Drugs used in the therapy of shock

Shock – State of accute circulatory failure.

Cardiac output is inadequate to provide tissue perfusion.

Causes – • Inflamation
• Infection of heart valve

Symptoms – • Shortness of breath
• Sweating
• Dizziness & fatigue
• Rapid breathing
• Pale skin

Types of shock

Type-1 – Hypovolaemic shock – Hypo = less
volaemic = volume

– **Cause** – Internal or external loss of blood, plasma, water.

– **Due to** – • Haemorrhage, • Trauma, • Vomiting, • Diarrhoea

– **Treatment** – Drugs or fluid replacement by
• Saline
• Plasma
• Blood

Type-2- Cardiogenic shock — Due to myocardial Infarction

- Cause - failure of heart to pump = Pump failure
- features - ↓ Cardiac output, peripheral resistance
- Treatment - To ↓ pain + Anxiety, ↓ Reflex vasoconstriction
  O_2 administration = Antagonize Hypoxia

Type-3 - Septic shock - Due to gram (-ve) or gram (+ve) bacteria

Type-4- Anaphylactic shock - Hypersensitivity reaction due to Antigen-antibody reaction.
↑ vasodilation

→ Drugs / Treatment

① Sympathomimetic amines - Noradrenaline, adrenaline, dopamine

↑ cardiac output, ↑ blood flow, ↑ tissue perfusion

② α-adrenoreceptor blocker - Phenoxybenzoamine
↓ vasoconstriction

③ Corticosteroids: vasodilation and (+ve) Inotropic effect
↑ Tissue perfusion

④ Oxygen (O_2) = ↓ Hypoxia – ↑ Cardiac output – ↑ Tissue perfusion

⑤ Cardiac Glycoside – Improve myocardial contractility, ↑ Cardiac output

⑥ Glucagon – ↑ Myocardial contractility – ↑ cardiac output

⑦ Dextrans – Effective plasma vol. expander – Effective in hypovolemic Shock

☆ **Hematinics** – one agent required in the formation of blood & used in the treatment & prevention of anemia.

Anemia –
- Blood loss [acute or chronic]
- deficiency of iron
- deficiency of folic acid & Vit. B_{12}
- destruction of RBC.

Iron –
- essential for haemoglobin production.
- Each molecule of haemoglobin has 4 iron containing residue.
- Total iron 2.5 - 5.0 g.
- Stored in ferric form with apoferritin.

$$\text{Apoferritin} + Fe^{3+} \longrightarrow \text{ferritin} \xrightarrow{\text{aggregates}} \text{Haemosiderin}$$

Distribution of Iron in the body –
- haemoglobin – 66%.
- ferritin or hemosiderin – 25%.
- myoglobulin (in muscle) – 3%.
- enzyme – 6%.

Daily Iron requirement –
- Adult male – 0.52 – 1 mg
- Adult female – 1 – 2 mg
- Children – 25 microgram / kg [4 g]
- Pregnency – 3 – 5 mg

Dietry Sources of iron –
- Rich – egg yolk
  dry fruit
  wheat
  liver

Medium- Meat
Chicken
fish
Banana
Apple
Spinach

Poor- Milk & its product.
root vegetables

- Iron absorption-

Dietry Iron

Hem
↳ meat, absorb faster as such

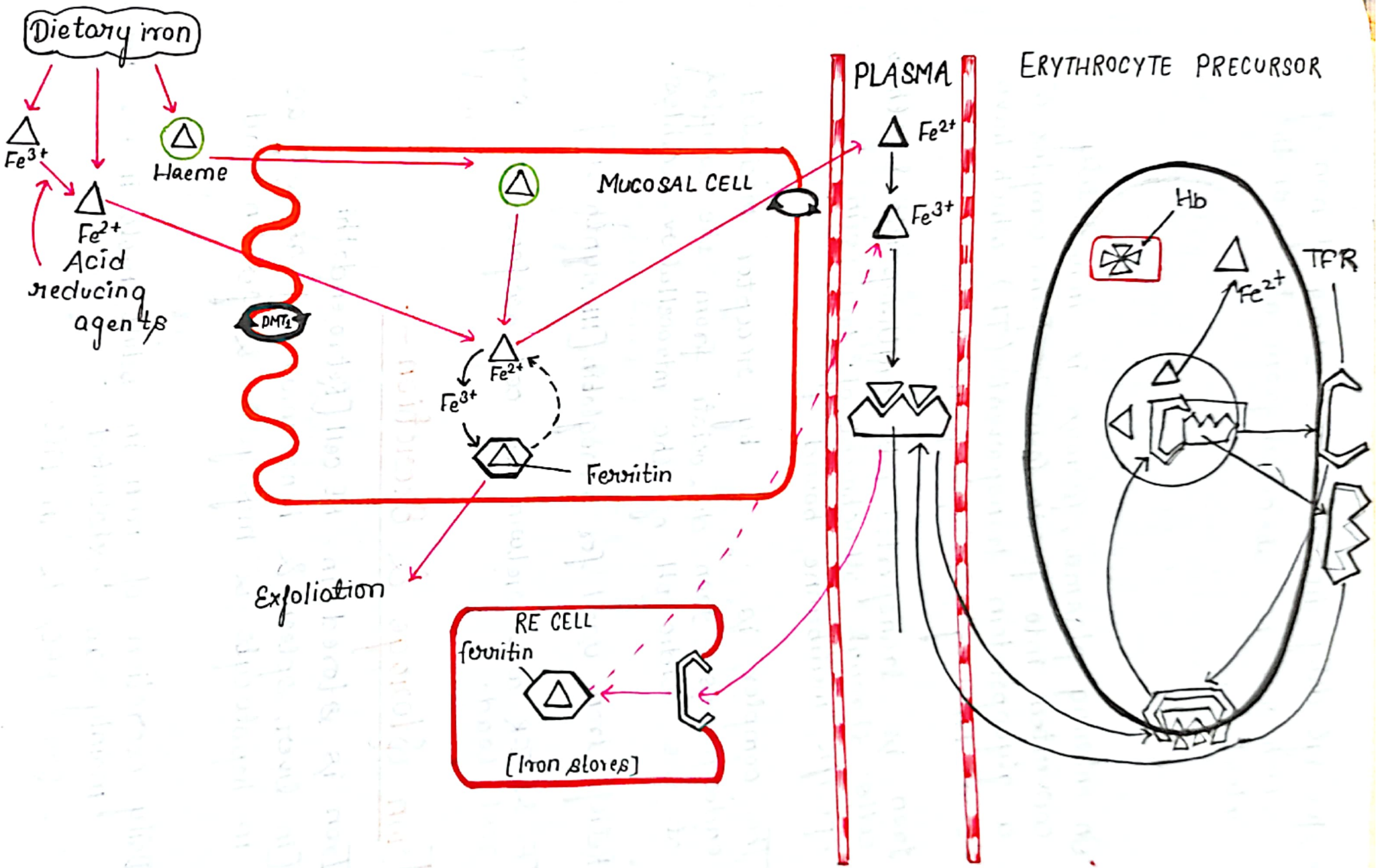
Inorganic Iron (Fe^{3+})
- grains & vegetables
- Slowly absorb
- needs to be dissociate from organic compound

