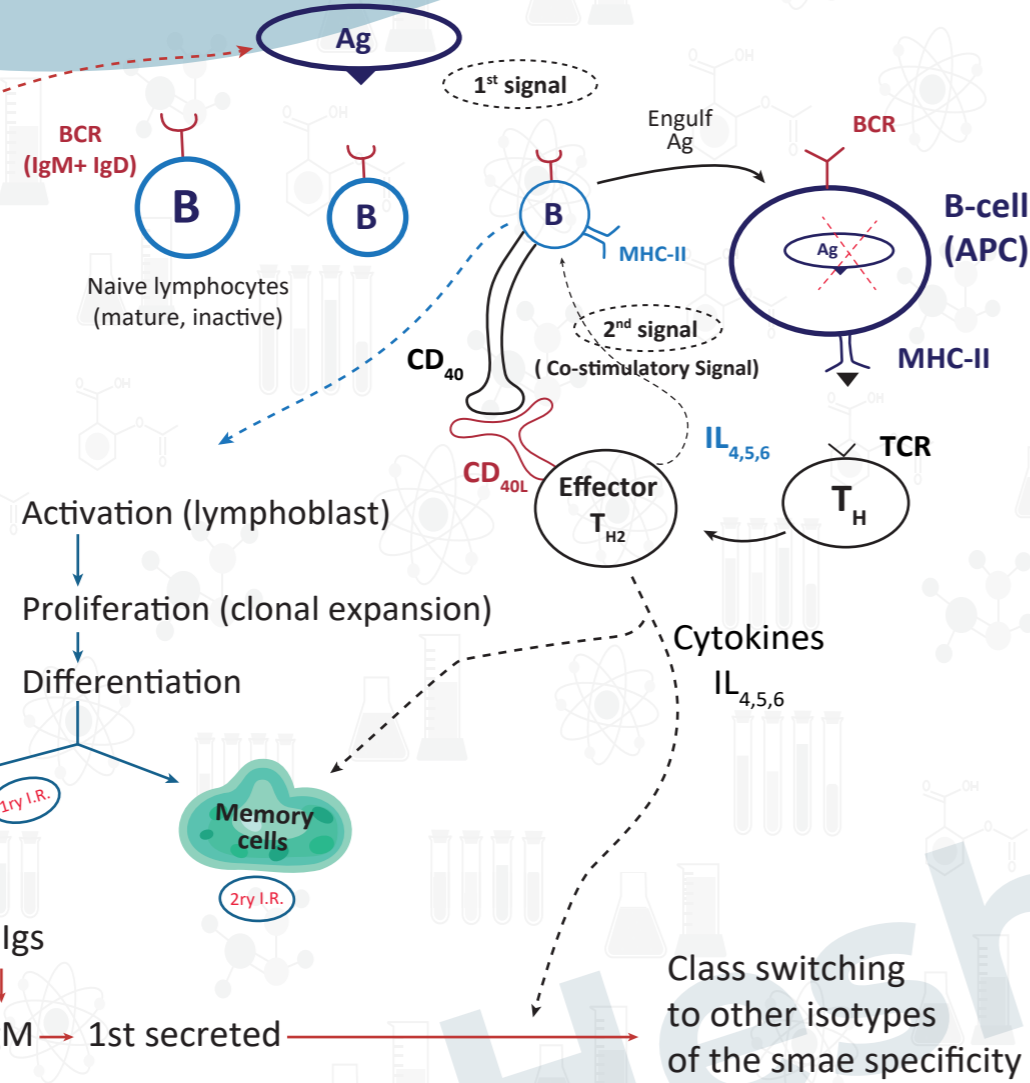


Chapter 6: Humoral imm.

- Destruction of E.C. pathogens (most bact.)
- Spread of I.C. pathogens (I.C. bact. and viruses as they move from cell to cell through E.C. fluids)

- **Origin:** B.M.
- **Maturation:** B.M.

