remain joined. Consequently this fragment is termed $F(\bar{a}b')_2$.



2. Functional properties

- a. IgG has the highest serum concentration of all immunoglobulins (700 to 1500 mg%) and a serum half life of 18 to 25 days.
- b. IgG adheres to cells that possess a receptor for the Fc fragment from IgG (Fcγ).
- c. IgG fixes complement, a series of enzymes resulting in cell lysis.
- d. IgG mediates placental passage of maternal antibody to the fetus.

Immunoglobulin M

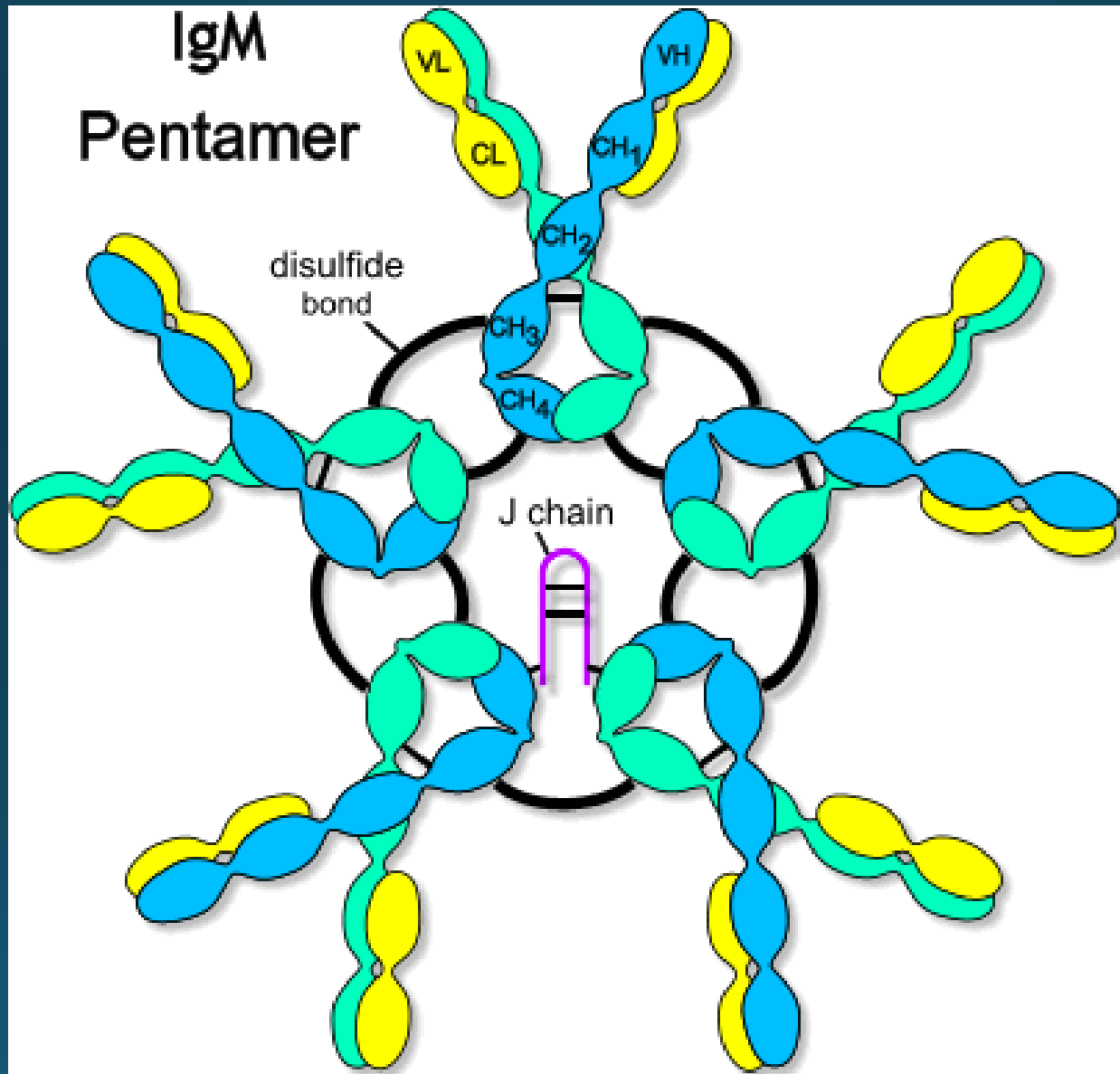
1. Structural properties

IgM exists in two structural forms:

- (1) A monomer is synthesized by B cells and retained on its membrane.
- (2) Secreted IgM exists as a pentamer (i.e., five monomeric IgM molecules joined together by a J chain).
 - (a) The pentamer is secreted following antigen and cytokine activation of B cells, with the hypervariable regions on the pentamer the same as those on the membrane bound monomeric receptor.
 - (b) Of the 10 possible epitope-binding sites on the pentamer, five are of high affinity and five are of low affinity.

