Type II or Cytotoxic Hypersensitivity

Type II hypersensitivity is mediated by antibodies directed towards antigens present on the surface of the cells or other tissue components.

Type II Cytotoxic or Cytolytic

Antigen - Red blood cell

- White blood cell

- Platelet

- Tissue

Antibody - IgG, IgM

Complement = + , -

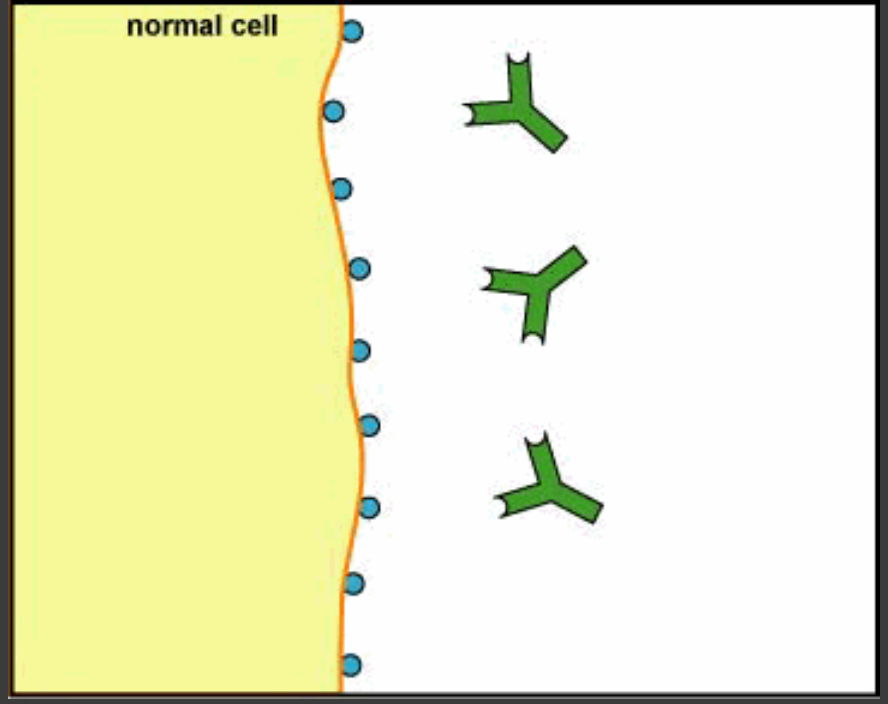
- involves antibody-mediated reactions .
- immunoglobulin class (isotype) is generally IgG.
- may also involve complement that binds to cell-bound antibody.
- The difference here is that the antibodies are specific for (or able to cross-react with) "self" antigens. When these circulating antibodies react with a host cell surface, tissue damage may result .

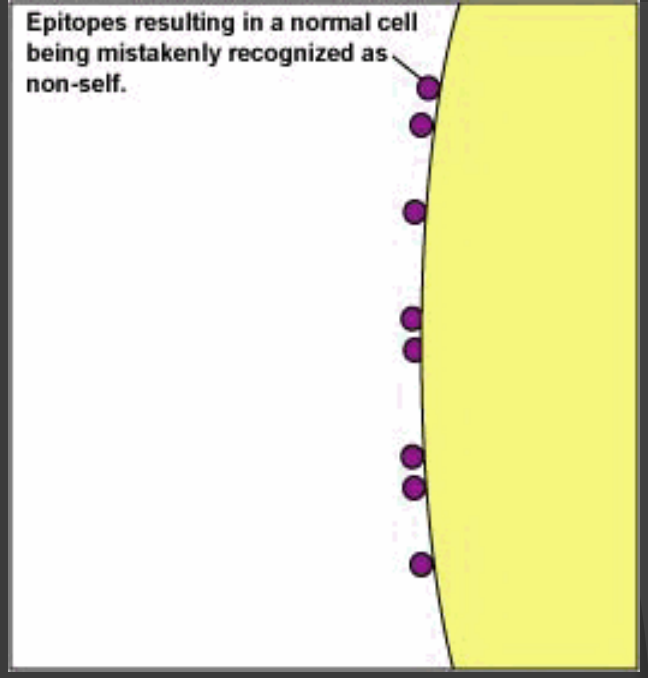
…

- [A] Complement Dependent Reactions
- [B] Antibody Dependent cell-mediated cytotoxicity
- [C] Antibody Mediated cellular Dysfunction

