

GENERAL

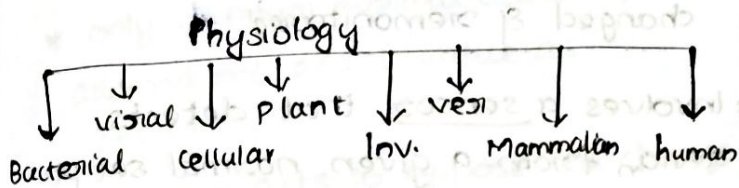
PHYSIOLOGY

• Describes the vital fn of living organisms, their organs, cells & molecules.

• Disordered / altered physiology
↳ disease.

• closely intertwined with medicine.

• Physiology gone abnormal
↳ clinical medicine



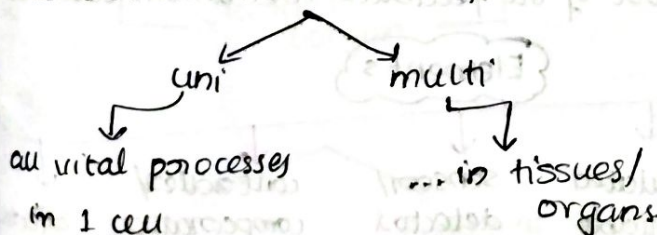
• General physiology
cellular principles common to the fns of all organs & tissues.
↳ cellular / molecular physiology.

• Pathophysiology
study of disordered body fn / physiological process.

Principles of homeostasis:

Milieu interieur:- "Claud Bernard"

to describe int. env. of cell.



Milieu exterieur: env. that physically surrounds whole organism.

Milieu interieur: Int. env. in which tissue / cells live.

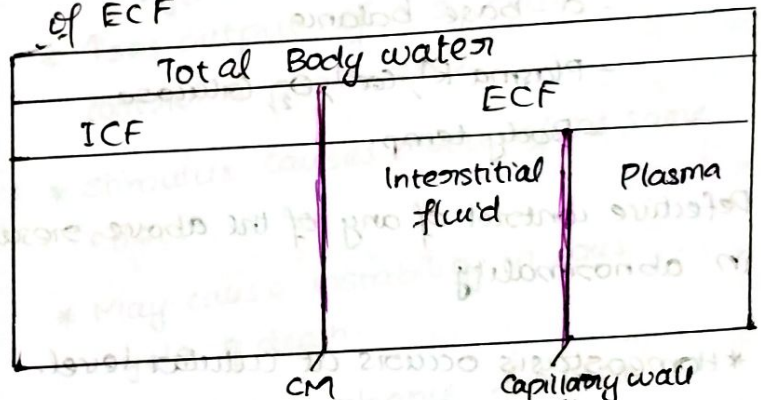
↓
extracellular fluid
↳ int. env. of cells.

60% of the adult body is fluid.
[Total body water]

- 2/3 : Intracellular fluid
- 1/3 : Extracellular fluid

Blood plasma Interstitial fluid

• Normal cell fn depends on constancy of ECF



↓
Impermeable to protein in plasma.

→ ECF → Na^+ , Cl^- , Bicarbonate ion

→ ICF → K^+ , Mg^{2+} & Phosphate ion

Normal fn depends on

↳ Normal availability of Int. env. of

• O_2 , glucose, ion

• Amino a, fatty a

Term homeostasis →

W.B. Cannon.

- Maintenance of nearly constant condition in the internal env. of cells of the body:

• Homeostasis is the control of a vital parameter.

Imp. constituents of ECF

O_2 - 40 → 35-45

CO_2 - 45 → 35-45

Na - 142 → 138-146

Homeostatic mechanism

Normal regulation occurs within range of values

* vital parameters controlled

- Arterial blood pressure
- $\bar{a}$ -base balance
- Plasma K^+ , Ca^{2+} , O_2 , Glucose
- Body temp.

Defective control of any of the above results in abnormality

* Homeostasis occurs at cellular level. [altering cell vol., energy level (ATP), inorganic ions (Na^+ , Ca^{2+})]

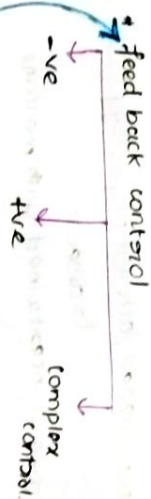
* Homeostasis continues under condition of env. variation, challenges from injury and diseases by **feedback control mechanism**

eg: Regulation of O_2 & CO_2 conc. in ECF

- : Regulation of plasma glucose
- : Buffering property of body fluids
- : Feedback control of arterial bp.

