OneShot 4.0

Physiology

DBMCI · 2026

DBMCI one

PHYSIOLOGY

“Success
is getting
what you want;
Happiness is
wanting what
you get.”

- Dr. Ashish Kumar

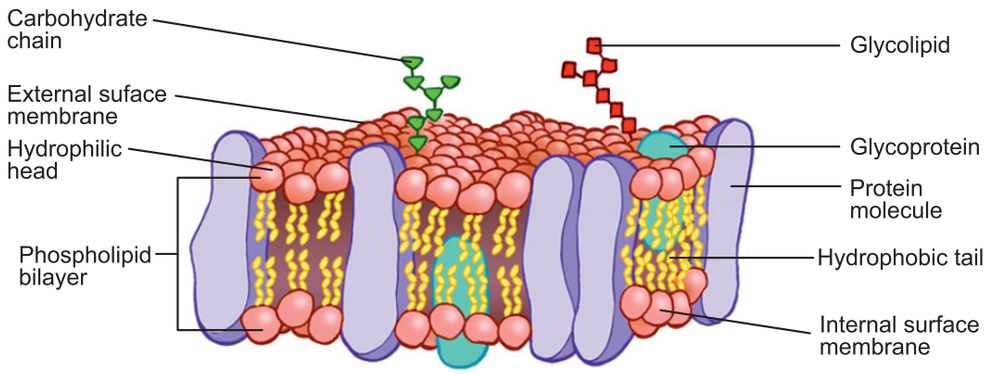
GENERAL & CELL PHYSIOLOGY

Unit of life is cell : Cell Membrane (CM) & Cytoplasm

CELL MEMBRANE (CM)

- Best Model for CM : Singer - Nicholson fluid Mosaic model
- CM contain lipids and proteins
- Main lipid are **Phospholipid**: Polar head by PO_4^{3-} groups (Hydrophilic) & Non-Polar tails made by lipid chain (hydrophobic)

Phospholipids are arranged as bilayers with proteins



Functions of lipids : Integrity, Flexibility & Solubility

- Lipid soluble substances can cross CM eg. gases, Fat soluble Hormones like Thyroid & steroid, Vitamin A D E K etc

Proteins of CM help water soluble substances cross & act across CM

1) Ions: use channels & pumps
2) Water: uses Aquaporin
3) Solutes like sugars, AAs, urea etc use CARRIER eg. GLUT
4) Water soluble hormones, Neurotransmitters use cell surface receptor
5) Proteins of CM also act as: enzymes, antigen, cell marker etc

BODY FLUIDS

60-70% of body weight is water called as TBW = Total body water

- 2/3rd is ICF & 1/3rd is ECF
- ECF = 25% PLASMA (inside vessels) & 75% IF (Interstitial fluid)
- IF is fluid b/w vessels & cells, also k/a Tissue fluid
- IF helps form LYMPH
- IF is same as plasma but no plasma proteins
- All exchange b/w cells & vessels occur in IF; It forms internal environment.
- It is maintained in a steady constant state Homeostasis; Best regulation is **Negative Feedback :** bring value back to normal.

ESTIMATION OF FLUID CHAMBERS

Dye Dilution Method

Vol= Amount of dye/Concentration

Dyes used

1. TBW = Heavy Water: D_2O, T_2O
2. ECF = Inulin, sucrose
3. Plasma = Radio labelled Albumin, Evan blue dye

TRASPORT ACROSS CM

1. Active

- Use ATP, Against gradient (uphill): Low to high Conc.
- Types: a) 1° Primary Active, Direct use of energy Eg. **Pump**
  b) 2° Secondary Active, coupled to Pump Eg. **Sodium symporter**
  Sodium AA Symport, SGLT: Sodium Glucose Linked transport
  GIT: SGLT-1 & Kidneys: SGLT -2

2. Passive

- No ATP, along gradient (Down hill): High to low Conc.
- Follow Fick's law
- Types: a) Simple Diffusion: No carrier, Eg. O_2, CO_2 Diffusion
  b) Facilitated Diffusion: Carrier used, Eg. GLUT

Cell Junctions (b/w cells)

1. **Gap Junctions:** Connexon protein - helps in ions, current spread from one cell to another. Eg. : Electrical synapses, heart, smooth muscles (viscera) like GIT, bladder, uterus etc. All fibers contract as one unit/Syncytium

2. **Tight Junctions:** Zonula Occludens, made by Occludin & Claudin proteins
   Act as BARRIER, Eg. BBB, Blood-Testis Barrier, Placenta Barrier, Kidney etc

3. **Desmosomes:** Cellular Cement/Macula Adherens. Made by Cadherin protein, Desmoglein (Dsg-1, 3 in Skin)

NOTES

DIGESTIVE SYSTEM / GIT

4 Layers

1. Mucosa: Innermost, contains Villi & Microvilli for Absorption
2. Submucosa : Vessels, nerves, lymphatics, glands → secretion
3. Muscularis: smooth muscles for Motility
4. Serosa: for attachment, absent in esophagus (adventitia)

Enteric Nervous system : Control GIT, 2 Parts

1. Meissner's or submucous plexus: in submucosa for ↑ secretion
2. Auerbach or myenteric plexus: in muscularis for ↑ movements

ANS: Autonomic Nervous System

Symp. system (fight or flight): ↓ GIT sec. & movements, ↑ Heart, ↑ Reflexes etc
Parasymp (Rest & Digest): ↑ GIT secretion & ↑ movement, urination, erection
Pacemaker of GIT : Cajal cells in Auerbach Plexus: make slow waves/BER

- Basal electrical Rhythm, BER + stimulus (food, distension, Ca^{2+}, Ach, GIT hormones etc) cause **Spike potentials** → Ca^{2+}: Bind **calmodulin** & activate Myosin Light Chain Kinase **(MLCK)** will break ATP → Contraction & Movements
- Max BER → Duodenum & Min. BER → Cecum (slow)

GIT MOVEMENTS

1. **Peristalsis:** Food movement in forward direction
   BER + food → Distension & Release Neurotransmitters, Ca^{2+} etc.
   Front/anterograde: VIP (Vasoactive Intestinal peptide) & NO: Relax
   Retro/back: Ach, S-HT, Substance P etc. cause Contraction
2. **Reverse/Anti Peristalsis:** Vomiting
3. **MMC:** Migratory Motor Complexes/Hunger Pangs/Broomstick or Housekeeping of GIT: produced by empty stomach & clear old contents to prepare for next meal
   Duration: 90-100 min, food will ↓ MMC & ↑ Peristalsis
   Motilin hormone from M_0 Cells of stomach, Duodenum: ↑ All movements
4. **Mass movements** for defecation by colon, rectum (Ganglionic cells in Auerbach Plexus). Frequency 1-3 times a day.

ABSENT IN HIRSCHSPRUNG DISEASE/MEGACOLON

We need good bulk of feces for proper bowel movements
↑↑ by dietary fibers (Cellulose, Lignin, Pectin, Chitin, Inulin etc.)