[A] Complement-dependent Reactions

- **Two mechanisms :**
- ***1. Direct Lysis of the cells***
- **Antibody (Ig G or IgM) react with the antigen present on the surface of the cells**
- **Activates complement system**
- **Formation of Membrane Attack Complex which disrupts membrane integrity by “drilling holes” through lipid bilayer & causes lysis**
- ***2. Opsonization***
- **Fixation of antibody or C3b fragment on cell surface**
- **Cells become susceptible to phagocytosis**





- **Opsonization& Phagocytosis** **MAC lysis**
- **In opsonization & Phagocytosis**

IgG antibodies react with epitopes on host cell membrane, phagocytes binds to Fc portion of IgG & discharge their lysosomes.

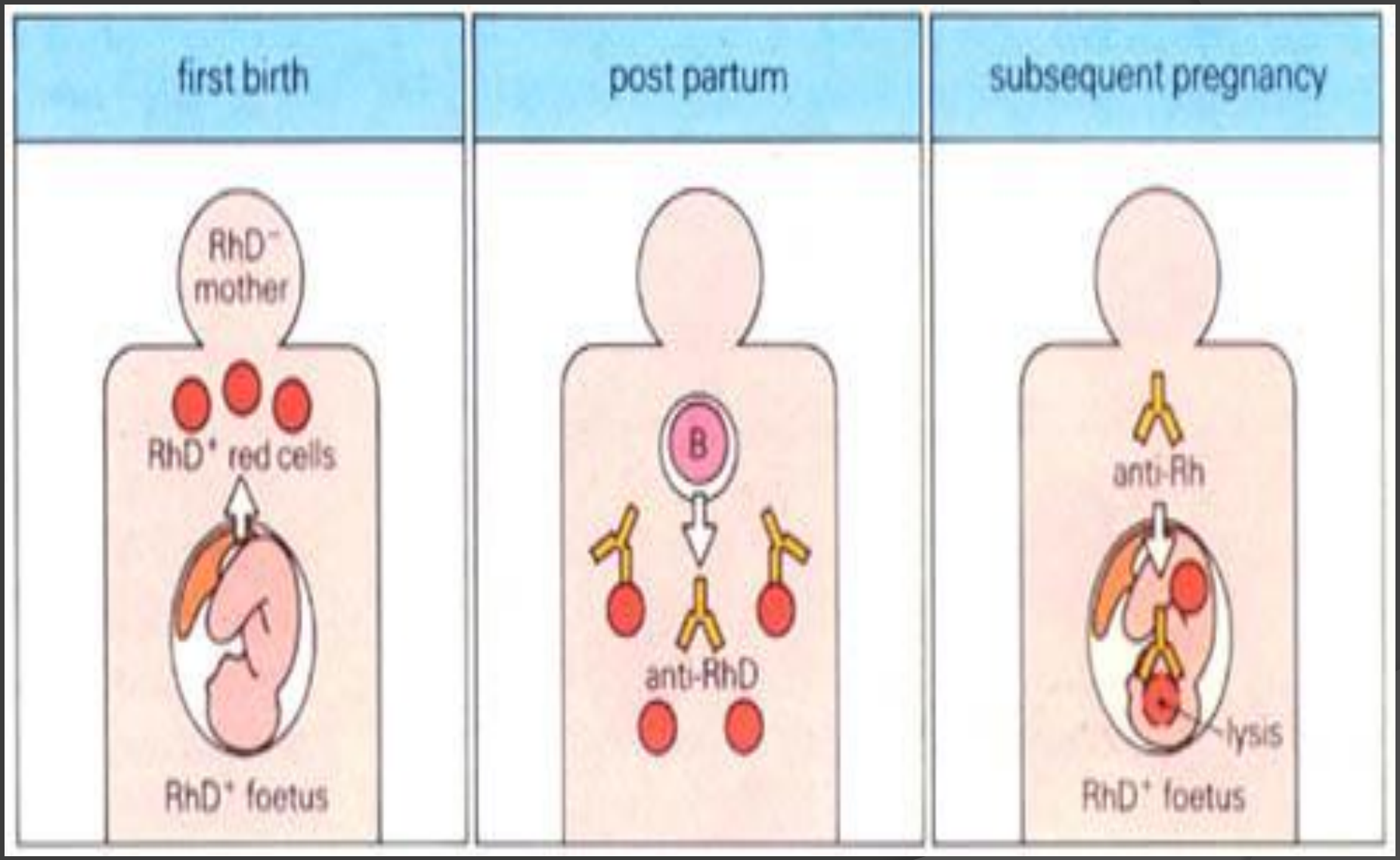
- **In MAC lysis, IgG or IgM react with epitopes on host cell membrane, activates classical complement pathway & formation of MAC complexes and lysis of the cell.**

