

# Physiology

**Edition 8.5**

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# HOMEOSTASIS

----- Active space -----

## Introduction

00:00:48

Homeostasis is the concept of **constancy**.

Central theme for bodily function.

Disturbance in homeostasis.



Disease.

Claude Bernard :

Coined the term **milieu interior** (Internal environment).

Walter Cannon :

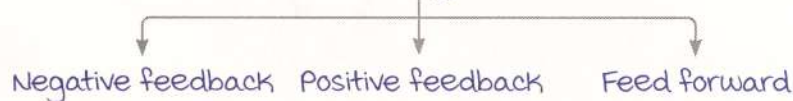
Coined the term homeostasis.

## Control Systems of Homeostasis

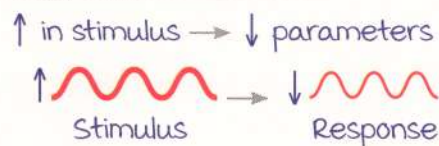
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mechanisms of the body to maintain homeostasis.

Control systems



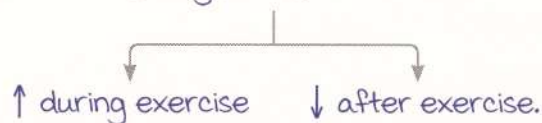
### Negative Feedback :



Eg :

1. **Baroreflex** :

Changes in BP

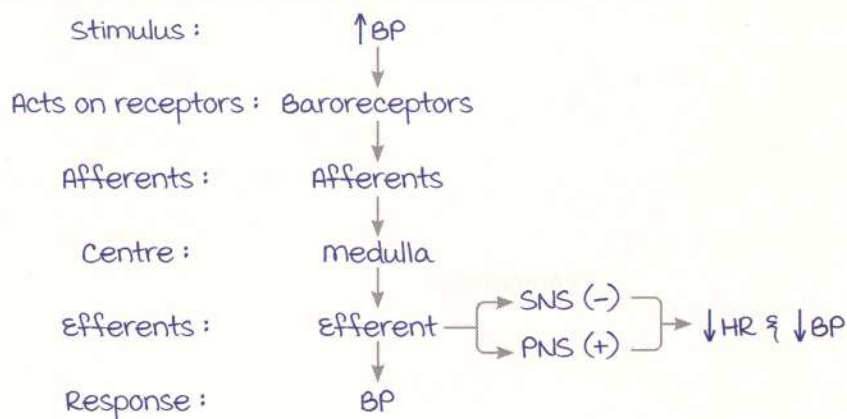


2. Endocrine hormone regulation (99%).

3. Gastric acid secretion.

----- Active space -----

Components of -ve feedback :



SNS : Sympathetic nervous system.

PNS : Parasympathetic nervous system.

Assessment of effectiveness of -ve feedback :

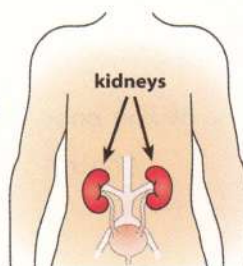
$$\text{Gain (G)} = \frac{\text{Correction by the System (C)}}{\text{Error remaining (E)}}$$

Infinite feedback gain :

When error becomes zero  $G = \frac{C}{0} = \infty$

$\downarrow$

Gain = Infinity



Eg :

Kidneys always correct blood pressure back to normal.

In HTN  $\rightarrow$  Kidneys are affected  $\rightarrow$  BP never comes back to normal.Positive Feedback :

- $\uparrow$  in initiating stimulus  $\rightarrow$  Further  $\uparrow$  in response.



- Amplification/cascade of reactions.
- AKA vicious cycle (Destabilizes our system).

Eg : CLAPS (mnemonic).