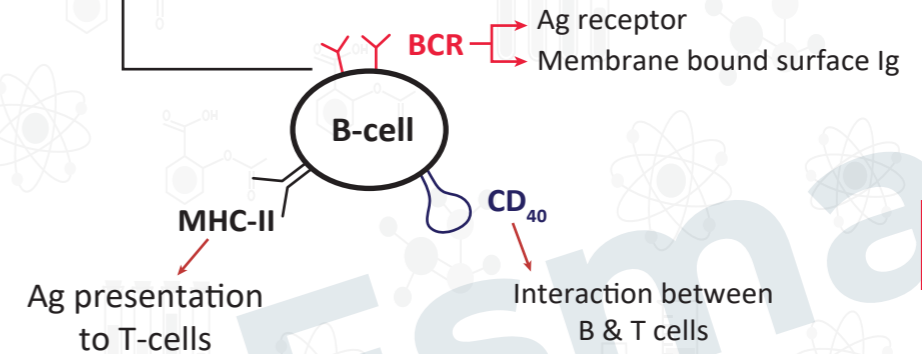
Thymus dependant Ag (TD)



Humoral imm. (Ab dependent imm.)

B- cell surface molecules

- All BCRs on single B-cell are of identical specificity
- Immature B-cell express only IgM
- Mature B-cell bear both IgM & IgD



Immunity (8)

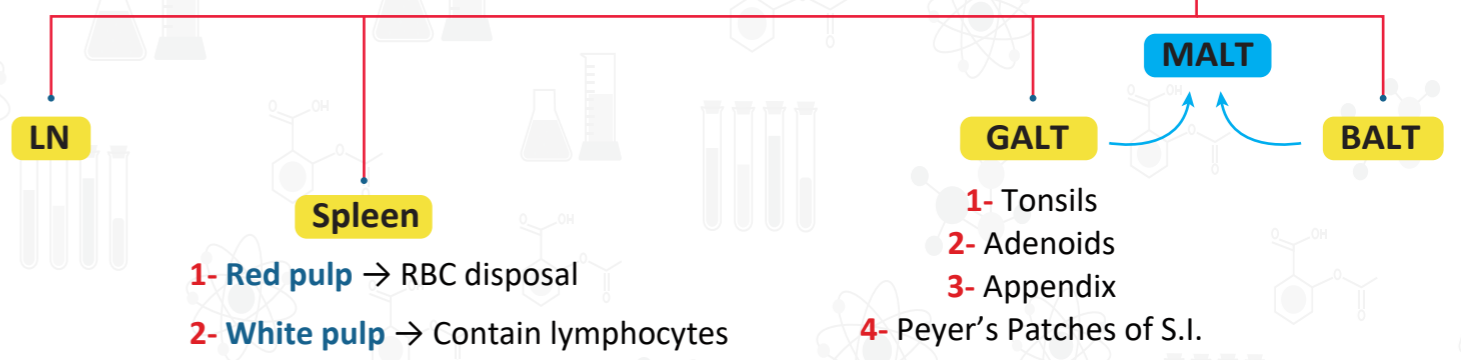
From Ch. (1) Lymphoid Organs

1 1ry lymphoid organs (central)

- Site of maturation of lymphocytes
- 1- B.M. → B-cell maturation
- 2- Thymus → T-cell maturation

2 2ry lymphoid organs (peripheral)

- Site of residence of lymphocytes → B & T cells meet Ags



Thymus independent Ag (TI)

Some Ags (bact. P.S.)