Baro-receptors: Rapid control mechanisms for maintaining BP

HOMEOSTATIC CONTROL SYSTEMS



* System in which state of a body condition is monitored, assessed, changed & re-monitored.

* Involves a sensor that detects deviation from a given normal set pt.

eg: thermo, baro, etc. receptors

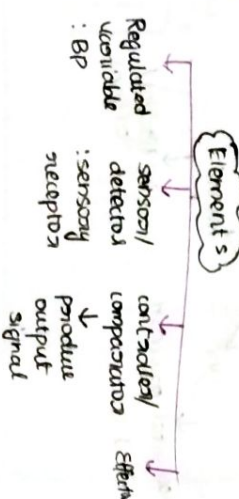
* Signals from the sensor trigger compensatory changes that continue till set pt is restored

-ve feedback mechanism

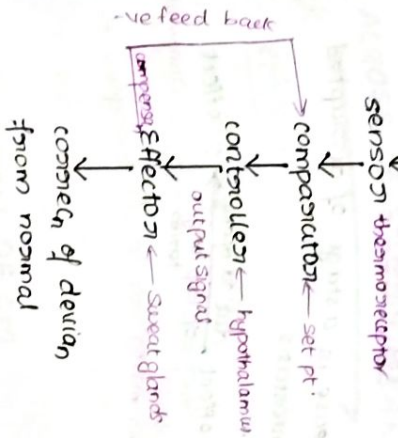
* connective mechanism involving an act that directly opposes a variation from normal limits

* Tend to push a variable in the direction opposite (-ve) to direction of original change

* Most of the feedback mechanism are -ve



eg: Input signal



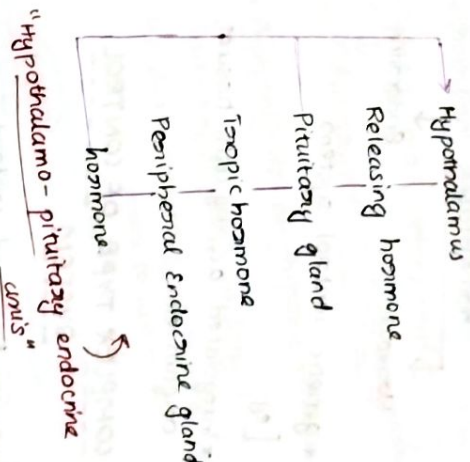
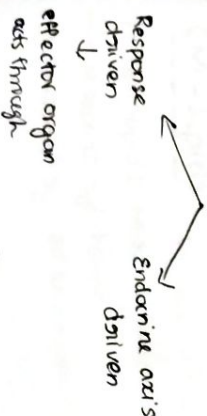
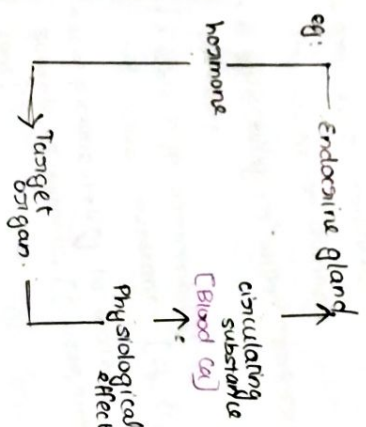
* Only a near normal value is attained not exact value as set pt.

* Effector acts to oppose the change

* Information flows along a closed loop.

* "gain" or proportionality factor. means effectiveness.

RESPONSE DRIVEN -ve FEEDBACK



+ve FEEDBACK

* eg: parturition, reflex during child birth

: coagulation cascade, generation of nerve impulse

* Uses output of a system to control a parameter

* stimulus causes more of the same effect.

* May cause instability vicious cycle & death

* Uses disturbance further.

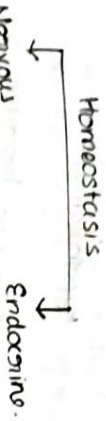
GAIN OF A CONTROL SYSTEM

* Effectiveness of a control system

Gain = correction/error.

