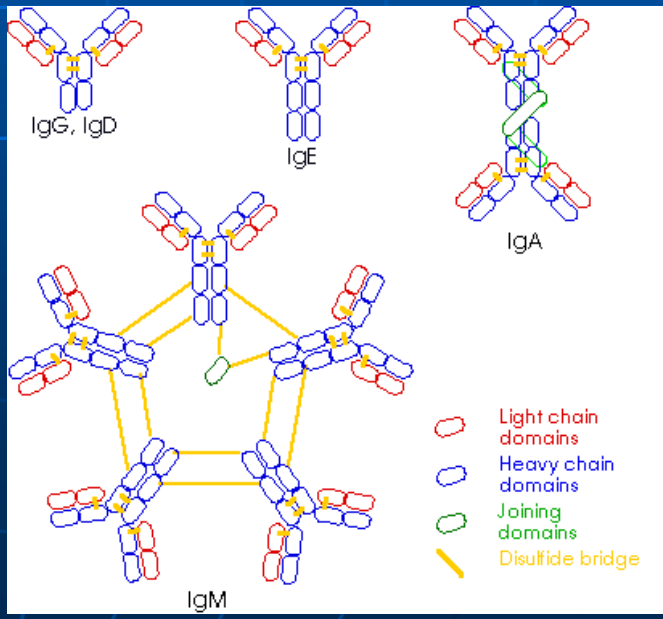
Antibodies or Immunoglobulins

* **Definition:**
  Glycoprotein in serum and tissue fluid

* **Produced by:**
  B-lymphocytes in response to exposure to antigen

* **React specifically with antigen**

* **Five classes of Antibodies:**
  IgG
  IgM
  IgA
  IgD
  IgE



IgG

Properties

- Major serum Ig
- Major Ig in extravascular spaces
- The only Placental transfer Ig
- Fixes complement
- Phagocytes - opsonization

IgM

Properties

- First Ig made by fetus and B cells
- Present in colostrum and mother milk protect newly born.
- Fixes complement

IgA

-Found in serum and body secretion:
Tears, saliva, gastric and pulmonary secretions

- Major secretory Ig on Mucous surfaces give Local Immunity by coating m.o, bacteria or viruses preventing their adherence to mucosal cells
- Does not fix complement (unless aggregated)
- Present in colostrum and mother milk protect newly born.

IgE

- Least common serum Ig
  - Binds to basophils and mast cells (Does not require Ag binding)
- Allergic and hypersensitivity reactions
- Parasitic infections (Helminths)
  - Binds to Fc receptor on eosinophils
- Does not fix complement

IgD

- Present in very small amount in serum
- B cell surface Ig
- Does not bind complement

Antibody Production

Clonal selection theory:

*B-cells display immunoglobulin molecules on surfaces

*Immunoglobulin serve as receptors for specific antigen

*The antigen binds to immunoglobulin receptor of B-cells

*B-cells is stimulated to divide and form a clone

*B-cells become plasma cells and secrete antibodies

*Some stimulated B-cells revert to small lymphocyte (memory cells)

*Memory cells proliferate on re-exposure to same antigen

Activation of B-cells

Two mechanisms:

1) T-dependent antigen:

. Most antigen require T-helper cells to activate B-cells

. Antigen is phagocytosed by macrophages or B-cells

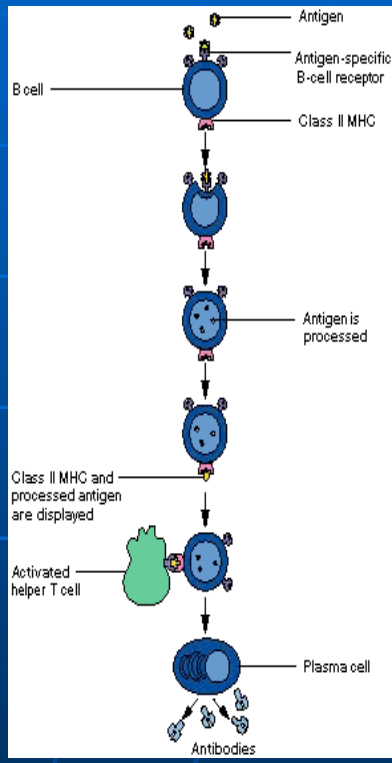
. Macrophages or B process present Ag to T-cells

. These activate T-cells to produce lymphokines

. lymphokines (IL-2,IL-4,IL,5) stimulate B-cells to divide and differentiate into plasma cells

. Plasma cells form → specific antibody
or → differentiate into memory cells

. All classes of antibody (IgG,IgM,IgA,IgD,IgE) are T-cell dependant



Activation of B-cells

2) T-independent antigens:

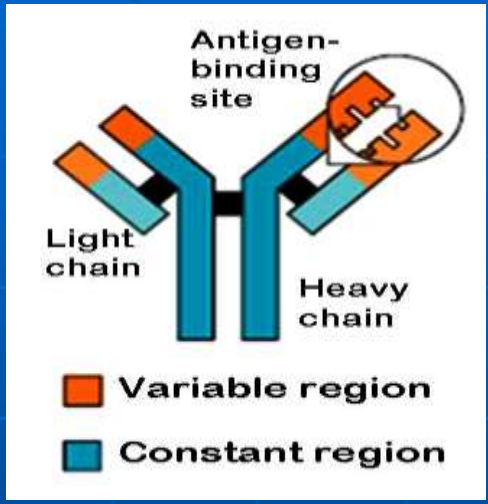
- Activation of B-cells directly without help of T-cells (e.g. bacterial capsular polysaccharides)

- IgM antibody is primarily produced

Antibody Structure

Immunoglobulins are glycoproteins made up of

- Four polypeptid chains (IgG):
  - a- Two light (L) polypeptide chains
  - b- Two heavy (H) polypeptide chains



- The four chains are linked by disulfide bonds

- Terminal portion of L-chain contains part of antigen binding site

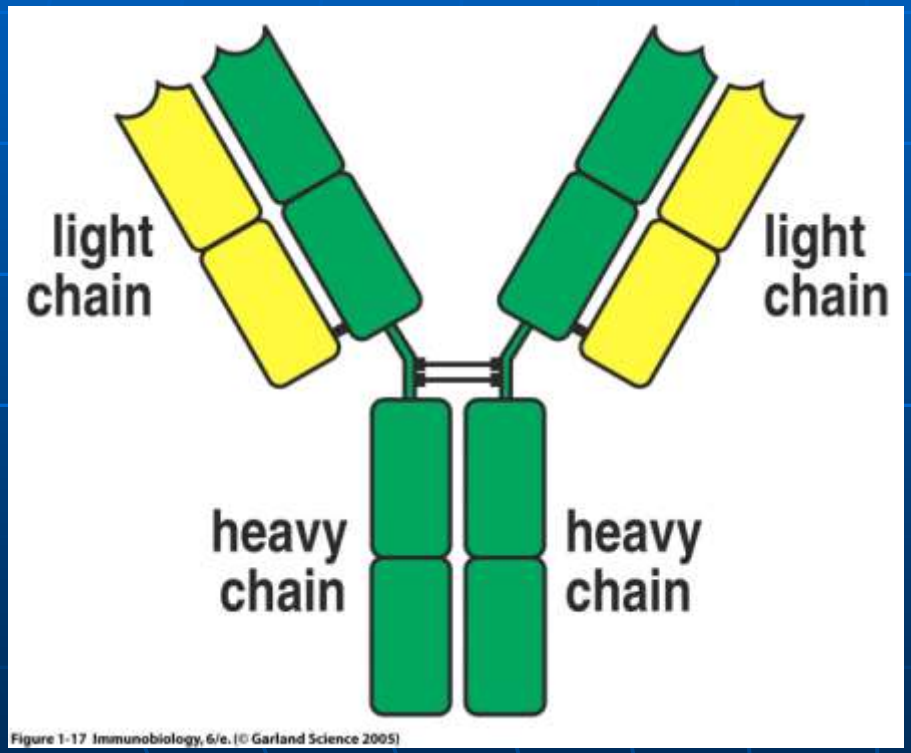
- H-chains are distinct for each of the five immunoglobulins

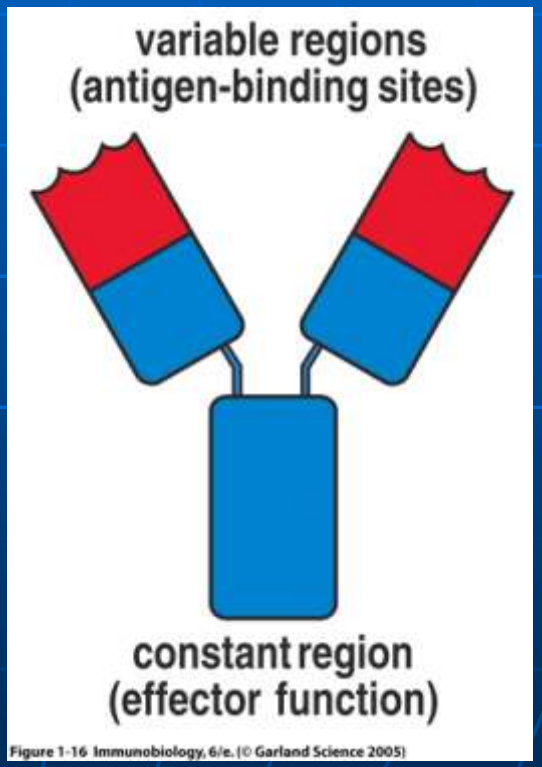
- Terminal portion of H-chain participate in antigen binding site

- The other (Carboxyl) terminal portion forms Fc fragment

ANTIBODY STRUCTURE

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 (C).