→ Activate B-cells directly without T-cell help

B-cell activation is delivered by the Ag only

In this case

- 1- Only IgM is produced → No class switching to other isotypes
- 2- Memory cells are not produced

Mature B-cells

Leave blood stream → Enter 2ry lymphoid organ → Migrate to T-cell zone

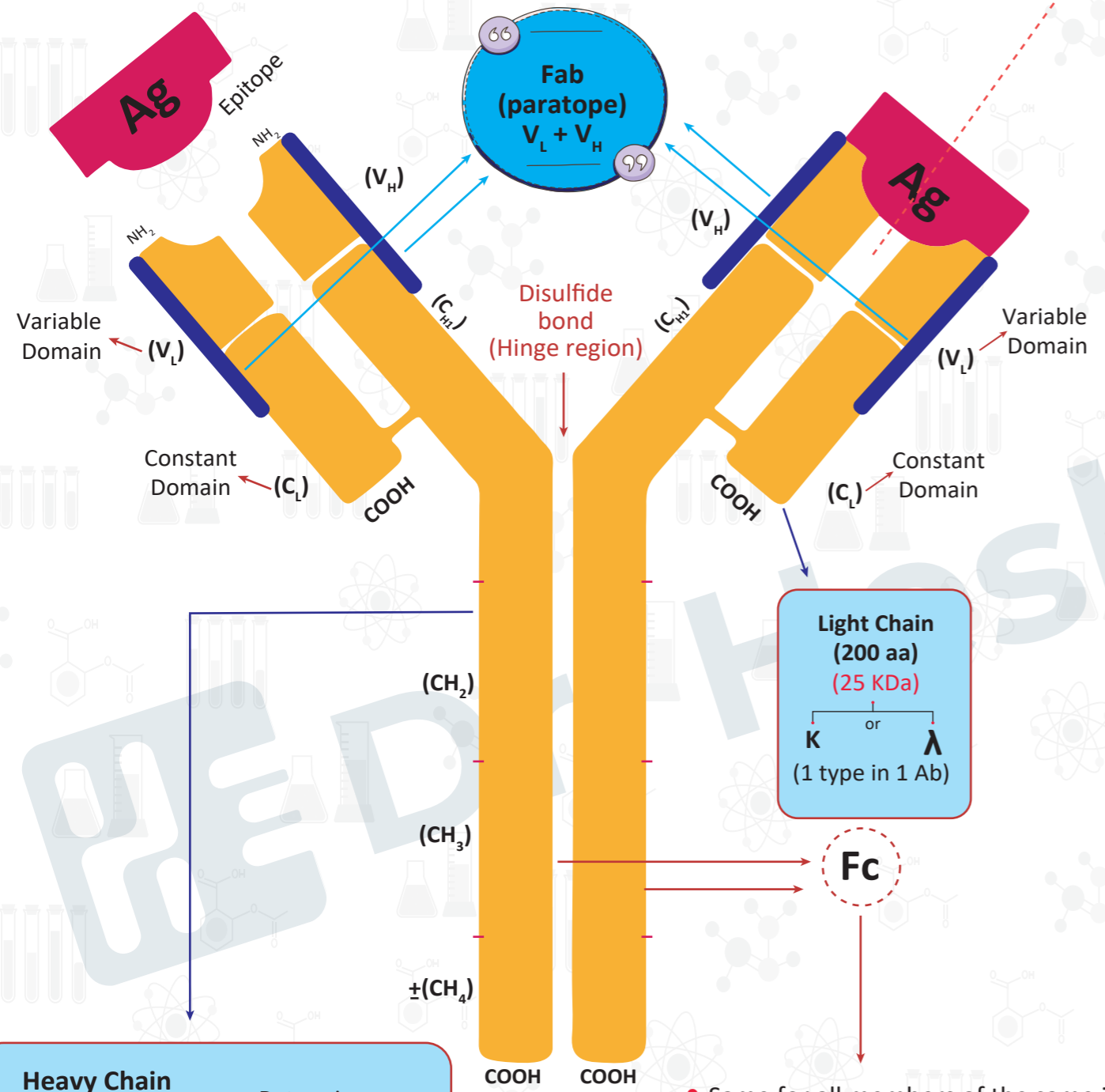
No target Ag → B-cell re-enter circulation