2. **Functional properties** IgM, the earliest antibody to appear after antigenic stimulus, fixes complement avidly.

IgM Pentamer



Immunoglobulin A

1. Structural properties

IgA exists in three forms: a monomer, a dimer (in which a J chain joins two monomers; and a dimer plus a secretory piece.

(1) The dimer is transported across respiratory and intestinal mucosal barriers into the lumen by the secretory piece, which is a receptor for the IgA Fc region ($Fc\alpha R$) on the mucosal epithelium.

(2) The secretory piece also protects IgA from proteolysis.

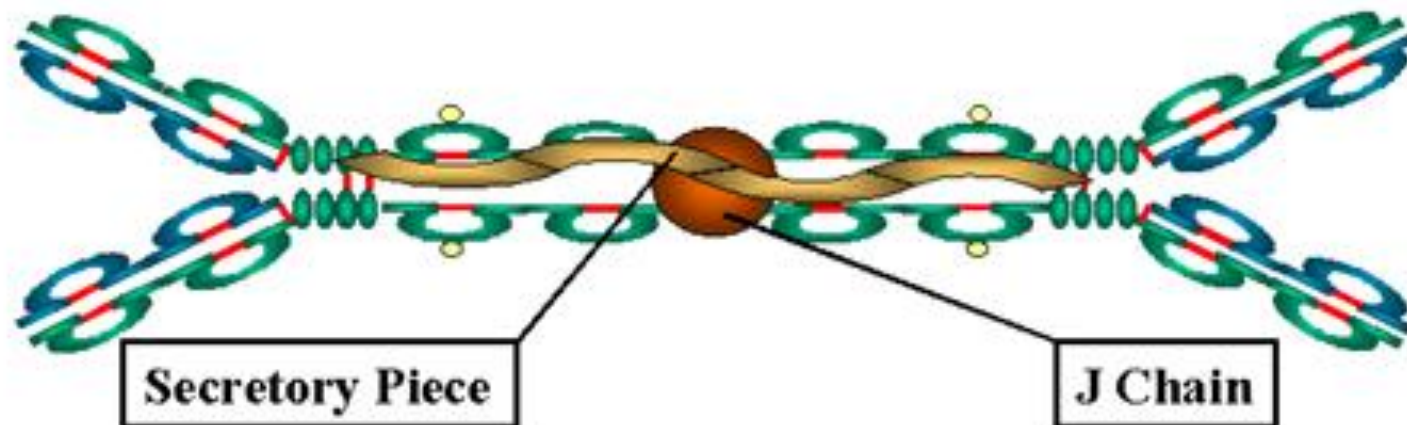
2. Functional properties

a. IgA is found in high concentrations in secretions; in serum, IgA exists mainly as a dimer with a half-life of 5 days.

b. IgA is located in and protects mucosal tissues, saliva, tears, and colostrum by blocking bacteria, viruses, and toxins from binding to host cells.

IgA

- Structure
 - Serum - monomer
 - Secretions (sIgA)
 - Dimer (11S)
 - J chain
 - Secretory component



Immunoglobulin E

1. Structural properties

- a. The IgE molecule is unstable at 56C and is called reagin.
- b. IL 4 mediates the B-cell switch to IgE production.

2. Functional properties

- a. IgE Fc region binds avidly to mast cells and basophils.
- b. IgE triggers the release of vasoactive amines (mainly histamine), resulting in atopic disease characterized by hives (a local reaction) and anaphylaxis (a systemic reaction).
- c. IgE does not cross the placenta or fix complement by the conventional pathway.
- d. The binding of IgE to IL 5 activated eosinophils results in elimination of parasitic Helminths.
- e. Both total and allergen specific IgE can be quantified.

. Immunoglobulin D

Functional properties

- a. IgD is found on the B-cell membranes of 15% of newborns and again on adult peripheral blood lymphocytes in conjunction with IgM; serum levels are very low. The serum half-life is 2 to 3 days.
- b. IgD is a receptor on B-cell membranes for antigen.