- **Most commonly involves Blood Cells (RBC, WBC, Platelets) but antibodies can also be directed against extracellular tissue (e.g. Glomerular basement membrane)**
- **Transfusion Reactions**
- Hemolytic disease of the new born(HDN)

  (Erythroblastosis fetalis)

- Rh incompatibility disease, - ABO incompatibility disease

- **Autoimmune haemolytic anaemia, agranulocytosis or thrombocytopenia**


first birth
post partum
subsequent pregnancy
RhD⁻ mother
RhD⁺ red cells
RhD⁺ foetus
B
anti-RhD
anti-Rh
lysis
RhD⁺ foetus

- Hemolytic dis. of newborn can be entirely prevented by adminstrating antibodies against the Rh antigene ,these Abs called Rhogam ,bind to any fetal red blood cells that enter the mothers circulation at the time of delivery before B cells activation and ensuing memory cell production can take place.
- The treatment depend on the severity of the reaction .the fetus can be given an intrauterine blood exchange transfusion to replace fetal Rh+ RBC with Rh-,the transfusion given every 10-21 days until delivery.
- In less severe cases a blood exchange transfusion is not given until after birth.
- Treating by plasmapheresis ;a cell separation machine is used to separate the mothers blood into cells and plasma ,the plasma is discarded and the cells reinfused into mothers in an albumin or fresh plasma.

Diagnosis

1. Coombs test (Antiglobulin test)
   * Direct Coombs test
     - bound Ab on Rbc
   * Indirect Coombs test
     - free Ab in serum
2. Direct immunofluorescence
     - Ab on tissue

- Certain drugs like Penicillin leads to ;

Drugs attached to the surface of red blood cells (RBC) and acts as hapten for the production of antibody which then binds the RBC surface leading to lysis of RBCs.

- Goodpasture's syndrome: Generally manifested as a glomerulonephritis, IgG antibodies that react against glomerular basement membrane surfaces can lead to kidney destruction.

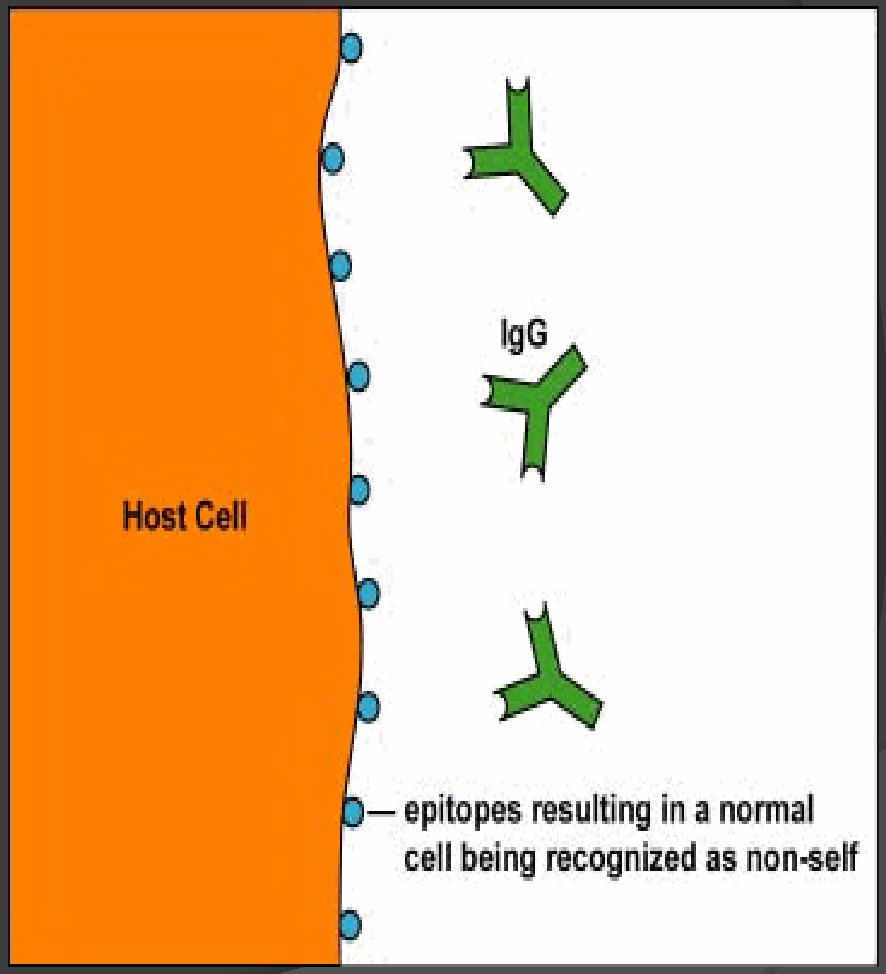
- Pemphigus: IgG antibodies that react with the intercellular substance found between epidermal cells.

