HYPERSENSTIVITY

- ✓ Typically, inflammatory responses rid the body of Ag and resolves the infection within days
- ✓ In some cases, the inflammatory response can have harmful effects - even result in death!
- ✓ -this type of IR is called 'hypersensitivity or 'allergy.
- ✓ Hypersensitive reactions develop during the course of either:
- ✓ -Humoral response or-Cell-mediated response
- ✓ Those reactions initiated by Ab or Ab-Ag complexes are called Immediate Hypersensitivities
- ✓ Those initiated by cell-mediated response are called Delayed-type Hypersensitivities

Gell Coomb Classification

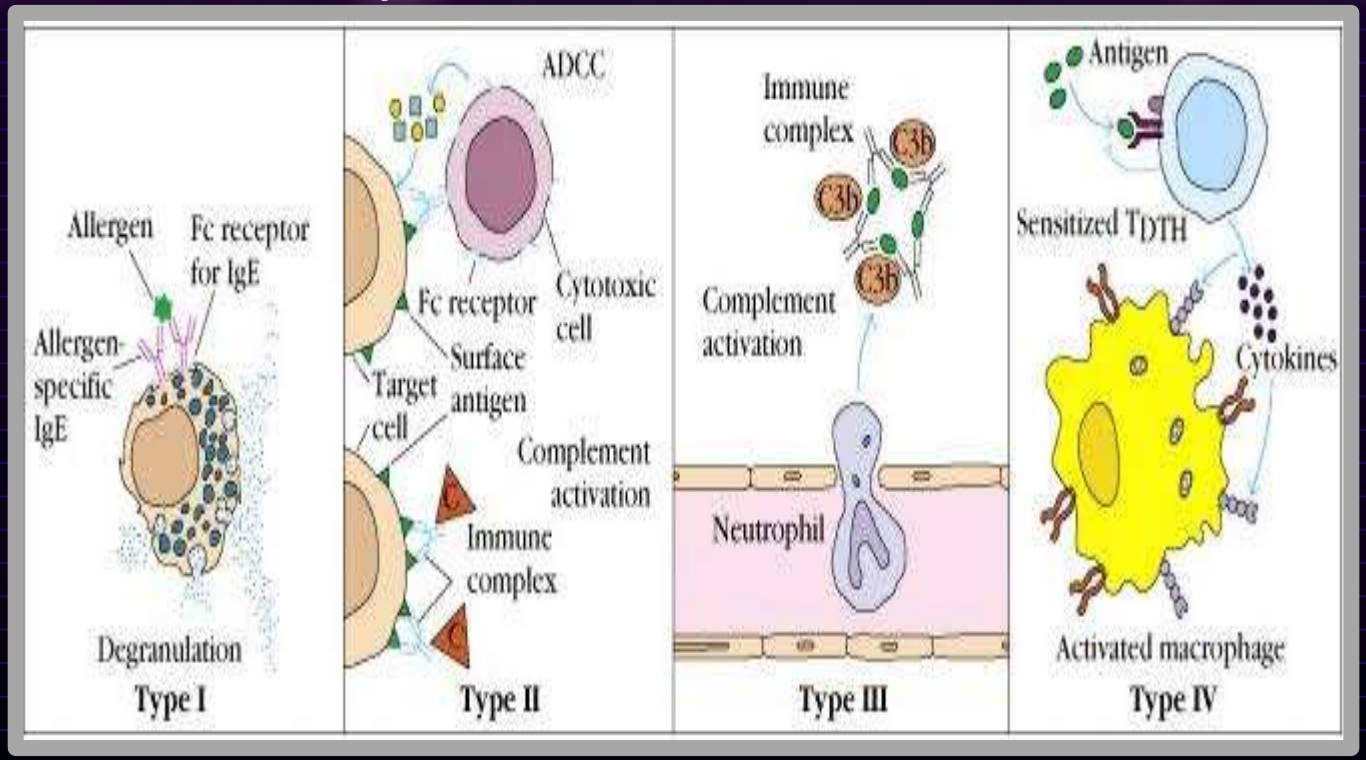
A. Type I Hypersensitivity: IgE mediatiated