3 Phases of Digestion

Name	Stimuli	Mediator	Response
Cephalic	Smell, sight of food	↑ Parasymp	↑ Saliva & 10% HCl sec.
Gastric	Food in stomach	Vagus (M_1) Gastrin (G-cell)	Max HCl sec. ↑ Gastric Emptying
Intestinal	HCl in Duodenum, Food, Vagus, Distension etc.	S- Cell: Secretin I-Cell : CCK- P2 Cell : GLP-1,2 Cell : GIP Enterogastrone VIP, Amylin etc.	↑ Alkaline $HCO3^-$ rich sec Pancreatic, Bile ↑ Insulin (GLP-1 & GIP) ↓ HCl secretion ↓ Gastric Emptying

Choleretics : ↑ BILE Sec : most potent are Bile salts & Acids (-cholic/cholate)

SALIVA

Max from Submandibular glands (70%), at Rest pH is 6.8 but on stimulation, secretion of Na^+, K^+, HCO_3^- causes more volume & makes pH alkaline 8.0

Functions

1) Lubrication
2) Taste
3) Mastication
4) Swallowing
5) Antibacterial: IgA, zinc, Defensin, Lysozyme etc.
6) Digestive Role by enzymes
   a) **S. Amylase/Ptyalin :** activated by Cl^- & Optimum pH = 6.7
      It break starch (Carbohydrates)
   b) **S. Lipase/Lingual Lipase & peptidase**

GASTRIC PHASE

Gastric glands → Main cells are

a) **Parietal/Oxyntic cells:** max at Fundus
   1) HCl secretion by Proton Pump (H^+/K^+ ATPASE & HCO_3^-/Cl^- exchanger: HCl in lumen & ↑ HCO_3^- in blood (post-prandial alkaline tide)
   2) **Intrinsic factor:** Bind Vit.B in duodenum & absorbed in Terminal Ileum.
      Defect causes: Megaloblastic anemia
   3) **Ghrelin:** Increase hunger & Growth Hormone

b) **Chief or zymogen cell** (Inactive enzymes): Pepsinogen $\xrightarrow{HCl}$ pepsin ↑ HCl sec by
1. Vagus - Ach (M_1) Receptor
2. ECL cells - (Enterochromaffin like cells) - secretes Histamine, SHT
3. G-cell at Antrum - Gastrin

Brunner gland in Upper duodenum protect from acid **burn** by making alkaline mucus with pH 10-11

DIGESTION & ABSORPTION

1. Proteins ⟶ AAs: AAs absorbed by Sodium AA Symporter
   Pancreatic enzymes (tail is exocrine part)
   Trypsinogen $\xrightarrow{\text{Enterokinase}}$ Trypsin (Active) in Duodenum
2. Fats ⟶ LCFA (Long Chain Fatty Acids)

   LCFA + Bile salts $\xrightarrow{\text{Emulsification}}$ Micelles (water soluble & absorbed)
   Enzymes: P. Lipase & Colipase (Pancreatic) Gastric Lipase etc.
3. Carbohydrates (polysaccharides)

   ↓ S. Amylase, Dextrinase, Pancreatic α -amylase

   Disaccharides ⟶ Monosaccharides & absorbed

   Maltose $\xrightarrow{\text{Maltase}}$ 2 Glucose

   Sucrose $\xrightarrow{\text{Sucrase}}$ Glucose + Fructose

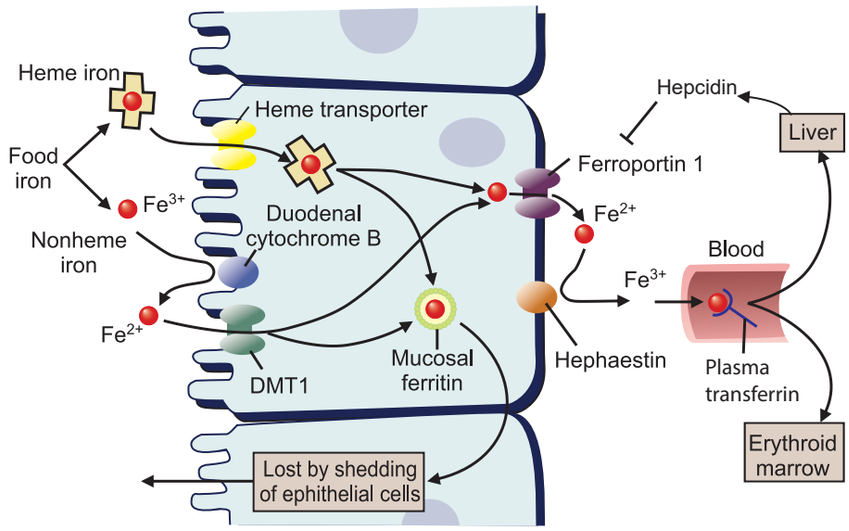
   Lactose $\xrightarrow{\text{Lactase}}$ Glucose + Galactose

Monosaccharides are absorbed by :
1) SGLT- 1: ORS contain both sodium & Glucose
2) GLUT-1 & 2: Glucose + Galactose
3) GLUT-5: fructose

Max absorption in Jejunum (Max area) after that Ileum & Colon

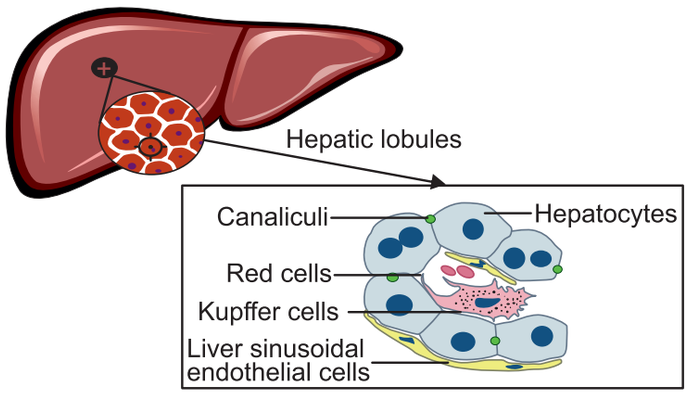
Exceptions i) Colon: Short Chain Fatty Acids
ii) T. ileum: Vit B_{12}, Bile Salt
iii) Duodenum: Iron absorption

Diet : Fe^{3+} to Fe^{2+} (Reductase/Cytochrome B)
Fe^{2+} enter duodenal cells by Apical/Luminal DMT-1 (Divalent Metal Transporter), can be stored as FERRITIN or leave cells to enter interstitium and then blood via Basal Ferroportin (FP), FP inhibited by liver Hepcidin
↑ Iron absorption : Vit C , HCl
↓ Iron absorption : Tannin, phytates



LIVER

All Substances from GIT reach LIVER for metabolism via Portal Vein C/A Entero-Hepatic Circulation



1. **Kupffer** *cells are resident liver macrophages*
2. **Ito cells** *(perisinusoidal fat-storing cells, stellate cells, lipocytes) of the liver are mesenchymal cells located in the Space of Disse. They are the main place of vitamin A storage in characteristic lipid droplets.*
3. **Hepatocytes**

NOTES

NOTES

RESPIRATORY SYSTEM

Weibel Airway classification: 23 generations

Trachea (generation zero)

↓

Bronchi (1st gen)

↓

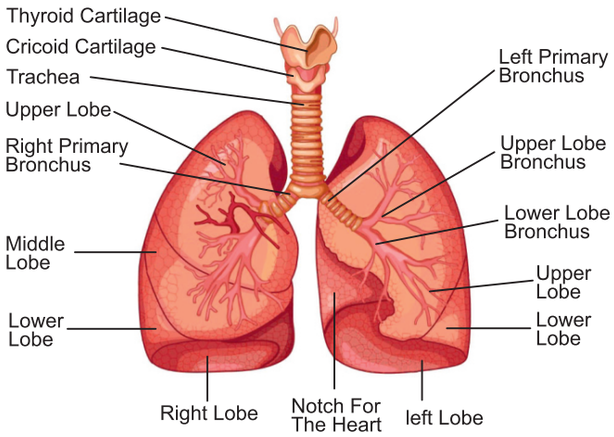
Bronchioles: Terminal (gen 16) & Respiratory (gen 17, 18, and 19)