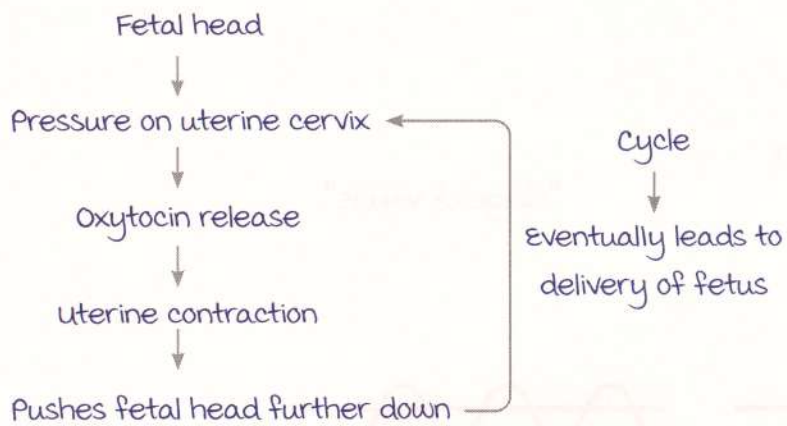
a) Coagulation cascade.

b) LH surge : Only exception for true feedback in endocrine hormone regulation.

c) Action potential.

d) Parturition (Normal delivery) :

AKA Ferguson reflex.



e) Shock :

Hemorrhagic shock (Eg : RTA) → Irreversible shock → Death (+ve feedback).

### Feedforward Control System :

Core theme : **Anticipatory control system.**

Body responds anticipating a stimulus (No actual stimulus).

Eg :

a) Anticipatory tachycardia & tachypnea : ↑RR and ↑HR before exercise.

b) Anticipatory motor control :

- Centre : Cerebellum
- Person driving on a highway → Applies brakes on seeing a cow (Anticipates danger).

c) Anticipatory regulation of core body temperature :

- Skin temperature → Shell temperature.
- Body organ temperature → Core temperature.

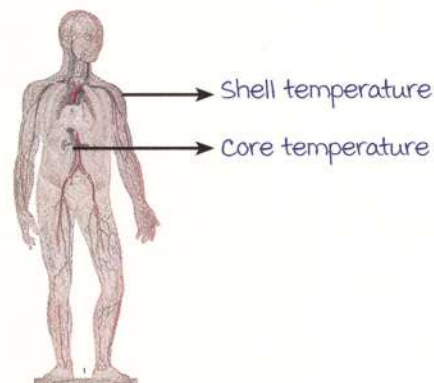
Cold environment.

↓ shell temperature.

**Hypothalamus** anticipates ↓ core temperature.

Corrective measures.

maintenance of core temperature.



----- Active space -----

## Properties of Homeostasis

00:28:04

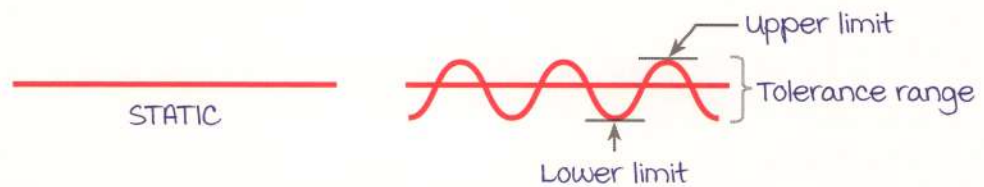
Dynamic constancy :

AKA **dynamic equilibrium**.

Homeostatic control systems maintain a "**range of values**"

Eg : Normal HR = 60-100bpm.

Normal RR = 12-18/min.



Prioritization of parameters :

- Priority of order of correction of parameters :