B. Type II Hypersensitivity: Antibody mediated

C. Type III Hypersensitivity: Ag-Ab Complex mediated

D. Type IV Hypersensitivity: Cell mediated (DTH)

Types of hypersensitive response

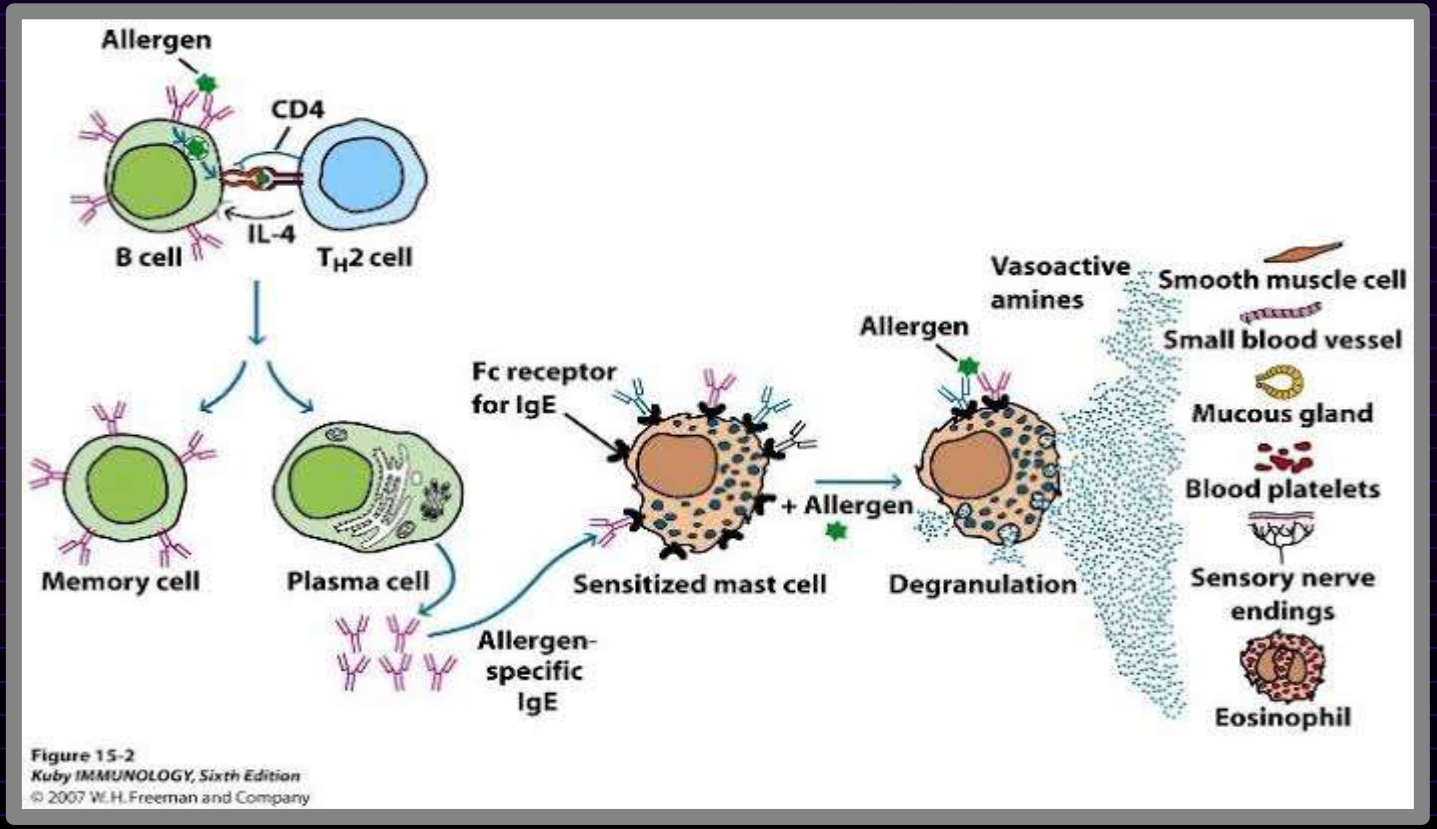


Type I hypersensitivity

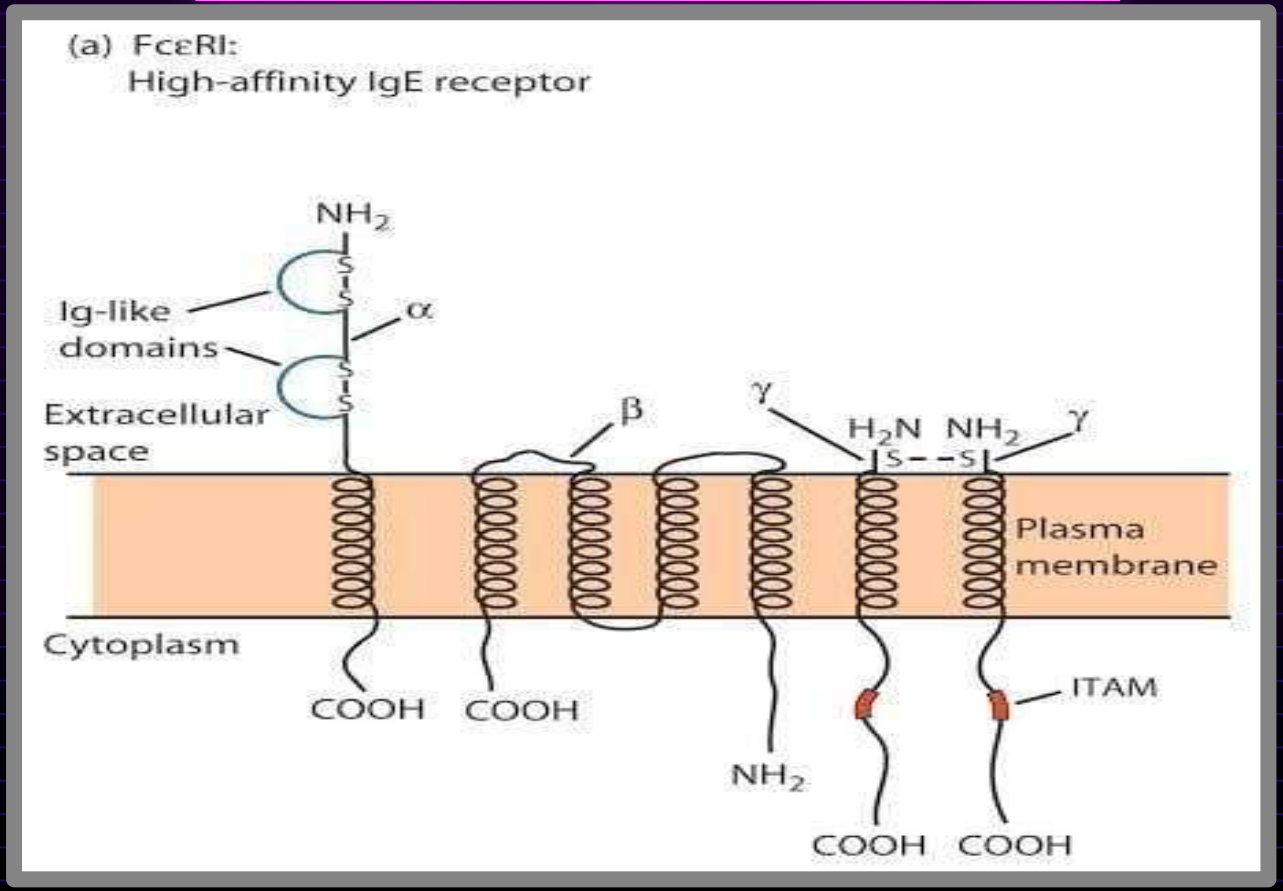
• **Allergens:** non-parasitic antigens capable of stimulating type I hypersensitive responses in allergic individuals