Target Ag present → B-cell bind by its BCR to Ag → Trapped before leaving T-cell zone → Full activation of B-cell

Immunoglobulin (IgA)=Abs

Glycoproteins → γ-globulins plasma proteins

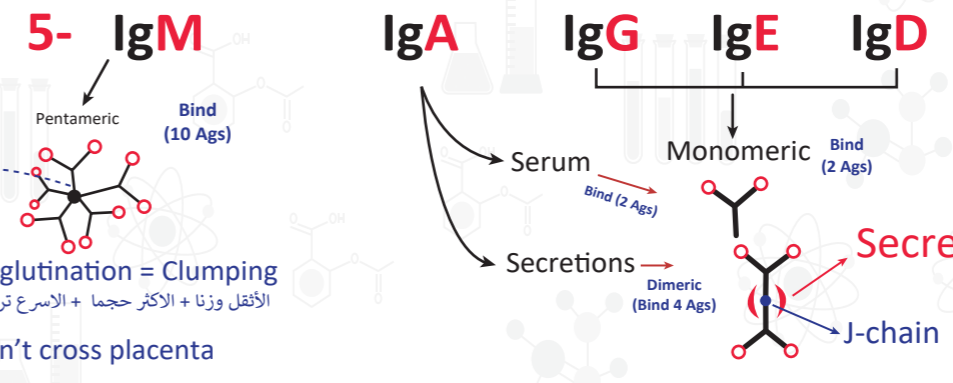
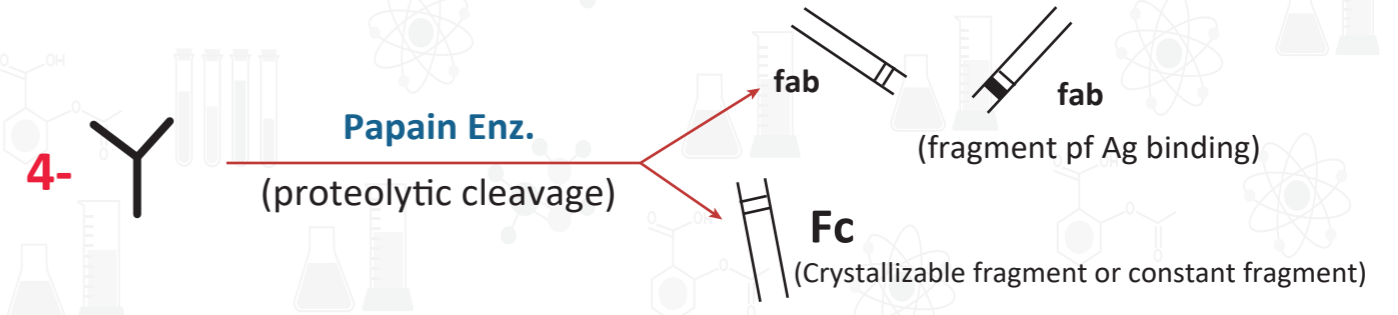
Ab structure



Hyper Variable region:

• Variability in α sequence in V_L and V_H is not spread evenly over the entire length → but restricted to short segments → called Hypervariable region or paratope → Ag binding site → complementary to epitope of Ag

- 1- Ab → 4 p.p. chains → 2 light (200 aa) + 2 heavy (400 aa) → connected together by disulfide bonds → region called **Hinge region**
- 2- * Light chain → kappa (κ) or lambda (λ) → only 1 type is present in 1 Ab
* Heavy chain → μ, α, δ, ε or γ → IgM, IgA, IgG, IgE and IgD
- 3- Each → * light chain → V_L and C_L
* Heavy chain → V_H and C_{H1,2,3,±4} → Fab = V_L + V_H
Fc