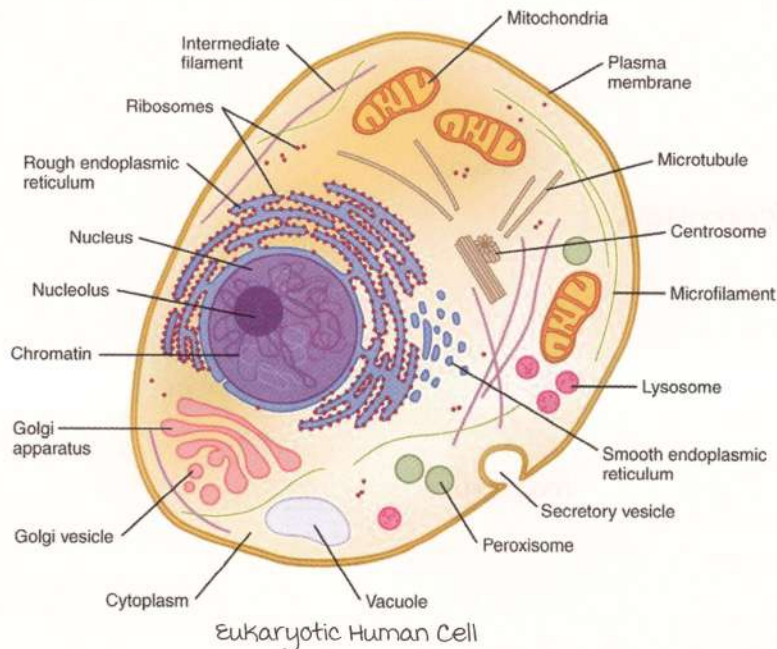
**pH** > BP > Temperature.

- pH changes are given more priority : As they affect the activity of enzymes  
→ Death.

## CELLULAR PHYSIOLOGY

----- Active space -----

Cell is the fundamental unit of all living organisms.



### Cell Membrane

00:01:13

AKA **plasma membrane**.

Function :

It is an outer barrier with selective permeability in the cell.

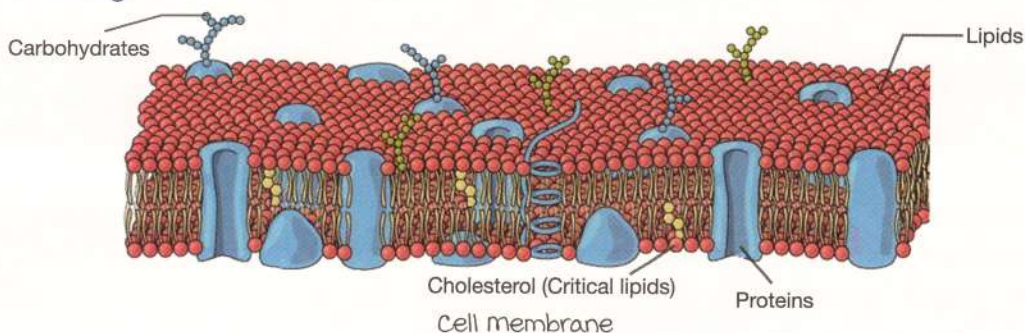
Structure :

Fluid mosaic model of cell membrane. Proposed by Singer and Nicholson.

Composition :

Macromolecules :

1. Proteins (55%) : Arranged in **mosaic pattern** in cell membrane.
2. Lipids (40%) : Responsible for fluidity of cell membrane.
3. Carbohydrates (5%).



----- Active space -----

00:04:40

## Lipids

### Introduction :

#### Structure :

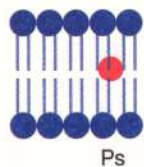
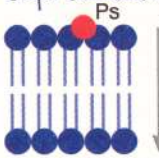
- Bilayer : Outer and Inner lipids.
- Asymmetry : Arranged specifically either on inner or outer side.

#### Types :

- Phospholipids ( $\text{PO}_4^{3-}$  group).
- Glycolipids (Carbohydrate side chain).
- Cholesterol (critical lipid).

### Phospholipids :

major lipid.