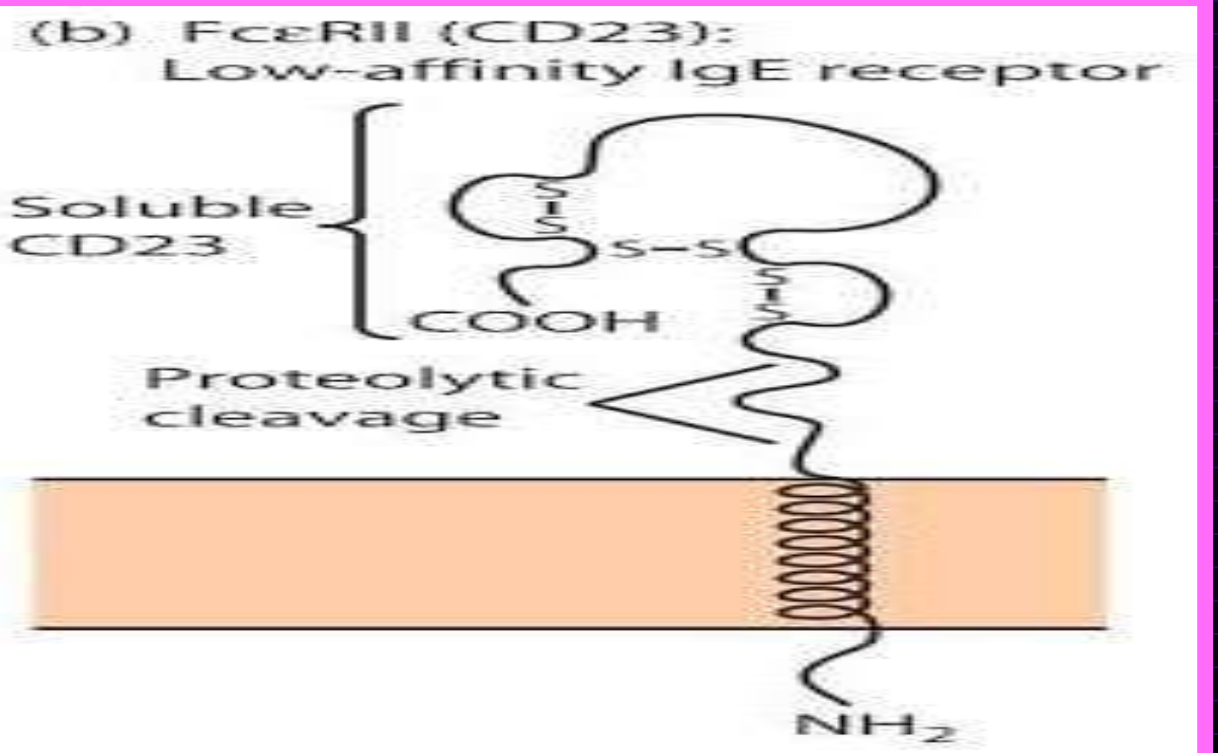
• **Atopic individuals:**
- IgE regulatory defects
- High levels of circulating IgE
- More no. of circulating eosinophils
- Susceptible to allergies