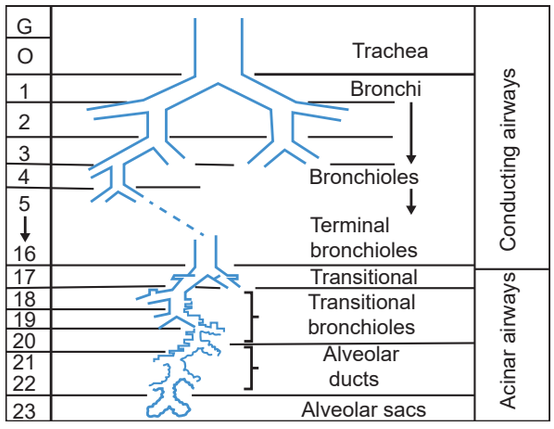
↓

Alveolar ducts (gen 20, 21, and 22)

↓

Alveoli (gen 23)





- Exchange/Respiratory zone: Gen. 17 -23
- Conduction zone: no exchange = Anatomical Dead space (150 ml)
  Trachea to Terminal bronchiole **(Max smooth muscle)**
  Boyle's Law: Pressure 1/α Volume

RESPIRATORY MOVEMENTS

1. Inspiration: Active process, uses muscles
   - Diaphragm (75%) & External Intercostal (25%)
   - Expand Thorax & ↓ pressure in Lungs, then pull air inside lungs
2. Normal Expiration: Passive process, no muscles just Elastic recoil
3. Forceful Expiration: Coughing, Shouting etc. It is active & uses muscles
   - Abdominal & Internal Intercostal
   - Compress thorax & lungs: ↑ pressure & push air out

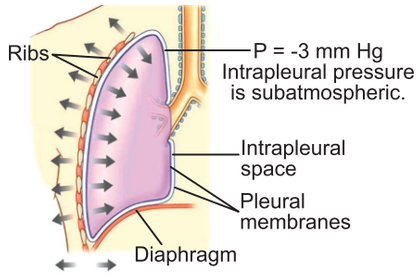
RESPIRATORY PRESSURES

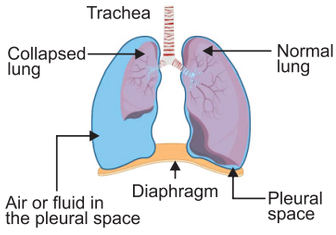
1. Intrapulmonary or Intra alveolar pressure (IAP)

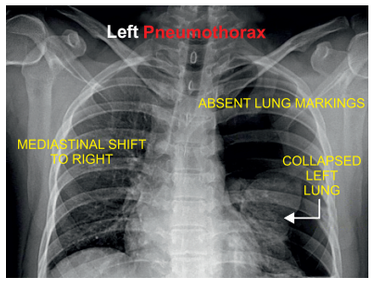
- Same as Atmosphere as lungs are connected to atmosphere by airways. Act as open cavity
- IAP at rest = 760 mmHg or 0 mmHg
- During Insp. = -1 mmHg/759 mmHg: pulls air inside
- During Exp. = +1 mmHg/761 mmHg: Lungs recoil and air is pushed out

2. Intra thoracic/Pleural Pressure (ITP)

- Pleural cavity surrounds lungs, has 2 layers: Parietal & Visceral
- Closed cavity = -2 mmHg at rest (-4 cmH_2O)
- This -ve ITP pulls lungs outwards & prevents collapse
- In pneumothorax, ITP becomes zero or +ve: lung collapse







COMPLIANCE: STRETCHIBILITY

- Normal lungs are elastic: Good Recoil & Compliance
- All lung Parenchymal diseases show poor Compliance due to fibrosis, inflammation, infiltration etc. Called RLD (Restrictive Lung Diseases)
  E.g. asbestosis, silicosis, pneumoconiosis, sarcoidosis etc.
- Only disease with high compliance is EMPHYSEMA (loss of Elastin protein, low recoil)
- If Airways narrow with Poor Turbulent Airflow called as OLD (Obstructive Lung Diseases)
- Compliance = $\frac{\Delta V}{\Delta P}$ = Δ is change
- Normal Lung Compliance = 220 ml/cm H_2O

SURFACE TENSION (ST)

- Inward force due to fluid & air inside alveoli
- **ST** will push air out. Alveoli can collapse (Atelectasis)
- Pull Fluid inside (Pul. Edema); Fluid + Fibrin make Hyaline Membrane
- ↓ Compliance & Difficult breathing: RDS (Respiratory Distress Syndrome
- ST reduced by surfactant, prevent RDS, Pul. Edema, collapse etc.

Surfactant: Produced by Type –II Pneumocytes & Clara cells

- Contain 70% phospholipids: Main is Di-palmitoyl phosphatidyl choline (DPPC or LECITHIN), minor is Sphingomyelin
- Surfactant protein (SP) - A, B, C, D: main is SP-B
- Surfactant production at 18-20 weeks, but secretion & action at 28 weeks
- Max secretion & Lung Maturity at 34 -35 weeks by steroids

PULMONARY FUNCTION TEST (PFT) BY SPIROMETRY

1. Normal Inspiratory & Expiratory Volume: **Tidal Volume (TV) = 500 ml**
2. Max forceful inspiration, above TV: **Inspiratory Reserve Vol. (IRV) = 3L**
3. Max forceful expiration after normal expiration: **Expiratory Reserve Volume (ERV) = 1.3 L**
4. Air left in lungs even after max forceful expiration: **Residual Volume (RV) = 1.2 L**

Since RV won't come out, it is not given by spirometer & prevents collapse

CAPACITY

Sum of 2 or more volumes

1) **IC** = TV + IRV: normal 3.5 - 4 L
2) **EC** = TV + ERV: normal 1.8 - 2L
3) **FRC (Functional Residual capacity)** = ERV + RV: normal 2.5L

- It is the air left in lungs after normal expiration or at rest
- As ERV won't come out and stays in lungs with RV, it is sum of both
- Spirometer fails to give RV & FRC

FRC estimation

1. Helium Dilution method
2. Single breath N2 washout/Fowler method: Gives Dead space also
3. Plethysmography in OLD
4. **VC (Vital Capacity):** It is max inspiration followed by max expiration
   VC = IRV+TV+ERV
   Normal VC in Males = 4.8 L & Females = 3.2 L
5. **TLC (Total Lung Capacity):** sum of all 4 volume
   - TLC = IRV + ERV + TV + RV: normal 6L
   - Spiro fails to give RV, FRC, TLC
   - TLC = VC + RV or IC + FRC

PFT IN DISEASES

- RLD: low VC due to poor compliance. All volumes are less
- OLD: normal VC or low VC (Due to air trapping)

TVC/FVC: Timed or Forced VC

- It is VC & time taken for example 5 L in 3 sec
- Divide TVC into FEV_1, FEV_2, FEV_3
- FEV_1 = Forced expiratory volume in 1^{st} sec
  - It is part of VC expired in 1st sec
  - $FEV_1\ \% = \frac{FEV_1}{TVC} \times 100 = 4/5 \times 100 = 80\%$
  - Normal FEV_1 % is 80% of TVC or 0.8
- Low FEV_1 % < 80% in OLD
- Normal FEV_1 % ≥ 80% in RLD
- Best investigation to differentiate RLD & OLD is FEV_1 %
- PEFR (Peak Expiratory Flow Rate): 250-500 L/min
- MEFR (Mid Expiratory Flow Rate): 150-300 L/min

VENTILATION

PV/MV (Pulmonary or Minute Ventilation): air going in & out of Lungs per min
= TV x RR (12 -16 breaths/ min)
= 500 mL x 12/ min = 6000 mL/min

AV (Alveolar Ventilation): air getting exchange per min in Lungs
AV = (TV - DS) x RR

- Dead space is air not getting exchanged in airway and alveoli
- Anatomical DS: normal 150 ml
- Alveolar DS: normal 0 ml
- Physiological DS = Anat DS + Alveolar DS

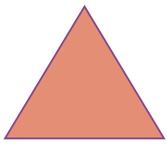
AV = (500 -150) mL x 12/ min = 4.2 L/min