* Magnitude of gain is a measure of effectiveness of feedback system.

* Temp control system is better than blood pressure system



* genetic control system

[eg]

* integrated acn by cells, tissues, organs etc.

COMPLEX TYPE OF CONTROL SYSTEM

* Feed-forward control

* Adaptive control: Delayed -ve feedback.

* continuous generates commands without directly sensing the regulated variable.

* open loop, moment - to - moment opening,

* operates when a change with time is delayed.

* control which anticipates change

* cerebral cortex: feed forward controller

* Acts in combination with -ve feedback systems.

ADAPTIVE CONTROL

* Brain corrects feed forward signals, sends to muscles next time the input is -ve.

* Delayed -ve feedback

HOMEOSTATIC COMPENSATION IN DISEASE

* Disease is a stage of disrupted homeostasis

* 1° effect due to opening of loop long term (physiological abnormality) → 2° effect (abnormality)

TRANSPORT MECHANISMS ACROSS CELL MEMBRANE

* CM/PM

CM/PM

• PM, envelops the cell

• Thin, pliable, elastic ~ 7.5nm thick

• composed 1/3 of proteins & lipids

• "the fluid mosaic model"

COMPOSITION OF CM

Proteins: 55%, Phospholipids: 25%, cholesterol: 13%, other lipids: 4%.

↓ fluidity/stability of CM
(glycolipids & glycoproteins)

• semi-permeable membrane

• Allow some substances to pass through & exclude others.

• Transport proteins

• Regulated ion channels

• A lipid bilayer with interspersed proteins

• enable high permeability to lipid-soluble substances [O_2 , CO_2]

• low permeability to water-soluble substances [glucose, amino acids, ions]

CM - Lipids

Phospholipids: most abundant:

→ phosphatidyl choline

→ phosphatidyl ethanolamine

• cholesterol, glycolipids

• sphingolipids, sphingomyelin

↓ in eukaryotes * in sig. transmission

→ Phospholipids - amphipathic molecule

Tail → hydrophobic → fatty acid

Head → hydrophilic → glycerol

exposed to water to

water

water

water

• phosphorylated glycerol backbone (head) and 2 fatty acid "tails"

• Amphipathic molecule.

phosphate head
hydrophilic
fatty acid tails
hydrophobic

→ Cholesterol

stabilize the membrane @ normal body temp.

→ Sphingolipids

• serve signal transmission in nerve cells

• protect from harmful env. factors

• forms adhesion sites for proteins

→ Proteins

• Proteins are interspersed in the lipid bilayer

• Av: 50%

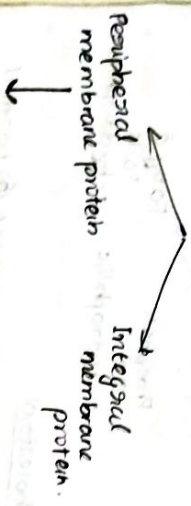
• Embedded in a "fluid mosaic model"

Integral proteins: - Span the membrane or are embedded in it (covalent bond to CM)

Peripheral proteins: - Present in only one side: [loose electrostatic attachment]

Membrane proteins

- Protein channels (for ions, & water) from ECF to ICF, protein pores (open/gated)
- Carrier proteins
- Enzymes
- Hormone receptors
- Cell-surface antigens, cell adhesive molecules



- Adhere to cytoplasmic or extra-cellular surface of CM.
- Non covalently bound: loose electrostatic interaction.
- Bind to integral proteins or polar head groups
- Enzymes, cell adhesion molecules, etc - peripheral membrane protein.
- Ankyrin " Anchors the cytoskeleton of RBC to an integral membrane protein (band-3)

Integral membrane protein

- Anchored to the CM by hydrophobic interactions/covalent bonds

① Trans-membrane proteins:

- Span the membrane one or more times - contact both the ECF & ICF

TMP - salt or something is enough to extract protein.

IP - detergent is needed & CM has to be completely removed

② Proteins embedded in the membrane do not span it.