$Fe^{+3} \xrightarrow[\text{reductase}]{\text{ferro}} Fe^{+2}$

- To separate iron transporter in the intestinal mucosal cells function to effect iron absorption.

1. Divalent metal transporter I [DMT-I]
   It carries ferrous iron into the mucosal cell.

2. ferro ⟶
   - Are bound with ferrous iron & pass through mucosal cell, directly into the blood stream.


Dietary iron
Fe^{3+}
Fe^{2+}
Acid reducing agents
Haeme
DMT1
MUCOSAL CELL
Fe^{2+}
Fe^{3+}
Ferritin
Exfoliation
RE CELL
ferritin
[Iron stores]
PLASMA
Fe^{2+}
Fe^{3+}
ERYTHROCYTE PRECURSOR
Hb
Fe^{2+}
TFR

- Average daily diet contain 10-20mg of iron of which 10% is absorbed from all over the intestine.

- On entering plasma, ferrous is immediately converted into ferric form & form complex ~ a glycoprotein transparent (TF) which have two binding site for ferric ion.

- Iron is transported into erythropoitic & other cells through attachment of transperin to specific membrane bound t

The complex is by receptor mediated endocytosis. Iron dissociate from the complex at the acidic pH of the intracellular vecihles.

Relief iron used for hemoglobin [Hb synthesis]

TF & TFR are return to cell surface to carry rest load.

* Iron Storage & Excretion →

- Iron is stored in RE cell [Retro endothi [in liver, spleen & bone marrow] as well as in hepatocyte & myocytes & ferritin and

- Daily excretion of iron in adult male in 0.5-1mg mainly as exfoliated . some RBCs & in Bile.

Other route →
Skin, little in urine & sweat

- In menstruating women, monthly men loss in 0.5 - 1mg/day.

* Oral Preparation →
  - Ferrous Sulphate
  - Ferrous succinate
  - Ferric ammonium citrate
  - Ferric gluconate
  - Iron choline citrate

* Oral Iron Adverse effect →
  - Epigastric pain
  - Nausea
  - Vomitting
  - Metallic
  - Constipation
  - Diarrehoe
  - Staining of teeth

* Parentral Iron →
  ① Given parentrally as deep IM & IV, only in following indication.
  - Oral iron is not tolarating.
  - Bowel upset

  ② Malabsorption —
  - failure to absorb oral iron.

Adr

- Pain at the site of injection.
- Headache, joint pain, nausea, urticaria (skin rash)
- Anaphylaxis (Allergic reaction)

Parenteral preparation

- Iron dextran
- Iron sorbitol citric acid
- Iron sucrose & sodium ferric gluconate

Acute Iron poisoning

- Iron toxicity
- More common in infants & and children
- 1-2g can be lethal (Dangerous)

- Symptoms

- Vomiting, abdominal pain
- Bloody diarrhoea
- Shock
- Haematemesis (Blood in vomiting)

Teacher's Signature : _____

Treatment

→ To prevent further absorption of iron from gut

(a) Induce vomiting or perform gastric lavage with sodium bicarbonate solution

(b) Give egg yolk and milk orally : to complex iron. Activated charcoal does not adsorb iron.

→ To bind and remove iron already absorbed

Desferrioxamine is given IV or IM to prevent iron absorption.

VITAMIN - B12

- Complex cobalt containing compounds Cyanocobalamin and hydroxocobalamin.
- Synthesized by microorganism, plants & animals

→ Dietary Sources : Liver, kidney, sea fish, egg yolk, meat, cheese.

- Vit. B_{12} occurs as water soluble, thermostable red crystals.

Expt. No.....

Page No.....