[2] Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC)

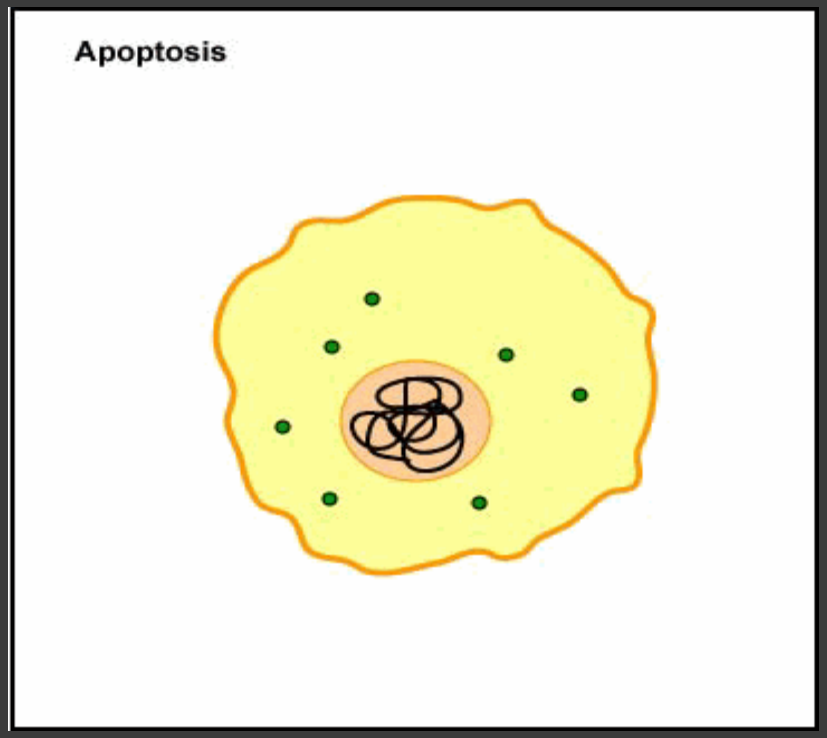
- **Doesnot involve fixation of complement but require co-operation of leukocytes**
- **Target cells coated with low concentration of IgG**
- **Nonsensitized cells bind target (IgG) by their Fc receptors**
- **Cell lysis proceeds without phagocytosis (too large a target to get phagocytosed e.g. parasites or tumour cells)**
- **May be mediated by Monocytes, Neutrophils, Eosinophils or NK cells**

ADCC destruction

- **Antobodies react with epitopes of host cell membrane & NK cells bind to Fc receptor of Antobodies. NK cells then lyse the cells with pore-forming perforins & cytotoxic granzymes.**