| Types                                  | Site                                                                                                                               | Significance                                                                                                                                                                                                                                                                                             |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Phosphatidyl choline (PC) AKA lecithin | Lungs : Surfactant                                                                                                                 | <ul style="list-style-type: none"> <li>• Prevent alveolar collapse.</li> <li>• major lipid in surfactant.</li> </ul>                                                                                                                                                                                     |
| Sphingomyelin                          | <ul style="list-style-type: none"> <li>• Nerve cell membrane.</li> <li>• Surfactant.</li> </ul>                                    | minor lipid in surfactant                                                                                                                                                                                                                                                                                |
| Phosphatidylinositol (IP3)             | Endocrine cells                                                                                                                    | <ul style="list-style-type: none"> <li>• Part of second messenger system (<math>\text{IP}_3 \rightarrow \text{DAG} \rightarrow \text{Ca}^{2+}</math>)</li> </ul>                                                                                                                                         |
| Phosphatidylserine (PS)                | Inner surface of cell membrane in all cells<br> | If expressed on outer surface.<br> <ul style="list-style-type: none"> <li>• Apoptosis (Programmed cell death).</li> <li>• Detected by Annexin V : Binds &amp; forms complex with PS. (Annexin V staining).</li> </ul> |
| Cardiolipin (CL)                       | Heart : mitochondria                                                                                                               | In syphilis : Serum anti-CL antibody + (Detected by VDRL test)                                                                                                                                                                                                                                           |

#### Note :

L (Lecithin)  
 S (Sphingomyelin) ratio :

- To assess fetal lung maturity.
- mature lung :  $\geq 2$ .

### Glycolipids :

| Types        | Site | Significance                                                |
|--------------|------|-------------------------------------------------------------|
| Cerebrosides | CNS  | -                                                           |
| Gangliosides | GIT  | Gm-1 gangliosides : Receptors for cholera toxin-Fragment B. |

## Cholesterol :

Site : Cell membrane of skin cells.

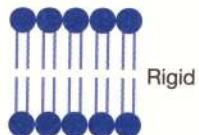
Significance :

- Precursor of vit.D.
- 7-dehydrocholesterol  $\xrightarrow[\text{(Skin)}]{\text{Sunlight}}$  vit.D
- **Fluidity buffer** : maintains membrane fluidity in optimal range.

## membrane Fluidity :

Lubricative property of lipid → maintain fluidity of membrane → Allows mobility.

### Characteristics of Fluidity :

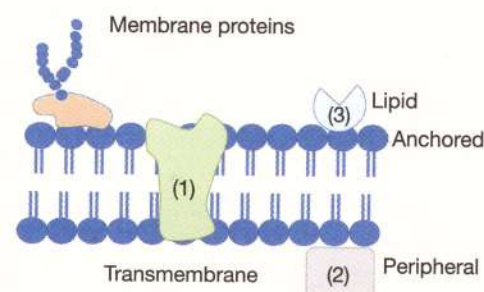
|                     | Increased fluidity                                                                                                                                                                                                                                                | Decreased fluidity                                                                                                                                                                                         |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Effect on health    | Good                                                                                                                                                                                                                                                              | Bad                                                                                                                                                                                                        |
| Type of fatty acids | unsaturated (Essential)                                                                                                                                                                                                                                           | Saturated (Trans)                                                                                                                                                                                          |
| Examples            | <ul style="list-style-type: none"> <li>• Linoleic acid.</li> <li>• Linolenic acid.</li> <li>• Arachidonic acid.</li> <li>• Omega-3 fatty acids : Abundant in fish.</li> </ul>  | <ul style="list-style-type: none"> <li>• Stearic acid.</li> <li>• Palmitic acid : (Abundant in junk food)</li> </ul>  |

## Proteins

00:24:00

Classification based on location in cell membrane :

1. Transmembrane proteins/integral membrane proteins : Present throughout.
2. Peripheral proteins : Present peripherally.
3. Lipid-anchored proteins : Requires lipids for attachment.

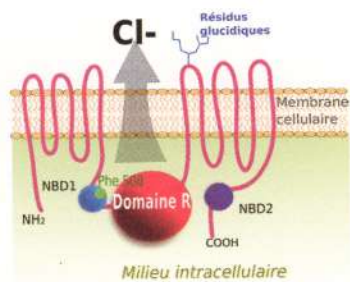


### Transmembrane Proteins (Integral membrane Protein) :

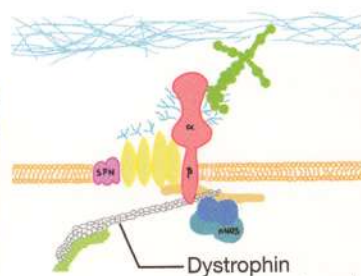
most important.

