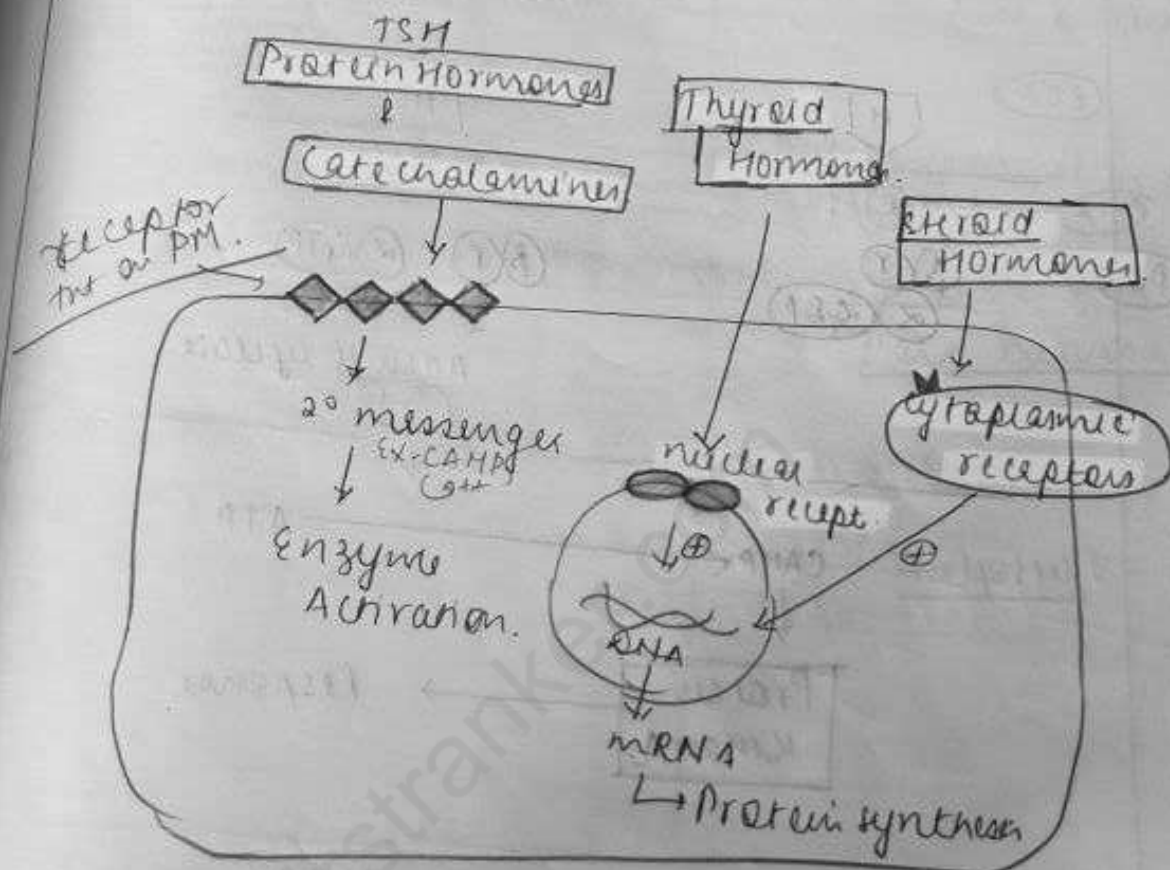


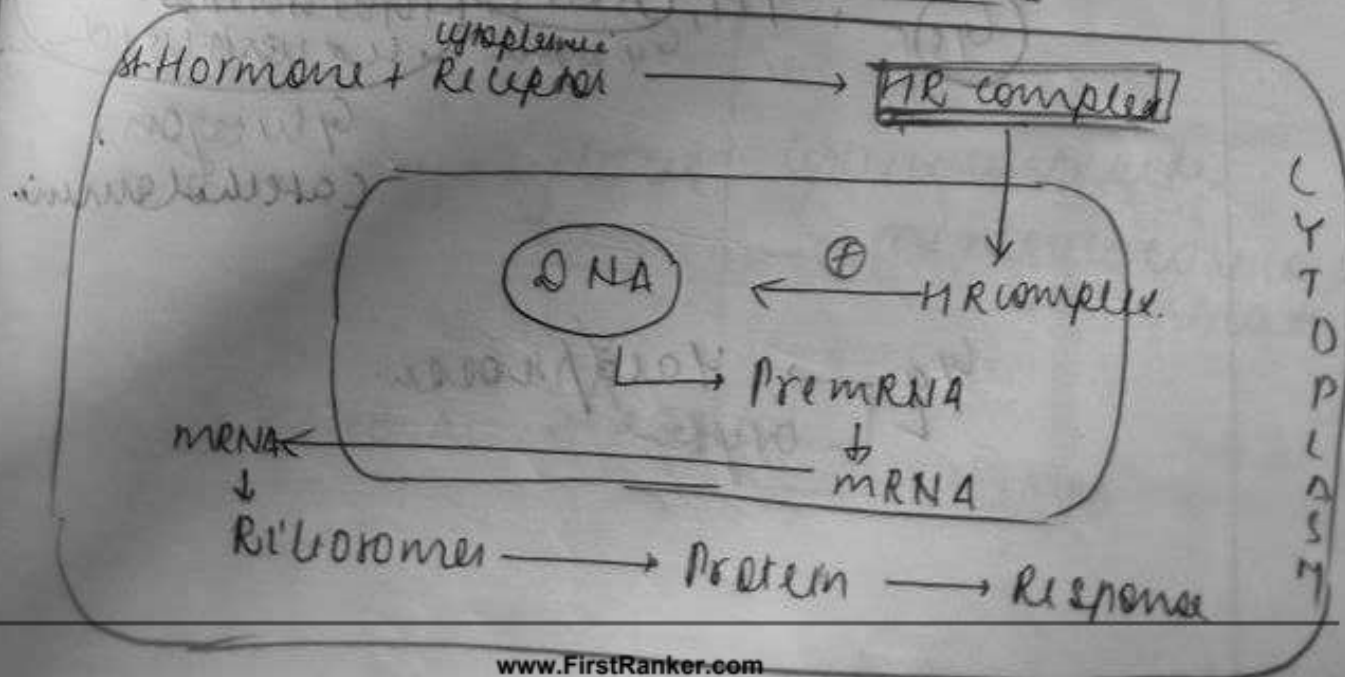
28 Jan 2019

HORMONES

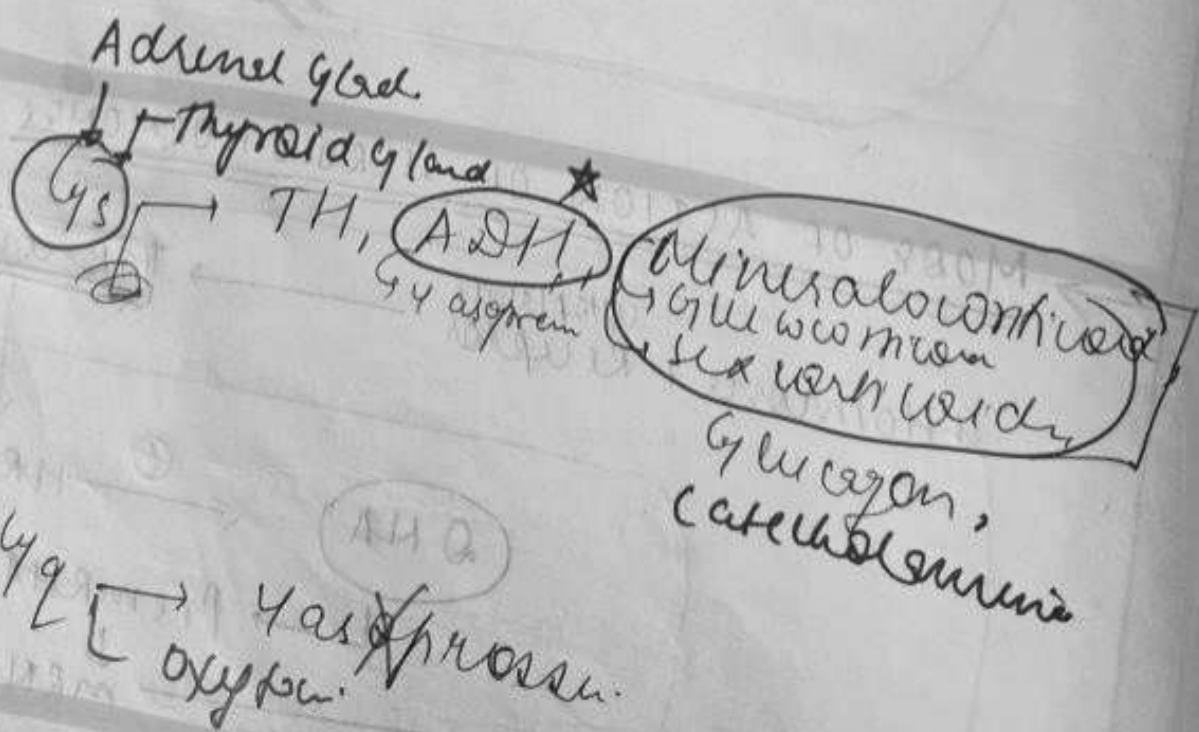
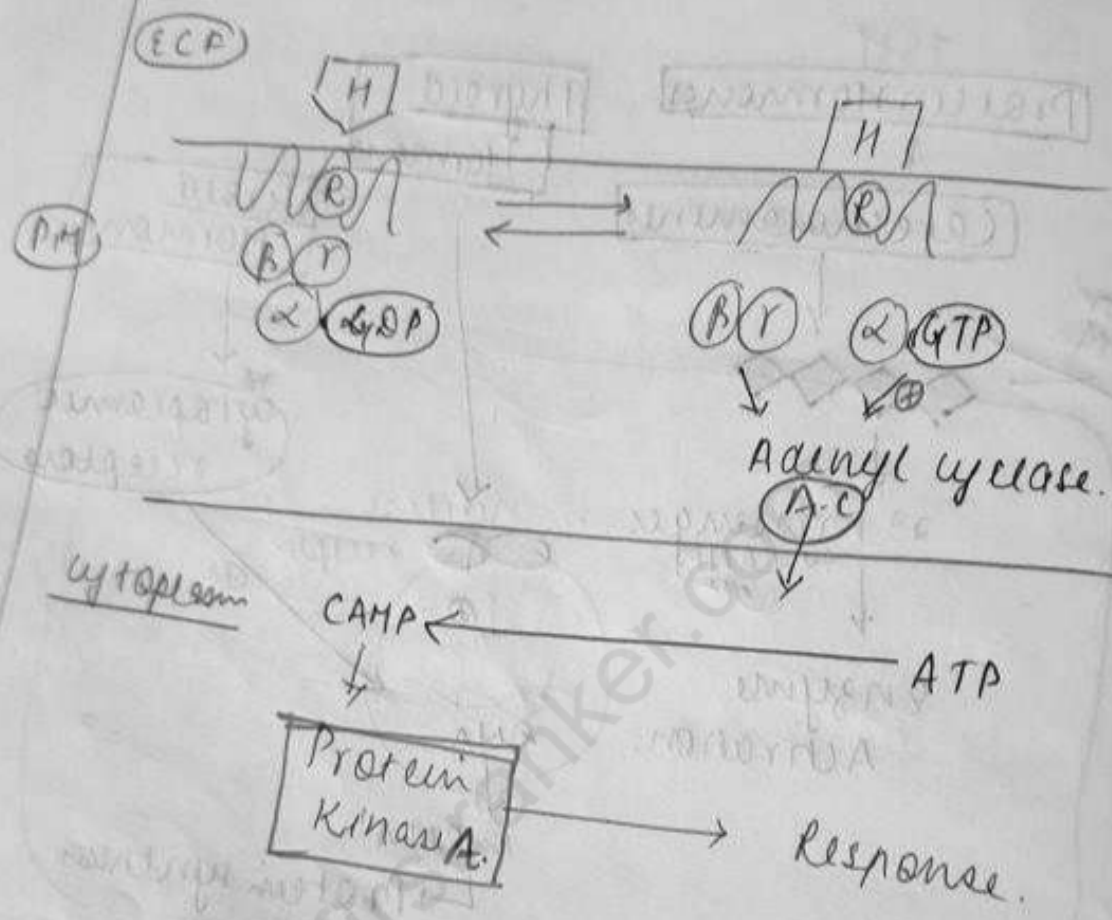
HORMONE RECEPTORS:



MODE OF ACTION OF STEROID HORMONES:



→ MODE OF ACTION OF PROTEIN HORMONES & CATECHOLAMINES



Sphenard bones
longevity in
20 in 'sella
Fursica

PITUITARY GLAND - situated in sella turcica

NEUROHYPOPHYSIS
Post. pituitary.

- neuroectoderm in origin
- developed from 3rd ventricle.

3 части

pass
distal

P. cas
intermedia

Pars
tuleradi

Pais nervosa.

124N → 7H, oxytocin

by unaccounted,
minerals consumed,
sex variation

supra optic n. → A2H

HORMONES OF ANT. PITUITARY

Adipophil
(70% of all
secretory
cells)

- (i) Somatotrophs / somatotropes - secrete GH / STH
somatomedin
- (ii) Lactotrophs / Lactotropes - PL
- (iii) Corticotrophs - ACTH & β-Lipotropin = Ado hormone & sex hormones
- (iv) Thyrotrophs - TSH
- (v) Gonadotrophs - FSH & LH

→ Classical Tropic Hormones - ACTH
TSH
FSH
LH

Ant. Pituitary

- staining property
- Chromophore - takes no stain; secrete no hormone
 - chromophil - take stain; secrete hormone

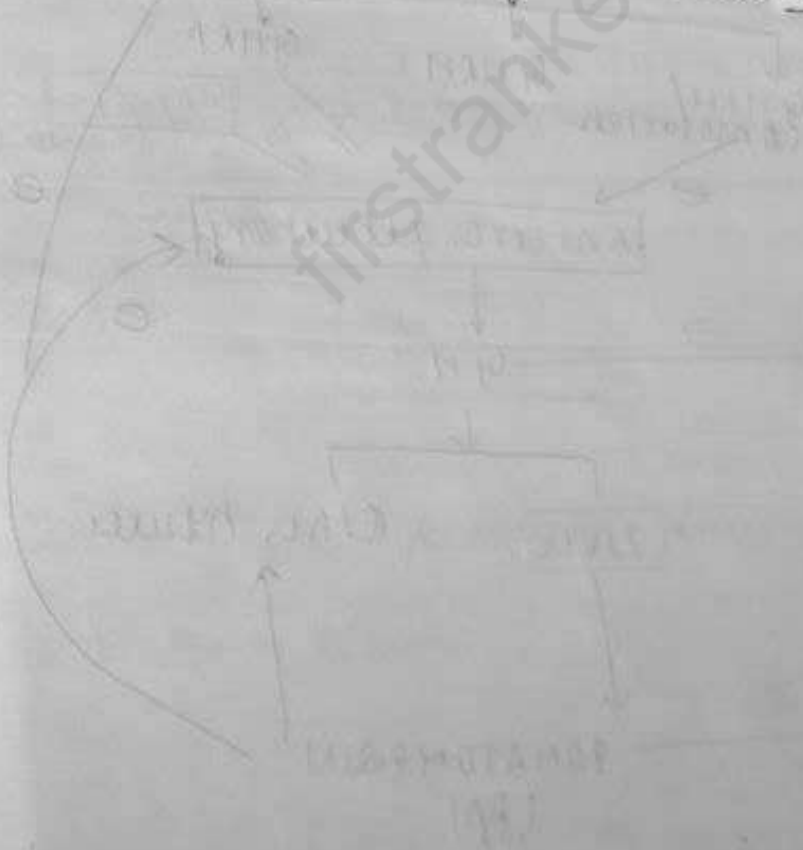
REGULATION OF ANT. PITUITARY SECRETION

→ Hypothalamus controls ant. pituitary by secreting releasing & inhibiting hormones which are called neurohormones. These hormones are transported to ant. pituitary through

hypothalamo-hypophyseal portal vessels.