V/Q : VENTILATION - PERFUSION RATIO

- It indicates gas exchange $V/Q = \frac{\text{Air coming/min.}}{\text{Blood coming/min}}$
- Ideal V/Q ratio = 1; Indicates best exchange
- If V/Q ≠ 1, called as V/Q mismatch: Poor exchange
- If V/Q > 1, Means air >> blood, Air left unexchanged, ↑↑ physio DS
  E.g. Pul. Embolism, Emphysema

- Hypoxic Hypoxia: all lung diseases, High Altitude, V/Q mismatch etc. Tissue get less O_2 as Lungs fail to oxygenate the blood : ↓ PaO_2 & SpO_2
  Other hypoxias have normal PaO_2
- Anemic Hypoxia: less Hb
- Stagnant/Ischemic Hypoxia: Less Blood flow to tissue – shock, Buerger's
- Histotoxic Hypoxia: Tissue fail to use O_2 despite normal blood O_2
  E.g. Cyanide inhibit complex IV of ETC

Normal V/Q ratio of whole lung = 0.8



Apex V/Q ratio = 1.3: Max due to poor perfusion
Physio. DS present, Max PO_2 at apex (TB: MC site)

Base V/Q ratio = 0.6: Min due to Max perfusion

Max Perfusion due to Gravity & Max Ventilation at base due to Max space

PARTIAL PRESSURE & GAS EXCHANGE

- Gas exchange by simple passive diffusion given by Fick's law
- Rate of diffusion depends on: Membrane, PP, Gas

Respiratory membrane: Type I Pneumocyte

a. Area: Normal 70 m^2

b. Thickness: Normal 0.5 µm

- ↓ Area & ↑ thickness: Poor O_2 diffusion called as membrane diffusion disorder e.g. ILD, ARDS, Pneumonia etc. Best Investigation DLCO
- Diffusion Capacity in lungs for CO (Carbon Monoxide)

CO_2 TRANSPORT

4 mL % or 200 ml/ min

1. Dissolved CO_2
2. **Bicarbonate: MAIN FORM**
3. Carbamino Hb (CO_2Hb)

O_2 TRANSPORT

250 mL/min or 5 ml%

Hb bound O_2 (99%)	Dissolved O_2 (1%)
• 1 Hb bind 4O_2 • 1 gm carry 1.33 ml O_2 • Normal Hb = 12- 16 gm% will carry 18-19 ml% O_2	• 0.3 ml % • PaO_2 depend only on dissolved O_2 called as HENRY LAW

O_2- HB DISSOCIATION CURVE

- Sigmoidal S shaped due to **relative affinity or co-operative binding**
- RRR: Right Shift, Release O_2 in tissue, called as BOHR effect
- High PCO_2 in tissue cause loading of CO_2 & unloading O_2 from Hb
- LLL: Left Shift, Hb bind O_2 in Lungs is HALDANE effect, High O_2 affinity
- Double BOHR & HALDANE in placenta

- 2,3 BPG bind β –chain of HbA and cause O_2 release
- **HbF:** 2 alpha & 2 gamma globin chain, No β -chain, No 2-3 BPG binding So, Hbf has higher O_2 affinity. Hence it extract O_2 from Maternal HbA
- CO poisoning: CO has 210 times more affinity for Hb than O_2
- It form CarboxyHb (COHb, Cherry Red, Fire in closed Room)
- It is abnormal Hb won't Release O_2, Death Occurs (anemic hypoxia)

Pacemaker of Respiration : in medulla called as **Pre Botzinger Complex (PBC)**

It stimulates Resp. muscles & produce automatic Involuntary breathing

- DRG = Dorsal Respiratory Group - acts on inspiratory muscles
- VRG = Ventral Respiratory Group - causes forceful expiration
- Pre-Botzinger Complex - gives Ramp signal to DRG
- AC = APNEUSTIC CENTER: Activates DRG, increases Depth of respiration
- PNEUMOTAXIC CENTER = Inhibits AC, Prevents Apneusis, increases Rate
  - Medulla lesion: Respiration stops - called apnea
  - Pons lesion: Irregular, shallow breathing
  - Mid pontine lesion and B/L Vagotomy: Apneusis (Resp. Stops in Inspiration)

Regulation of Respiration *by Chemoreceptor: Sense & correct hypoxia & Hypercapnia (↑ $PaCO_2$) by stimulating Respiratory centers in Brainstem.*

This results in Hyperventilation (↑ TV, ↑ RR) to ↑ PaO_2 & ↓ $PaCO_2$ to normal

Central Chemoreceptor (CC)	**Peripheral Chemoreceptor (PC)**
- Ventral medulla	Carotid Bodies: Bifurcation of **CCA:** IX Nerve
- Only stimulated by ↑ H^+ in CSF	Aortic bodies: Arch of **Aorta:** X Nerve

- PC stimulated by blood changes: ↑ $PaCO_2$, ↓ PaO_2 & ↑ H^+ in blood
- PC contain O_2 sensitive K^+ channels in Glomus cells (Type-I)
- PC not stimulated by Anemic Hypoxia. All others can stimulate PC
- CO_2 can cross BBB & stimulate both PC & CC (By making H^+ in CSF)
  So, it is the main stimulus (Hypercapnic Drive) for Respiratory Regulation

NOTES

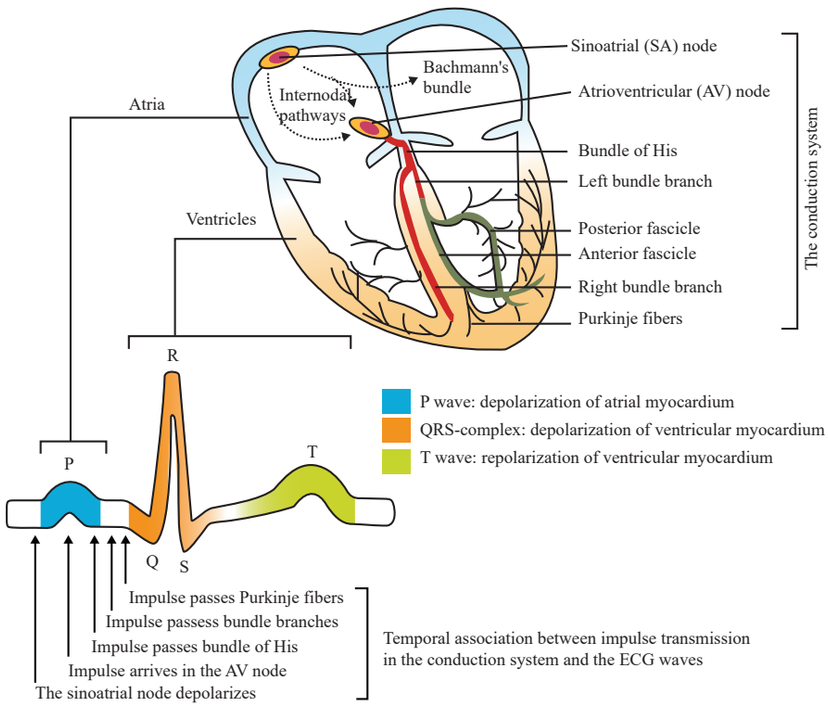
CARDIOVASCULAR SYSTEM

Pacemaker of Heart is SA Node *due to max frequency 70-100/min*

- *It makes automatic Action Potentials due to phase IV Pacemaker Potential.*
- *Pacemaker Potential caused by*
  - *a. Funny/Leaky Na^+ channel*
  - *b. Ca^{2+}t channel (transient)*

CONDUCTING PATHWAY

SA node (Atria)
↓
AV node
↓
Bundle of HIS
↓
Bundle branches
↓
Purkinje fiber (Ventricle)



Max Gap Junctions

- *Purkinje fibers: Fastest 4m/sec*
- *AV node: Slowest 0.05m/sec*
- *AV Delay: 0.1 sec*