Daily requirement — 1-3 µg
3-5 µg in pregnancy

-> Deficiency of Vit B_{12}

Vit B_{12} deficiency occurs due to

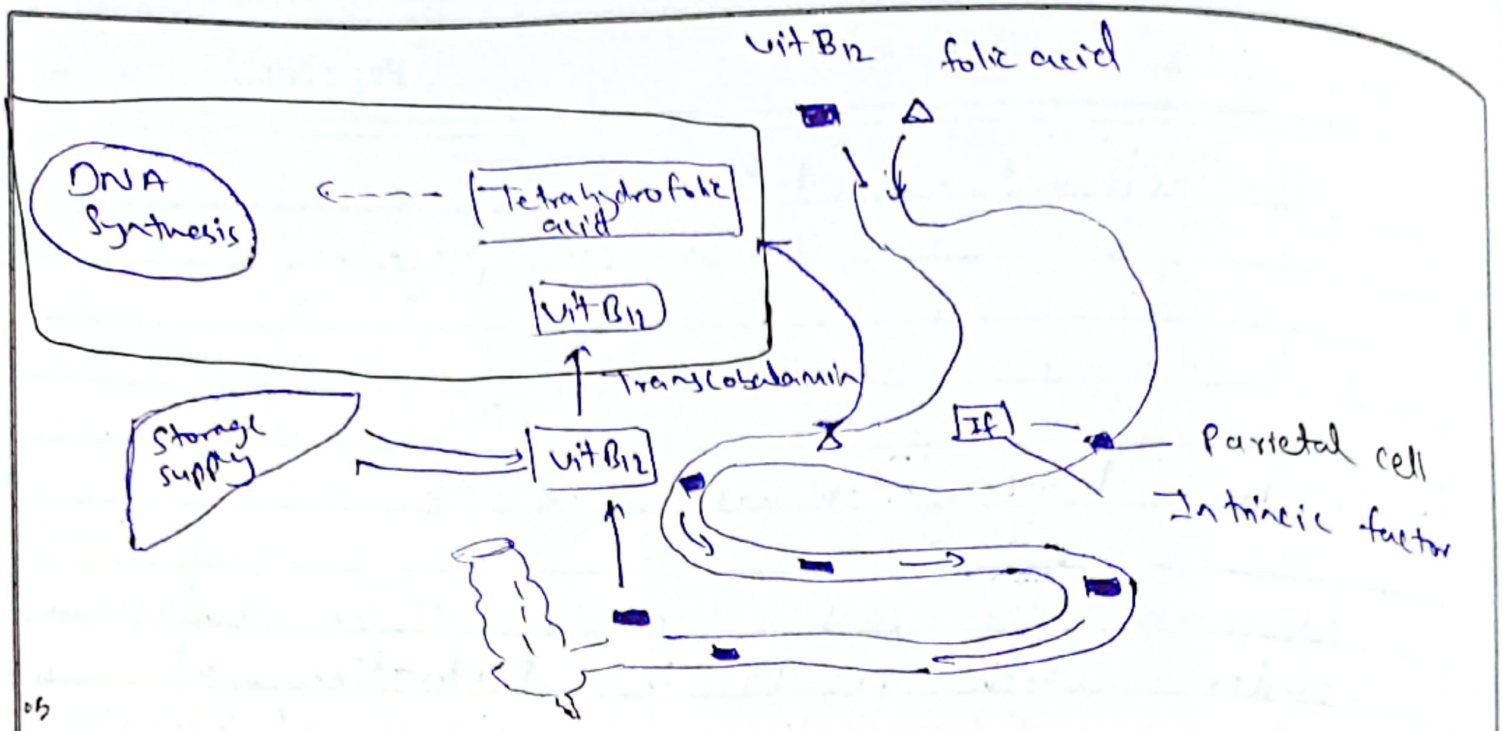
1- Addisonian pernicious anaemia: is an autoimmune disorder which results in destruction of gastric parietal cells → absence of intrinsic factor → inability to absorb Vit B_{12}

2. Other causes:
- Chronic Gastritis
- Malabsorption
- Gastrectomy (Surgical removal of a part of stomach).

Vit B_{12} and folate metabolism

Vit B_{12} is absorbed in the intestine with the help of Intrinsic factor. It is transported in the blood by Transcobalamin II to the liver for storage or to erythropoietic cells to facilitate conversion of methyltetrahydrofolic acid to tetrahydrofolic acid, important in DNA synthesis. Vit B_{12} is not degraded in the body, excreted mainly in bile.

Teacher's Signature : _____



Preparation and uses of Vit B12

- Vit B_{12} is directly and completely absorbed after IM or deep SC injection.
- Cyanocobalamin - 35 µg/5 ml inj
- Hydroxocobalamin - 500 µg, 1000 µg inj

Uses

- Treatment of Vit B_{12} deficiency
- Megaloblastic anaemia: defects in the metabolism of vitamin B_{12} or folic acid.
- Pernicious anaemia: Body isn't able to absorb orally vitamin B_{12} due to a lack of intrinsic factor so given parentrally.
- Prophylaxis - 3-10 µg daily.
- Neurological condition - multiple sclerosis, psychiatric disorders

Expt. No.

Folic Acid

It occurs as yellow crystals which are insoluble in water, but its sodium salt is freely water soluble.

Chemically, it is Pteroyl glutamic Acid (PGA) consisting of pteridine + paraamino benzoic acid (PABA) + glutamic acid.

Dietary sources – liver, green leafy vegetables, yeast, egg, milk.

- Present in food as poly-glutamates
- Absorption – in the duodenum and jejunum
- Transported in the blood as methyl- THFA by active and passive transport.
- Stored in cells as polyglutamate, liver takes up a large part and secretes methyl- THFA in bile.

Functions

FA $\xrightarrow{\text{folate Reductase}}$ DHFA $\xrightarrow{\text{DHFRase}}$ THFA

THFA - essential for biosynthesis of purines

Teacher's Signature : _____

Deficiency & Manifestation

- Megaloblastic anaemia
- Dietary deficiency
- Malabsorption
- Epithelial damage
- Weight loss
- Drugs – Phenytoin, phenobarbitone, methotrexate can induce folate deficiency.

Therapeutic use

- Megaloblastic anaemia
- folic acid deficiency
- Protect epithelial cell
- Growth in infants
- In pregnancy

Preparations

- folic acid - liquid oral, injectable
- folinic acid - ~~Calcium~~ fastovorin 3mg
  Calcium Leucovorin 3mg/ml inj.

Erythropoietin

Erythropoietin (EPO) is a sialoglycoprotein (sialic acid + Glycoprotein) hormone (MW 34000) produced by peritubular cells of the kidney that is essential for normal erythropoiesis (production of RBCs)

- Kidney cells release EPO in response to anaemia & hypoxia.
- Binds to EPO receptors on red cell progenitors and stimulates red cell production.
- Induce haemoglobin formation and erythroblast maturation.
- Releases reticulocytes (immature RBCs) in the circulation.

Recombinant human erythropoietin

- Epoetin α & β is administered by I.V. or S.C. injection and has a plasma $t_{1/2}$ of 6-10 hr, but action lasts several days.

Therapeutic uses

In treatment of Anaemia due to:

- Chronic renal failure if Hb < 8 mg/dl
- Zidovudine therapy in AIDS patients
- Cancer chemotherapy
- Multiple myeloma and cancer of bone marrow.

Teacher's Signature : _____

Adverse Effects

~~with~~ Adverse are related to sudden increase in haematocrit (ratio of vol. of RBC to the total vol of blood.), blood viscosity and peripheral vascular resistance.

These are –

- Increased clot formation in the A-V shunts
- Hypertensive episodes
- flu like Symptoms

Expt. No.....