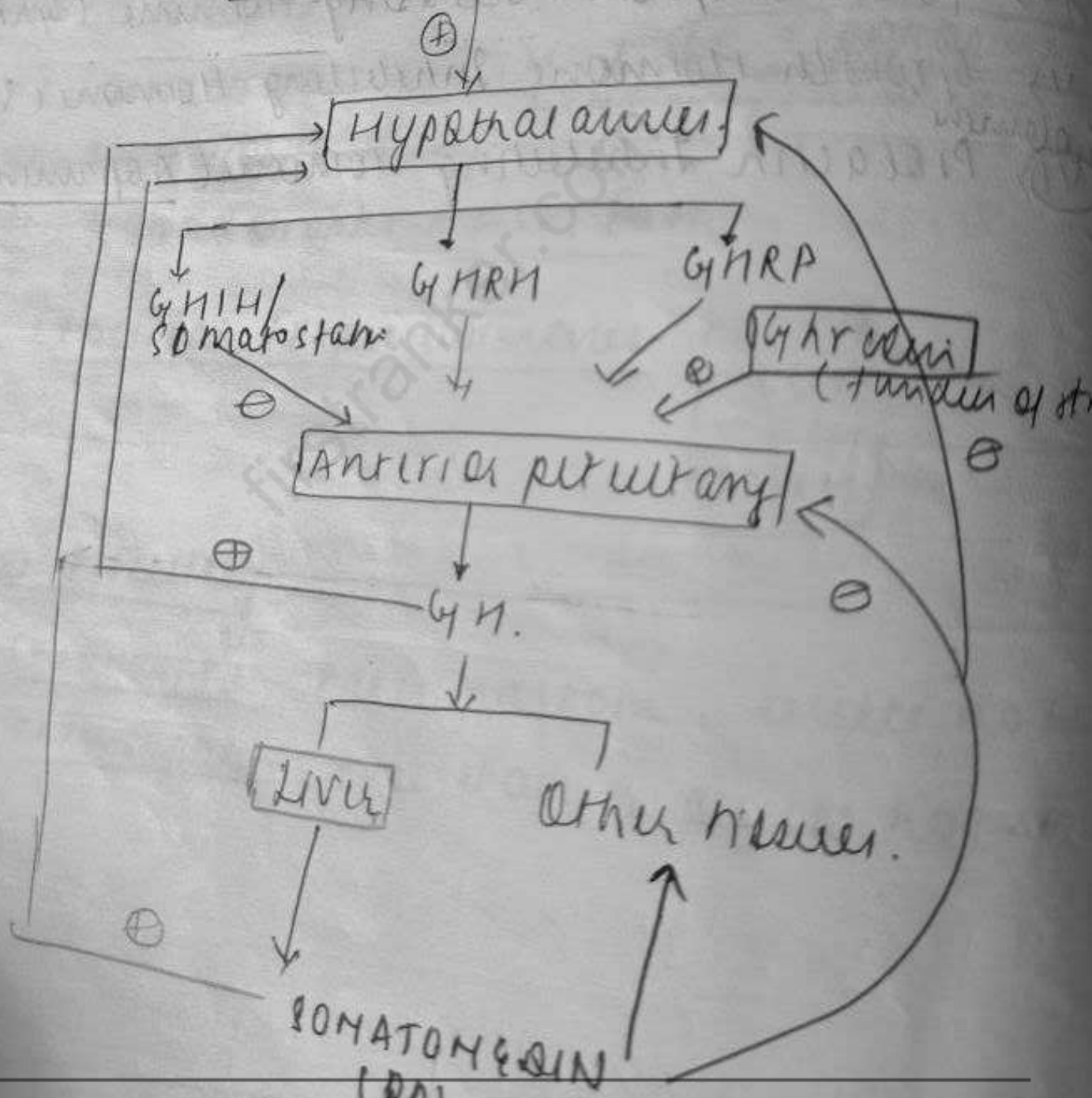
HORMONES OF HYPOTHALAMUS: (all are peptide hormones except Dopamine)

- i> Growth Hormone Releasing Hormone (GHRH)
- ii> Corticotrophic Releasing Hormone (CRH) -
- iii> Thyrotrophin Releasing Hormone (TRH) -
- iv> Gonadotrophin Releasing Hormone (GnRH) -
- v> Growth Hormone Inhibiting Hormone (Somatostatin)
- vi> Prolactin Inhibiting Hormone (Dopamine)



REGULATION OF GH / IGF-1 SECRETION

(↓ GH)
Hypoglycemia, fasting, starvation,
exhaustion, stress, trauma.



→ Action of GH:-

- GH acts on bones, growth & protein metabolism through somatomedin secreted by liver.

→ Somatomedin: substance through which GH acts.
 (GH related to insulin except that C-chain is shorter)
Types ↓

IGF-I / Somatomedin C

- acts on bones & protein metabolism.

IGF-II

- insulin like GF.
• role in faster growth

→ DURATION OF ACTION:

GH

- loose binding with plasma pr. → binds with plasma pr. strongly.
- ↓
- released from plasma protein rapidly

action lasts for short duration

~20 min

IGF-I / Somatomedin C

- ↓
- released slowly from plasma pr.

acts continuously for long duration

~20 hrs

→ MODE OF ACTION OF SOMATOMEDIN C / IGF-I

via 2^o messenger - (cAMP)*

→ GH Receptor / GHS [Growth Hormone secretagogue]

GH + GHS (transmembrane receptor)
 ↓
 cytosolic family

↓ mainly liver cells

↓
HR complex

Liver

↓
 intracellular enzyme pathways

↓
 somatomedin secretion.

Action of GH

HORMONES OF POST- PITUITARY

i) ADH / Vasopressin made up of
ii) oxytocin - pituitary

- Neurohypophysis ≠ secret any hormones
- ADH & oxytocin - synthesized in hypothalamus.

Hypothalamo-hypophyseal tract (axonic flow)

post-pituitary.

stored at Nerve endings.

- When myelites from Hypothalamus reach post-pituitary, hormones are released from Nerve endings.

NEUROHORMONES

Neurophysin

binding protein which transport ADH & oxytocin from Hypo → post-pituitary via hypothalamo-hypophyseal tract.

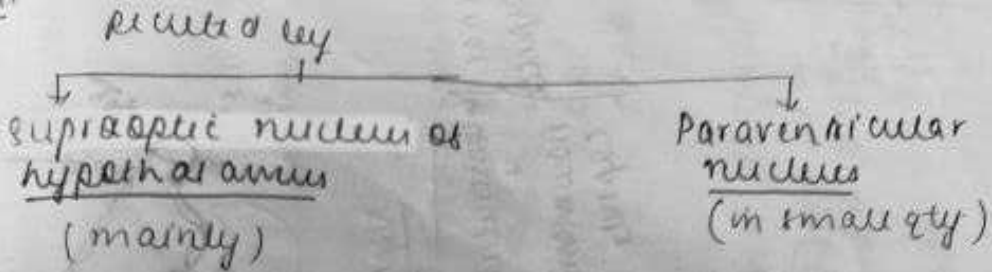
NEUROPHYSIN I / OXYTOCIN NEUROPHYSIN

binding protein for oxytocin.

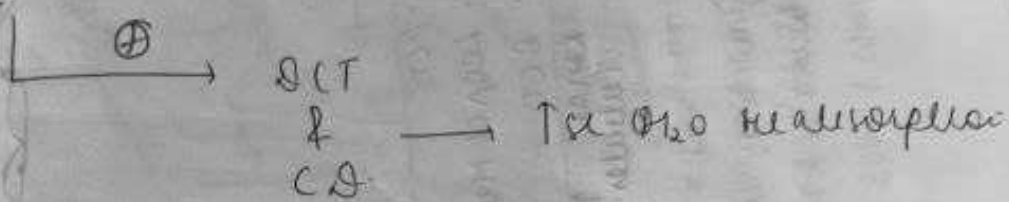
NEUROPHYSIN II / ADH NEUROPHYSIN

binding protein for ADH / Vasopressin.

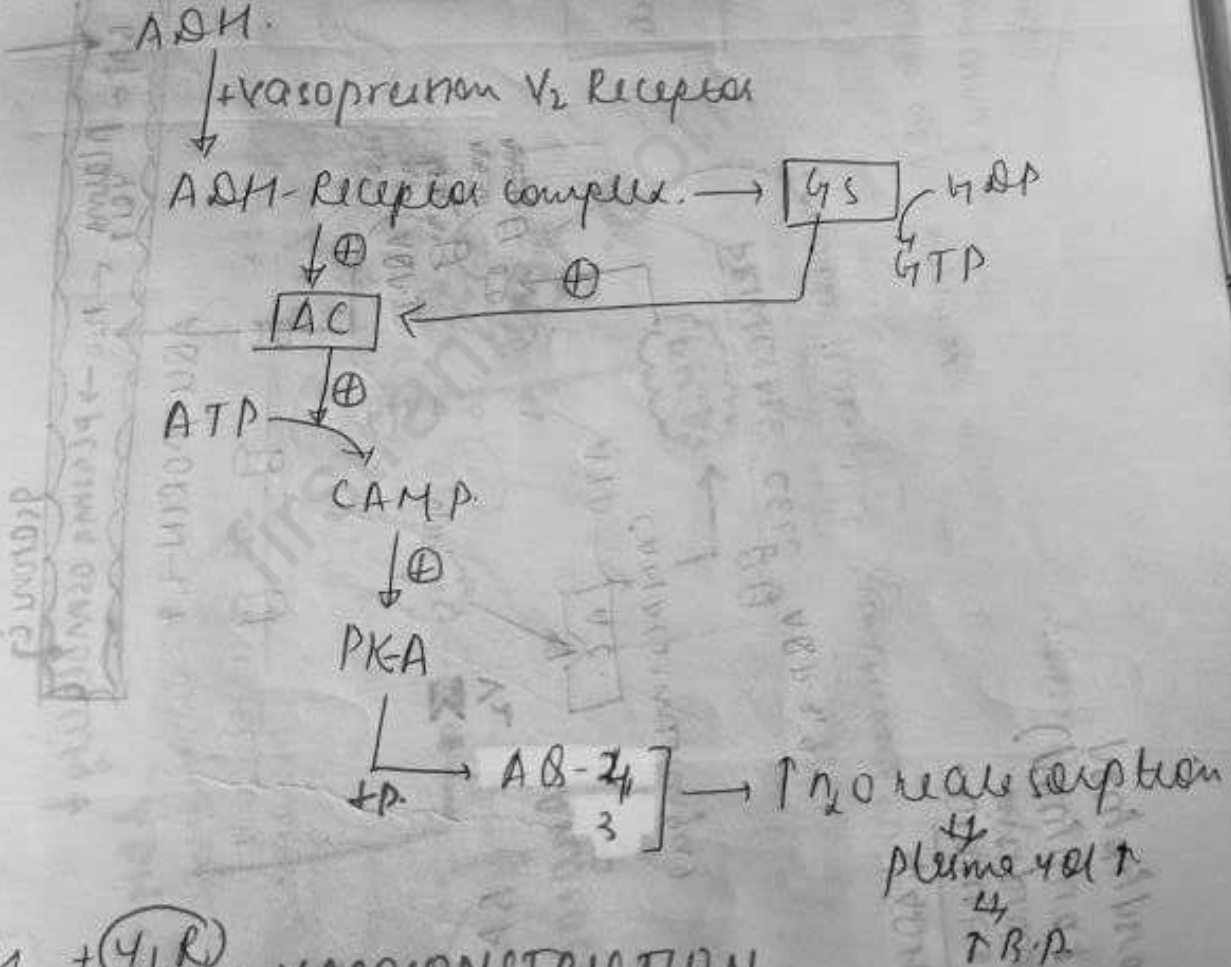
ADH:-



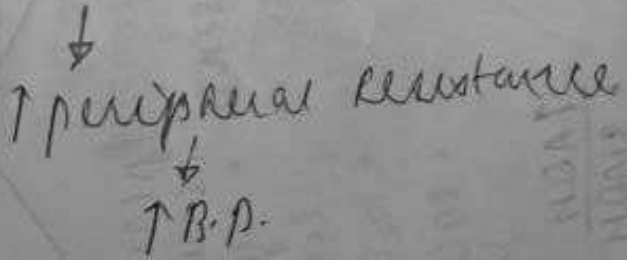
ACTIONS:

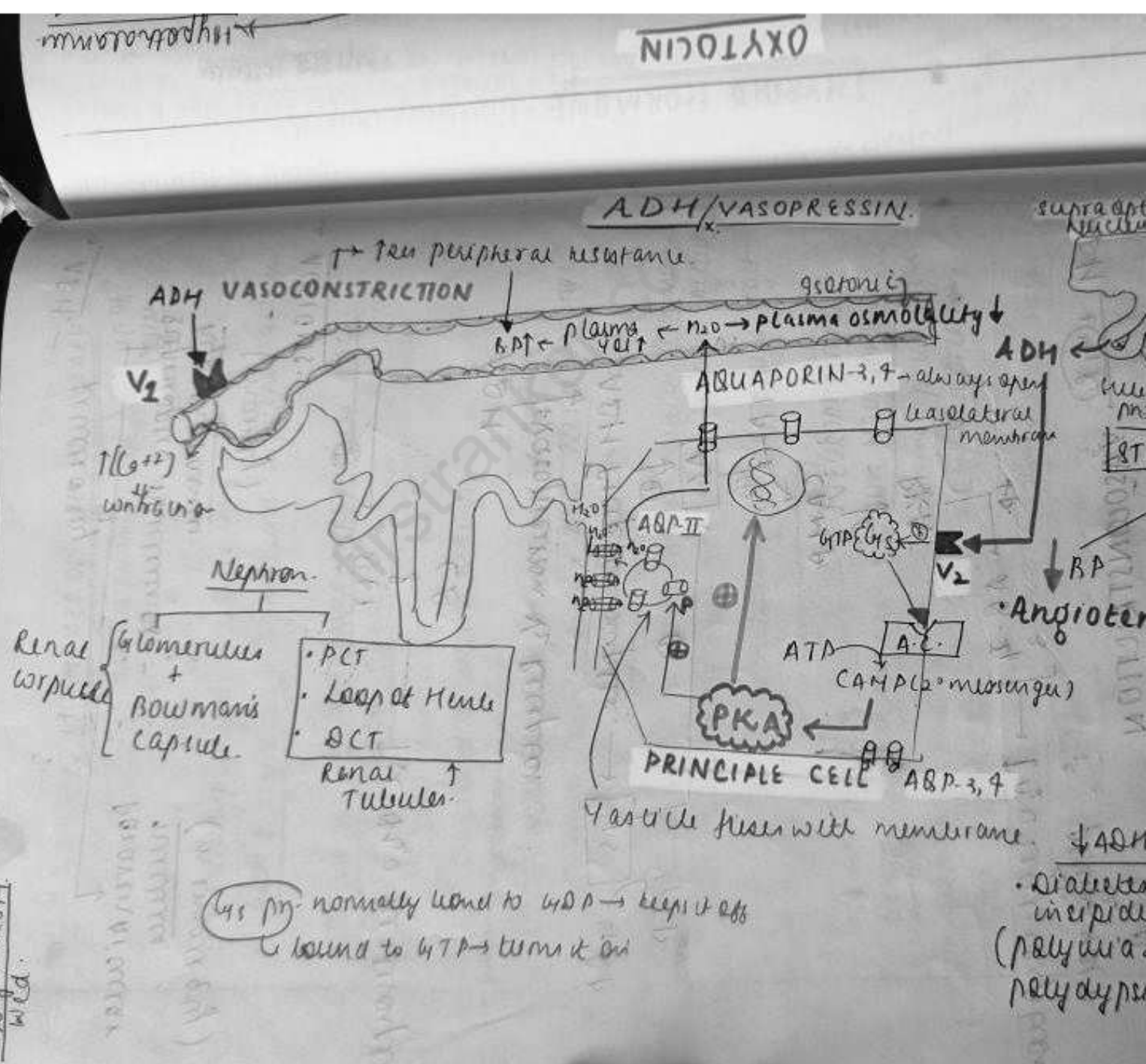


①



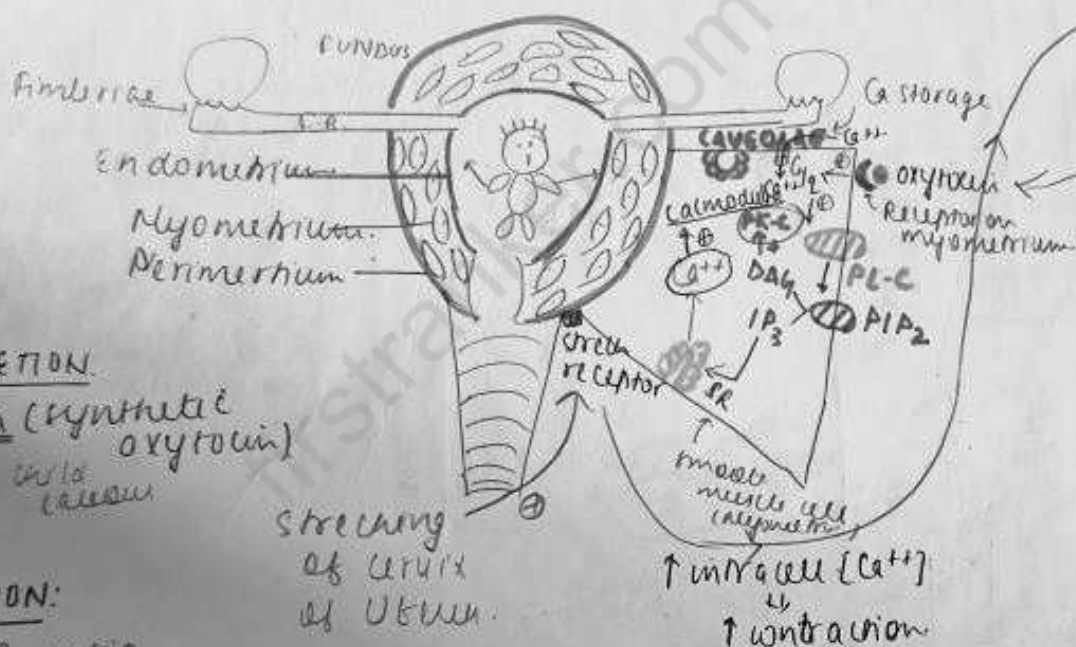
② ADH + (V₁R) → VASOCONSTRICTION





30 Jan 2019
Wed.

OXYTOCIN

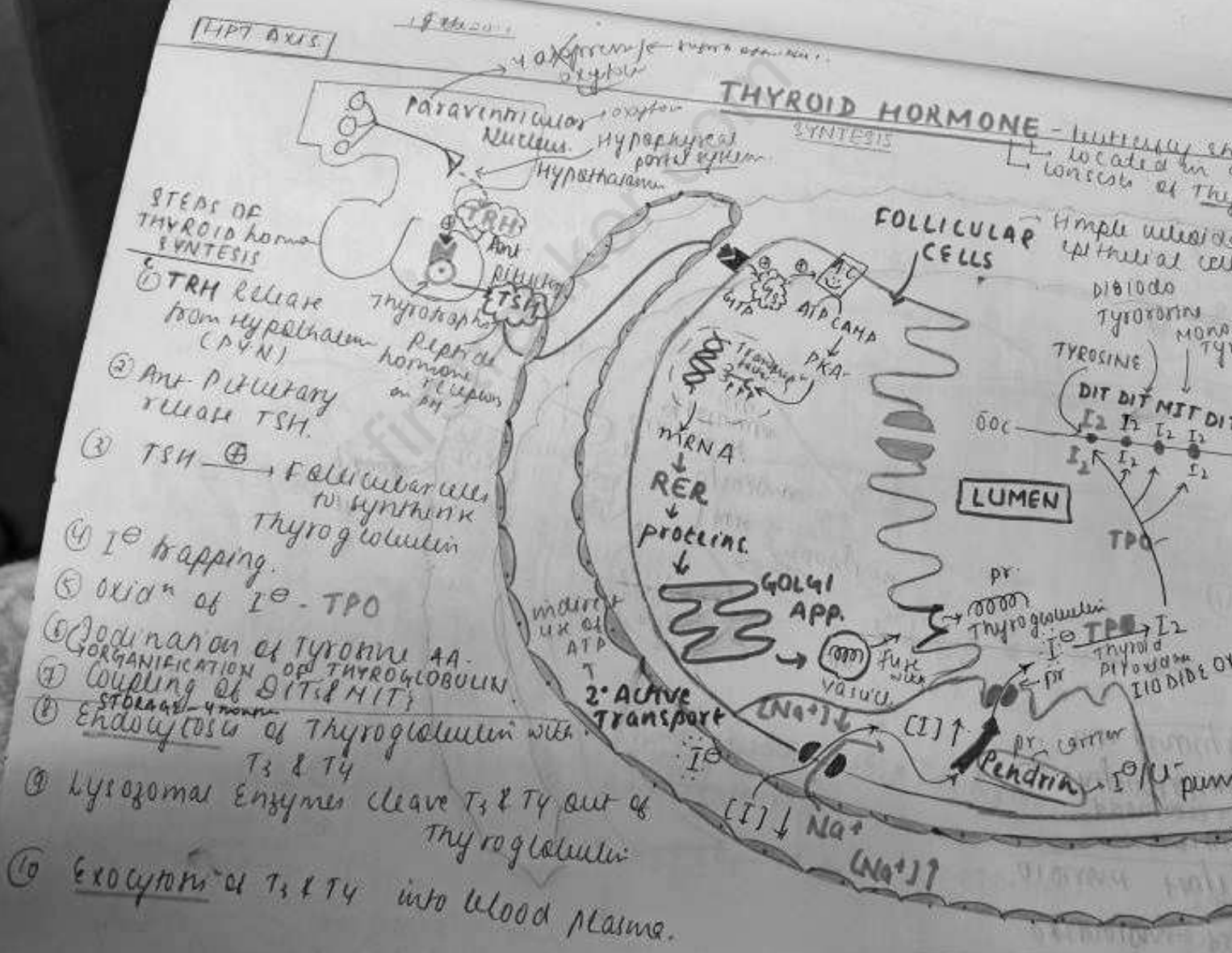


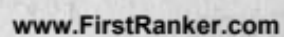
HYPERSECRETION

- **PPMS** (synthetic oxytocin) given during child labour

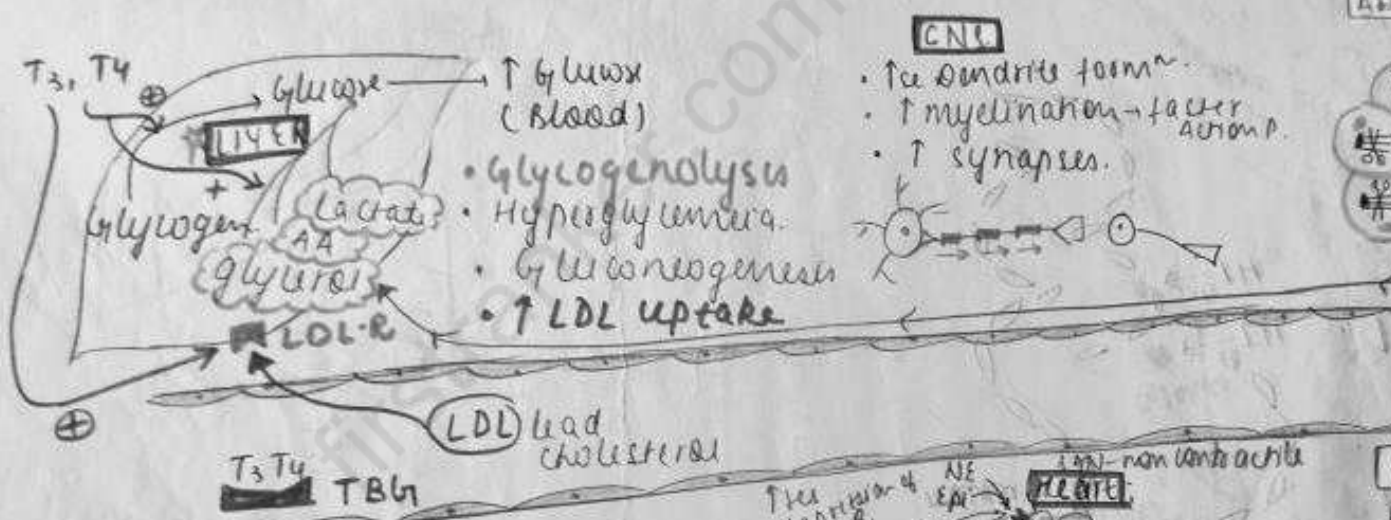
HYPOSECRETION:

- Uterine inertia
- Postpartum Haemorrhage.
- ↳ > common in ant-Pituitary.