Components of Type I Rxns

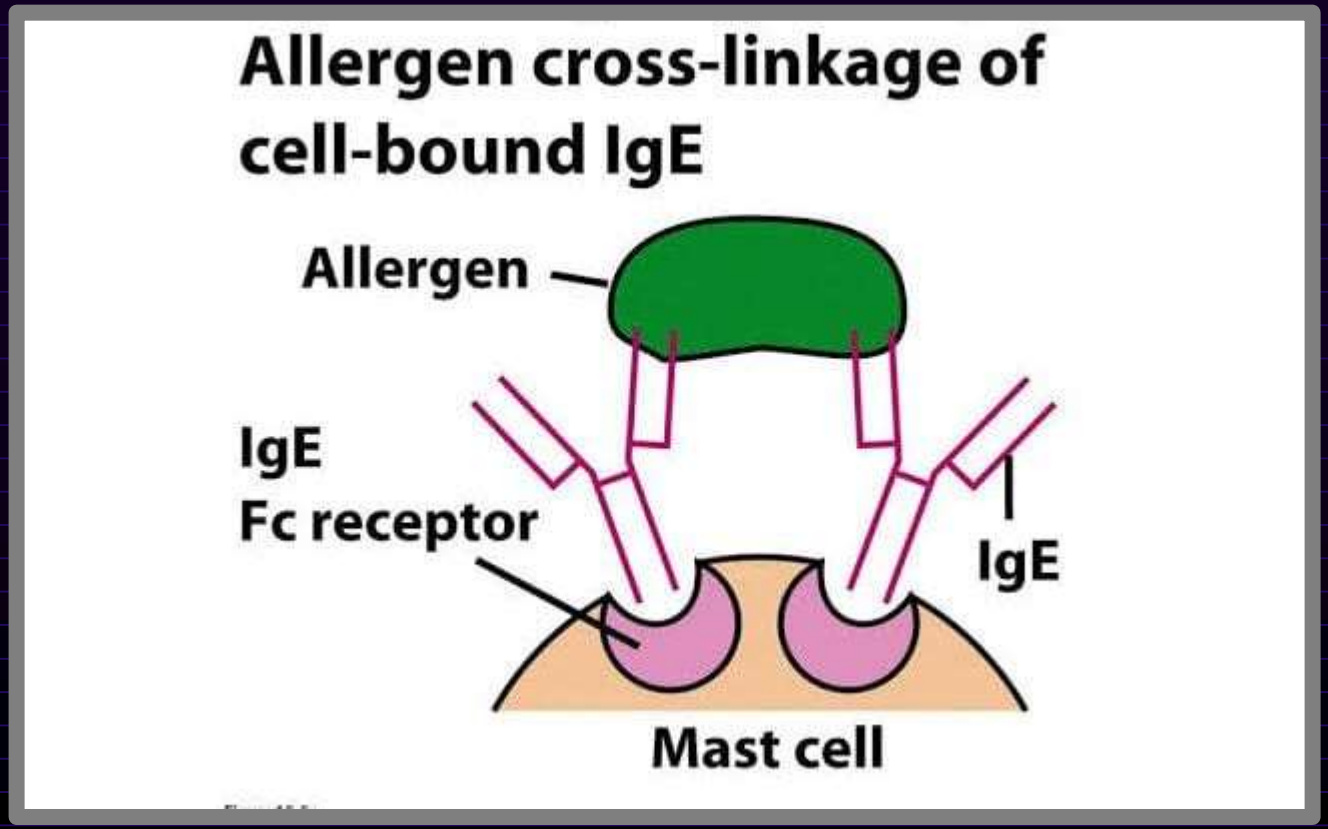


FC RECEPTORS FOR IGEFC RECEPTORS FOR IGE

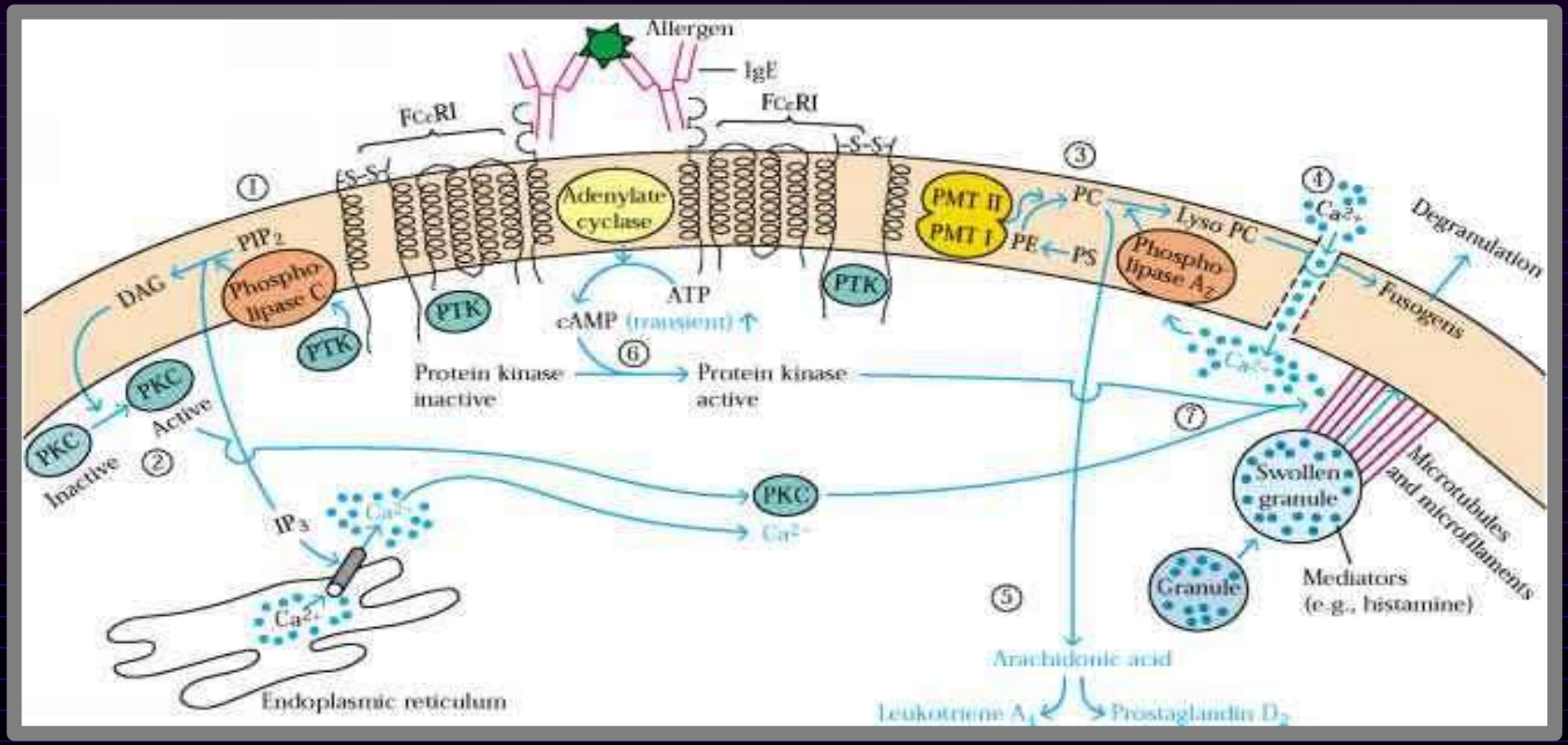



(b) FcεRII (CD23):
Low-affinity IgE receptor
Soluble
CD23
S–S
COOH
Proteolytic
cleavage
NH2

Cross -linking of IgE by allergens



Mechanism of mast cell degranulation



Mediators

- **Primary mediators**: are produced before degranulation & are stored in granules. E.g.: histamine, proteases, heparin

. **Secondary mediators:** are produced during degranulation process. E.g.: leukotrienes, prostaglandins, platelet activating factor.