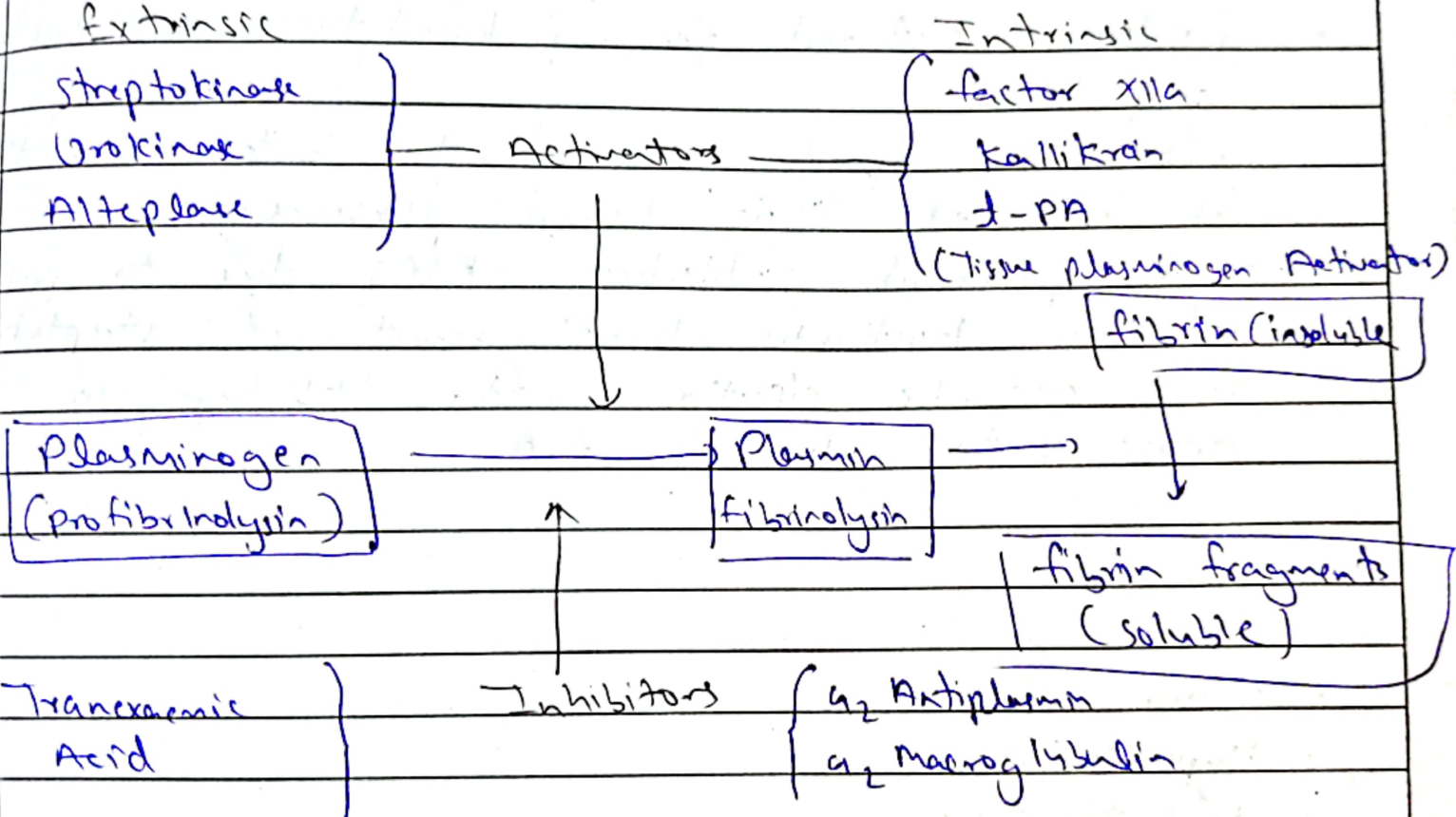
Date.....

Page No.....

fibrinolytics & Anti-platelet drugs

fibrinolytics -

- Drugs that are used to lyse the thrombi or clot by activating the natural fibrinolytic system.



- Thrombolytic (Another name)
- Venous thrombi are lysed more easily than arterial.
- They have little effect on thrombi > 3 days old.

Teacher's Signature : _____

Clinical important fibrinolytics are:

- Streptokinase
- Urokinase
- Alteplase
- Tenecteplase

Streptokinase

- Protein obtained from β hemolytic streptococci group C.
- Non-fibrin specific. i.e activates both circulating as well as fibrin bound plasminogen.
- Antistreptococcal antibodies (ASA) due to past infections inactivates large amount of streptokinase
- will not be effective after 4-5 days of administration due to ASA.

Adverse effects

- fever
- Hypotension
- Arrhythmias

Date.....

Expt. No.....

Page No.....

Urokinase

- An enzyme isolated from human urine.
- Commercially prepared from cultured human kidney cells.
- It activates plasminogen directly and has a plasma $t_{1/2}$ of 10 to 15 min.
- Adv – Non antigenic, not destroyed by ASA. But not fibrin selective.

Alteplase (rt-PA)

- Recombinant DNA technology
- Specific for fibrin-bound plasminogen.
- Non antigenic, not destroyed by antibodies
- Rapid acting, short $t_{1/2}$, given by slow I.V infusion
- More potent
- Nausea, mild hypertension, fever may occur
- Expensive.

Teacher's Signature :

Reteplase and tenecteplase

- Recombinant mutant variants of t-PA
- Resistant to inhibition by plasmin activator inhibitor
- Longer duration of action, injected IV as a single bolus dose (tenecteplase).
- Similar to t-PA in efficacy & toxicity.

– Contraindications to thrombolytic

- Intracranial haemorrhage
- Ischaemic stroke in past 3 months
- Head injury in past 3 months
- Active bleeding / bleeding disorders
- Peptic ulcer

Uses of fibrinolytics

- Acute myocardial infarction
- Deep vein thrombosis
- Pulmonary embolism
- Acute ischemic stroke

Expt. No.....

Date.....

Page No.....