③ Trans-membrane integral proteins

eg: Na⁺-K⁺ pump (transport protein)

- receptors for hormone eg neurotransmitters.
- Ion channels.
- GTP binding proteins (span the CM)

② Proteins embedded in bilayer without crossing it

③ Lipid-anchored proteins linked by covalent bond to lipid component or to a fatty acid derivative

④ GPI anchors [glycosylated phosphatidyl inositol]

Glycophospholipid linked proteins

eg: enzymes, cell surface antigens

- Anchored to the outer leaflet of membrane
- Enzymes: Alkaline phosphatase
- Cell surface antigens
- Cell adhesion molecules

Membrane carbohydrates

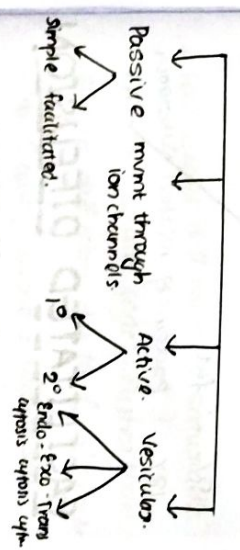
glycolipids &

• Provide -ve surface charge to the cell

• Act as receptors for binding hormones eg: Insulin

• Some CHO moieties enter into immune rxn.

TRANSPORT MECHANISM ACROSS CELL MEMBRANE



• Down an electrochemical gradient

Simple diffusion
facilitated diffusion

• Against Electrochemical gradient

1° Active tr. requires direct input of metabolic energy
2° Active tr. utilizes indirect input of metabolic energy

Diffusion

A gas or a substance in sol. expands because of motion of its particles, to fill all available vol.

• Energy: of the normal kinetic motion of matter

Diffusion through CM

• Occurs through intermolecular spaces or in combination with a carrier proteins.

• Simple diffusion: by random thermal motion of molecules.

- through lipid bilayer or through watery channels

- not carrier mediated

- Facilitated diffusion: carrier mediated.

Active transport

• transport across membrane in combination with a carrier protein against an energy gradient



Lipid soluble substances

• O₂, CO₂, N₂ dissolve directly in lipid bilayer.

• Rate of diffusion directly proportional to lipid solubility

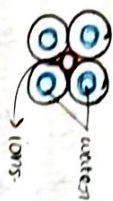
Diffusion through protein spaces

• Tubular pathways extending from ECF to ICF

• Integral proteins, always open (not gated)

- selectively permeable: to water, ions, urea etc.

- Aquaporins: selective channels for water, tetrameric structure



- Pore is narrow. Diameter of pore electrical charge of selectivity

Net rate of diffn

- Flux or flow (J) depends on:

- Conc gradient, diffn coefficient, thickness of membrane, SA, availability for diffn.

$$J = -DA \frac{\Delta C}{\Delta x}$$

Labels: ΔC → conc. gm., Δx → thickness, DA → Diff. fac.

$D \propto \frac{1}{\text{radius viscosity}}$ $\propto \frac{1}{D \uparrow \text{diff. easily}}$

FICK'S LAW OF DIFFUSION

- Magnitude of diffusing tendency (J)

- J $\propto$ Area of across diffn taking place

- Conc. gradient $\propto$ [conc. diffn / thickness]

$$J = -DA \Delta C / \Delta x$$

J $\rightarrow$ net rate of diffn

$$\text{conc. diff} = \frac{C_0 - C_1}{\text{distance}}$$

- Driving force for net diffusion
- Diffusion rate of ion/electrolyte depends on P.D across CM of charge of diffusing ion.

Diffusion potential.

When a charged solute diffuses across a membrane, down a conc. gradient, that diffusion itself generate a P.D across the membrane.

$\hookrightarrow$ D.P.

BODY FLUID COMPARTMENTS

- Maintenance of relatively const. env. is homeostasis

In 70 kg adult man,
60% total body water
17% intracellular

15% fat
18% proteins & related substances

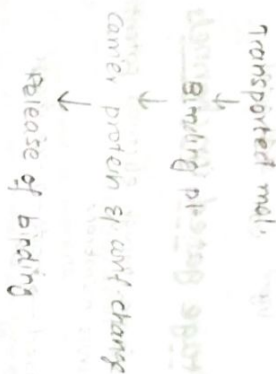
FACILITATED DIFFUSION

- carrier mediated (facilitated) passive diffusion
- carrier protein moves substances down an electrochemical gradient — requires no input of metabolic energy.
- Uniporins (facilitated transporters)

- Fundamental event for a carrier is a cycle of conformational change.

- Binding sites in a carrier are limited
- each cycle can transport only a fixed no. of solute particles.