Localized anaphylaxis

- Reaction limited to specific tissue
- Involve epithelial cell surfaces.

- Allergic rhinitis
- Asthma
- Atopic dermatitis

Systemic anaphylaxis

- Shock like fatal state
- Antigens involved: venom of bee, wasp, hornet: drugs like penicillin, insulin; seafood.
- Drug of choice: epinephrine

Regulatory factors

The following factors influence IgE response to allergens:

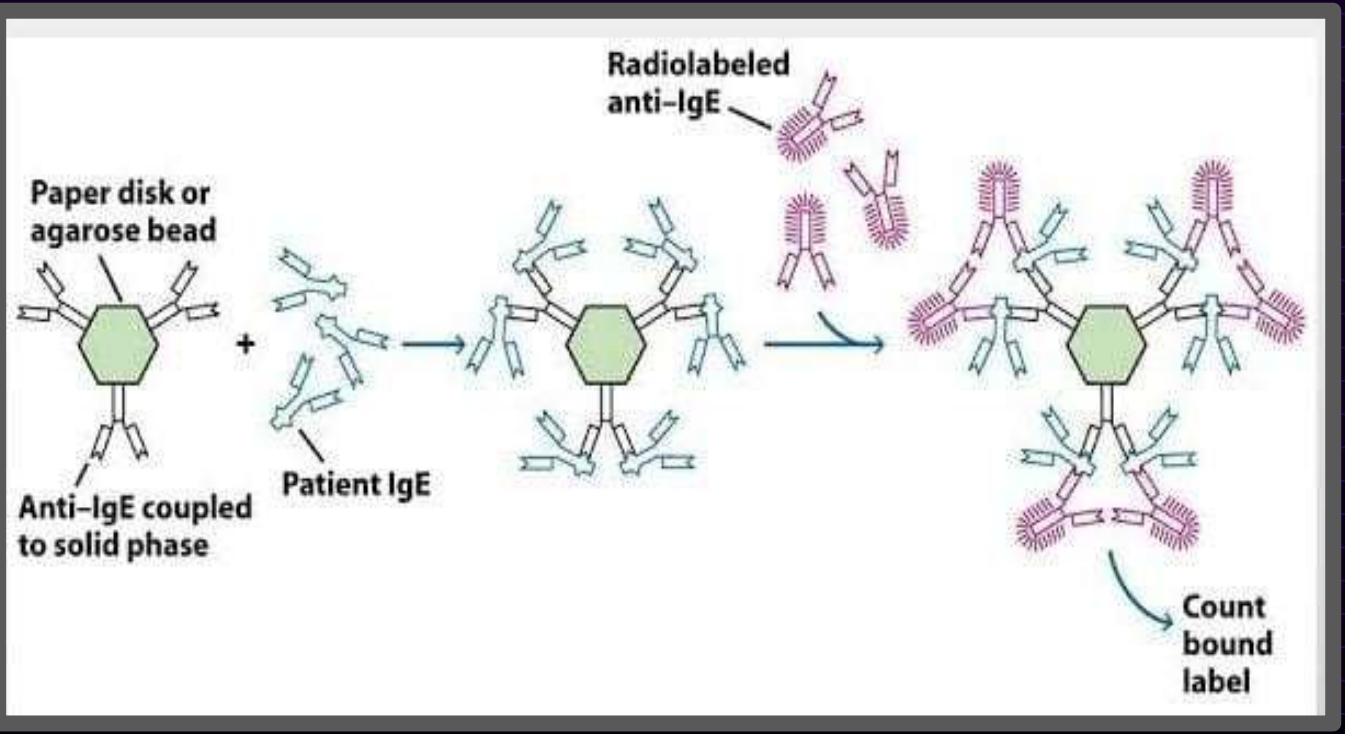
- Level of Ag dose
- Mode of antigen presentation
- Relative presence of TH1 and TH2 titres
- TH2's release IL-3.4.5, and 10
- TH1's release IFN gamma

Atopic vs non-atopic individuals express qualitatively different Type I responses to allergens...

- Atopic responses involve TH2 → production of IgE from B cells
- Non-atopic responses involve TH1 → production of IgM or IgG

Detecting allergies

- Skin tests
  - injections or scratchings
  - Local Mast cells-Produces wheal and flare
  - Inexpensive and quick
  - May sensitize one to new Ag's-May late-phase rxn in some Immuno assays for serum IgE
  - Radio immuno sorbent test (RIST) – Radio allergosorbent test (RAST)


Radiolabeled
anti–IgE
Paper disk or
agarose bead
+
Patient IgE
Anti–IgE coupled
to solid phase
Count
bound
label

Therapy

- ✓ Avoidance of contact
- ✓ Antihistamine drugs
- ✓ Immunotherapy

Type II Hypersensitivity

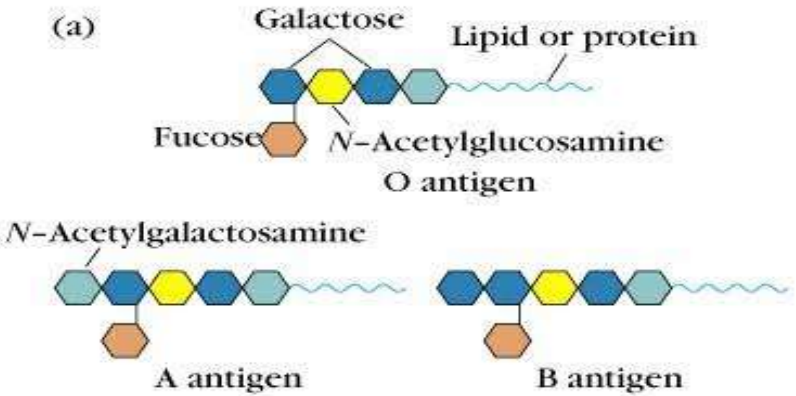
- Antibody Dependent Cytotoxicity
- Antibody Dependent Cell mediated Cytotoxicity
- Target antigens are found on cell or tissues
- Antibody binds to Target Antigen- complement activated cell destruction
- Ig binds to Fc receptors on NK cells