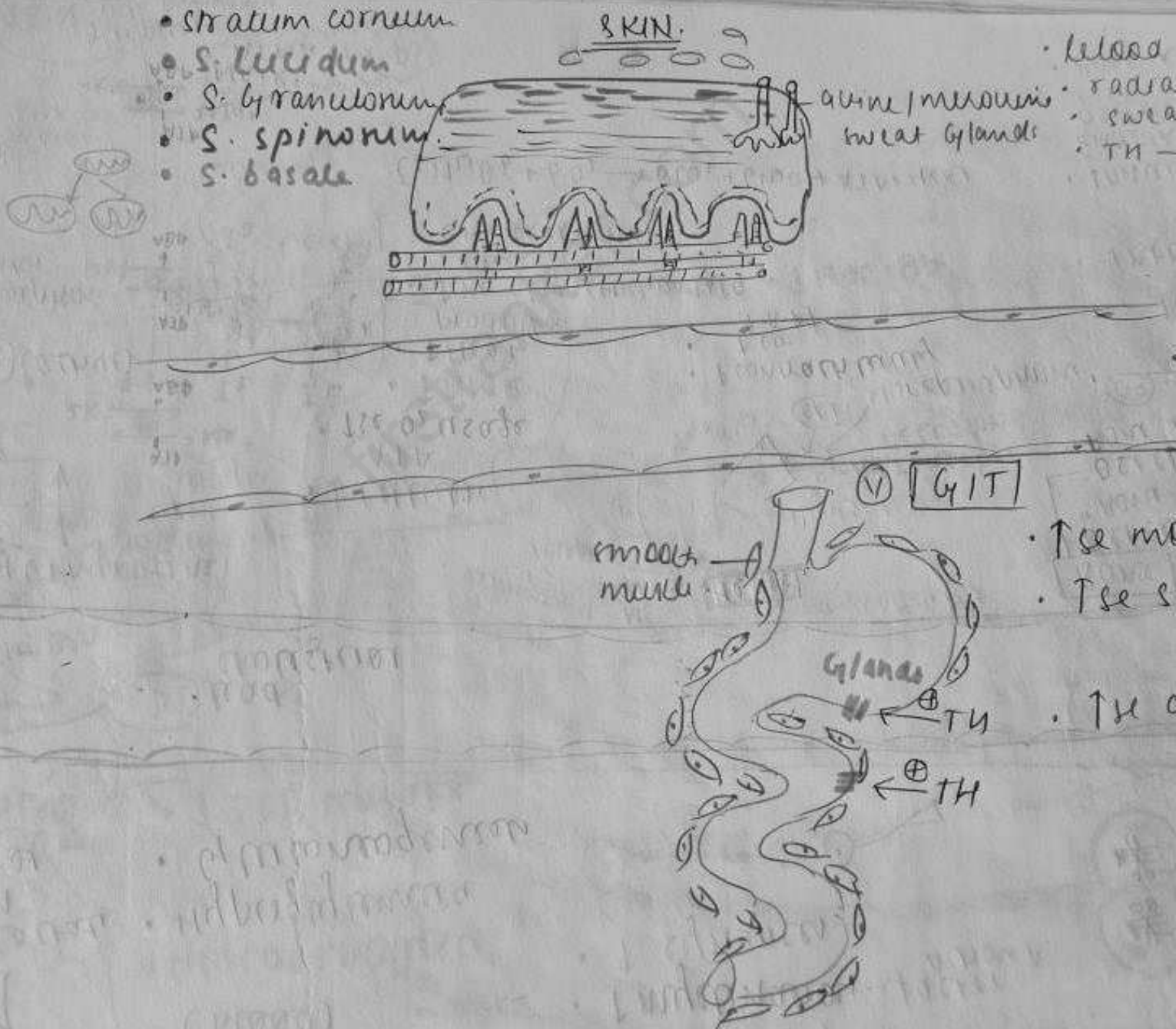


ACTION OF THYROID HORMONE



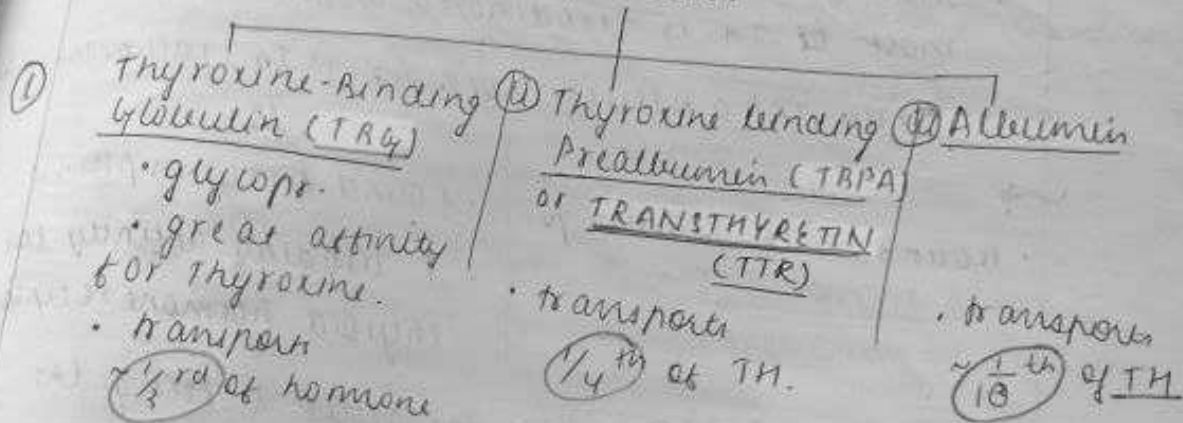
MODE OF ACTION:-



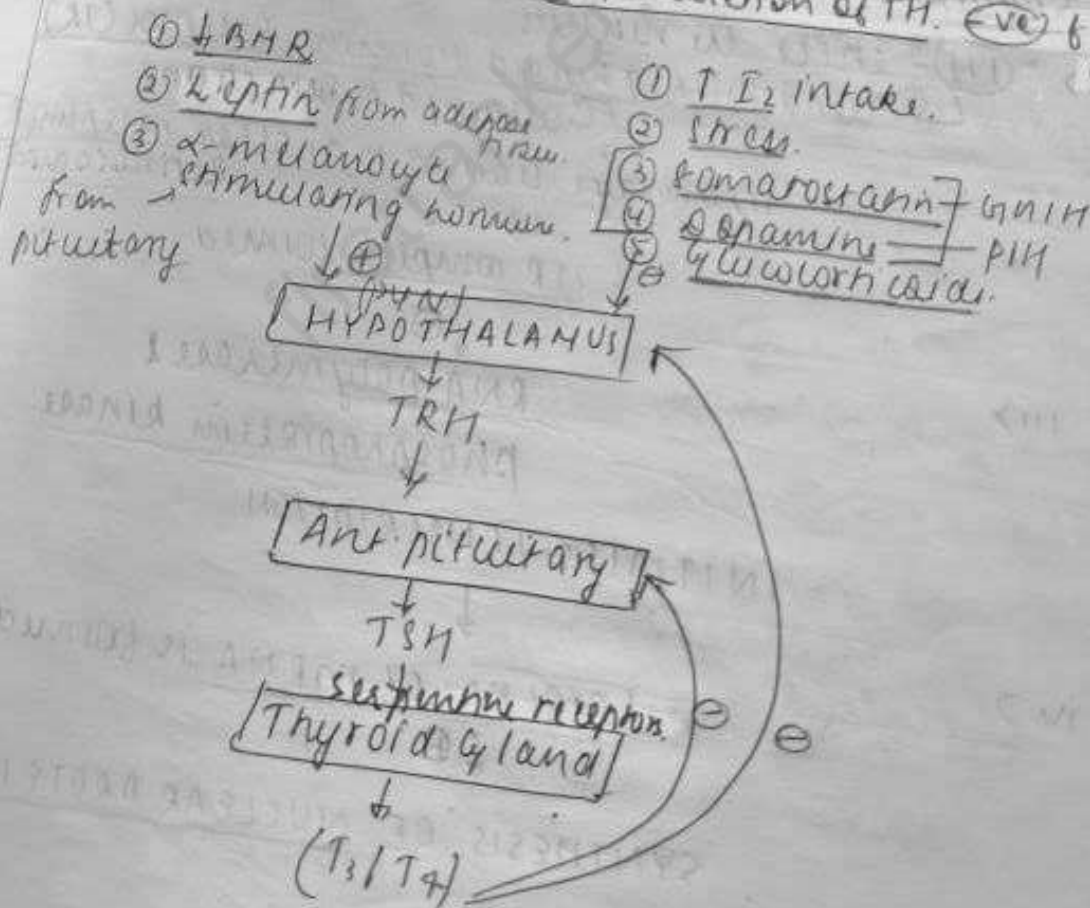


TRANSPORT OF THYROID HORMONES

by 3 types of proteins:



REGULATION OF secretion of TH. (-ve) feedback control.



22 Feb 2019

MODE OF ACTION:

• In target cells of liver, muscle & kidney, most of T_4 is deiodinated to form T_3 .

• True intracellular hormone is T_3 , rather than T_4 .

<u>T_4</u>	<u>T_3</u>
• bound with plasma p.	• found freely in plasma.
	• ↑ binding affinity for thyroid hormone receptor.

→ TH act by activating the genes & using the GENETIC TRANSCRIPTION.

Sequence of events:-

- i) T_4 - enter the nucleus
 ↳ bind with Thyroid Hormone Receptor (TR)
 { Attached to DNA strand
 ii) always bound to another receptor Retinoid RXR
 ↓
TR complex formed

↓ ⊕
RNA polymerase & phosphoprotein kinase

INITIATES TRANSCRIPTION

↓
Large no. of mRNA is formed.
 ↓ ⊕

SYNTHESIS OF NUCLEAR PROTEINS

FUNCTIONS OF THYROID HORMONES

i) ↑ BMR

ii) stimulate growth in children.

i) BMR:

- ↑ O_2 consumption of tissues
- ↑ BMR
- ↑ heat production
- CALORIGENIC ACTION

ii) PROTEIN METABOLISM:

↑ synthesis of protein

• ↑ catabolism of protein

⊗ ↑ the translation of RNA

⊗ ↑ the transcription of DNA to RNA

⊗ ↑ the Activity & NO. of mitochondria: ↑ ATP product

⊗ ↑ the Activity of cellular enzymes like

α-glyceral phosphate dehydrogenase & oxidative enzymes

iii) CARBOHYDRATE METABOLISM:

• accelerate glyconeogenesis

• ↑ glycogenolysis

• ↑ glucose absorption from GI tract

iv) FAT METABOLISM:

• Thyroxine decreases fat storage by mobilising it from adipose tissues. Mobilised fat is converted into free FA & transported by blood.

↓
↑ free FA in blood

vii) CVS: i) HR - acts directly on heart.

ii) Force of contraction:

iii) Blood vessels: ↑ metabolic rate
↓
↑ qty of metabolites produced
↓

VASODILATION

iv) Arterial B.P. - ↑ ^H ↑ Force of contraction
↓
↑ ^{L.D.} L.D.
↓
B.P. ↑

- Mean Press - unchanged
- Systolic B.P. - ↑
- Diastolic B.P. - ↓
- Pulse P. Press

~~viii)~~ CNS: - Thyroxine - essential for development & maintenance of normal functioning of CNS.

i) CNS development: Thyroxine - imp. for brain development during fetal life & in few yrs of post-natal life.

ii) On normal function of CNS:

- Thyroxine - stimulating factor for CNS, especially brain
- ↑ blood flow to brain
- Normal functioning of brain needs the mu of T₄

HYPERSensitivity of T₄ - excess stimulates CNS.
↳ excess worried

CRETINISM

→ hypothyroidism in children, - stunted growth

→ CAUSES:-

- ① Congenital - no of thyroid gland.
- ② genetic disorder.
- ③ Lack of I₂ in diet.

→ SYMPTOMS:

- ① New born baby, ^{with thyroid deficiency} appears normal at the time of birth (∵ T₃ ^{from} might have been supplied from mother).
- Few weeks after birth, baby starts developing signs
 - sluggish movement.
 - croaking sound while crying.
- Unless treated immediately, the baby will be mentally retarded permanently.
- ② skeletal growth more affected than soft tissue.
 - stunted growth + beaked body.
 - Tongue so big that hangs with dripping of saliva.
 - obstructs swallowing & breathing.

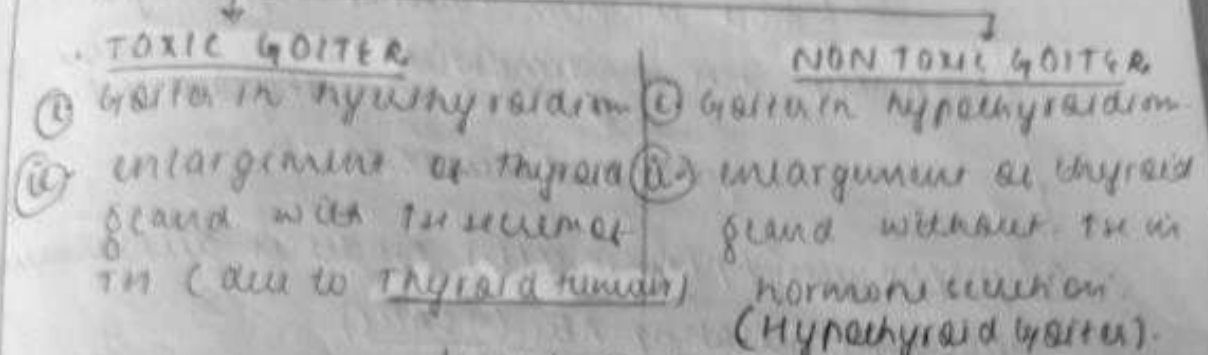
CRETIN

- ① mental retardation.
- ② body is disproportionate.
- ③ reproductive function affected.

PITUITARY DWARF

- CNS - normal.
- body parts - proportionate.
- may be normal.

GOITER - enlargement of thyroid gland.



Based on cause.

ENDEMIC COLLOID GOITER

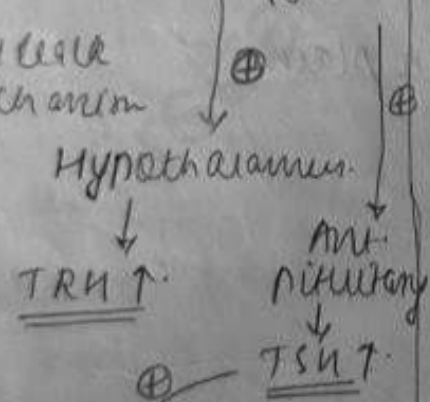
I₂ deficiency goiter

- non toxic goiter due to I₂ deficiency.

Intake < 50 µg/day

∴ lack of I₂ → no hormone form.

• By feedback mechanism



Thyroid cells secrete Thyroglobulin into thyroid follicles.

- As there is no hormone to be cleaved, Thyroglobulin remains as it is & is accumulated in follicles of gland → Inc in size of gland.

IDIOPATHIC NON TOXIC GOITER

(unknown cause)

- enlargement without I₂ deficiency

CAUSE: may be due to

- ① thyroiditis
- ② deficiency of enzymes.
ex - peroxidase, TPO, iodinase, 5-deiodinase.

Required for TH synthesis

- ③ some food stuff contains goitrogens & TH synthesis
(ex - turnip, caulage, brussels)
becomes active during ↓ I₂ intake.

HYPERTHYROIDISM.

• GRAVE'S DISEASE: autoimmune disease.

↳ most common cause of hyperthyroidism.

Normally, TSH combine with surface receptors of thyroid cells.
↓
synthesis & secret of TH.

• B lymphocytes (plasma cells) produces autoimmune Abs
Thyroid stimulating Abs (TSAs)

↳ act like TSH.
binds with membrane receptors of TSH.

↓ ⊕
CAMP system of thyroid follicular cells.
↓
hypersecretion of TH. ⊕ → TSH production.

• TSAs - last for long time upto 12 hrs.
TSH - last for an hr.

• $[TSH] \approx 0$ or ↓ in plasma.

Mon.
18 Feb 2019

ADRENAL GLAND

- life saving gland /
- essential endocrine gland.

ADRENAL CORTX

- outer portion
- 80% of gland.

ADRENAL MEDULLA

- central portion
- 20%

Zona
glomerulosa

Zona
fasciculata

Zona
reticularis

- all adrenocortical hormones are steroidal in nature.

∴ name corticosteroids.

steroidal in
cytoplasmic receptor

Mineralocorticoids

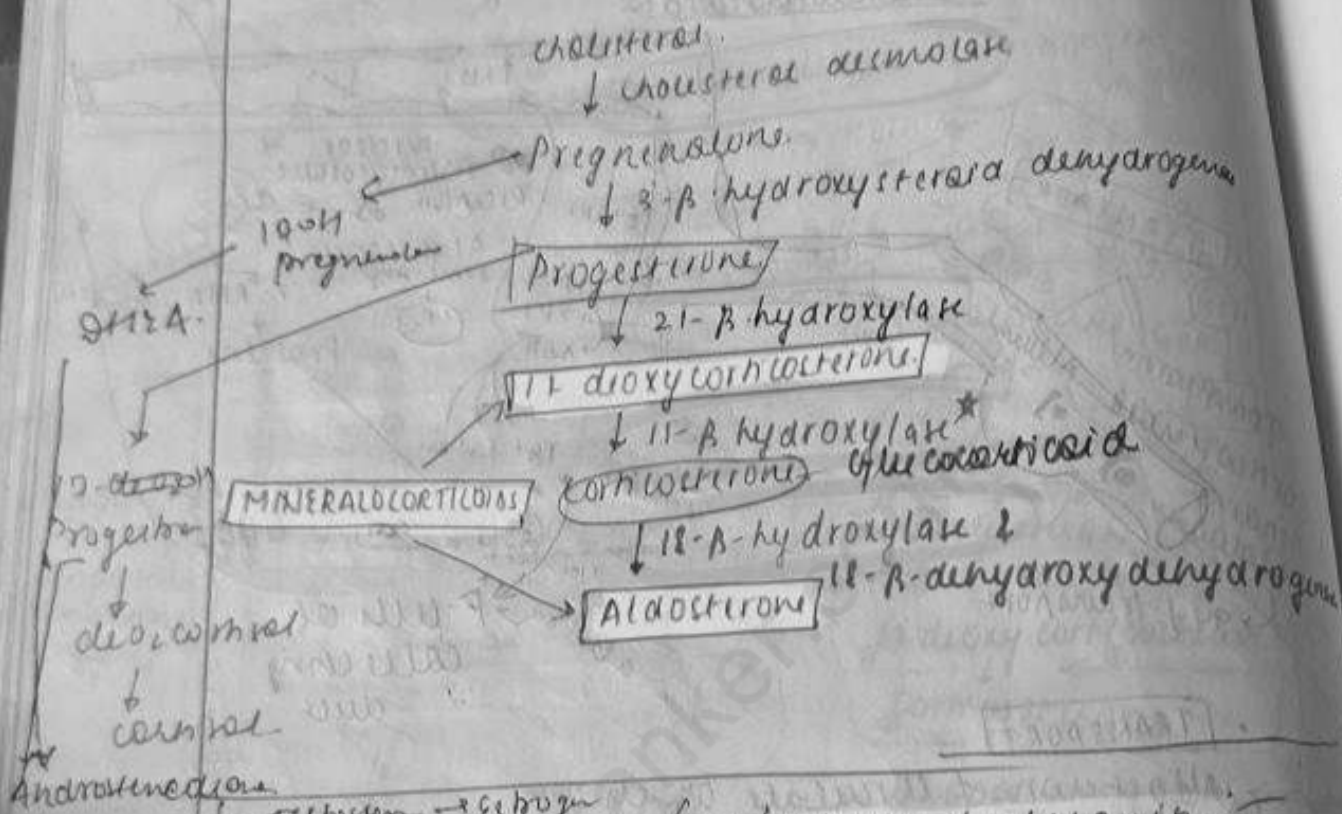
Glucocorticoids

Sex hormones

CYANIDE SLS



SYNTHESIS OF ALDOSTERONE



CONN'S SYNDROME / 1° hyperaldosteronism

Cause - prolonged excess secretion of Aldosterone from Adrenal cortex due to adenoma / tumour of 2° glomerulus

Features:

- 2° to Na⁺ absorption & its exchange with H⁺ & K⁺ in DCT
- (i) Hypertension → ↑ Na⁺ → ↑ ECFV & ↑ B.P.
- (ii) Excretion in urine → Hypokalaemia
- (iii) muscular weakness
- (iv) Metabolic alkalosis → ↓ free Ca⁺⁺ → Tetany
- v) Hypokalaemic neuropathy (renal tubular damage)
polyuria, polydipsia, ↓ conc. ability of Kidney

vi) Aldosterone escape

↓ - deficit of extracellular vol.