Antiplatelet Drugs

- Drugs which inhibit platelet aggregation
- Useful in the prophylaxis thromboembolic disorders.
- The principal function of platelets is to prevent bleeding - by Thrombus (platelet plug formation)

Classification

1. PG Synthesis Inhibitors - Aspirin
2. Phosphodiesterase Inhibitor - Dipyridamole
3. ADP antagonists - Ticlodipine, clopidogrel
4. Gp IIb / IIIa receptor Antagonist - Abciximab
   Eptifibatide
   Tirofiban
5. Others - PGI_2, cilostazole

Platelet plug formation

1- Platelet adhesion
2- Platelet activation
3- Platelet aggregation

Teacher's Signature : _____

After the injury → the platelet adhere at that site and causes Activation of platelets

↓

leads to generation of Arachidonic acid, The arachidonic acid release the ADP Cresponsible for direct platelet aggregation.

↓

Arachidonic acid in presence of COX leads to generation of PGH_2 & PGH_2 (unstable prostaglandin & then to TXA_2 (Thromboxane A_2) → which causes platelet aggregation.

Arachidonic Acid

Aspirin ✕ ↓ ← Cox

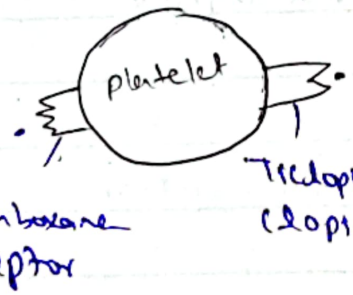
PGH_2

↓

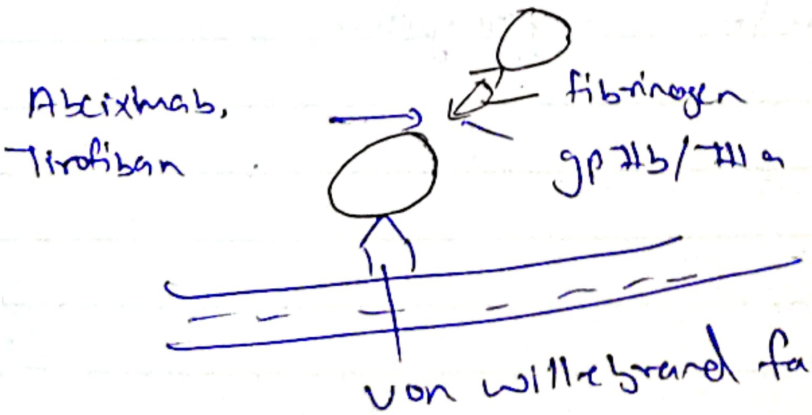
PGH_2

↓

TXA_2 ⟶ Platelet aggregation



→ Direct platelet aggregation



Expt. No..... Page No.....

Aspirin

- TXA_2 synthesis inhibitor
- The prostaglandin TXA_2 promotes platelet aggregation.

Mechanism of Action

- Aspirin irreversibly acetylates and inhibits the enzyme COX-1 & TX-synthesis in platelets.
- Platelet cannot synthesize fresh enzyme, so antiplatelet action lasts for 5–7 days.
- Daily aspirin dose is 75 – 100 mg

At high doses, it also inhibits PGI_2 prostacyclin (a potent inhibitor of platelet aggregation)

Dypyridamole

- Phosphodiesterase inhibitor which interferes with platelet function by increasing the platelet cAMP level & ↑ endogenous PGI_2 level.
- Used along with aspirin or warfarin for the prophylaxis of thromboembolic in patient with prosthetic heart valves.
- Can be used in patients with transient ischemic attacks or strokes.

Teacher's Signature : _____

ADP Antagonist (clopidogrel, Ticlopidine)

Prodrugs → Active metabolite

↓

Irreversibly block the ADP receptor (P_2Y_{12})

↓

Prevent activation of platelet

↓

Inhibit platelet aggregation

GP-IIb/IIIa receptor Antagonists

- Potent platelet aggregation inhibitors

Mechanism – The GP IIb/IIIa is a receptor on platelet surface for fibrinogen and von willebrand factor through which agonists like collagen, thrombin, TXA_2, ADP, etc. finally induce platelet aggregation. Thus, GP IIb/IIIa antagonists block aggregation induced by all platelet agonists

Therapeutic uses

- Coronary artery disease
- Cerebrovascular disease
- Venous thromboembolism
- Peripheral vascular disease

Plasma volume expanders

Plasma volume expanders are the i.v. fluid solutions which increases the plasma volume by increasing osmotic pressure.

- High molecular weight substances
- Generally they are used to replace fluids that are lost due to illness, burns, trauma or hemorrhage.
- In emergency, immediate volume replacement is important to maintain the blood pressure & tissue reperfusion.
- Blood volume is directly proportional to the blood pressure in the body, and when both decrease the flow of blood to important tissue may be inhibited.
- Hypovolemic shock occur when tissue oxygenation drops due to a decrease in blood volume.
- Plasma volume expanders when infused IV retain fluid in the vascular compartment

Teacher's Signature : _____

and thus correct hypovolemia due to loss of plasma or blood.

Ideal properties of plasma expanders

- Exert oncotic pressure comparable to plasma
- Should remain in circulation and not leak out in tissues, longer acting.
- Pharmacologically inert.
- Should be stable & cheap
- Should not interfere with grouping & Cross matching of blood.
- Non-antigenic & non-pyrogenic

Mechanism of Action

- Generally works on the principle of osmosis
- Increase plasma osmotic pressure, drawing water into plasma from interstitial fluid preventing it from leaking out into the tissues & increases intravascular blood volume
- Since the lost blood is replaced with a suitable fluid, the diluted blood flows more easily.
- Increase central venous pressure, ↑ CO, ↑ SV, ↑ BP, improve oxygen flux

Date.....

Expt. No.....

Page No.....

Types of plasma volume expanders

Colloids
- Dextrans
- Gelatin
- Hydroxymethyl starch
- Polyvinyl pyrrolidine
- Human albumin
- Blood

Crystalloids
- Normal saline
- Dextrose
- Ringer Solutions

Colloids

Colloids volume expanders contain larger insoluble molecules, such as gelatin or hydroxyethyl starch, and theoretically increase the intravascular volume but not interstitial and intracellular volume.