Postulated mechanism for facilitated diffusion



- Rate of transport depends on

$\rightarrow$ rate @ which carrier undergoes conformational change
 $\rightarrow$ limited no. of binding sites on the carrier.

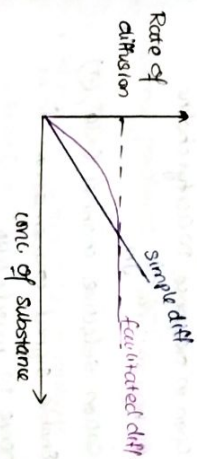
- * Facilitated diffusion is saturable.

- At low solute conc.: - faster than simple diffusion, due to fn of carrier.

- At $\uparrow$ conc., carriers become sat.

- Transport maximum [Tm]:

Pt. when all the binding sites are occupied & saturation achieved.



- Glucose, most amino acids

- Glucose transporter (GLUT)

- GLUT 4: Transports glucose into skeletal muscle & adipose cells.

stimulated by insulin

- GLUT 2: Transports glucose out of intestinal & renal epithelial cells.

GLUT 4: mediated facilitated diffn of glucose in insulin sensitive tissues

GLUT 2: mediated absorption

Features of carrier-mediated transport

- Saturation

- Stereo specificity: D-glucose, not L-glucose. (not by binding site)

- Competition: D-galactose, Phlorizin are competitive solutes. (near both of glucose)

Transport through ion channels

- Simple aqueous channels with tightly regulated pores that are gated, by some conformational changes

voltage ligand $\rightarrow$ shear

- Ions move down the electrochemical gradient.

- * cause transport of charge across membranes & set up electrical potential; imp. for function of excitable cells.

Selective permeability of channels

- selective for 1 or more ions.

- selectivity results from:

- Diameter
- Shape
- electrical charge along inside surface
- selectivity filter.

Types of protein channels

(A) K^+ channels: Tetramers



(B) Acetylcholine receptors:

Five identical subunits



(C) Aquaporin water channels:



very narrow

(D) Cl^- channels



Dimer

Structure of K^+ channel

• Tetrameric structure with a central pore

• Selectivity filter is lined by carbonyl groups for K^+ is formed by 'pore loops'

Sodium channel

• selectivity filter lined with strong negative charges

- Pull dehydrated Na^+ into these channels

Gating of ion channels

- channels undergo conformational transitions b/w closed & open states
- Provides control of permeability
- Ligand-gated
- opened/closed in response to ligand

Voltage gated

- Gated by alteration in membrane potential

• Phosphorylation gated

• stretch gated (Pressure gated)

eg: Ca^{2+} channel

ligand volt stretch gated

Voltage gated ion channels

• conform, through electrical potential across membrane

• closed $\rightarrow$ inside $\rightarrow$ -ve charge

• $cm \rightarrow$ lose -ve charge $\rightarrow$ influx

Na⁺ channel

Activation gate Inactivation gate

Resting $-70mV \rightarrow$ activated $+35mV$



Ligand gated channel

- Acetylcholine receptor ion channel
- Open in response to acetylcholine
- @ neuromuscular jn
- cation selective channel (Na^+ , K^+)
- Enable signal transmission from nerve to muscle cells

Clinical imp

• channelopathies (mutation in ion channels)

• $Allosteric$ activation/inactivation of ion channels

- ion selectivity

• Diseases mostly affect muscle & brain

brain

Osmosis

pulling force: osmotic pressure diff.

set by conc. diff.

$\rightarrow$ flow of solvent molecules across a semi-permeable membrane

• Depends on no. rather than type of solute

Osmolarity:

No. of osmoles/litre of soln.

• Affected by solutes in soln & temp.