FUNCTIONS OF MINERALOCORTICIDS

ALDOSTERONE

↳ life saving hormone.

Ⓜd Ⓢ → death within 2 days → weeks.

① Na^+ : act on DCT & collecting duct (P cells)
Ⓜd Ⓢ → Ⓢ → ↑ Na^+ absorption.

↓
Hypernatremia

② ECF:

Na^+ absorbed from renal tubules.

↓
simultaneously H_2O is also absorbed.

↓
↑ ECF volume

[↑ Na^+ absorption ≠ ↑ $[\text{Na}^+]$
↳ H_2O absorbed simultaneously]

③ B.P.:

↑ ECF vol & ↑ blood vol.

↓
↑ B.P.

ALDOSTERONE

ESCAPE

④ K^+ :

↑ K^+ excretion through renal tubules.

↓
Hypokalemia.

⑤ H^+ :

↑ Na^+ reabsorption from renal tubules

↓ (Na^+ - H^+ antiport pump)

tubular secretion of H^+

↓
↓ $[\text{H}^+]$ in ECF

Aldosterone maintain Acid base balance.

Adaptation

↑ Hyposecretion

ALKALOSIS

↓↓ Hyposecretion

ACIDOSIS.

Conn's syndrome

- ALDOSTERONE x ESCAPE - 2^o effect of excess Mineralocorticoids
- escape of kidney from salt-retaining effects of excess administration / secretion of Aldosterone.

↑ Aldosterone level → ⊕ → ENaC

↓
↑ absorption of Na & H₂O from renal tubules

↓
↑ ECF volume

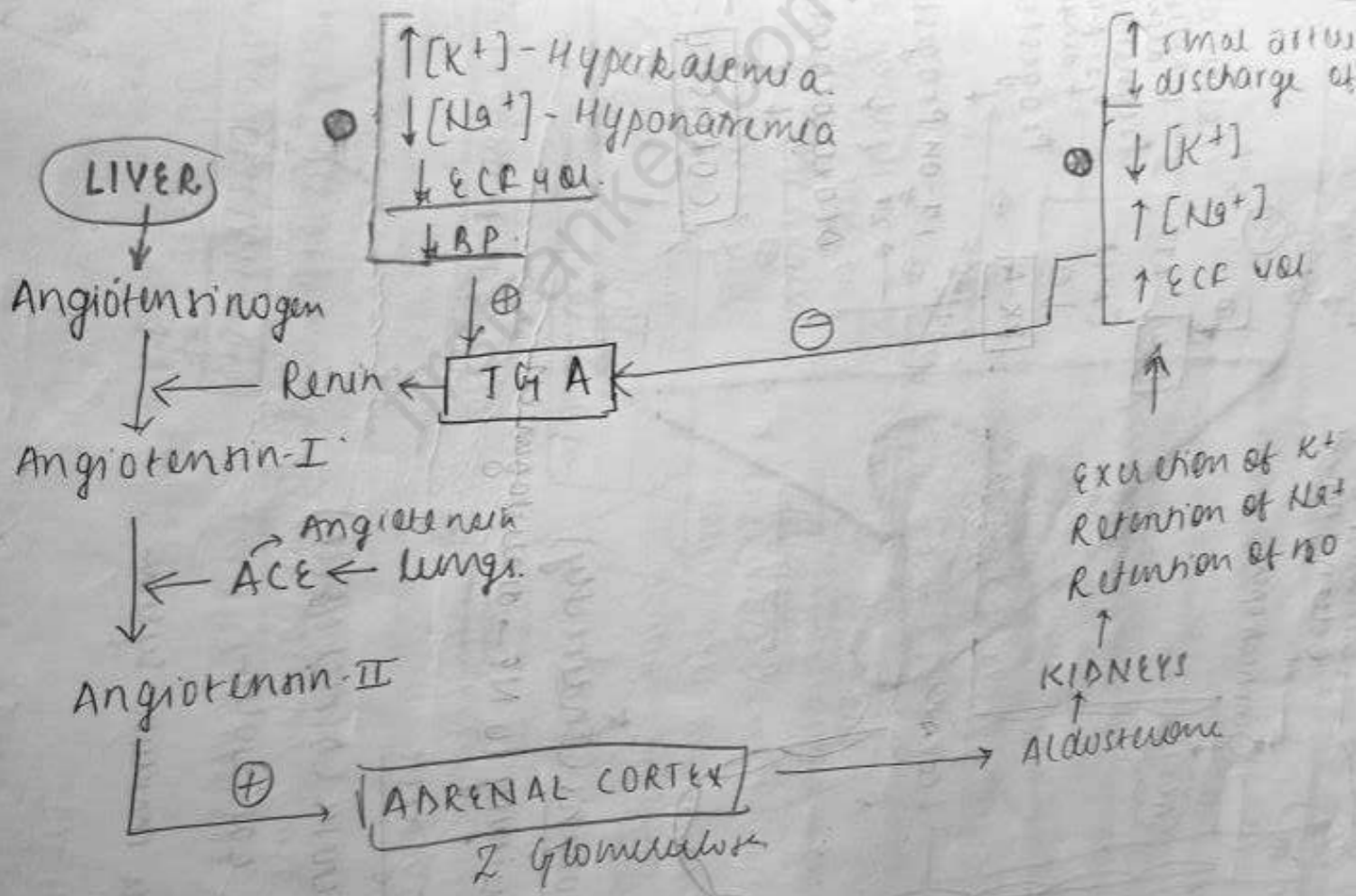
↓
↑ arterial B.P.

↓
Release of
★ ANP, BNP & CNP
(C-type natriuretic peptide) from cardiac muscles
↓
excretion of Na⁺

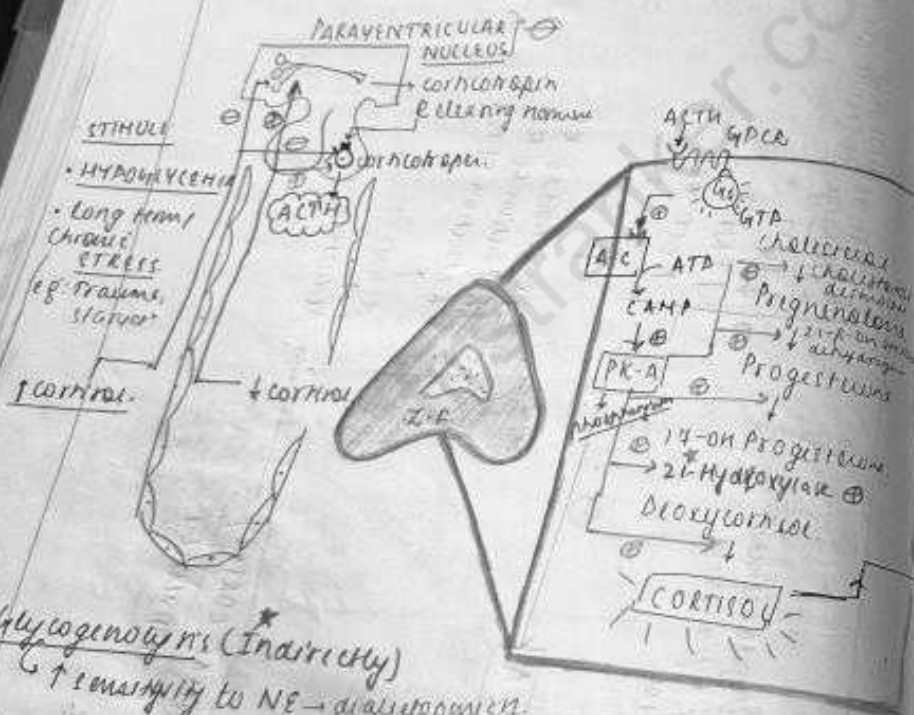
↓
Pressure diuresis

↓
⊖
excretion of Na⁺ & H₂O through urine

↓
↓ ECF volume



ZONA FASCIOLATA



- **Glycogenolysis (Indirectly)**
↑ sensitivity to NE → adrenaline
- **Gluconeogenesis**
- **Glycogenesis (Direct effect)**
- **Protein Catabolism**
↑ A.P.
depresses immune system

FUNCTIONS



14 Feb 2019 Tuesday

GLUCOCORTICOIDS

- (i) cortisol - most potent; 95% of glucocorticoid activity
- (ii) corticosterone.
- (iii) cortisone.

CORTISOL - LIFE PROTECTING HORMONE

↳ helps to withstand stress & trauma in life

FUNCTIONS OF GLUCOCORTICOIDS

(1) Carbohydrate Metabolism:

↑ blood glucose level.

- Promote GLUCONEOGENESIS in liver from AA, glycogen, lactic acid
- Glucocorticoids stimulate proteolysis in muscle.

↓
inhibit the uptake & utilisation of glucose by peripheral cells

ANTI INSULIN ACTION

(2) Protein Metabolism: promote protein catabolism by

- releasing AA from body cells (except liver) into blood.

- The uptake of AA by hepatic cells from blood.

Leads to:

- i) ↓ cellular protein
- ii) ↑ AA in plasma.
- iii) ↑ protein content in liver

③ Fat Metabolism: mobilisation and redistribution of fat.

- i) Mobilisation of FA from adipose tissue.
- ii) ↑ FA conc. in blood.
- iii) ↑ utilisation of fat for energy.

④ WATER METABOLISM: maintain H_2O balance
↳ ↑ excretion.

⑤ ↑ retention of Na^+ & excretion of K^+ $\leftrightarrow$ Aldosterone

⑥ BONES: → ↑ bone resorption - OSTEOCLASTIC ACTIVITY

• ⊖ bone formation & mineralisation - OSTEOBLASTIC ACTIVITY

⑦ RESISTANCE TO STRESS: by

i) release & transport of AA from tissues to liver.

ii) release of FA from adipose tissue.

iii) ↑ sensitivity of noradrenergic receptors to NE.

⑧ ANTI-INFLAMMATORY EFFECTS: by cortisol $\rightarrow$ $\ominus$ Response

i) ⊖ release of chemical substances from damaged tissue $\rightarrow$ prevents vasodilation.

ii) causes vasoconstriction through action of catecholamine.

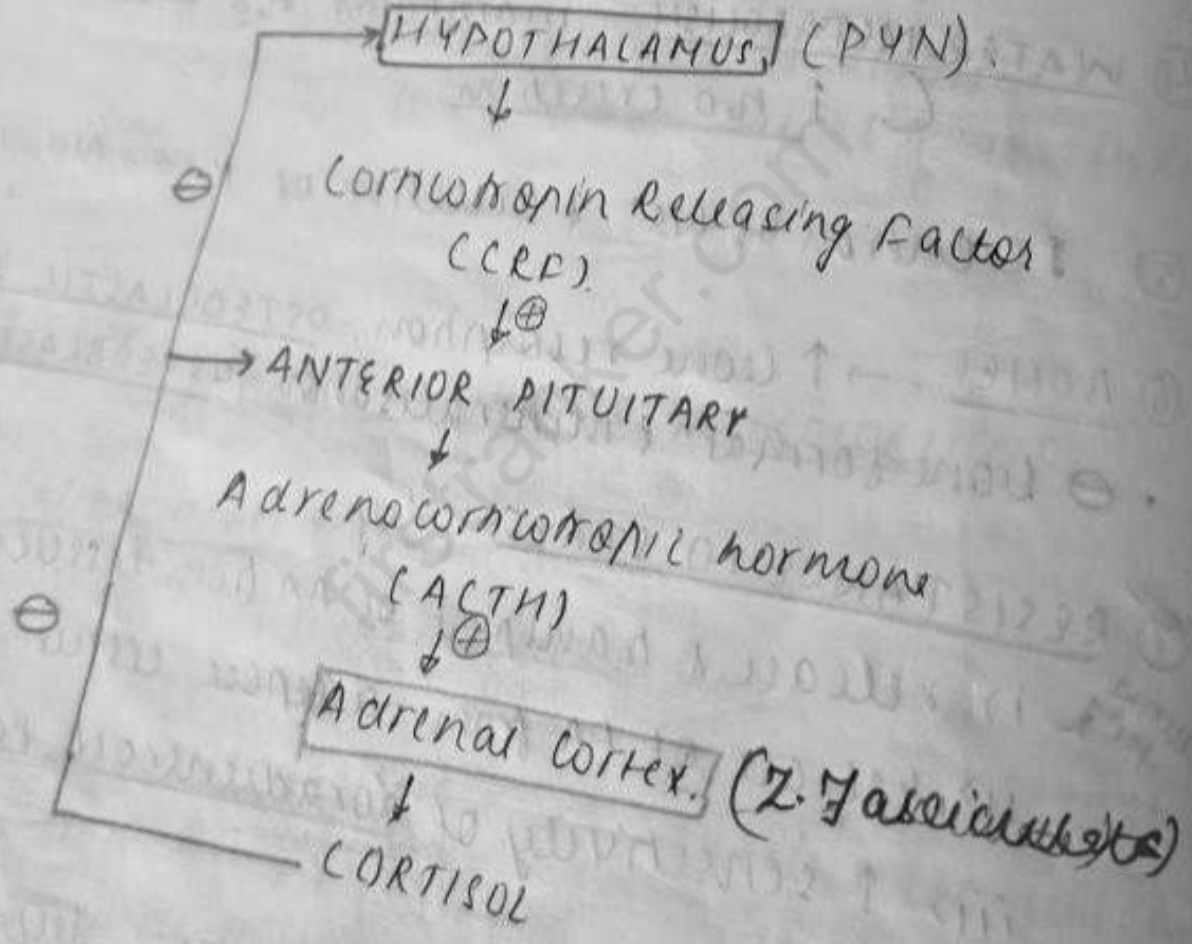
iii) ⊖ migration of leukocytes to affected areas.