Type II Hypersensitivity: Antibody mediated cytotoxic Transfusion reactions

- ✓ Hemolytic disease of the newborn
- ✓ Drug induced hemolytic anemia
- ✓ ABO blood group antigens - Antibodies IgM (Isohemagglutinins)
- ✓ hemolysis on transfusion
- ✓ Immediate or delayed type reaction

Antibody-mediated Hypersensitivity, Type II

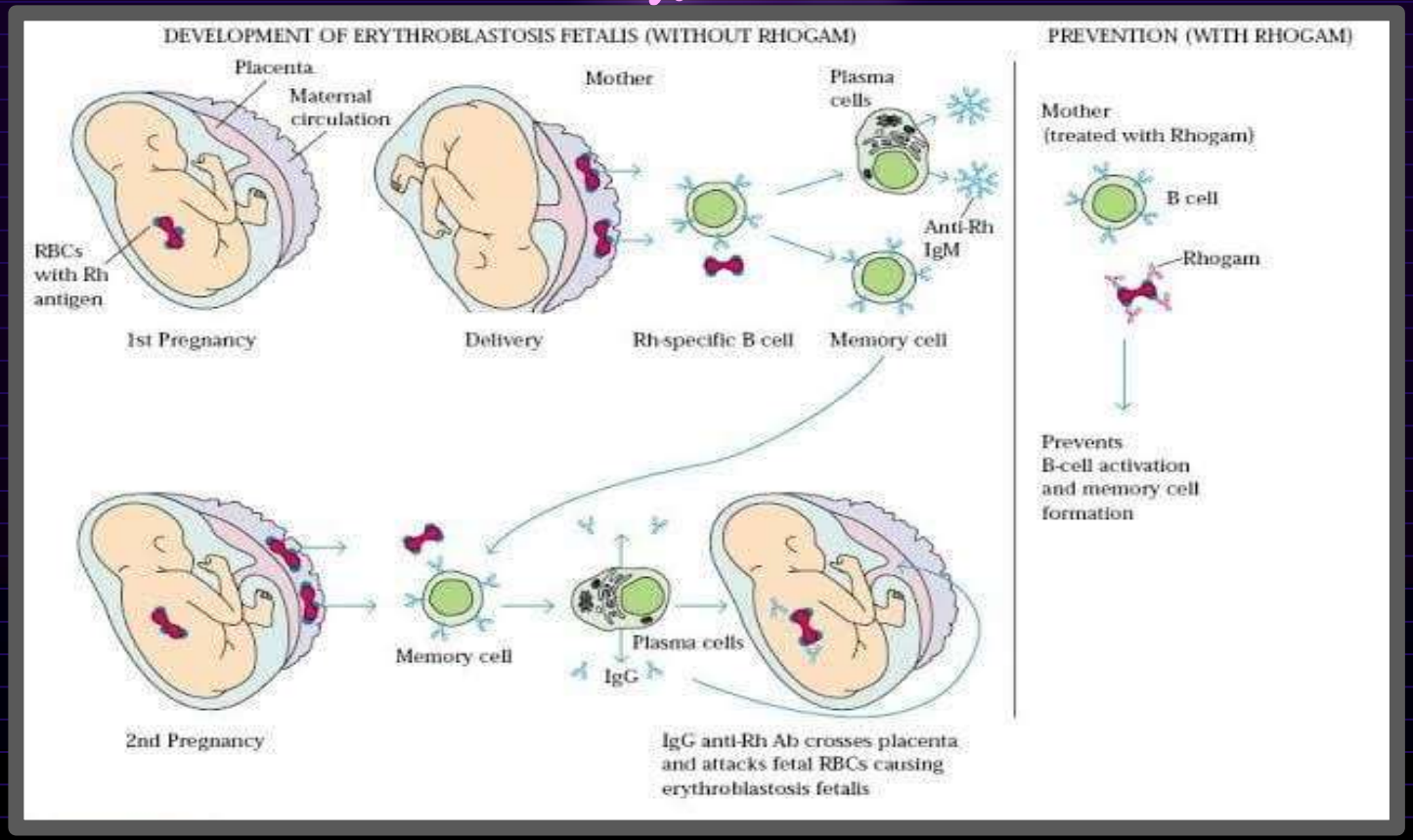
(a)



(b)