| Functions               | Examples                                                                                                                                                                                                        |
|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Hormone receptors (m/c) | GPCR (G-protein coupled receptors).                                                                                                                                                                             |
| Pump channels           | $\text{Na}^+ - \text{K}^+$ ATPase                                                                                                                                                                               |
| Ion channels            | <ul style="list-style-type: none"> <li>• <math>\text{Cl}^-</math> channel (CFTR).</li> <li>(Cystic fibrosis transmembrane conductance regulator.)</li> <li>• In cystic fibrosis → CFTR mutation (+).</li> </ul> |

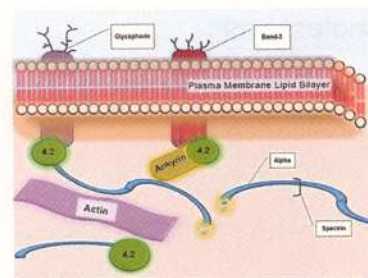
----- Active space -----



Transmembrane protein :  
Cl<sup>-</sup> channel (CFTR)



Peripheral protein



### Peripheral Proteins :

Functions :

1. Support shape of cell :

| Cell                    | Protein    | Diseases due to mutations                                                                                                                                                                                                                                                          |
|-------------------------|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RBC<br>(Biconcave disc) | Spectrin   | Elliptocytosis                                                                                                                                                                                                                                                                     |
|                         | Ankyrin    | Spherocytosis                                                                                                                                                                                                                                                                      |
| Skeletal muscle         | Dystrophin | <ul style="list-style-type: none"> <li>Duchenne muscular Dystrophy (DMD).</li> <li>muscular weakness. Typical presentation.</li> <li>Gower's sign : Climb on own body to stand up (knee → Hip → Stand).</li> <li>Respiratory paralysis (Weakness of diaphragm) → Death.</li> </ul> |

2. Cell surface receptors.

### Lipid Anchored Proteins :

In RBC :

- PIGA (Phosphatidylinositol Glycan-A) gene synthesises proteins :
  - CD55 (Decay accelerating factor).
  - CD59 (membrane inhibitor of reactive lysis).
  - C8 binding protein.
- Proteins bind to lipid : **Phosphatidylinositol**.
  - Significance :
    - Normal gene : Prevent hemolysis.
    - mutated gene : Paroxysmal Nocturnal Hemoglobinuria.

Paroxysmal nocturnal hemoglobinuria :

Pathology : mutated or absent PIGA gene.

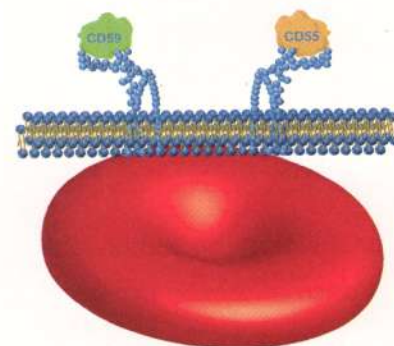
During sleep (Night)

↓ pH

Activates complement proteins : C5-C9 (membrane attack complex)

Attacks RBC membrane

Hemolysis (Hemoglobinuria).



Lipid anchored proteins in RBC.

Treatment :

- Anti C5 monoclonal antibody : Supportive.
  - Eculizumab.
  - Ravulizumab (Long acting).
- Hematopoietic stem cell transplant : Definitive.

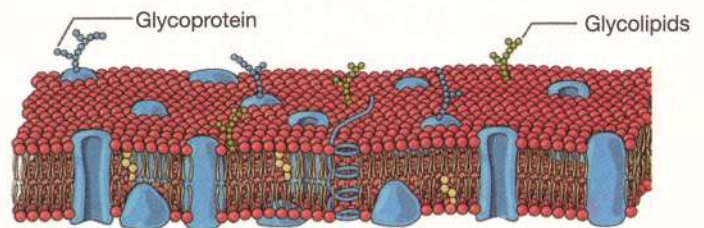
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## Carbohydrates

00:41:30

Classification :

1. **Glycoprotein** : Attached to proteins.
2. **Glycolipids** : Attached to lipids.