⑨ IMMUNOSUPPRESSIVE EFFECT:

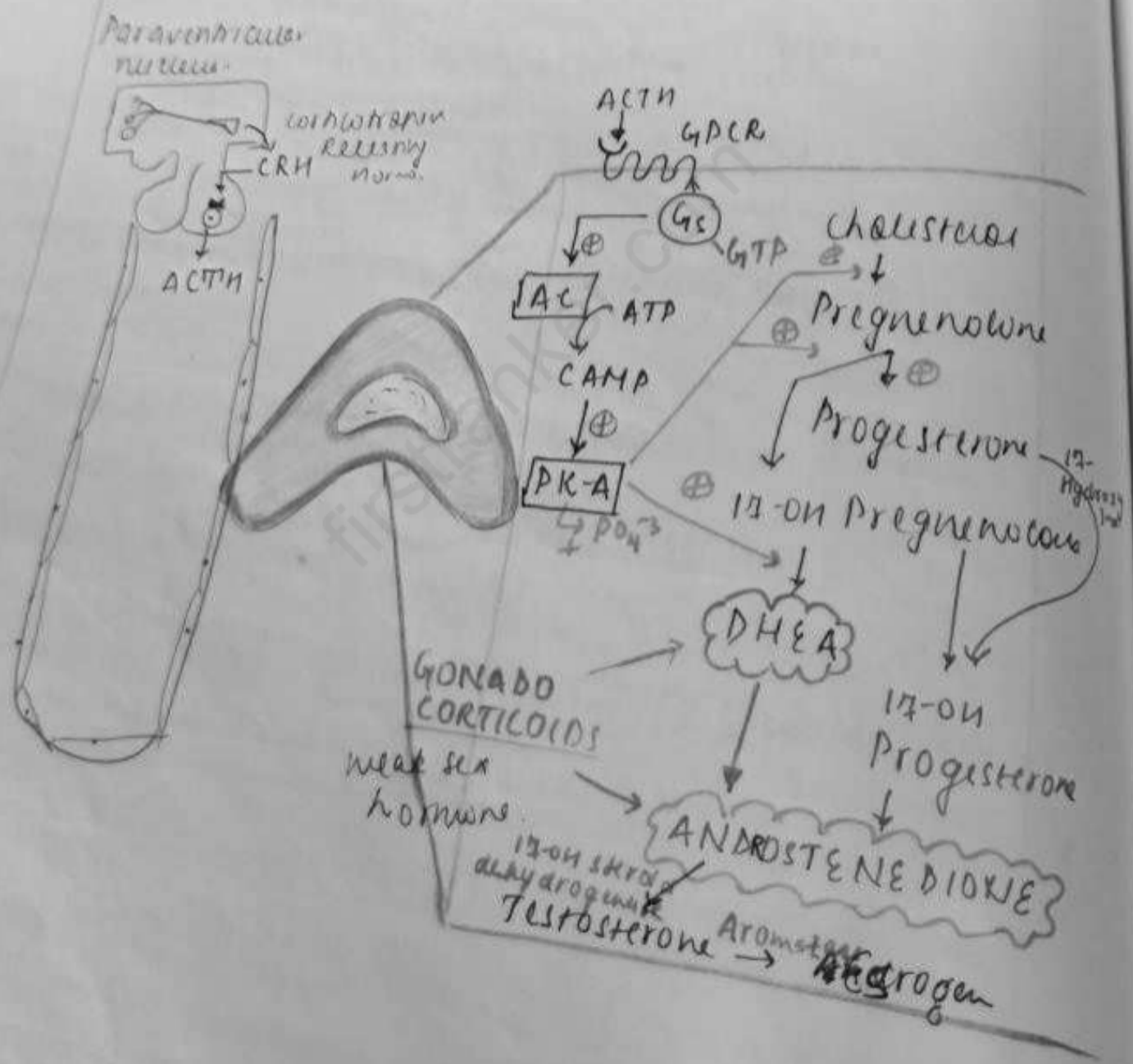
⑩ anti-allergic.

REGULATION OF CORTISOL SECRETION

Emotion, stress, trauma,
influence of circadian rhythm.
↓⊕



ZONA RETICULARIS



Dehydroepiandrosterone

Weak Androgen

FUNCTIONS of DHEA & ANDOSTERONE :-

♂

• Testosterone ↓

- helps to produce hair growth.
- pubic, axillary & facial
- sebaceous secretion.
- "LIBIDO" / sex drive.

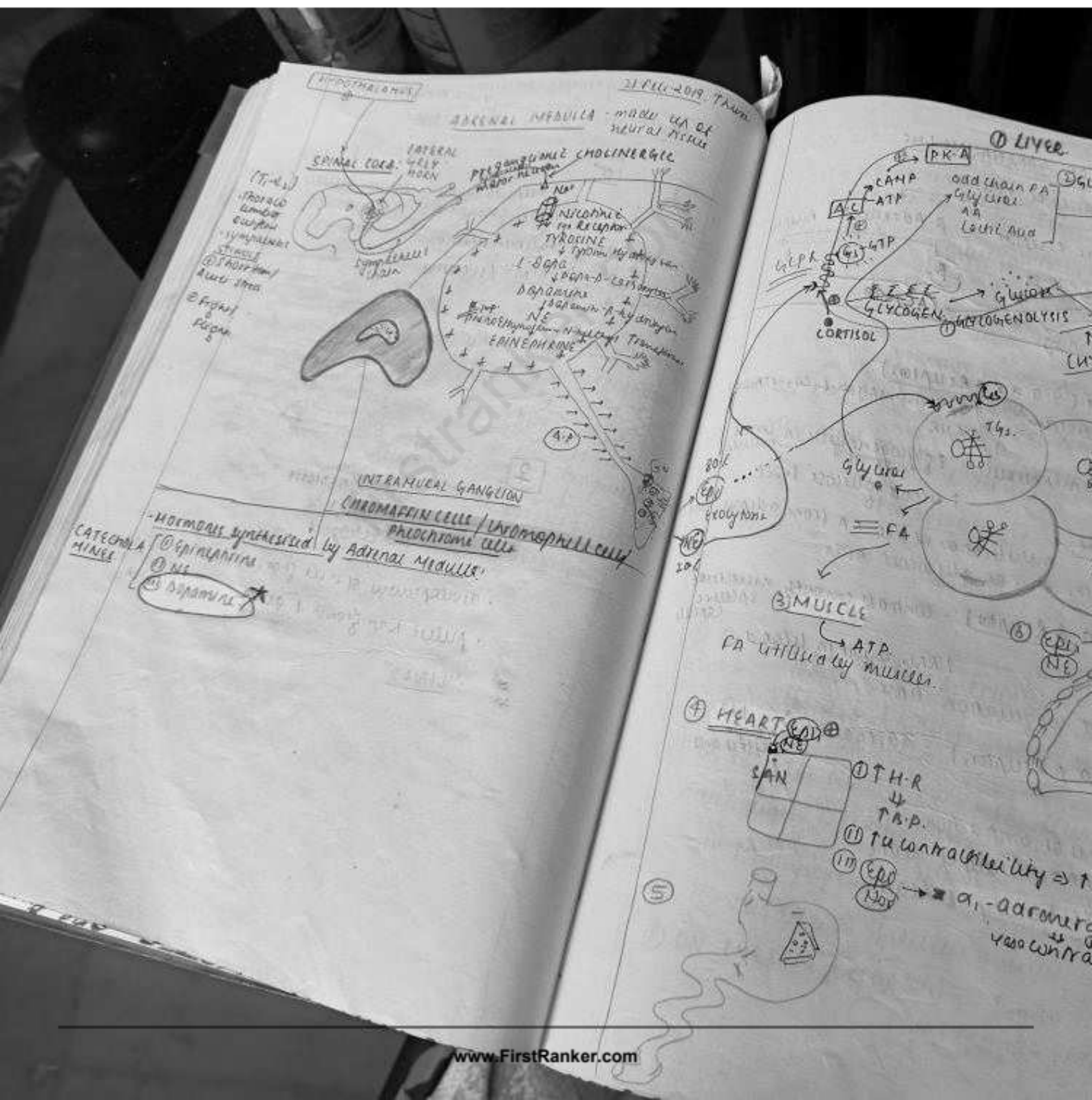
♀

ANDOSTERONE

↓
Estrogen

- development of 2^o sex characteristics i.e. breast.
- pubic hair growth & axillary hair growth.

• "LIBIDO"

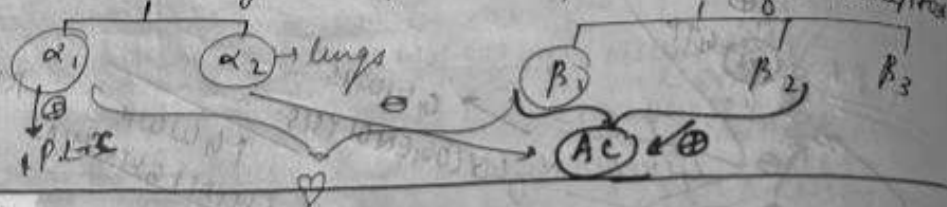


ACTION OF ADRENALINE & NE

act via 2 classes of receptors

α -Adrenergic receptors

β -Adrenergic Receptors



ACTION:

① ON METABOLISM (via α & β Receptors):-

i) General metabolism:- $\uparrow$ O_2 consumption & CO_2 removal
 $\uparrow$ HR

ii) Carbohydrate metabolism: $\uparrow$ glycogenolysis in liver & muscle
 $\downarrow$
 $\uparrow$ blood glucose level

iii) FAT METABOLISM:

mobilisation of free FA from adipose tissue
needs the mu of glucocorticoids.

② ON BLOOD (via β Receptor):- contract smooth muscles of spleen & capsule $\downarrow$ $\uparrow$ RA in blood $\downarrow$ $\uparrow$ blood coagulation time.

③ ON HEART (via β Receptors):- Adrenaline & NE strengthen effect on

- ① $\uparrow$ HR
- ② $\uparrow$ force of contraction
- ③ $\uparrow$ conductivity of heart
- ④ $\uparrow$ excitability of heart

Adrenergic Receptors
 β_1 β_2

CO_2 removed

in liver & muscle level

adipose tissue

muscles of placenta capsule

① ON BLOOD VESSELS (via α & β_2 Receptors)

needs the release of glucose from liver & muscle
 • NE - vasoconstriction of blood vessels throughout the body via α receptors $\Rightarrow$ $\uparrow$ total peripheral resistance
 • Adrenaline -
 - constriction of blood vessels through α_1 receptors
 - dilation of blood vessels in skeletal muscle, liver, heart through β_2 receptors

$\downarrow$
total peripheral resistance $\downarrow$

② ON B.P (via α & β Receptors): needs the release of GLUCOCORTICOID

Adrenaline - $\uparrow$ force of contraction & $\uparrow$ C.O. $\downarrow$ total peripheral resistance

$\uparrow$ SYSTOLIC B.P.

$\downarrow$ DIASTOLIC B.P.

NE -

General vasoconstrictor

$\downarrow$
 $\uparrow$ total peripheral resistance

$\downarrow$
 $\uparrow$ DIASTOLIC B.P.

③ ON RESPIRATION (via β_2 Receptors):

• $\uparrow$ rate & force of respiration.
 • BRONCHODILATION

④ ON SKELETAL MUSCLES (via α & β_2 Receptors):

Adrenaline - $\uparrow$ severe contraction & quick fatigue of skeletal muscles

ii) $\uparrow$ glycogenolysis & release of glucose from muscle

iii) vasodilation in skeletal muscles.

⑤ ON CNS (via β Receptors): - $\uparrow$ activity of brain.
 (fight/flight reaction)

HYPERSECRETION

PHEOCHROMOCYTOMA

phaeochromocytoma
Cushing's syndrome

• hypersecretion of catecholamines

Cause:

- i) tumour of chromophil cells of Adrenal medulla
- ii) caused rarely by tumour of sympathetic ganglia

SYMPTOMS: HYPERTENSION - endocrine / 2° hypertension

- ① Flushing
- ② Tachycardia
- ③ Polyuria & glycosuria
- ④ Sweating
- ⑤ Chest pain
- ⑥ Palpitation
- ⑦ Hypoglycemia

ADRENERGIC RECEPTORS

Mode of Action

Response

1. α_1 Receptor

① IP_3 through PL-C
② A.C & CAMP

mediates NorAdrenaline & Adrenaline action

2. α_2 Receptor

① A.C & CAMP

Mediates Adrenaline = NE

3. β_1 Receptor

① A.C & CAMP

Adrenaline = NE

4. β_2 Receptor

① A.C & CAMP

22 Feb 2019 Friday

CUSHING SYNDROME

particularity cortisol ^{obesity} hypersecretion of glucocorticoids

• May be due to

• Pituitary origin

• CUSHING'S DISEASE

• ↑ ACTH secretion

↓
hyperplasia of Adrenal cortex

↓
↑ secretion of glucocorticoids

• ACTH secretion ↑ due to

✓ Tumour in pituitary cells
i.e. basophilic cells which
secrete ACTH

ii) Malignant tumour of non
endocrine origin like
cancer of lungs & abdominal viscera

iii) Hypothalamic disorder
↑ secretion of CRH

ACTH
independent

• Adrenal origin

• CUSHING'S SYNDROME

Cortisol secretion is ↑ due to

i) Tumours in zona fasciculata
of Adrenal cortex

ii) Carcinoma of Adrenal with
visceral

iii) Prolonged treatment of
chronic anti-inflammatory
diseases like Rheumatoid
arthritis with ↑ dose of corticosteroids

• CUSHING'S SYNDROME (Remedy)

ACTH dependent C.S.

• hypersecretion of ACTH

ACTH Independent C.S.

• secretion of ACTH normal

• due to abnormal membrane
Receptors for some peptides like
IL-1, Gonadotropin Releasing
Hormone & VIP in cells of
Zona fasciculata

• The binding of these peptides

SYMPTOMS:

① disproportionate distribution of body fat.
② Moan face: edematous facial appearance.

fat accumulation & retention of water.

③ Buffalo hump: fat deposit on neck & shoulder.

④ Pot belly: fat accumulation in upper abdomen.

⑤ Purple striae: reddish purple stripes on abdomen due to stretching of abdominal wall due to excess subcutaneous fat.

⑥ Thinning of extremities: rupture of subdermal tissue due to stretching.

⑦ Protein depletion: protein depletion.

⑧ Thinning of skin & subcutaneous tissues: thinning of skin & subcutaneous tissues.

⑨ Weakening of muscles (pr. depletion): weakening of muscles (pr. depletion).

⑩ Bone resorption / osteoporosis (pr. depletion): bone resorption / osteoporosis (pr. depletion).

⑪ Hyperglycemia: hyperglycemia.

⑫ Immunosuppression: immunosuppression.

⑬ Poor wound healing: poor wound healing.

hyposecretion

ADDISON'S DISEASE / CHRONIC ADRENAL INSUFFICIENCY

→ failure of adrenal cortex to secrete corticosteroids

Types:

- ① 1° A.D.
adrenal cause . failure of adrenal cortex to secrete ACTH.
- ② 2° A.D.
pituitary to secrete ACTH.
- ③ 3° A.D.
failure of (Pituitary) hypothalamus to secrete CRH.

CAUSES:

- ① Atrophy of adrenal cortex due to autoimmune disease
- ② Destruction of gland (Tuberculosis)
- iii) Destruction of hormone secreting cells in Adrenal cortex by malignant tissue.
- iv) Congenital failure to secrete cortisol

→ SYMPTOMS: deficiency of CORTISOL & ALDOSTERONE

- i) Pigmentation of skin & mucous membrane due to excess ACTH secretion, induced by cortisol deficiency.
→ pigmentation by melanocyte stimulating agent (MSH)
- ii) Muscular weakness.