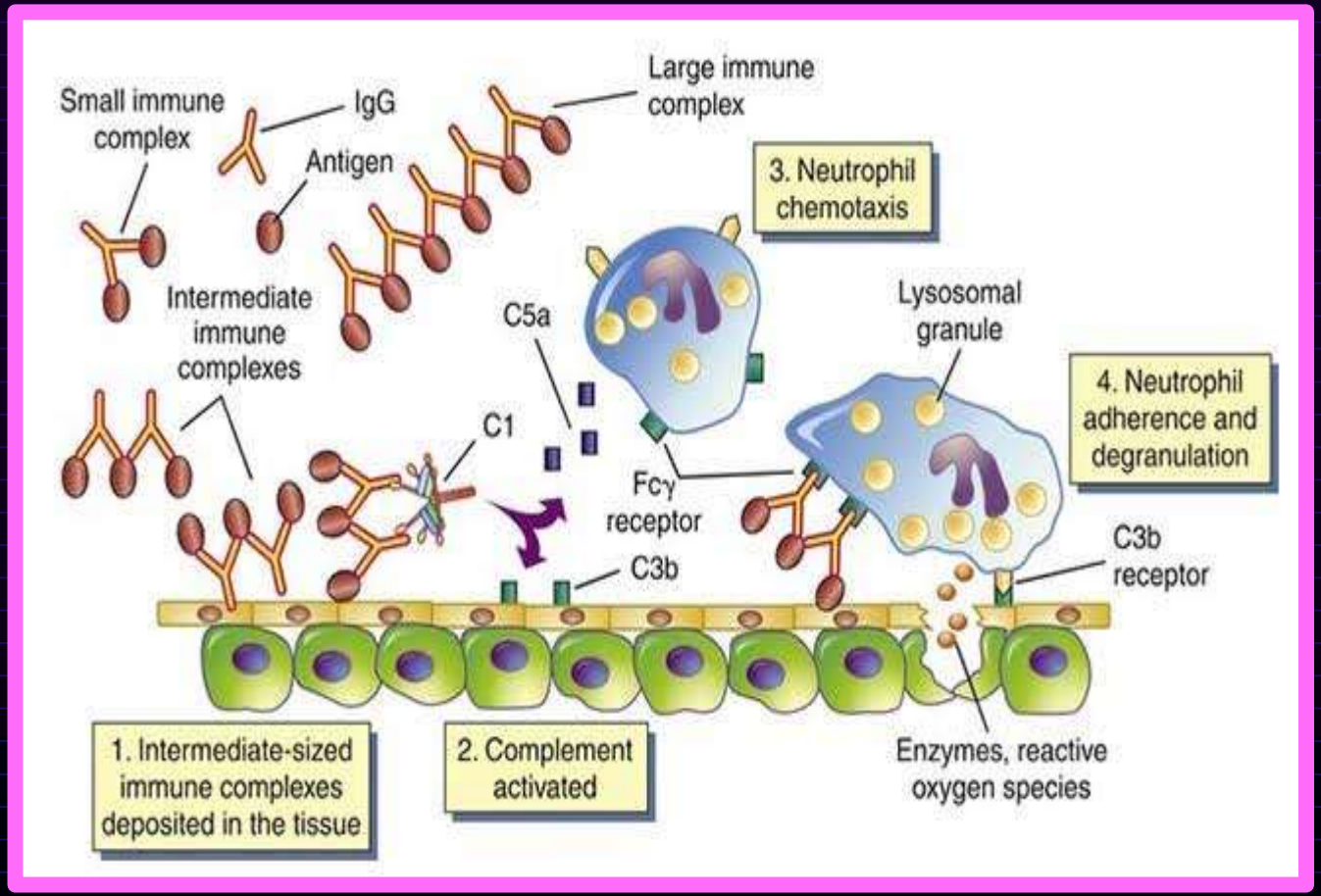
Genotype	Blood-group phenotype	Antigens on erythrocytes (*agglutinins*)	Serum antibodies (*isohemagglutinins*)
AA or AO	A	A	Anti-B
BB or BO	B	B	Anti-A
AB	AB	A and B	None
OO	O	None	Anti-A and anti-B

Antibody-mediated Hypersensitivity, Type II



Type III Hypersensitivity

- ✓ Immune Complex Reactions
- ✓ Antigens are in solution in plasma or interstitial fluids. Abs combine with these Ags, fix complement and initiate the consequences of the complement cascade / phagocytosis
- ✓ Large amounts of immune complexes can lead to tissue-damaging type III hypersensitive reactions


Small immune complex
IgG
Antigen
Large immune complex
3. Neutrophil chemotaxis
Intermediate immune complexes
C5a
Lysosomal granule
4. Neutrophil adherence and degranulation
C1
Fcγ receptor
C3b
C3b receptor
1. Intermediate-sized immune complexes deposited in the tissue
2. Complement activated
Enzymes, reactive oxygen species

❖ Localized reactions

- Arthus type skin reactions
- complex mediated glomerulonephritis

❖Generalized reactions

- Serum sickness Within days or weeks after exposure to foreign serum antigen Fever, weakness, generalized vasculitis (rashes) with edema and erythema, lymphadenopathy, arthritis, and sometimes glomerulonephritis

Type IV Hypersensitivity

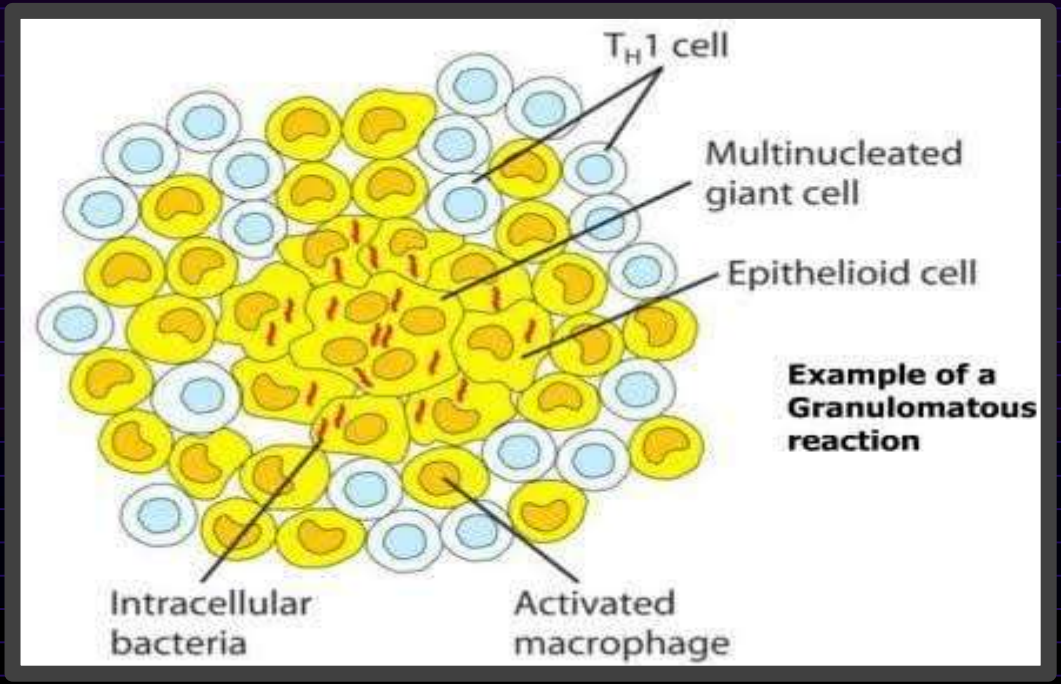
- ✓ 1-2 weeks
- ✓ T Dтн Cells
- Tc
- TH1

