GROUP – A

VERY LONG ANSWERS

(12 MARKS)

ENDOCRINE SYSTEM

GROUP-A (12 MARKS)

1. What are the hormones secreted by adrenal cortex. Describe the principal functions of the mineralocorticoids. What is Conn's syndrome?[3+7+2][2014]
2. Enumerate the functions of calcium in our body. How its homeostasis is maintained by involving different hormones? What are the sources of these hormones? Name the features of Rickets and Osteomalacia. [2+4+2+4][2013][2017]
3. What is blood calcium level? Name the physiological functions of Ca^{2+} in the body. Discuss briefly how the blood calcium level is maintained? [1+3+8][2008][2005][2017]
4. Describe the physiological effects of thyroid hormones. What is thyroid storm? [10+2][2012][2017]
5. Name the various layers of adrenal cortex and the hormones secreted from them. What are the effects of glucocorticoids ? Describe Cushing's syndrome.[2+7+3][2011]
6. Enumerate the hormones secreted from thyroid gland. Describe the functions of thyroxin. Write a brief note on Cretinism. [2+7+3][2010]

7. Enumerate the hormones of anterior pituitary gland. Describe the functions of thyroxin. Mention the cells from where the hormones are secreted. Describe the features of gigantism and acromegaly. What are somatomedins? [2+2+3+3+2][2007]
8. Outline the steps of synthesis of thyroid hormones. List the main actions of thyroid hormones. Mention the features of clinical conditions related to the hypo-functioning of the gland.[3+4+5][2006]
9. Classify the hormones of adrenal cortex. State the steps of biosynthesis and functions of aldosterone. What is aldosterone escape phenomenon? [3+3+3+3][[2004]
10. Name the hormones of islets of Langerhans. State the functions of insulin. Why polyphagia occurs in diabetes mellitus? [2+7+3][2015]

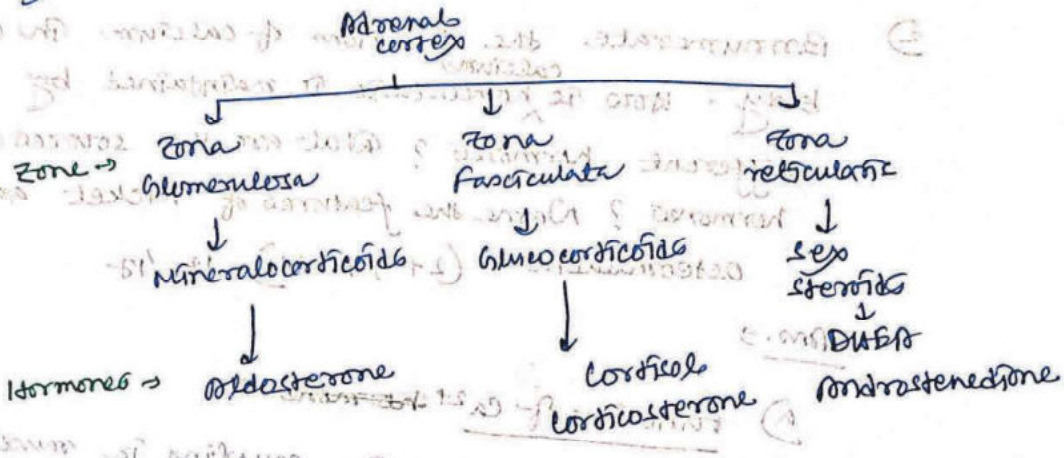
11. Enumerate the layers of adrenal cortex and the hormones secreted from them. Explain how aldosterone controlls extracellular fluid volume. What is aldosterone escape?. [3+7+2] [2019]

Group B

1) What are the hormones secreted by adrenal cortex? Describe the primary form of the mineralocorticoids. What is Conn's disease? (3+7+2) 14