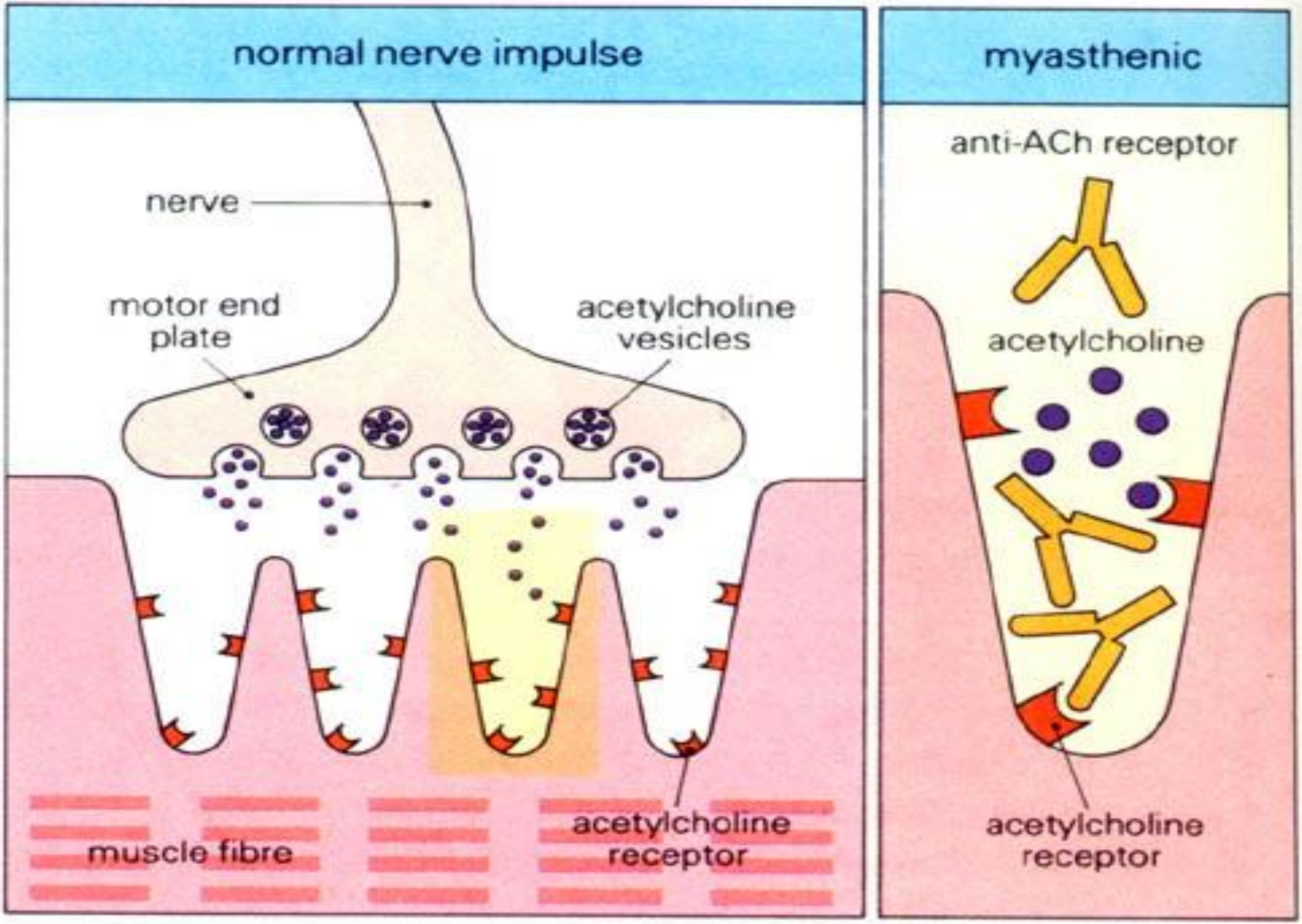
ADCC apoptosis



- **ADCC apoptosis by NK cells**

[3] Antibody-Mediated cellular Dysfunction

- **Antibodies directed against cell surface receptors impair or dysregulate function without causing cell injury or inflammation**
- **E.g. in Myasthenia Gravis , antibodies reactive with acetylcholine receptors in motor end plates of skeletal muscles impair neuromuscular transmission & causing muscle weakness**
- **While in Grave's Disease antibodies against thyroid-stimulating hormone receptors on thyroid cells stimulate the cells causing hyperthtyroidism**


normal nerve impulse
nerve
motor end plate
acetylcholine vesicles
muscle fibre
acetylcholine receptor
myasthenic
anti-ACh receptor
acetylcholine
acetylcholine receptor