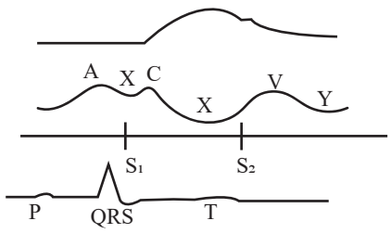
CARDIAC CYCLE (0.8 SEC)

Events occuring in one heart beat

1. Systole (S_1-S_2): Isovolumetric Contraction & Ejection
2. Diastole (S_2-S_1): Isovolumetric Relaxation & Filling

Jugular Venous Pressure (JVP) from Internal Jugular vein, shows RA changes

- **A**tria contract = **a** wave
- RV **C**ontract = **c**- wave (TV bulge into RA)
- Atria rela**x** = **x** descent
- Atria fill by **v**ena cava = **v** wave
- Atria empt**y** when TV open = **y** descent



VOLUME CHANGES

1) **EDV** (End Diastolic Volume): blood filled in Ventricle during diastole, Normal is 120 - 130 ml. It depends on **VENOUS RETURN**. ↑ EDV will ↑ load on ventricle even before contraction called as **PRELOAD**
2) **SV** (Stroke Vol): blood pumped per beat, normal is 70-80 ml
3) **EF** (Ejection Fraction): Percent of blood ejected per beat, normal is 65%

   EF = SV/EDV x 100
4) **ESV** (End systolic volume): blood left after Ejection, normal is 40-50 ml

   ESV = EDV -SV

CARDIAC OUTPUT (CO)

- Blood pumped by each ventricle per min, Same in RV & LV
- CO estimation by
  - ECHO
  - Dye Dilution method
  - Thermodilution method
  - CO = SV x HR = 5 L/min
- During exercise CO increase up to **20 -25 L/min** called as **Cardiac Reserve**

1. Frank Starling Law

(EDV ∝ SV): more filling (↑EDV)

Cause more pumping (↑SV)

E.g. Exercise, i.v. Fluids

↑ EDV, SV, CO etc.

2. Inotropic effect

↑SV due to Left Shift of FS curve

More contractility due to higher Ca^{2+}

Inotropic agent: E, NE, dobutamine (β_1)

Digoxin by ↓ Na^+ K^+ pump & ↑ Ca^{2+}

β_1 Symp causes

- ↑ HR: (+) Chronotropic
- ↑ SV: (+) Inotropic
- ↑ Conduction: (+) Dromotropic
- ↑ Excitability: (+) Bathmotropic

TYPES OF VESSELS

1. **Wind Kessel Vessel:** Large elastic arteries like Aorta. They stretch in systole & Recoil Inwards in Diastole. This compresses blood to produce Diastolic Pressure (DBP) 80 mmHg & Maintain blood flow in diastole.

2. **Capacitance Vessels:** Systemic veins. They have high compliance, they stretch & store blood (contain 50-60% blood). Help compensate loss of blood

3. **Exchange Vessels:** Capillaries
   a. Permeable, Simple squamous endothelial cells
   b. Min. Blood Volume (5% of blood)
   c. Low pressure & Low Resistance
   d. Slowest speed: good exchange & silent laminar flow
   e. Max cross sectional area (CSA): Due to billions of capillaries in parallel

Arteries: Max speed, turbulent flow: noisy

4. **Resistance vessels**
   a. Muscular arteries & arterioles
   b. Smooth muscles: contract & relax
   c. Change diameter & control Blood flow

Arterioles: Main Resistance Vessel: Max smooth muscles & Symp. Supply

α_1	β_2
Vasoconstriction : ↓ FLOW	Vasodilation : ↑ FLOW
Everywhere skin, GIT, kidney muscle etc.	Few sites: Muscles, sweat glands, uterus

Arterioles offer Resistance at tissue level - main site of Peripheral Resistance

↑PR will ↑load on ventricle after they start contraction called as AFTER LOAD

Blood Flow Regulation: Flow = Pressure/Resistance

- Organs can control their own blood flow by changing their Resistance called as Autoregulation of flow. E.g. ↑ Flow to muscle = ↑ **Pressure** by ↑ Symp Activity
- Local Metabolites: Lactic acid, ↑ PCO_2, ↓ PO_2, K^+, H^+, Adenosine, ↑ temp etc does vasodilation: ↓ Resistance & ↑ flow (METABOLIC AUTOREGULATION)
  Best autoregulation in Brain & Heart

$$R = \frac{8\eta l}{\pi r^4}$$

R = Resistance
η = Viscosity of blood
l = Vessel length
r = Vessel radius

Double radius: r (increase 2 times)
= 2^4 times (16 times) Fall in resistance

Blood Pressure [BP= CO x PR]

1. SBP= 120 mmHg
   It is due to ventricular contraction & depends on CO mainly
2. DBP = 80 mmHg
   It is due to elastic Recoil & depend on PR mainly

3. PP (Pulse pressure) = SBP-DBP: indicates Blood flow & arterial compliance
4. MBP/MAP (Mean BP) = 95-100 mmHg
   MBP = 2/3 DBP + 1/3 SBP or MBP = DBP + 1/3 PP

CVS Regulatory Centers In Medulla

VMC (Vasomotor Center)	CVC (Cardio Vagal Center)
• RVLM: Rostro Ventrolateral medulla • ↑ Symp: ↑ SV, ↑ HR, ↑BP etc	• Vagal nuclei = NTS, NA • ↑ parasympathetic by vagus Nerve Ach (M_2): ↓ HR, ↓ CO, ↓ BP, Conduction etc

Baro Receptor (BR)

- Control BP, They are stretch Receptor in Arteries,
- Sense & regulate MBP, Range of 60 - 180 mmHg. They act by Negative Feedback and always ↑ BR, ↑ HR by (+) CVC (NTS) & (-) VMC
- Destroy BR: ↑BP as VMC acting uncontrolled (Neurogenic Hypertension)
- Location: same as peripheral chemoreceptors
- Aortic sinus BR (Xth Nerve) & Carotid sinus BR (IXth Nerve)

CVS Reflexes

1. **Bainbridge reflex** is a compensatory reflex resulting in an increase in heart rate following an increase in cardiac preload (I.V. Fluids).

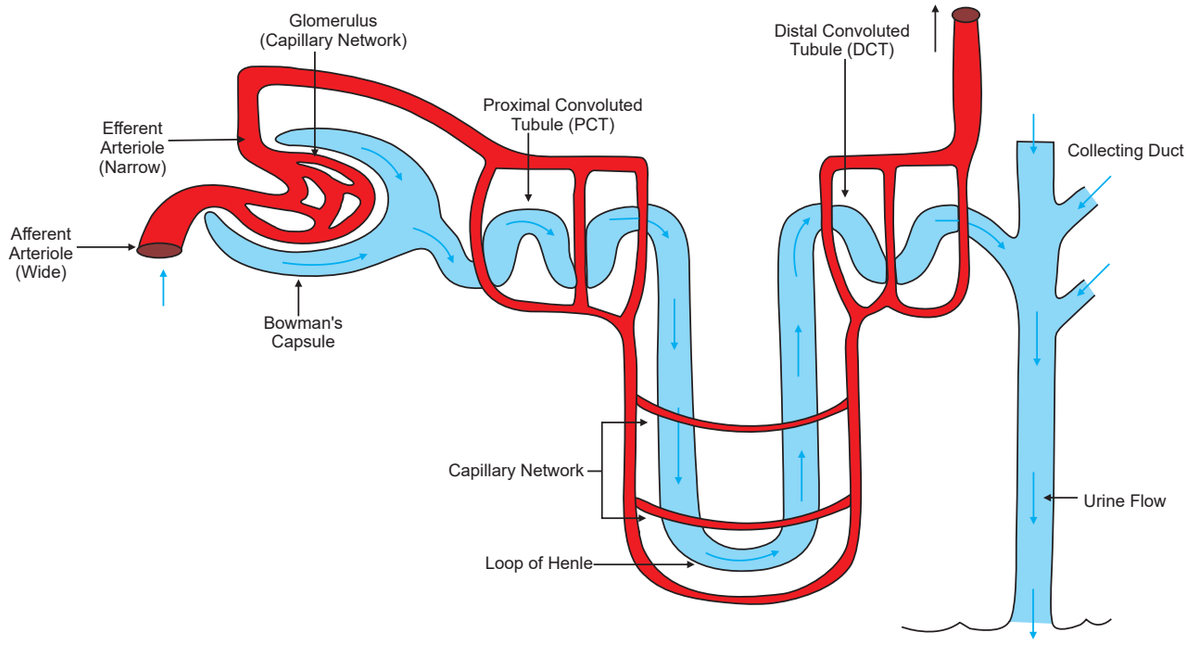
2. **Bezold-Jarisch** reflex is a triad of responses (apnea, bradycardia, and hypotension) following i.v. injection of Capsaicin, Veratridine, 5HT etc
   Similar to J-Reflex in lungs by J Receptors