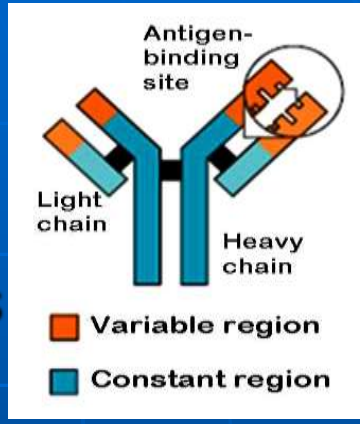


Amino acid sequences were determined from myeloma proteins.

Fig. 1-17,1-16

Variable(V) and Constant (C) Regions

- Each **H**-chain and each **L**-chain has **V**-region and **C**-region



- **V**-region lies in terminal portion of molecule
- **V**-region shows wide variation in amino a. sequences
- Hypervariable region form region complementary to Ag determinant
- It is responsible for antigen binding
- **C**-region lies in carboxyl or terminal portion of molecule
- **C**-region shows an unvarying amino acid sequence
- It is responsible for biologic functions

Antibody Fragments

- Fab fragment: antigen binding site

- Fc (crystallizable fragment):

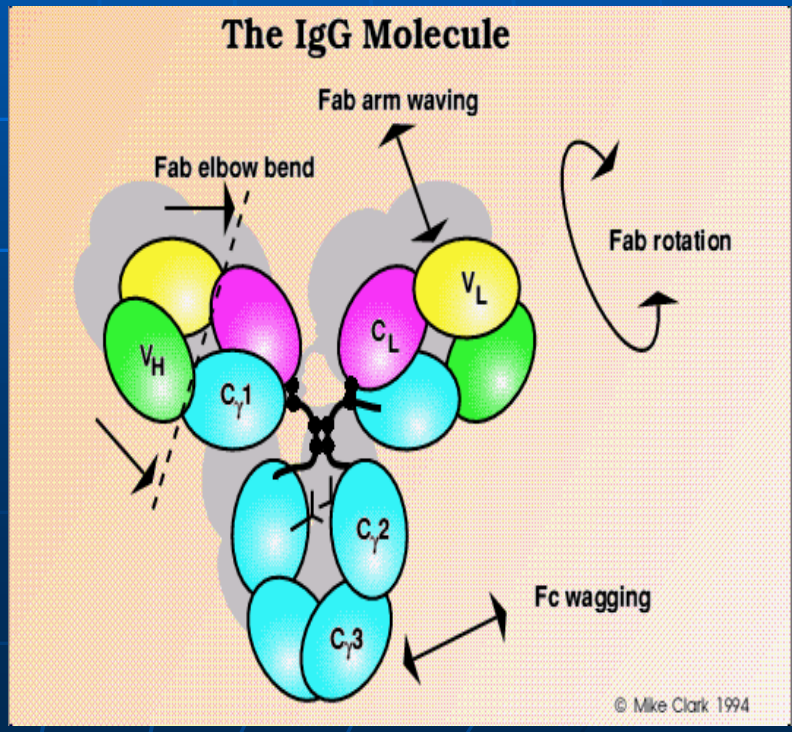
  a- Complement fixation (IgM and IgG)

  b- Opsonization (IgG)

  C- Placental attachment (IgG)

  d- Mucosal attachment (IgA)

  e- Binding to mast cells (IgE)



Properties of Immunoglobulins

Property	IgG	IgA	IgM	IgE	IgD
Heavy chain symbol	γ	α	μ	ε	δ
Molecular weight	150 KDa	170-400 KDa	900 KDa	190 KDa	180 KDa
Percentage in serum	75 %	15 %	10 %	0.004 %	% 0.2
Complement fixation	Yes	No	Yes	No	No
Transplacental passage	Yes	No	No	No	No
Opsonization	Yes	No	No	No	No

Antibody Diversity

*Immunoglobulins are protein (antigenic)

*Immunoglobulins subdivided into :

a- Isotypes: Antigenic difference in C-region
five immunogl. classes are different isotypes

b- Idiotypes: Ag difference in V-region of immunogl.

c- Allotypes: Antigenic feature of immunogl. that vary among individual under genetic control
Ag difference in C-region of H and L chain

Primary and Secondary antibody response

Primary antibody respone	Secondary antibody response
* first exposure to antigen	* Subsequent exposure
* lag period: days or weeks (slow onset)	* Lag period: hours (rapid onset)
* Small amount immunogl. low Ab level with gradual increase	* large amount immunogl. high Ab with rapid increas
* Ab Persist for short duration Weeks then decline rapidly	* Persist for long periods (monthes or years)
* Antibody is IgM	* Antibody is IgG

Primary and Secondary antibody response