✓Cytokines
- IL-2, MIF, TNF, Interferon

✓Macrophages
- lytic enzymes

Type IV Granulomas

Effective against intracellular parasites
- Granulomatous lesions
- M. leprae, M. tuberculosis



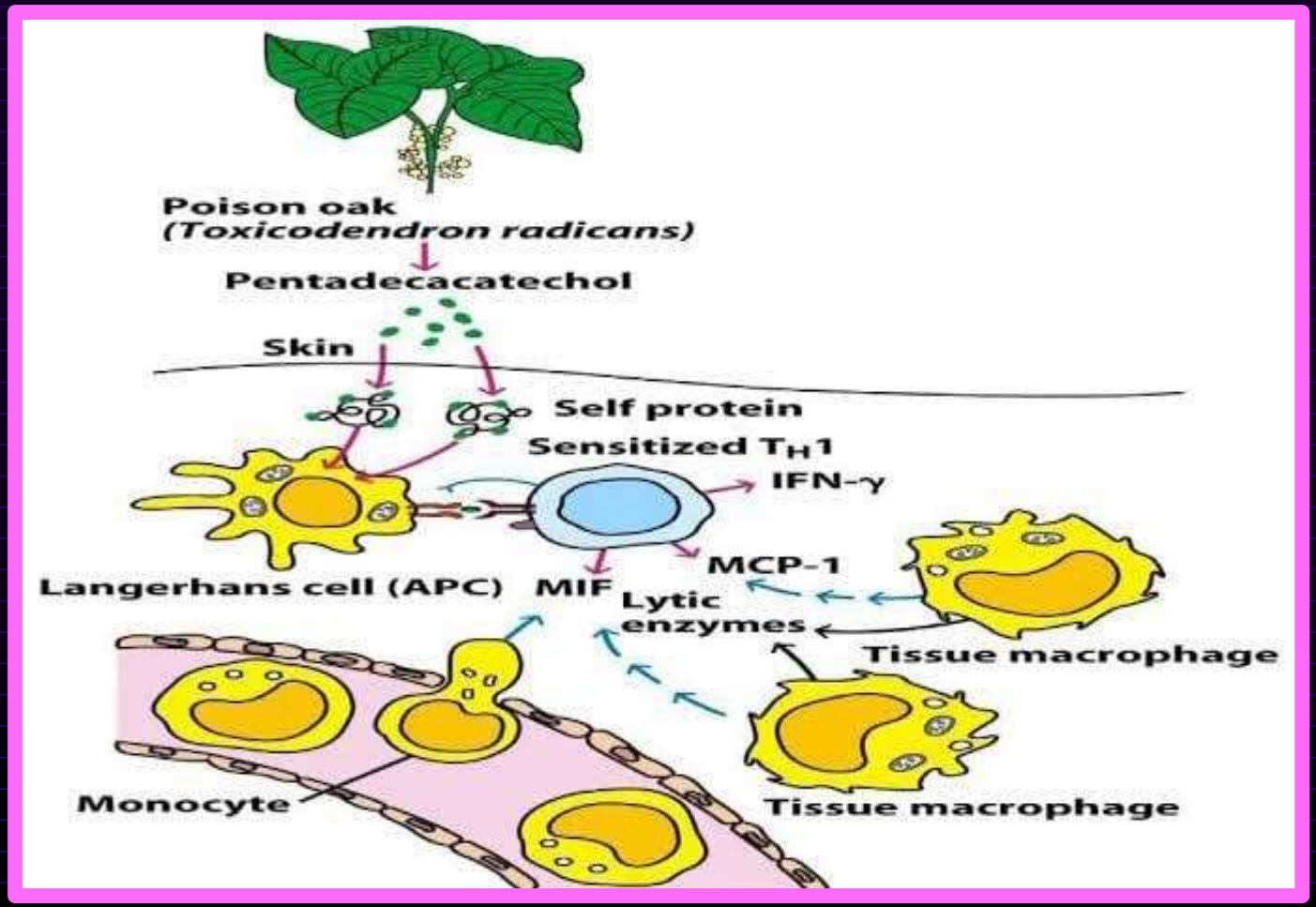
Type IVContact Hypersensitivity

- Small molecules complex with skin proteins

- pentadecacatechol poison ivy, poison oak
- cosmetics, hair dyes
- solvents formaldehyde, turpentine
- nickel rubber

- Complex internalized by APC
- MHC-II

- Response 48-72 hours


Poison oak
(Toxicodendron radicans)
Pentadecacatechol
Skin
Self protein
Sensitized T_H1
IFN-γ
MCP-1
Langerhans cell (APC)
MIF
Lytic enzymes
Tissue macrophage
Monocyte
Tissue macrophage


THANKS