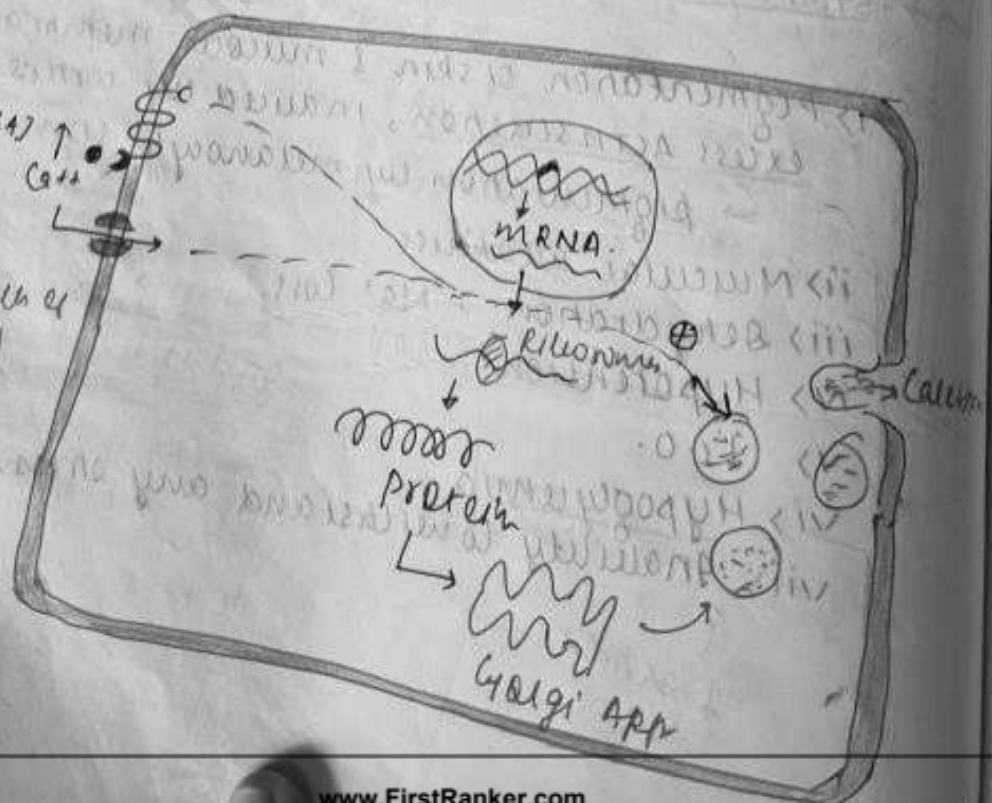
PARATHYROID GLAND

24 Feb 2019
on par. aspect of thyroid glands

★ Ex. of HUMORAL STIMULI



(HYPERCALCAEMIA) ↑ Ca⁺⁺
Calcitonin (parafollicular cells of thyroid glands) → C-cells



PARATHYROID HORMONE - linear polypeptide
 - MW - 9500
 - 84 AA. residue.

CHEMISTRY:

SYNTHESIS:

synthesized as

Prepro PTH (115 AA)
 ↓
 ER

leader sequence removed from N₂ terminal

P10 PTH (90 AA)
 40 41 42

PTH (84 AA) - packaged in secretory granules.

MECHANISM OF ACTION:-

PTH receptors - 3 types.

PTHrP

PTHrP 1 / hPTH

PTHrP Receptor

also binds to PTH related protein

PTHrP produced by active tumour at local

PTHrP 2 / (hPTH 2-R)

Receptor

• ≠ bind to PTH related pr.

• not in brain, placenta, parathyroid.

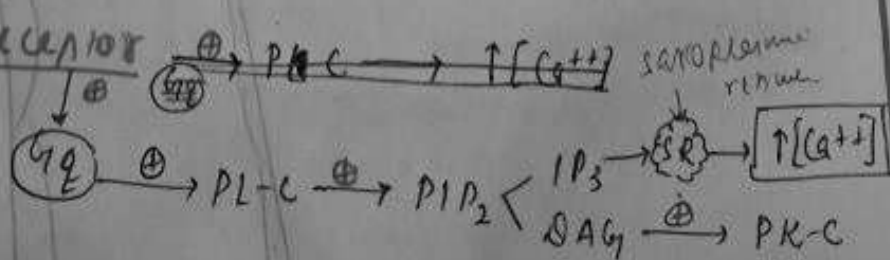
PTHrP 3

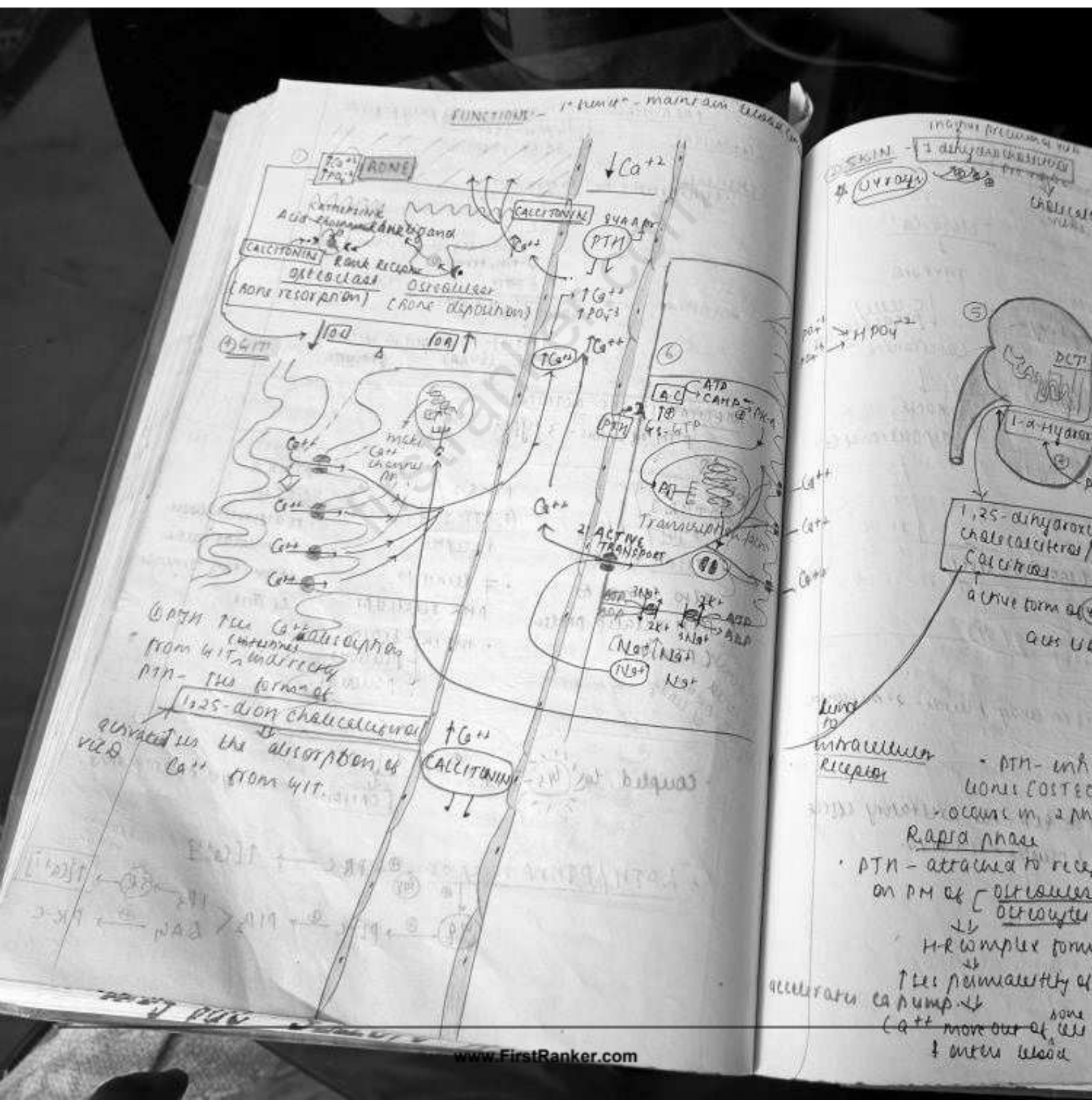
PTHrP

• reach with C-terminus rather than N₂ terminus of PTH

• coupled to G_{12} - GTP → $A-C$ → ATP → $PK-A$ → $CAMP$ 2nd messenger of hormone.

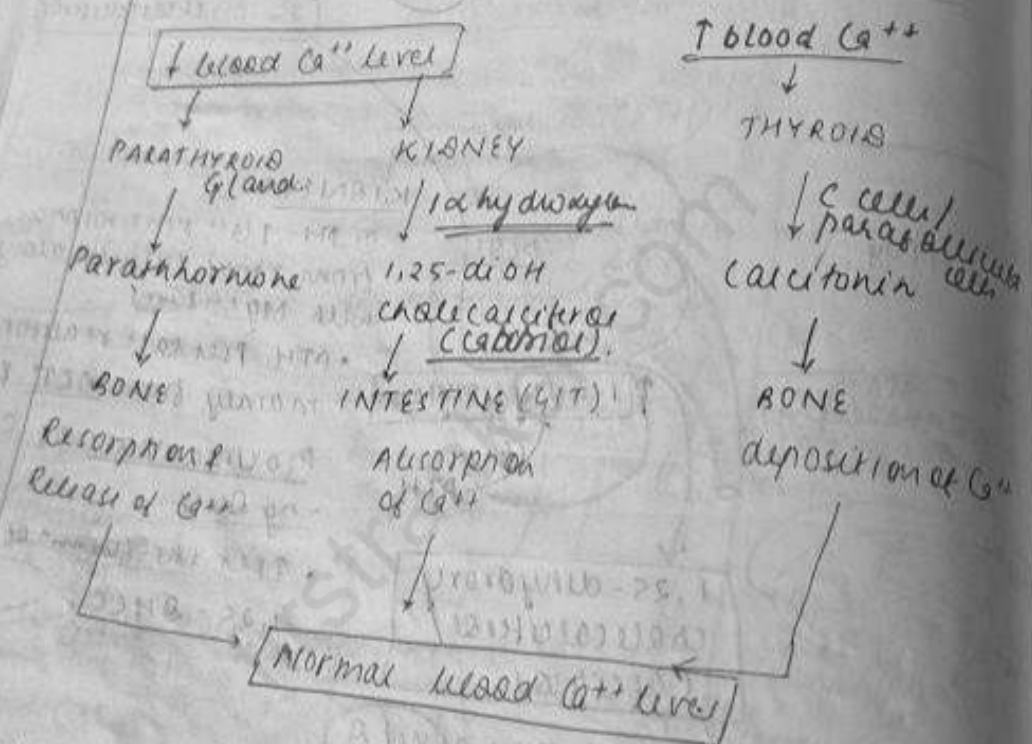
hPTH / PTHrP receptor





26 Feb 2019

REGULATION OF BLOOD Ca^{++} LEVEL

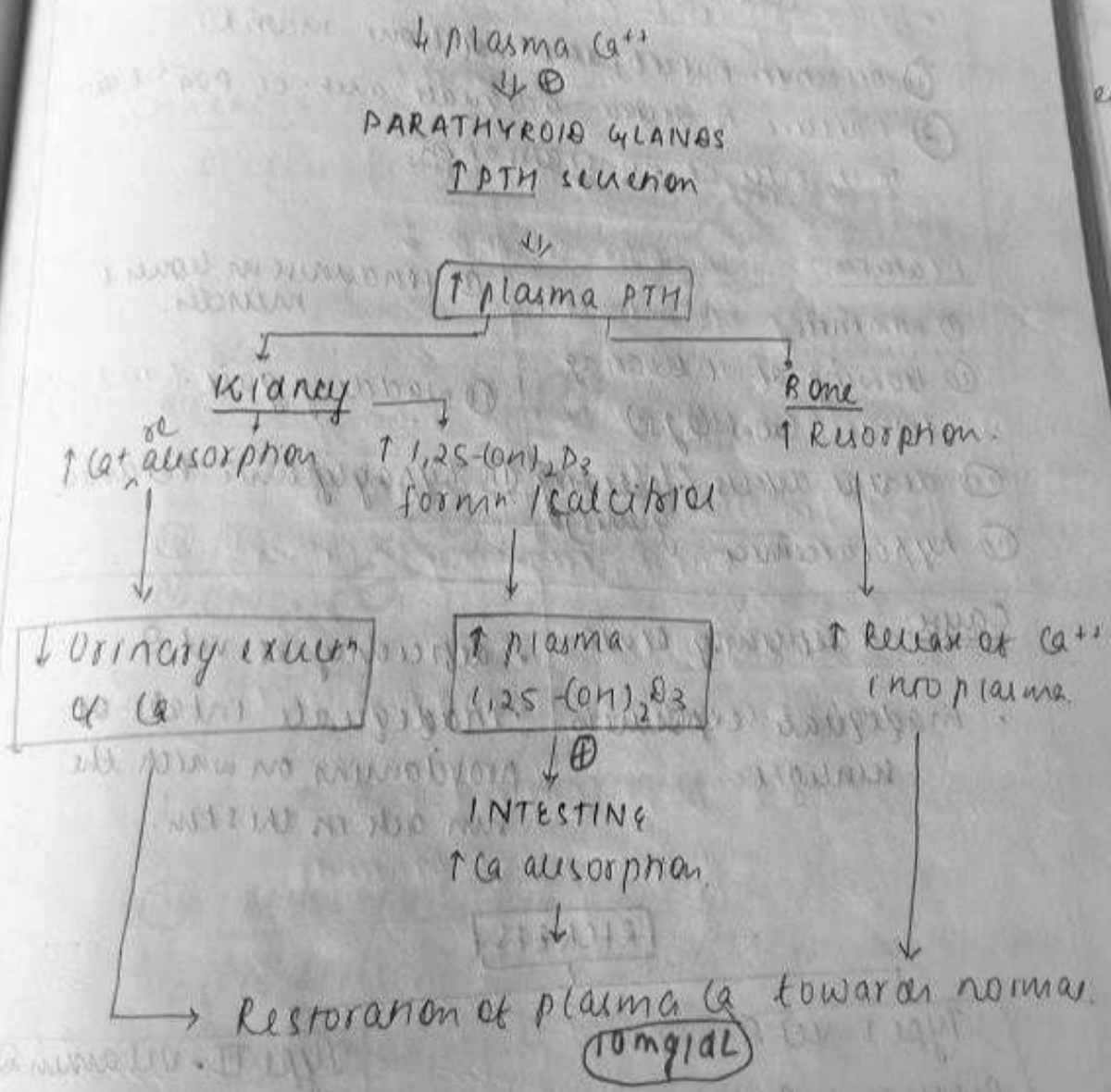


* Normal plasma $Ca^{++} \sim 10 \text{ mg/dl}$

FUNCTIONS of Ca^{++} :

- (i) Free, ionized form (Ca^{++}) in body fluids - 20 mEq/L
- (ii) Blood coagulation.
- (iii) Muscle contraction.
- (iv) Nerve function: $[Ca^{++}]$ in ECF - net excitatory effect on nerve & muscle - in vivo.

REGULATION OF WHOLE BODY ~~BODY~~ Ca^{++} HOMEOSTASIS



Vit D deficiency 2017
RICKETS (child) OSTEOMALACIA (adult)

- ① defective calcification of bone matrix.
- ② Failure to derive adequate amt. of PO_4^{3-} from the sites of mineralisation.