Immunity (9)

| Heavy Chain (400 aa) (50-75 KDa) | | Determine Ig isotype | | |
|----------------------------------|-----------|----------------------|-------------|-----------|
| Mu (μ) | Alpha (α) | Gamma (γ) | Epilson (ε) | Delta (δ) |
| IgM | IgA | IgG | IgE | IgD |

- Same for all members of the same isotype
- Detect functional properties of isotype
- Differs in different Ab isotypes → different biological functions

- Synthesized by local mucosal cells
- 1- ++ Passage of IgA through epith. cells
- 2- Protect it # proteolytic digestion

Functions of Abs

Ab isotype determines the effector mechanism

1 Agglutination

- Clumping of pathogen (particulate Ag)

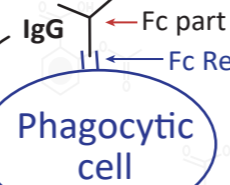
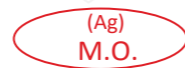
-- Its dissemination

++ Its removal by phagocytosis



2 Opsonization

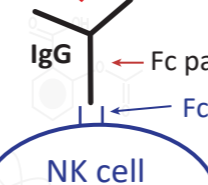
IgG



++ phagocytosis and I.C. killing of pathogen

3 ADCC

IgG



++ Cytotoxicity (E.C. destruction)

4 Complement activation

IgG or IgM



++ Complement

5 Neutralization

Sec IgA or IgG

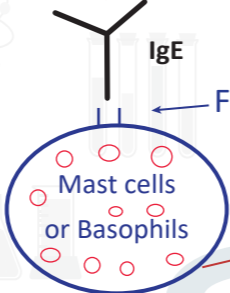
-- Attachment of pathogen to their specific receptors on their target cells



Target host cell

6 Mast cell & Basophil

IgE (ايحييه)

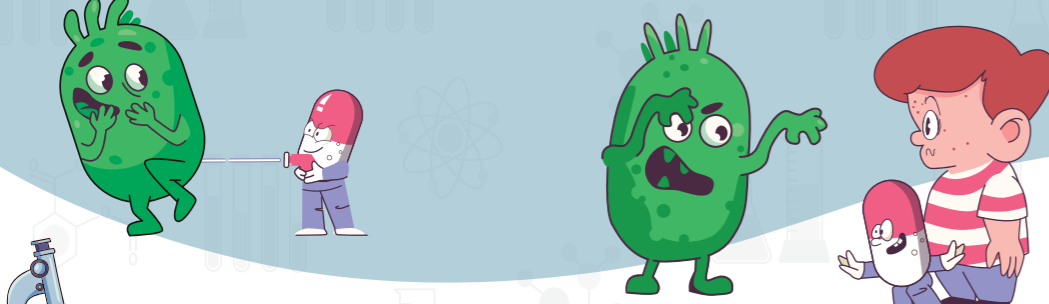


Degranulation → ++ histamine

Immunity (10)

Ig classes (Isotypes)

| الأكثر تركيزا و الأصغر حجما | الأكبر حجما | | | الأقل تركيزا |
|--|--|--|-------------------------------|---|
| IgG (75%) | IgM (8-10%) | IgA (Serum 15-20%) | IgD (< 1%) | IgE (trace amounts) |
| Gamma heavy chain | Mu | Alpha | Delta | Epsilon |
| Monomeric → 2Ags | Pentameric → 10 Ags (held together by disulfide bonds) | 2 types: 1- Serum → monomeric → (2Ags) 2- Secretory → Dimeric → (4Ags) | Monomeric → 2Ags | Monomeric → 2Ags |
| | J-Chain | <ul style="list-style-type: none"> • J- chain • Secretory components:- <ul style="list-style-type: none"> * synthesized by local mucosal cells * ++ passage of IgA through epith. cells * protect IgA from proteolytic digestion | | |
| Major Ab in 2ry IR | Major in 1ry IR | | | |
| Can cross placenta (contain Fc Rec.) → Passive protection to the newborn during 1st few months of life | Can't cross placenta → so, its presence in newborn blood =intrauterine infection | N.B. sec IgA is produced by submucosal plasma cells → & found in mucosal sec. (Saliva, tears, colostrum, Resp, GIT, Gut secretions) | | |
| Anti-Rh Abs | Anti-ABO Abs (Only Ab # thymus independent Ag) | | | |
| Biological activation: 1- Opsonization 2- ADCC 3- Complent activation 4- Neutralization | 1- Agglutination → <i>IgM is the most efficient</i> 2- Complement activation → <i>IgM is the most efficient</i> 3- Acts as BCR on mature B-cells | Serum IgA → uncertain functions Sec. IgA → neutralization ↓ local immunity at mucosal surfaces | Acts as BCR on mature B-cells | 1- Binds to Fc Rec. on mast cells & basophils → ++ histamine → Type-I Hypersensitivity 2- Bind to Fc rec. on eosinophils → ++ imm. to parasites (eosinophils release toxins on surface of parasites) |