- Blood itself is a colloid. Commonly used colloid are albumin, Dextran & starch.

Advantages	Disadvantages
• Longer duration of action	• Allergic reaction possible
• Vascular permeability is low → HMW → stay for longer	• Expensive • Various effect on blood coagulation.

Teacher's Signature : _____

Dextran

Dextrans are polysaccharide obtained from sugar beet & is available in two forms.

- Dextran - 70 (MW 70,000)
- Dextran - 40 (MW 40,000)

Dextran - 70

- More commonly used, Osmotic pressure is similar to plasma.
- Slowly excreted by glomerular filtration as well as oxidized in the body over weeks.
- Allergic reactions are common
- It may interfere with coagulation blood grouping & cross matching.

Dextran - 40

- It is 10% solution of dextrose & saline.
- Reduces blood viscosity and prevents RBC sludging : improves microcirculation
- Rapidly filtered at the glomerules : and may get highly conc. in the tubule if oliguria develops
- Cheap
- Can be stored for 10 years.

Expt. No.....

Date.....

Page No.....

Degraded gelatin polymer

- Synthetic polymer of MW - 30,000
- Exerts osmotic pressure similar to albumin and is not allergic, hypersensitivity reactions are rare.
- Doesn't interfere with blood grouping & cross matching.
- Used for priming the heart - lung & dialysis machines.
- Duration of action : 12 hrs
- Long shelf life

Hydroxyethyl starch

- It is a complex mixture of 90% ethoxylated amylopectin of various molecular sizes; average MW 4.5 lacs.
- Maintains blood volume for longer time
- Doesn't cause acute renal failure or coagulation disturbance.

Adverse effects

- fever, chills
- Vomiting
- Anaphylactic reaction

Teacher's Signature : _____

Polyvinyl pyrrolidone

- Synthetic water soluble polymer, used as a 3.5% soln.
- fraction of PVP is stored in reticuloendothelial cells, Kupfer cells in liver, skeletal muscles and skin for a long time.
- Partly excreted through kidneys
- Interfere with blood grouping causes histamine release.

Human Albumin

- Obtained from pooled human plasma
- Given as 5% or 20% solution, 100ml of 20% soln is osmotically equivalent to 500ml of whole blood.
- Nonantigenic, doesn't interfere with coagulation & blood grouping.
- Used in burns, hypovolemic shock.

Expt. No.....

Page No.....

Crystalloids

- Electrolyte solutions with small molecules that can diffuse freely throughout the extracellular space
- Relatively low tendency to stay intravascular
- Principal component is inorganic salt sodium Chloride (NaCl)

eg- Normal saline
Dextrose
Ringer soln

- Advantages
- NO allergic reactions
- Inexpensive
- low effect on blood coagulation

- Disadvantages
- Shorter duration
- Required in larger quantity
- Excessive use can cause oedema.

Teacher's Signature :

Normal Saline

- Isotonic fluid, osmolarity nearly equal to that of ECf.
- 0.9% Sodium chloride
- Normal sterile saline is a sterile, non pyrogenic solution
- Should be avoided in heart failure, pulmonary edema.

Dextrose

- Hypertonic fluid : used as 5% soln
- Plasma volume expansion is minimum
- Dextrose gets metabolised and water get distributed in all compartments.
- Infusion of 1 ltr of dextrose can raise the plasma volume by just 100ml.
- Should be injected slowly.

Expt. No..... Page No.....

Diuretics

Diuretics are the drugs which increase excretion of sodium and water from body through urine, thus increase urine output (diuresis).

- Act by inhibiting the reabsorption of ions at various sites of renal tubule.

Classification

1- High efficacy diuretics (Inhibitors of Na^+-K^+-$2Cl^-$ co transport)
- Sulphamoyl derivatives — • furosemide
  • Bumetamide
  • Torasemide

2- Medium efficacy diuretics (Inhibitors of Na^+-Cl^- symport)

(a) Benzothiadiazines (thiazides) -- • Hydrochlorothiazide
  • Benzthiazide

(b) Thiazide like — Chlorthalidone
  Clopamide

3- Weak diuretic:

(a) carbonic anhydrase inhibitors - Acetazolamide

Teacher's Signature : _____

(b) Potassium sparing diuretics

(i) Aldosterone Antagonist: spironolactone

(ii) Inhibitors of renal epithelial Na^+ Channel
- Triamterene, Amiloride

(c) Osmotic diuretics
- Mannitol
- Isosorbide
- Glycerol

Mechanism of Action of loop diuretics

Secreted by organic acid transporters in the proximal tubule

↓

Reaches Thick ascending limb of Henle's loop

↓

Block Na^+ K^+-2Cl Symporter, present on the luminal membrane of TALH

↓

Inhibit reabsorption of Na^+ Cl^-

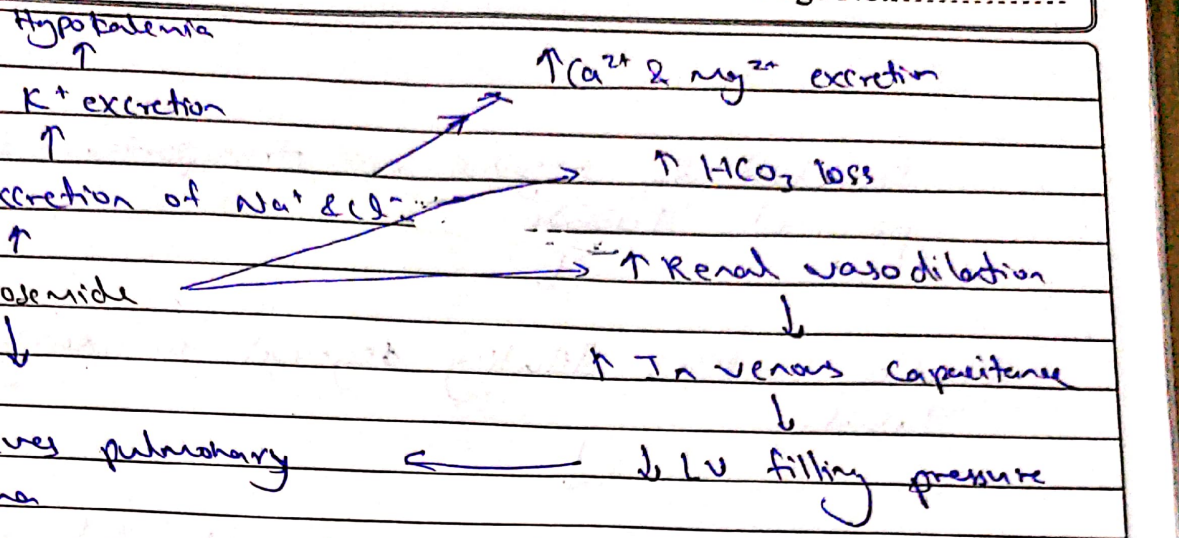
↓

↑ excretion of Na^+ & Cl^- in the urine

Expt. No.....