Significance :

Glycolipids on RBC membrane : **Determine blood groups.**

|                     | Blood Type |   |    |   |
|---------------------|------------|---|----|---|
|                     | A          | B | AB | O |
| Red Blood Cell Type |            |   |    |   |

Note :

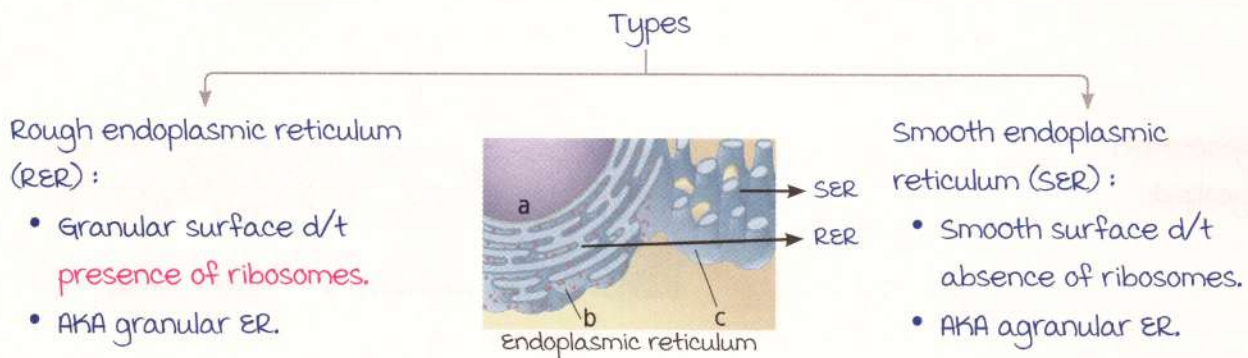
- membrane with highest protein : Inner mitochondrial membrane.
- In nerve cell membrane (myelin) : **Lipid (80%) : Protein (20%).**
- Repair of damaged cell membrane is by resealing of lipid bilayer.
- Deficiency of lecithin in pre-term baby : **Hyaline membrane Disease.**

----- Active space -----

# CELL ORGANELLES

## Endoplasmic Reticulum

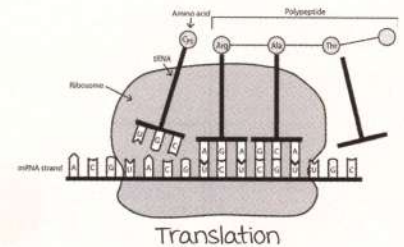
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### Rough Endoplasmic Reticulum :

Functions :

- Protein synthesis/translation.
- Folding of proteins :  
using chaperones/heat shock proteins (HSP).
- Degradation of misfolded proteins & quality control of proteins by unfolded protein response or ER stress response.  
 $\uparrow \uparrow$  misfolded proteins  $\rightarrow$  ER  $\rightarrow$ 
  - Halts protein synthesis.
  - Endoplasmic reticulum associated degradation (ERAD).



ERAD :

misfolded proteins are tagged to **ubiquitin** (kiss of death)

Protein-ubiquitin complex

moves to **proteasome** (Graveyard of the cell)

Degradation.

Applied aspect : misfolded protein diseases.

- Alzheimer's disease** : more common.
  - Due to accumulation of misfolded **Aβ amyloid protein**.
- Prion disease :
  - PrP<sup>C</sup> (Normal protein in CNS)  $\rightarrow$  **PrP<sup>Sc</sup>** (Prion protein : misfolded).
  - Eg : Creutzfeldt Jakob disease (very fatal).

## Smooth Endoplasmic Reticulum :

----- Active space -----

Functions :

1. **Synthesis of steroid hormones :**
  - Adrenal cortex : Aldosterone, cortisol.
  - Testis : Testosterone.
  - Ovary : Estrogen.
2. Storage of  $\text{Ca}^{2+}$  : SER of skeletal muscle stores  $\text{Ca}^{2+}$  (Sarcoplasmic reticulum).
3. Drug detoxification (Xenobiosis) :
  - major site : Liver SER.
  - Enzyme : **Cytochrome P450 (CYP450)**.