Osmolality

No. of osmoles/kg of solvent

* Total plasma osmolality

: 290 mOsm/L

due to ions, $[Na^+]$, $[Cl^-]$, $[HCO_3^-]$

• Imp. in assessing

- dehydration

- Overhydration

- Electrolyte abnormalities

• Plasma proteins contribute

$< 2 \text{ mOsm/L}$

• Glucose & Urea also contribute

$\sim 5 \text{ mOsm/L}$

- become large in hyperglycaemia & uremia

Tonicity

• Describe the osmolality of a soln, relative to plasma

0.9% $NaCl \rightarrow$ isotonic to plasma

• 5% glucose soln (nearly

isotonic) is infused intravenously to treat dehydration

Gramong & Sullivan

Active transport

• Transport of molecule or ions in both directions with a carrier protein against a concentration gradient or electrical gradient

• Requires additional source of energy besides kinetic energy provided by hydrolysis of ATP

Substances actively transported

• Na^+ , K^+ , Ca^{2+} , Fe^{2+} , Cl^- , I^- , several sugars, most amino acids

• According to source of energy used:

1. active transport: Directly from

ATP hydrolysis

2. active transport: Indirect input of metabolic energy

3. carrier protein is capable of imparting energy to the transported substance to move it against the electrochemical gradient

• carrier: Mostly ATPase enzymes (pumps)

Diagram

Pumps in active transport

- $\text{Na}^+ - \text{K}^+$ ATPase :- In all CM
- $\text{H}^+ - \text{K}^+$ ATPase :- In gastric mucosa, renal tubules.

- Ca^{2+} ATPase :- In sarcolemmal & endoplasmic reticulum.

PMCA :- Ca^{2+} out of cell.
Plasma membrane Ca^{2+} ATPase

$$\text{ECF } \text{Na}^+ > \text{ICF } \text{Ca}^{2+}$$

- Proton ATPase: Acidity intracellular organelles.

In Active transport

- Carriers mediate coupled modes of transport
- In the form of

→ Pumps

→ Cotransporters: Symports:

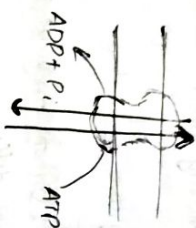
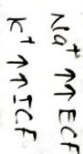
→ Exchangers: Antiports (countertransporters)

Na-K Pump ($\text{Na}^+ \text{K}^+$ ATPase)

- First enzyme recognized to be an ion pump
- Jones & Skou showed 1997 Nobel Prize in Chemistry

- In CM, in all parts of body.
- Mostly on basolateral side of epithelial cells.
- Active transport for $\text{Na}^+ \text{K}^+$

- Actively pumps Na^+ from ICF to ECF & K^+ from ECF to ICF



- ATP is hydrolysed to ADP & P_i , releasing energy from high-energy phosphate bond
- Terminal phosphate is transferred to the transport protein, initiating a cycle of phosphorylation & dephosphorylation

Na-K Pump electrogenic

- For each cycle, 3Na^+ extruded & 2K^+ taken in
- Coupling ratio of 3:2
- Net extrusion of 1 net charge

$\text{Na}^+ - \text{K}^+$ Pump : Subunits

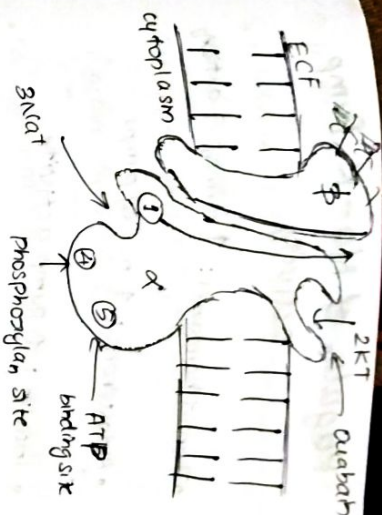


- Heterodimer with α & β subunits

- α subunits: Catalytic subunit that mediates active transport

- β subunit: Single membrane-spanning domain

- Separates of subunit eliminates activity



- $\text{Na}^+ \text{K}^+$ transport occurs through the α subunit

- Intracellular portion of α subunit has

- Na^+ -binding site
- Phosphorylation site
- ATP binding site

- Extracellular portion has

- K^+ -binding site
- Ouabain binding site

β subunit

- Glycoprotein with 3 ex EC glycosylation sites

- Essential for

- proper assembly of pump
- Membrane targeting

- α & β subunits are heterogeneous

- $\alpha_1, \alpha_2, \alpha_3$ isoforms

- $\beta_1, \beta_2, \beta_3$

- Isoforms represent specialisation for specific tissue function

- Member of $\text{E}_1 - \text{E}_2$ (P-type) ATPase family intracellularly
- cycles b/w E_1 & E_2 conformational states.