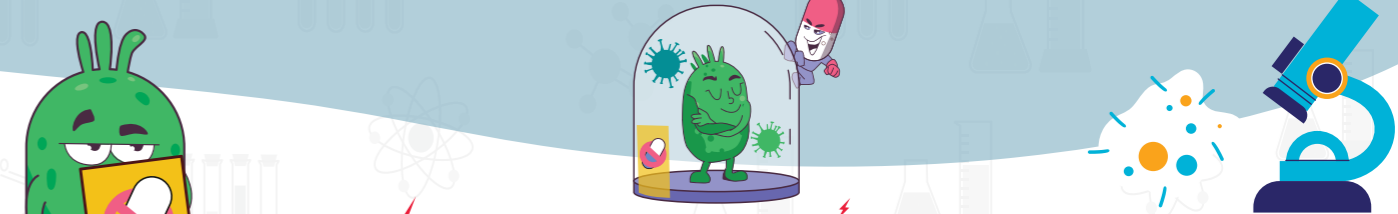
| | 1ry I.R | 2ry I.R |
|-------------------------------|---|---|
| Ab level | | |
| Defination | IR following 1st exposure to Ag | IR following subsequent exposure to the same Ag |
| Lag (induction) period | Long (7-10) days Time needed to undergo activation, proliferation and differential to plasma cells | Short (few hours to few days) |
| Ab level | Low | High (10 time greater) |
| Duration | Short (Abdecline rapidly) | Long (months) |
| Ig class | Mainly IgM | Mainly IgG |
| Memory cells | Develop at the end | Present from the start |

For this reason, most Vaccines are given in more than 1 dose (booster dose)

Immunity (11)

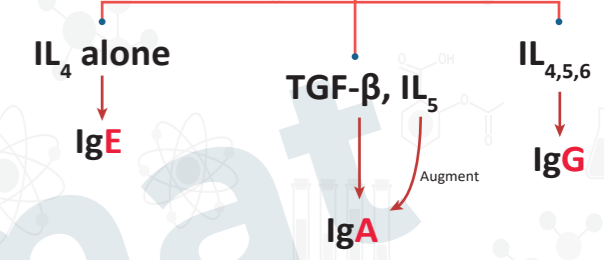
Heterophile Abs (cross reacting Abs)

- See Heterophile Ags (ch.3)



Ig class switching

- Plasma cells switch from producing IgM to produce IgG, IgA or IgE
- Depends on cytokines released from T-cells
- By changes of $C_H \rightarrow$ No change in tight chain or $V_H \rightarrow$ Ig produced is of the same specificity as original IgM but differs in biological characters



Monoclonal Abs (MCA)

- Highly specific Ab # single epitope
- Produced by single clone of B-cells
- Uses

Diagnosis

- In Ag detection (serological reaction)
- e.g. Detection of lymphocyte markers (CD)

ttt

- Ttt of drug toxicity (digital toxicity)