3. **MAREY'S LAW :** BP 1/∝ HR
   a) **Shock :** ↓ BP but ↑ HR by (↑ symp) Reflex Tachycardia
   b) **Cushing Reflex:** ↑ ICT (Head Injury) cause ↑BP but ↓ HR by Baroreceptors called as Reflex Bradycardia

NOTES

URINARY SYSTEM: KIDNEY

Functional unit of kidney is Nephron = 1-1.3 million/each kidney



Glomerular capillaries (GC) → filter plasma mainly on size basis

After Filtration, substances enter Tubules

Reabsorption	Secretion
- Good solutes like glucose, water, AAs, Na^+ etc - Enter blood (PC: Peritubular Capillaries) from urine (tubules)	- Bad & waste solutes like drugs, toxins, metabolites, urea, uric acid are removed from blood (PC) to urine (tubules)

3 STEPS of Urine formation & Plasma Clearance

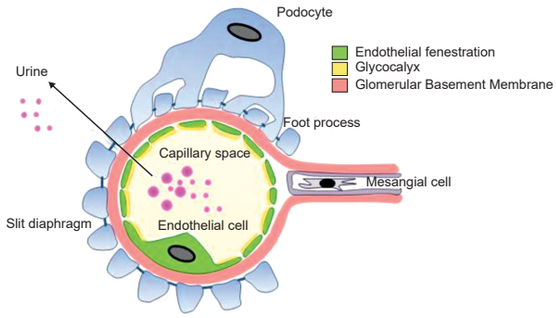
1. Filtration: glomerular function
2. Reabsorption: tubular function
3. Secretion: tubular function

Glomerular Filtration Membrane

1. Endothelial cells of GC: opening b/w cells are fenestrations 70-90 nm .
2. Basement membrane: contains –Ve charged Sialoproteins and Heparan sulphate. They repel & prevent filtration of - Vely charged plasma proteins
3. Epithelial cells of BC: Podocyte & foot process with Filtration slit 10-20nm

Net pore size: 4-8 nm

- Substances < 4 nm size are freely filtered
  Inulin, glucose, Na^+
- > 8 nm are not filtered: RBC, WBC, Platelet
  β macro globulins. Hb binds
  to Haptogloblin to prevent filtration.
- If B/w 4-8 nm depends on charge
  eg. Albumin = 7 nm, Filterable by size But
  not filtered due to -ve charge.
- Loss of charge in nephrotic syndrome cause albuminuria



PCT: Max ATP, O_2 & blood flow because max sec. & Reabsorption occur

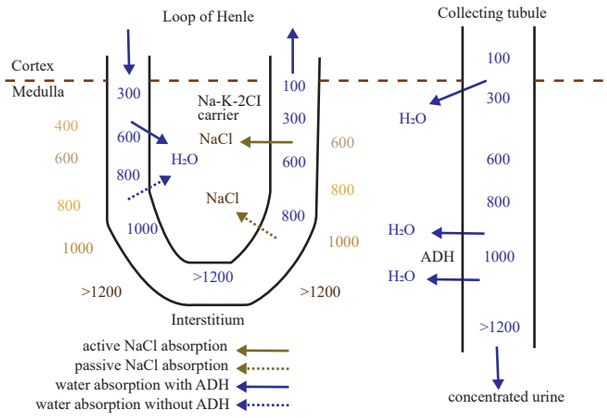
- All sub max Reabsorption in PCT except Mg^{2+} in Ascending Loop
- All sub max secreted in PCT except K^+ in P-cell & urea in Thin loop
- Max acid sec in PCT. Max buffers in PCT to maintain pH
- Main Buffer is Bicarbonate (HCO_3^-): need carbonic anhydrase
- Minor Buffers are Ammonia & Phosphate

LOH: Medulla has more osmolarity (1200 mOsm/L), 4 Times more than plasma (300 mOsm/L) called as HYPERTONIC

- Medulla will pull water from Urine & make concentrated hypertonic
- Urine, upto 1200 mosm/L in Desc. Loop & CD (need ADH)
- Longer the loop → more conc. power called as Juxtamedullary nephrons
- Descending Loop is water permeable = hypertonic urine
- Ascending Loop is solute permeable = hypotonic urine

Counter Current System (CC) : ↑ Conc. of urine

CC Multiplier	CC Exchanger
Asc. Loop Create high medulla osmolarity (1200) by accumulating solutes	Vasa Recta Maintains medulla osmolarity by water Reabsorption



DCT: Early part
Na^+Cl^- Co-Transport (NCC)

CD: 2 types of cells (in DCT also)

1. I-cells: Intercalated cells for Acid secretion, most acidic urine, min pH of urine is 4.5 called as limiting pH
2. P-cells: Principal cells, K^+ sec (↓ Blood K^+) & Na^+ Reab (by ↑ S. Na^+) by ENac (Epithelial sodium channel). It is blocked by Amiloride Diuretic Doc: Liddle syndrome & Lithium Induced DI

   P-cells stimulated by aldosterone : ↑ S. Na^+, ↓ S.K + & Metabolic Alkalosis

CD : Water & urea permeable with ADH

- UT-3 (Urea Transport -3): make urea enter medulla, increase Osmolarity
- ↑ Water Reabsorption by Aquaporin- 2 (V2 Receptors of ADH) in P-cells

SIADH: More Adh	D. Insipidus: Less ADH
CD: ↑ water permeable	↓↓ water permeable
↑↑ water reabsorption	Less water reabsorption
Hypertonic urine (1200 mosm/L)	Hypotonic urine (50-100 mosm/L)
Low urine Volume	High urine volume, polyuria, polyuria

RBF = Renal blood flow = 1200 ml/ min

RPF = Renal plasma flow = 625 ml/min

GFR : Amount of plasma filtered/min = 125 m/min (180L/day)

Clearance (CL) = UV/P

1. If only filtration occurs (No Sec & No Reabsorption): CL = GFR
   e.g. inulin CL used for GFR Estimation
2. If secretion also occurs : ↑↑ CL
   - CL >> GFR eg. creatinine CL: 130 min/min
   - It is sec & filtered both but little secretion. Hence, CL is close to GFR
   - Most accurate for GFR: Inulin
   - Most used for GFR: Creatinine

If full secretion, then 100% plasma cleared: CL = RPF

eg: PAH: Para amino Hippuric acid, used for RPF estimation

3. If Reabsorption: CL < GFR

   Eg. Urea CL = 70-90ml/min (filtered & Reabp for CC system)

   If 100% reabsorbed, 0% cleared in urine, CL is zero Eg: Glucose, AAs

   Glucose is 100% reabsorbed in PCT by SGLT -2 (Apical) & GLUT- 2 (Basal)

T_MG = Transport max of Glucose: max glucose that can be reabsorbed per min in Tubules- It is 375 mg/min.