- Extension of 3Na^+ , uptake of 2K^+ for each ATPase

Transport cycle of Na-K pump

- Cycle begins with pump in E_1 state bound to ATP.

- E_1 state: $\uparrow$ affinity for Na^+ , ion binding sites face ICF

- 3Na^+ ions bind, ATP is hydrolysed, P_i is transferred to phosphorylation site

- Major conformational change occurs to E_2 state

- In E_2 state: $\uparrow$ affinity for K^+ & Na^+ affinity for Na^+

- 3Na^+ ions are released to ECF

- 2K^+ ions bind extracellularly

- P_i is released (Dephosphorylation)

- A major conformational change occurs, releasing 2K^+ into ICF

- An ATP molecule binds, reorienting the pump to ATP bound E_1 state ready to begin another cycle

Na⁺ - K⁺ Pump Functions

Regulation of Na-K Pump activity

- Responsible for creating large conc. gradients for Na⁺ & K⁺ across CM.
- keeps intracellular (Na⁺) low & [K⁺] high
- Energy of the gradients is used for counter transport & transport of solutes.
- create & maintain the resting membrane potential (RMP)
- maintains a RMP (-ve) inside CM
- Basis of neuron & signal transmission
- Direct electrogenic contribn: Due to coupling ratio of 3:2
- Indirect contribn.
- Na⁺ - K⁺ ATPase is necessary to create & maintain the K⁺ conc. gradient which establishes the RMP.
- Prevents swelling & bursting of cells
- Imp. for controlling cell vol.
- Impermeant anions inside a cell attract K⁺, Na⁺ which cause osmosis of water into cell.
- Aldosterone: ↑ no. of pumps
- Thyroid hormones: ↑ formation & activity
- Insulin: ↑ pump activity
- Dopamine: Phosphorylates & inhibit the pump in kidney

APPLIED IMPORTANCE

- cardiac glycosides (ouabain, digitalis) inhibit Na⁺ - K⁺ ATPase
- ouabain binds near K⁺ - binding site & makes the pump non-functional
- Digoxin: ↑ cardiac contracta.
- Used in treatment of cardiac failure

H⁺ - K⁺ Pump

- ① Found in parietal cells of gastric gland & collecting duct of kidney.
- Active extrusion of H⁺ & uptake of K⁺ across apical membrane of parietal cell
- mechanism for secreting HCl in stomach.
- Omeprazole, inhibitor of H⁺ - K⁺ ATPase
- Used to ↓ H⁺ secret. in peptic ulcer

② In kidneys: intercalated cells of CD.

- H⁺ secreted from blood into renal tubular fluid
- Eliminate excess H⁺ from body fluid.

Active transport of Ca²⁺

- Ca²⁺ maintained @ low conc. in ICF
- By 2 Ca²⁺ pumps

① PM Ca ATPase (PMCA)

- ② Sarcoplasmic & endoplasmic reticulum Calcium ATPases (SERCA)

PMCA

- In PM of most cells
- One Ca²⁺ ion extruded in exchange one H⁺ for each ATP hydrolysed

SERCA

- on membrane of intracellular organelles
- Active sequestration of Ca²⁺ into intracellular stores

2^o active transport

- Active transport of Na⁺ coupled to transport of solutes
- Energy is 2^o derived from: basically dissected Na⁺ gradient, set up by the Na-K pump.
- Indirect utilization of ATP.

8/12/2022 Energy 2^o derived from: basically dissected Na⁺ gradient, set up by the

- Solutes transported uphill

- glucose
- amino acids
- K⁺
- Cl⁻

- coupled to downhill transport of Na⁺

Types of 2^o transport

- cotransport (symport): All substances bound to carrier trans in same dir across CM

- In epithelia of small intestine & renal tubule

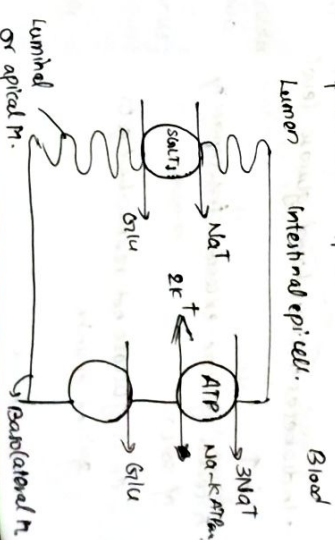
- Na⁺ - glucose co.
- Na⁺ - amino acids co.