Date.....

Page No.....



Pharmacokinetics

- Rapidly acting, well absorbed orally
- Quick onset of Action: I.V. 2-5 min, oral- 20-40 min
- Duration of action = 4-6 hrs

Adverse Effects

- Hypokalemia
- Hypovolemia
- Hyponatremia

Uses

- Hypertension
- Acute renal failure
- Edema due to CHF

Teacher's Signature : _____

Thiazides

Secreted by organic acid transporters in the proximal tubule

↓

Reaches Cortical diluting segment or early Distal Tubule

↓

Binds to Na^+-Cl^- Symporter located on the luminal membrane

↓

Inhibit reabsorption of Na^+ Cl^-

↓

↑ excretion of Na^+ & Cl^- in the urine

- Pharmacokinetics

- Well absorbed orally
- Action starts within 1hr
- Duration of action: 8-48 hrs
- Dose - 25-100 mg

- Uses

- CHF
- Hypertension
- Hyper calciuria

Expt. No.....

Date.....

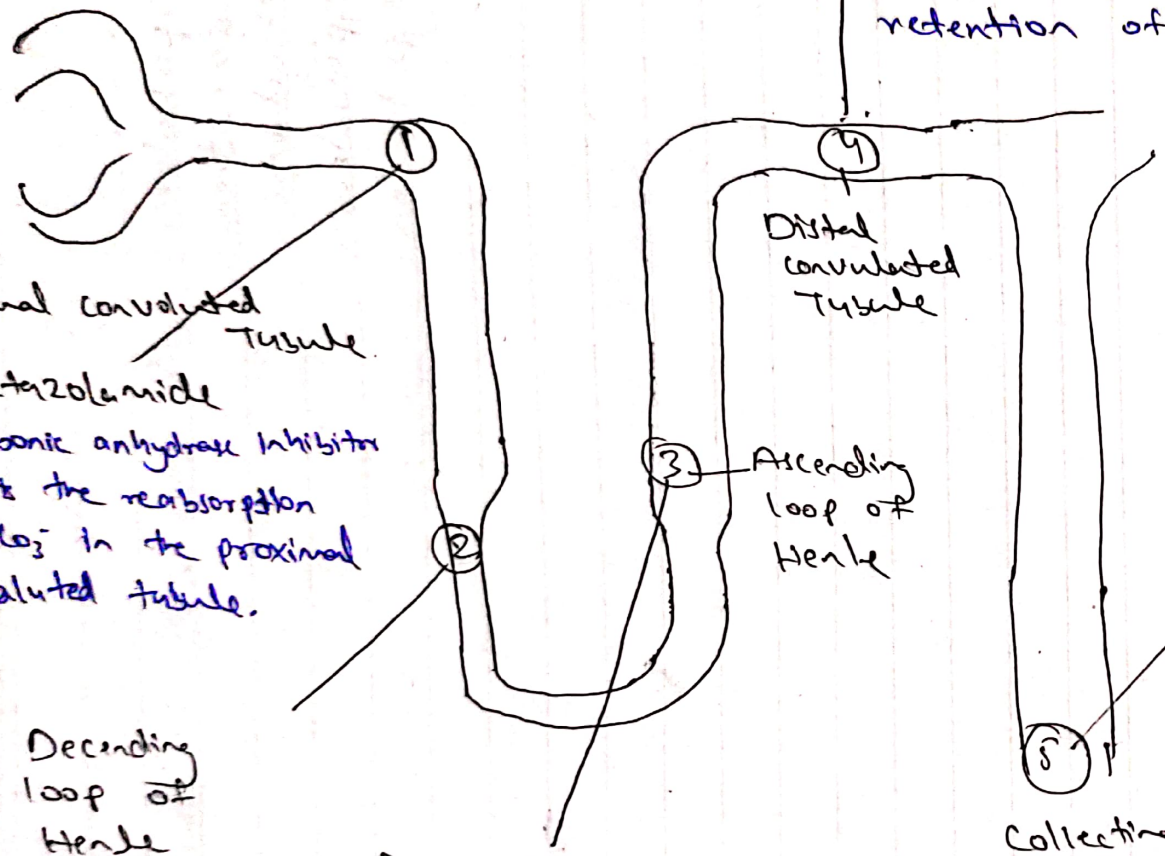
Page No.....

Adverse effects

- Hypokalaemia & metabolic alkalosis
- Hyponatremia
- Dehydration
- Hypovolemia
- Hypotension

Thiazide & Thiazide like

- Inhibit reabsorption of Na^+ & Cl^- in the distal convoluted tubule, resulting in retention of water in the tubule.



- Acetazolamide
- A carbonic anhydrase inhibitor inhibits the reabsorption of HCO_3^- in the proximal convoluted tubule.

- Furosemide, Bumetanide, Torsemide
- Loop diuretics inhibit the Na^+-K^+-$2Cl^-$ cotransport in the ascending loop of Henle, resulting in retention of Na^+, Cl^- in the tubule

- Spironolactone, Amiloride
- spironolactone inhibit aldosterone mediated reabsorption of Na^+ & secretion of K^+
- Amiloride block Na^+ Channel
- These agents prevent loss of K^+ that occurs with thiazide or loop diuretics.

Expt. No.....

Date.....

Page No.....