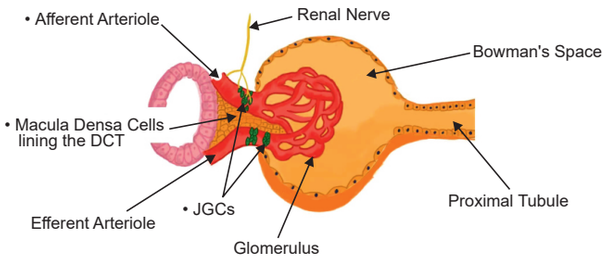
FL: Filtered load: amount of substance filtered per min (GFR x Plasma Conc) If FL> T_MG not 100%. Reabsorbed, Glycosuria occurs.

↑↑ Filtered load	↓T_MG (less reabsorption = Tubular D.)
High load cause glycosuria	Fanconi syndrome
E.g. DM	Acute Tubuler Necrosis

JG apparatus: 3 Types of cells

1. Lacis cells: Mesangial cells

   Act as Macrophages



2. JG cells in Afferent arterioles sense RBF & release Renin if poor flow (Shock ↓BP, Symp, ↓Na^+) etc

3. Macule Densa cell in DCT & Ascending Loop for GFR Regulation called as Tubulo Glomerular feedback.
   Ist sense GFR by Na^+, Cl^- levels in Tubular fluid then correct GFR by Intraglomerular Mesangial cell Contractile cells around Glomerulus: Contract → ↓ GFR
   - Efferent Arteriole Constriction by AT-II : ↓ RBF but Blood accumulates in Glomerulus , ↑ hydrostatic pressure & ↑ GFR
   - Afferent Arteriole Dilation by dopamine: ↑ RBF, ↑ hydrostatic Pressure, ↑ GFR

NOTES

NOTES

CENTRAL NERVOUS SYSTEM (CNS)

Neurons & Glial cells

- Neurons: 100 billion, no new Neurons formed after birth except hippocampus
- Glial Cells: more in numbers & can form new cells: Gliosis/Glioma

Types of glial cells

1. Microglia: CNS Macrophages for phagocytosis
2. Oligodendrocytes: make myelin in CNS
   PNS: Schwann cells make myelin
3. Ependymal Cells: Lining cells of ventricles
4. Astrocytes: Supporting cells to Neurons & help in BBB: Tight Junction

CSF: 150 ml, daily production = 500 ml/day or 20 ml/hr

- Sec: choroid plexus
- Absorption: Arachnoid villi

Normal pressure: 50-130 mm H_2O or 5-10 mmHg

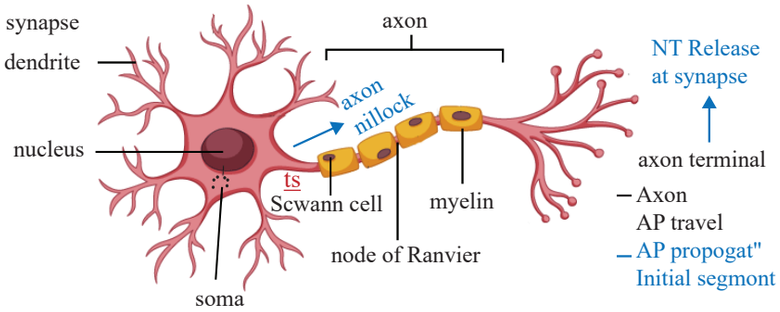
CSF Functions

- Nutrition (O_2, glucose, AAS, Pons etc)
- Waste Removal
- Maintain Temp, pH, osmolarity etc
- Shock Absorber

CSF is similar to plasma but Lower conc (glucose is 60%)

Except PCO_2, HCO_3, Mg^{2+}, Cl^- in higher concentration in CSF

Neuron Anatomy



Nissl granules in cell body are free Ribosomes: protein synthesis

Neuronal Injury (Wallerian Degeneration): Ist change is break down of Nissl granules called as Chromatolysis

AP genesis at Axon Hillock

RMP & AP

Membrane is selectively permeable, at rest permeable to K^+, Cl^- (Diffusible ions). But not permeable to Na^+, Ca^{2+}, Po_4^{3-}, proteins etc

There is uneven Distribution of Ions across Membrane Called as Gibbs Donnan equilibrium

	ICF (inside)	ECF (outside)
Cations	K^+	Na^+, Ca^{2+}
Anions	Po_4^{3-}, Protein	Cl^-

Due to unequal concentration Na^+, Ca^{2+} will come inside & K^+ will go outside. This Potential is called as Equilibrium Potential (EP) & given by Nernst equation

$$Vk \approx -60\ mV \log_{10} \frac{[K]in}{[K]out}$$

EP Values

1) Na^+ = + 60 mV (Cation Coming inside creates +ve EP)

2) Ca^{2+} = + 100 mV (Cation Coming inside creates +ve EP)

3) Cl^- = - 70 mV (Anion coming Inside creates -ve EP)

4) K^+ = - 90mV (Cationt but going outside, loss of (+) inside creates - ve EP)

RMP - Resting membrane potential

Depends on K^+ & Cl^- as Membrane is not permeable to Na^+ at rest but Permeable to K^+ & Cl^-. Since, both have -ve EP the RMP is always -ve.

Main cause of RMP is K^+ (Most permeable)

RMP values

1) Neurons = -70 mV

2) Skeletal & Cardiac muscles = -90 mV

3) Smooth muscle, Thyroid = -50 mV

4) RBC = -12 mV

5) Rods & Cones = -30 mV

6) Cochlea Hair cells = -40 mV

Depolarization at Synapse by NT: **EPSP** (Excitatory post synaptic potential)

Hyperpolarization at synapse by NT: **IPSP** (Inhibitory post synaptic potential)

NT at Synapse, bind Receptor open Ion channels to produce EPSP/IPSP

1) Na^+ channel opening: Na^+ entry cause Depol/EPSP

E.g. Glutamate by NMDA Receptor (main Excitatory NT in CNS)

2) Ca^{2+} channel opening: Ca^{2+} entry = Depol/EPSP

E.g. Substance P: Stimulate SG cells of spinal cord (Substantia)
Ist Neuron of pain pathway cause pain sensation = Algia/Algesia/Dolor

3) K^+ channel opening : K^+ efflux = Hyperpol/IPSP
Eg: Morphine inhibit SG cells by μ opioid Recepter (-) pain: analgesia

4) Open Cl^- channel: Cl^- enter to cause hyperpol/IPSP
Eg: glycine in S. Cord & GABA in Brain (Main Inhibitory NT)

AP: Threshold stimulus (+15 mV) Cause AP, if less stimulus then no AP. This is called as **all or none law**.

1. Threshold stimulus (+15 mV): change RMP from -70 to -55 mV
2. -55 mV is FL (Firing Level) : Voltage gated Na^+ channal open (m-gate)
3. Na^+ enter & Cause Big Depol upto +35 mV (over shoot or spike potential)
4. Na^+ channels close (h-gate): Depol is over
5. K^+ ch open: K^+ goes out. Membrane returns to RMP (Repolarization)

Na^+ K^+ pump: Pump 3 Na^+ out 2 K^+ in.

To restore Ionic Equilibrium

- High Na^+ in ECF
- High K^+ in ICF

Memory stored at Synapses in NEO CORTEX NEURONS

Repeat stimulus: ↑ NTs & ↑ Receptors at Synapses called synaptic plasticity ↑ Recall & faster response

Long Term Potentiation (LTP) by ↑ NMDA receptors of glutamate by Hippocampus CA1 Neurons use LTP to convert Short Term Memory into LTM (Long Term Memory)

Sensory System

Receptor	Pathway	Cortical Centers
Make AP	Take AP to Cortex	Perception, memory

Properties of Receptors

1) **Threshold:** min stimulus needed to give Response eg: hearing at 20Hz.