## Golgi Apparatus

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Location : Close to RER.

Functions :

1. Post translational modifications:

Proteins synthesised by RER

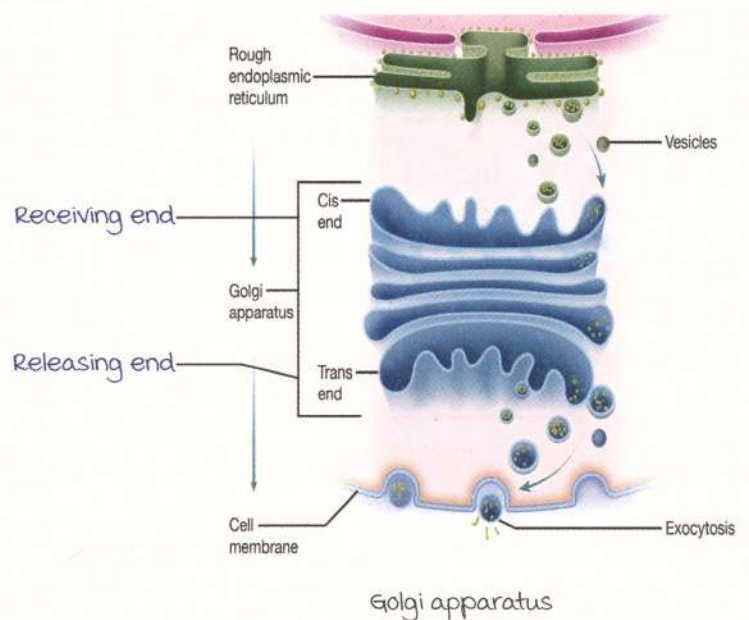
↓  
Cis end of Golgi apparatus (GA)

↓  
**Glycosylation** (Carbohydrate side chain is added to the protein)

↓  
Glycoprotein (↑ stability of protein)

↓  
Stored in vesicles  
↓ Stimulus

Released from trans end



GA are abundant in secretory cells.

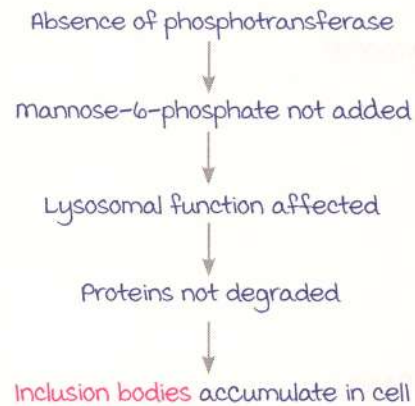
Eg :

- Antibody secreting plasma cells.
- Goblet cells of GI tract.

2. Sorting of proteins :

- GA determines where a protein is delivered.
- Eg : Protein  $\xrightarrow{\text{Phosphotransferase}}$  Protein + mannose-6-phosphate
  - ↓
  - moves to lysosome
  - ↓
  - Degraded.

----- Active space -----

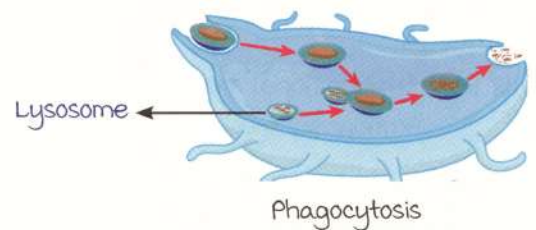
Applied Aspect :I cell disease :Lysosomes

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Recycle bin of the cell.Functions :

Acid mediated destruction :

- $H^+$ ATPase acid hydrolase.
- Acid hydrolase enzyme.

Note :

Acid in the lysosome can destroy itself : Suicidal bags/residual bodies.

Autophagy : Destruction of cell's own part.

Clinical Application :

Neutrophil : High content of lysosomes.