Antidiuretics

Antidiuretics are the drugs that reduces urine volume

Inhibit water excretion (anti-aquaretics) without affecting salt excretion

Primary indication: Diabetes insipidus

Classification of Antidiuretics

- Antidiuretics hormone (ADH): vasopressin (AVP)
- vasopressin analogues: Desmopressin, lypressin, Terlipressin
- Thiazide diuretics - chlorthiazide
- Miscellaneous - chlorpropamide
  - Carbamazepine

Antidiuretic hormone (ADH)

- vasopressin - Secreted by posterior pituitary along with oxytocin.
- Synthesized in supraoptic & paraventricular nuclei of the hypothalamus, transported along the hypothalamohypophyseal tract to the posterior pituitary.
- Vasopressin helps prevent the loss of water from the body by reducing urine output & helping

Teacher's Signature : _____

the kidneys reabsorb water in the body.

- Vasopressin also raises blood pressure by constricting blood vessels.

Physiological stimuli for ADH release:

- Dehydration
- Rise in plasma osmolarity

- ADH receptor

Vasopressin receptors – G-protein coupled receptor

V_1 receptor → vasoconstriction
V_2 " → water retention in collecting tubules

V_{1a} – present in vascular & other smooth muscle, CD cells, urinary bladder

V_{1b} – Anterior pituitary

V_2 – Present in collecting duct principal cells in kidney.
&
Ascending loop of henle.

Date.....

Expt. No.....

Page No.....

ADH Actions

- Kidneys — Acts on collecting duct principal cells, make them water permeable — water reabsorbed — conc. urine passed.
- Blood vessels: Constricts through V_1 receptor — rise blood pressure but at higher dose
- Dilates through V_2 receptors

Mechanism of Action

V_2 receptor on basolateral side of CD cell membrane

↓

Increases cAMP formation

↓

Phosphorylation of relevant protein promotes exocytosis of aquaporin 2 (water channel in apical membrane)

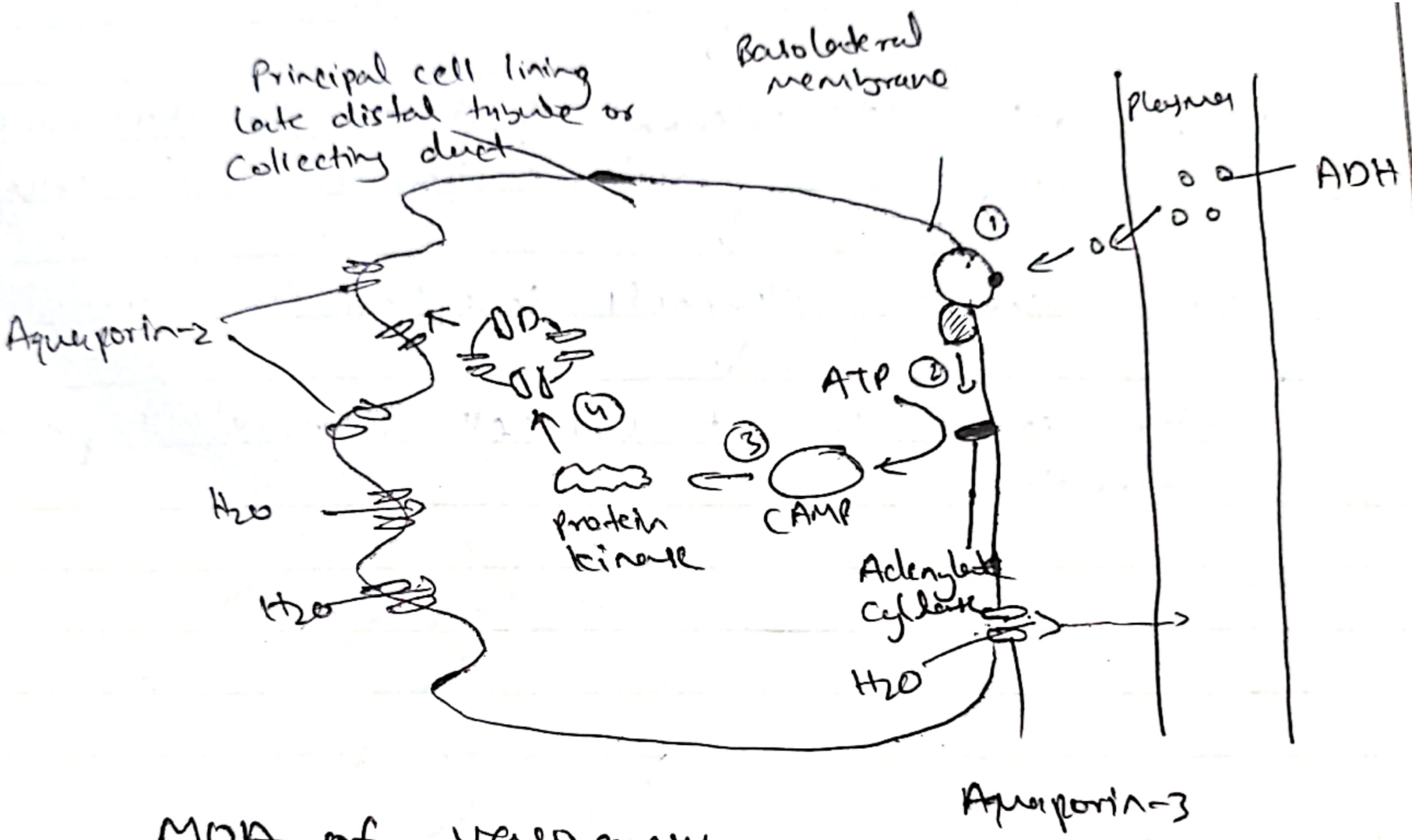
↓

More aqueous channels inserted in apical membrane

↓

Water permeability of CD cell increased & prevent urination.

Teacher's Signature : _____



MOA of vasopressin

Vasopressin analogues

- Desmopressin
  - Selective V_2 agonist so fewer side effects than others.
  - 12 times more potent anti-diuretic than ~~vaso~~ vasopressin
  - Duration of action 8–12 hrs

- Lypressin
  - Less potent than vasopressin
  - Acts on both V_1 & V_2 receptors
  - Longer duration of action
  - Used in place of ADH