2) **Specificity:** Receptor respond mainly to their type of stimulus eg: Light by Rods & Cones

3) **Adaptation:** Less sensation on constant stimulation

- Rapid adapting: Touch, smell
- Slow adapting: Proprioception (position)
- Non adapting: Pain felt all the time till healing occur.

4) **Weber-Fechner** and **Steven Power law**

Intensity (I) of sensation felt is proportional to power of Stimulus $(S)^A$

SPECIAL SENSES :

1. Vision

Receptors	Pathway	Cortical Centers
Rods & Cones	Optic pathway	Area 17, 18, 19 occipital lobe Colour vision: V_4 Area

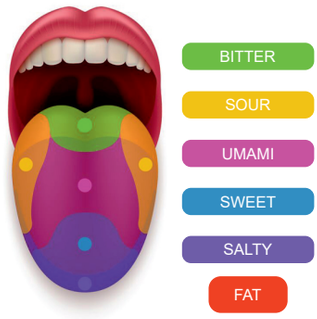
Dark: Rhodopsin (Vit A) show 11 cis Retinaldehyde + opsin chain

Light: All Trans Retinaldehyde leads to closure of Na^+ channel by Transducin (G-protein), this produce Hyperpolarization all other receptors produce Depol. Only Rods & cones Cause Hyperpolarization

2. Auditory System

- Inner hair cells at organ of corti in cochlea
- K^+ high in endolymph of scala media
- K^+ channel open = CMP - Cochlear Microphonic Potential
  - Auditory pathway COLIMA
  - Auditory cortex: Area 41, 42
  - Superior Temporal Gyrus Area 22 is Wernicke's Area for language
  - Angular Gyrus Area 39 for word Memory

3. TASTE : Papilla of Tongue



1) Fungiform papilla: Tip of Tongue
2) Foliate: Side of Tongue
3) Circumvallate (Disc like) Back of Tongue (Bitter)
   - Salty:
   - Sour:
   - Sweet:
   - Bitter :
   - Umami: MSG = Mono sodium glutamate: ajinomoto, meat etc

Chilly is not Taste but pain, it contains Capsaicin Bind Vanilloid Receptor (VR or TRPV1)

4. SSS = SOMATO SENSORY SYSTEM

- Sensations from body like pain, temp, touch etc

Receptors of SSS

1) **Merkel Disk** in epidermis for sustained touch & pressure, 2-point discrimination is best at fingertips & lips (1-2mm): Help blind read Braille script
2) **Meissner's Corpuscles:** Tip of dermal papilla
   Fine Touch & Low frequency Vibration

3) **Pacinian Corpuscles:** Onion shape in Deep Dermis
   High frequency Vibration & Pressure
4) Ruffini Endings
5) Krause End Bulbs for cold
6) Free Nerve endings for Pain, temp, itching, sexual sensations

PAIN	
Fast	**Slow**
A Delta myelinated Nerve fibres • E.g. skin injury • Superficial somatic pain • Sharp well localised	C-unmyelinted autonomic Nerve fibres • E.g. Angina, colic, headache • Deep, Visceral Pain • Dull, Diffuse, Radiation & Referred Pain

Ascending Sensory Tract in Spinal cord (white matter)

1) **Dorsal column:** Fine touch, pressure, vibration, Proprioception,
   Stereognosis (Identify object held in hand), Graphesthesia etc
2) **Lateral spinothalamic Tract :** Pain & temp (STT)
3) **Anterior STT:** Itching & crude touch/pressure

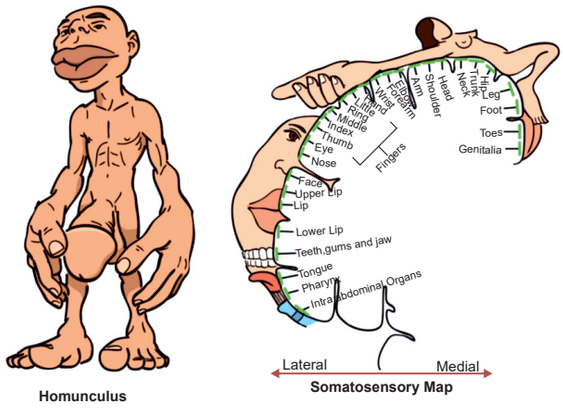
PARIETAL LOBE

Post central gyrus: Sensory Cortex

- PRIMARY AREA : 3, 1, 2
- SECONDARY AREA : 5, 7

Max Area in sensory homunculus

FACE (LIPS) & HAND (THUMB)



Motor Cortex : Area 4, 6 in Pre central Gyrus has Betz cells (UMN), they give corticospinal (CST) or Pyramidal Tract (PT). 85-90% fibers cross at lower end of Medulla Pyramids. PT helps in vol. fine skilled movements. PT stimulates LMN in anterior horn (αMN are LMN) of Spinal Cord

UMN Control LMN via Tract (PT, EPT)

Tract lesion (PT, EPT) is UMN Lesion: Spastic Paralysis (high Tone & Reflex)

LMN Control Muscle by Motor nerve like Alpha MN which release Ach at NMJ

LMN Lesion cause flaccid paralysis

Muscle

Length: sensed & regulated by muscle spindle (MS)

Tension: Golgi Tendon organ

MS: Stretch Reflex/DTR: Deep Tendon reflex

↑ Length sensed by muscle spindle then stimulate Alpha motor neuron to cause contraction (↓ length back to normal)

Gamma Motor Neuron: cause muscle tone (continuous muscle contractions) by stimulating muscle spindle. Tone helps in posture, balance, gait etc.

Basal ganglia: planning of movement, Dopamine from Substantia Nigra increases movements by stimulating striatum (Caudate nucleus & Putamen)

Cerebellum: Co-ordination & correction of movement. **Lesion causes ATAXIA**

Emotions produced by limbic system in Temporal lobe
Control of Emotion & Cognition (thinking) by Frontal lobe

Main Functions of The Hypothalamic Nuclei	
Nuclei	**Major hormones and/or their functions**
Supraoptic	• Osmoregulation by antidiuretic hormone • Regulation of uterine contraction and milk ejection by oxytocin
Paraventricular	• Osmoregulation by antidiuretic hormone • Regulation of thyroid function by thyrotropin-releasing hormone • Regulation of adrenocortical function, regulation of the sympathetic nervous system and adrenal medulla, regulation of appetite by corticotropin-releasing hormone
Suprachiasmatic	• Regulation of circadian rhythms and pineal function
Arcuate	• Stimulation of growth hormone • Regulation of pituitary gonadotrophins (follicle-stimulating hormone and luteinising hormone) • Dopamine functions as prolactin-inhibiting hormone • Inhibition of growth hormone-releasing hormone • Regulation of appetite
Periventricular	• Inhibition of growth hormone-releasing hormone
Ventromedial	• Stimulation of growth hormone • Inhibition of growth hormone-releasing hormone • Function as a satiety centre
Dorsomedial	• Focal point of information processing involved in feeding, drinking, body-weight regulation and circadian activity

Lateral hypothalamus	• Functions as a hunger centre
Preoptic area	• Role in thermoregulation • Regulation of thirst, inducing sleep and regulating male sexual behaviour
Anterior hypothalamus	• Thermoregulation 'cooling centre' (the thermoregulatory centre) • Regulation of thirst
Posterior hypothalamus	• Thermoregulation 'heating centre' - the thermoregulatory centre has receptors capable of detecting the temperature of the blood flowing through the brain

EEG & SLEEP

0-3 Hz :	Delta wave	Deep sleep
4-7 Hz :	Theta wave	Light sleep
8-13 Hz :	Alpha wave	Awake, Eye closed
4-7 Hz :	B- wave	Awake, Eye open, Busy mind

NOTES