Features:

- | | |
|---|---|
| <ul style="list-style-type: none"> ① weakness. ② bowing of wt. bearing bones (bow legs) ③ dental defects (bleeding gums) ④ hypocalcaemia. | <ul style="list-style-type: none"> ① tenderness in lower muscles. ② waddling gait (duck walk) ③ hypoglycaemic tetany |
|---|---|

Cause:

- | | |
|---|---|
| <ul style="list-style-type: none"> • deficiency of vit D • inadequate exposure to sunlight. | <ul style="list-style-type: none"> • deficiency of vit D • inadequate intake of provitamins on which the sun act in the skin. |
|---|---|

RICKETS

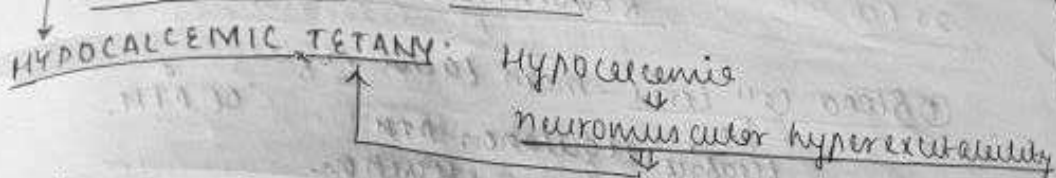
Type I vit D-Resistant Rickets

- inactivating mutations of the gene for renal 1 α -hydroxylase severe renal / liver diseases in which there is no response to vit D.
- normal response to 1,25-dihydroxycholecalciferol (Calcitriol).

Type II-vitamin D Resistant Rickets

- inactivating mutations of the gene for 1,25-dihydroxycholecalciferol Receptor.
- deficient response to both vit D & 1,25-dihydroxycholecalciferol (Calcitriol).

EFFECT OF PARATHYROIDECTOMY:
OSTEOMALACIA: TETANY



CHARACTERISTICS:

- ① extensive spasm of skeletal muscles.
→ involuntary muscle contract.
especially muscles of hand & feet & larynx.
- ② Laryngospasm can become so severe that airway is obstructed & ASPHYXIA is produced.
- ③ Ca^{++} - imp. role in blood clotting.
Fatal tetany occurs before compromising clotting rxn.
- ④ plasma $PO_4^{3-} \uparrow$; plasma $Ca^{++} \downarrow$
- ⑤ CHVOSTEK'S SIGN: quick contraction of facial muscles caused a gentle tap over facial nerve at the L of jaw.
• due to hyperirritability of facial Nv.
- ⑥ TROUSSEAU'S SIGN: spasm of hand after 3 min after arresting blood flow to lower arm & hand.
• flexion of wrist & thumb
• extension of fingers
• Blood flow to lower arm & hand is arrested by inflating the A.P. cuff 20 mmHg above patient's systolic P.

29 Feb 2019

REGULATION OF PTH SECRETION

① Blood Ca^{++} level - main factor regulating the secretion of PTH.
↓
feedback regulation of PTH secretion.

• $[Ca^{++}] \text{ level} \rightarrow \downarrow \text{ secretion}$

• Condⁿ when PTH secretion ↓ :-

- i) ↑ qty. of Ca in diet
- ii) ↑ vit. D in diet
- iii) ↑ reabsorption of Ca from kidney by some kidney diseases

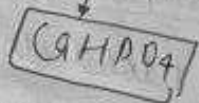
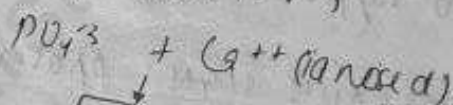
$[\downarrow Ca^{++}] \text{ in blood} \rightarrow \uparrow \text{ PTH secretion}$

↳ Rickets, pregnancy, lactation.

② Blood level of PO_4^{3-} :-

• PTH secretion & blood PO_4^{3-} level

when, blood PO_4^{3-} level is ↑,



∴ ionised Ca^{++} level in blood is ↓.
↓
PTH secretion.

③ 1,25-dihydroxycholecalciferol: acts on PT gland.
↓
↑ Ca^{++} → ↓ preproPTH mRNA

④ Magnesium: maintain normal parathyroid secretory response.

28 FEB 2019

PANCREAS - Endocrine gland

Endocrine Exocrine

Cells: β cells

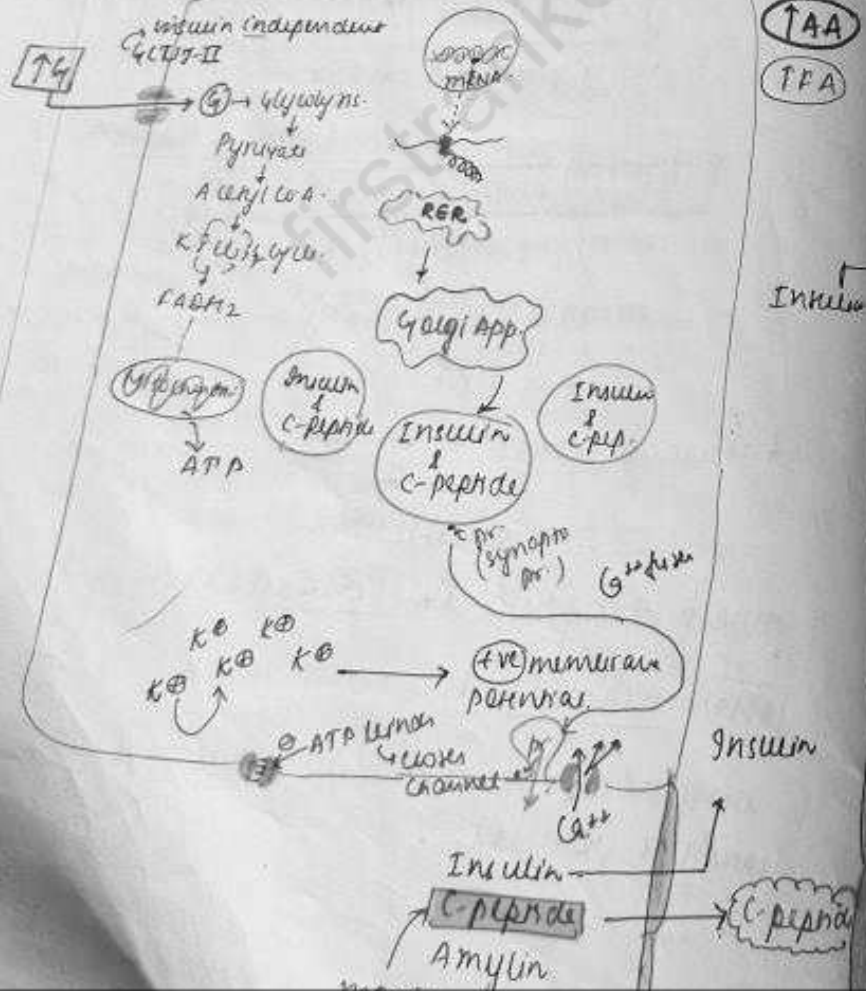
Glycogen Insulin

HYPOGLYCEMIA HYPERGLYCEMIA

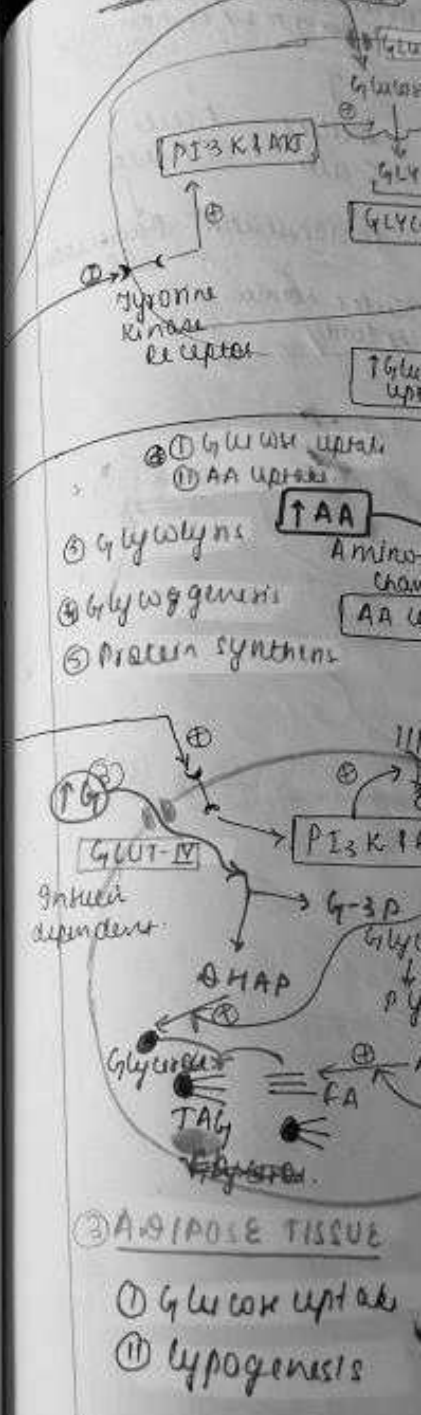
Avg blood gluc = 80-120 mg/dl

ISLET OF LANGERHANS

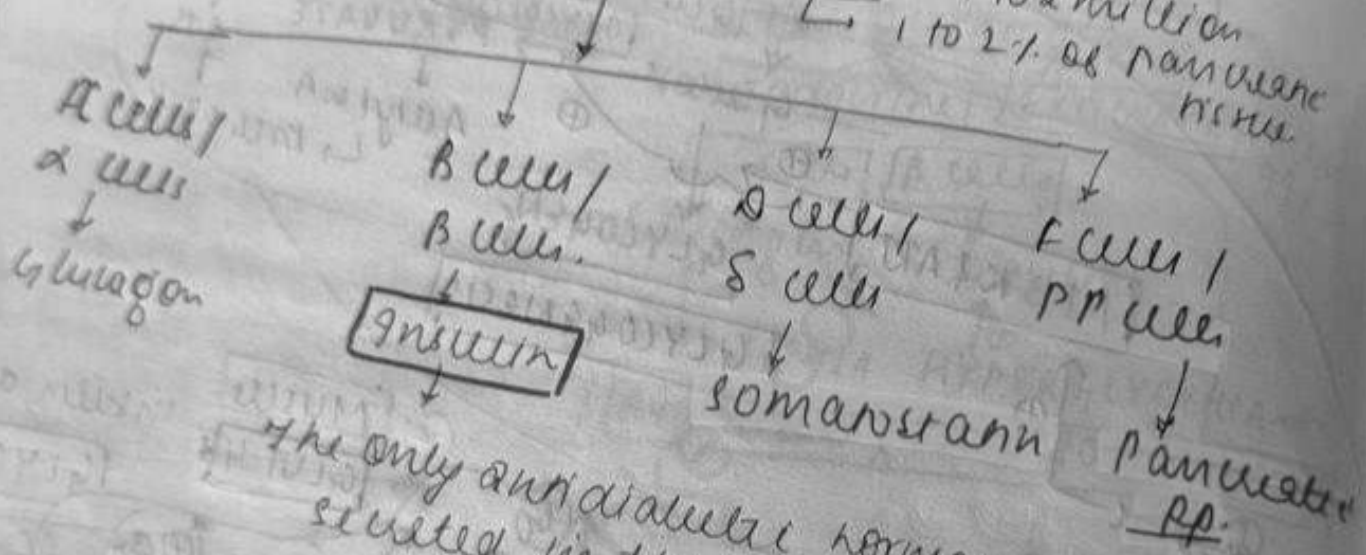
β CELL



FUNCTIONS of Insulin



ISLETS OF LANGERHANS - 1 to 2 million
1 to 2% of pancreatic tissue.

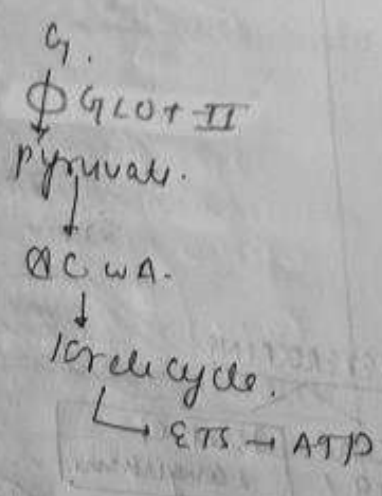


The only antidiabetic hormone
secreted in the body.

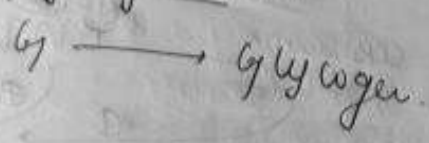
FUNCTIONS OF INSULIN:-

① Liver:-

① Glycolysis



② Glycogenesis

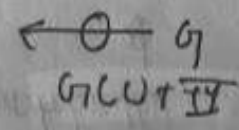


② Muscle

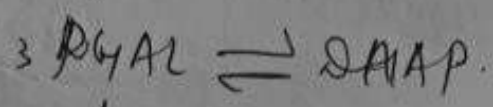
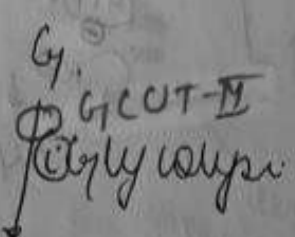
① ↑ AA uptake

protein synthesis

② Glycolysis



③ Adipose tissue



↓
TAG

③ Lipogenesis

④ ↑ Glucose uptake



DIABETES MELLITUS - insulin deficiency at tissue level

TYPE 1 diabetes /
Insulin Dependent Diabetes
Mellitus (IDDM)

Cause: Autoimmune
destruction of β cells of Pancreatic
islets.

- usually not in children.

THERAPY:

- provision of EXOGENOUS INSULIN,
carefully titrated to
dietary intake of glucose.

Type 2 diabetes /
Non Insulin Dependent
Diabetes Mellitus (NIDDM)

- dysregulation of
insulin release from β cells

Insulin resistance in
peripheral cells like
skeletal muscle, brain &
liver.

- historically not in overweight /
obese adults, nowadays
diagnosed in children as
childhood obesity type 2.

- lifestyle changes

↓ alteration in diet
↑ exercise.

delay symptoms at early stages.

- INSULIN-SENSITISING DRUGS -
2nd line agents.

CHARACTERISTICS OF DIABETES:

- ① Glycosuria - excretion of glucose through urine.
- ② OSMOTIC DIURESIS - excess glucose in renal tubules draws water & develops osmotic effects.

↓
↓ renal Reabsorption of water from renal tubules

DIURESIS

- ③ POLYURIA: polyphagia & polydipsia.
passage of large vol. of urine.

- ④ POLYDIPSIA (excessive drinking) :- Excess water loss.
↓
↓ water content & salt content in body
↓
⊕
THIRST CENTER in Hypothalamus.

- ⑤ wt. loss in spite of POLYPHAGIA :- (Tired appetite).

- ⑥ ACIDOSIS :- During insulin deficiency, glucose is not used by peripheral tissues for energy.
CAUSE
① Large amount of fat is broken to release energy.
↓
↑ KetoAcids (AcetoAcetate, β -Oxybutyrate, Acetone).
↓
ACIDOSIS

- ② KetoAcids are excreted in combination with Na^+ through urine [KETONURIA]

• Na^+ is exchanged for H^+ , which diffuse from renal tubules into ECF $\rightarrow$ ACIDOSIS.

- ⑦ KETOSIS - ↑ production of ketone bodies.

VII COMA:

↑ rate & depth of respirations due to acidosis
↓
During Kussmaul breathing
↓
↑ qty of CO_2 lost during expiration
↓
obscure redⁿ of H_2O_3
↓
severe ACIDOSIS
↓
SEVERE DIABETES MELLITUS.

VIII HYPERGLYCEMIA:

→ FUNDAMENTAL DEFECTS to which most of the abnormalities can be traced:-

- ① reduced entry of glucose into various peripheral tissues.
[INTRACELLULAR GLUCOSE DEFICIENCY]
- ② ↑ liberation of glucose into circulation from liver.
[EXTRACELLULAR GLUCOSE EXCESS]