- In renal tubule: Na⁺ - K⁺ - 2Cl⁻ cotrans.

Sodium glucose cotransport

SGLT (Na⁺ - glucose transport protein)

- Downhill movement of Na⁺ coupled with uphill movement of glucose



SGLT₁

- 2 binding sites: for Na^+ , glucose
- Both Na^+ & glucose bind to the sites on SGLT₁

• conformational change occurs, both Na^+ & glucose are trans. to the inside of cell.

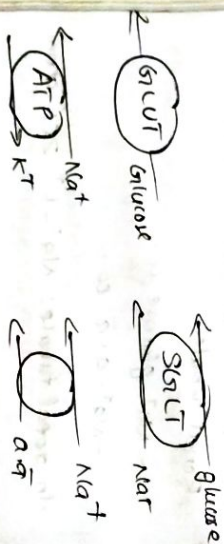
• Neither get tr. in absence of other Na^+

Across basolateral mem.

- glucose moved out by fac. diff. into the interstitial fluid.

[through SGLT₂]

Glucose reabs. in kidney



Applied importance

Trans. max for glucose transport in kidney

• SGLT₂ in kidney exhibit saturation of Na^+

• In diabetes mellitus blood glucose level is $\uparrow$

is $\uparrow$

• Filtered glucose exceeds the capacity of SGLT

- excess glucose not reabsorbed gets spilled in urine

Counter trans.

- opp. directions
- Na^+ & H^+ exchanged for Ca^{2+} or H^+ (pH)

Na^+ - Ca^{2+} counter trans.

- 3 Na^+ ex. for 1 Ca^{2+} ion
- conf. change delivers Ca^{2+} to exterior of cell & Na^+ to int.

Applied imp

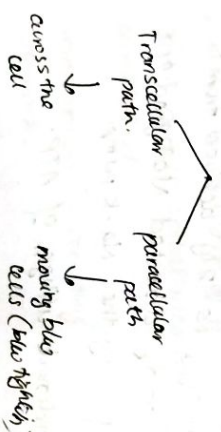
Digitalis glycosides $\uparrow$ cardiac contract. by inhibiting Na^+ - Ca^{2+} pump

- $\uparrow$ Na^+ (intracellular) $\downarrow$
- $\downarrow$ Na^+ influx & Ca^{2+} efflux $\downarrow$
- Ca^{2+} $\uparrow$ (intracellular) $\uparrow$ contract.

Na^+ - H^+ antiport

- In proximal tubules of kidney:
- Na^+ move into tubular cell
- H^+ exchanged into lumen & unabsorbed

Ac. trans. across epithelia

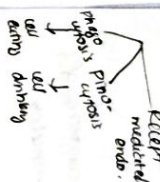


Vesicular transport

endocytosis

specialized

in of cell



transcytosis

from ICF

$\rightarrow$ ECF

exocytosis

- Requires Ca^{2+} , energy & docking protein
- SNARE protein

Seen of protein from cell.

non-constitutive (regulated)

- processing occurs before exocytosis
- endocrine cells, exocrine cells, neurons
- Plasma cells secreting Ig
- fibroblast secreting collagen

Endocytosis

2 non-cytoplasmic sides of membrane fuse.

Phagocytosis (cell eating)

- Ingestion of large particles (bacteria, cell debris)

• Imp. in immune cells system (macrophages, neutrophils)

Pinocytosis (cell drinking)

- Nonspecific uptake of small molecules and water into the cell.

• vesicles much smaller & substances ingested are in sol.

• means of entry of protein molecules into cells.

• Prominent feature of endothelial cells - that line capillaries.

- Requires energy (from ATP) & Ca^{2+} ions

Receptor-mediated endocytosis

- Sp. receptors are present on cell surface for transport.

• involves acc. proteins like

— clathrin, Actin, Dynamin

• clathrin mediated endocytosis

- receptors are conc. in small coated pits on membrane
- clathrin: A fibrous protein beneath the pit.

• process req. ATP, Ca^{2+} ions

Importance

- responsible for internalization of - proteins, nerve growth factors, LDL
- Role in synaptic transmission

vesicle docking & fusion involves proteins

- SNARE prot. - bridge b/w vesicle & target membrane

• latch & initiate fusion