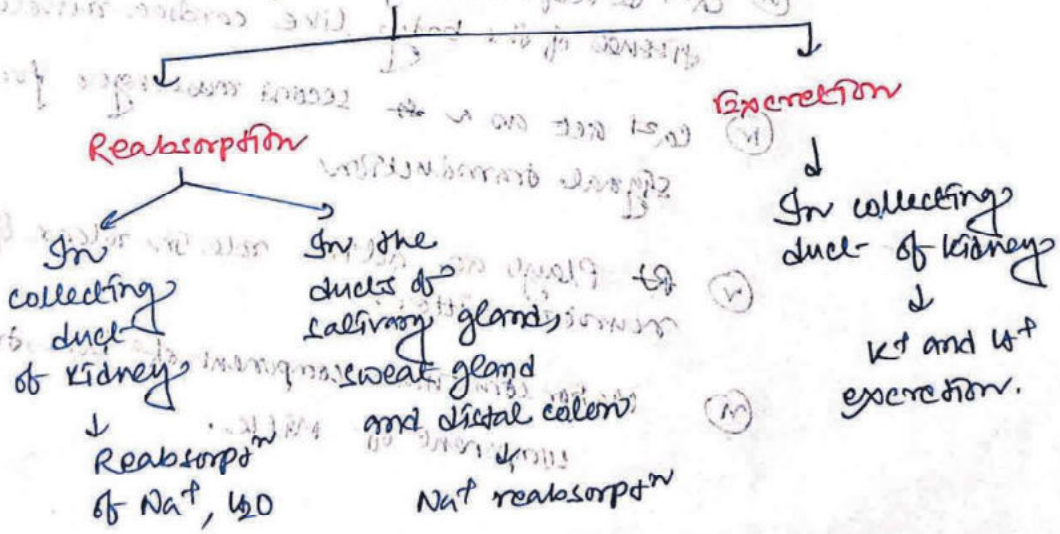
Ans. →

a) The hormones secreted by adrenal cortex →



b) Function of mineralocorticoids →

Aldosterone
aka 'Life saving hormone'



c) Conn's Syndrome → aka Primary hyperaldosteronism

i) Cause → Tumor in aldosterone secreting cells in zona glomerulosa.

ii) Clinical Features →
1) Hypernatremia
2) Hyperkalemia
3) Mild metabolic alkalosis
4) Hypertension
5) Polyuria and polydipsia

(vii) No edema formation occur due to "Aldosterone escape".

(viii) Paralysis due to depressant effect of Low Extracellular K^+ on AP transmission by nerve fibers.

2) Enumerate the functions of calcium in our body. How is calcium homeostasis is maintained by different hormones? What are the sources of these hormones? Name the features of Ricket and Osteomalacia. (2+4+2+4). '13, '17

Ans:-

a) Functions of Ca^{2+}

(i) Excitation - contraction coupling in muscle contraction

(ii) Hemostasis → Ca^{2+} are essential in clotting process.

(iii) Ca^{2+} is responsible for AP in many excitable tissues of the body like cardiac muscle.

(iv) Ca act as a second messenger for signal transduction

(v) Plays an active role in release of neurotransmitter.

(vi) Major structural component of bone, teeth. component of Milk.

CALCIUM (Ca^{+2}) REGULATION

- 3 Hormone — 3 Organ model

1. Parathormone } ↑ Ca^{+2}	1. Bone → Bank for Calcium
2. Vitamin-D } ↑ Ca^{+2}	2. GIT (Gastro-Intestinal Tract)
3. Calcitonin – ↓ Ca^{+2}	3. Kidney

PARATHORMONE (PTH) 00:07:47

- Source → Chief cells of Parathyroid Gland
- Parathormone contains 84 Amino acids
- Drug form of parathormone → Teriparatide

Actions of Parathormone:

1) Bone

- Bone has Two cells → 1) Osteoblasts
  2) Osteoclasts

Parathormone Receptor is present on the Osteoblast

↓

Produces RANK-Ligand

↓

The RANK-ligand acts on the Osteoclast

↓

Results in increase in Differentiation of osteoclast

↓

Increase in osteoclastic Activity results in Bone Resorption

- So, in the Treatment of osteoporosis

↓

RANK ligand Blocker is used (Denosumab)

Parathormone in Bone causes Bone resorption by eventually influencing osteoclast

↓

- Which is mediated by Acid proteases Present in the osteoclast
- Calcium in the Bone is stored in the form of $Ca^{+2}.Po_4^{-3}$ crystal (Hydroxyapatite)
- Acid proteases destroys this Hydroxyapatite crystals

↓

Results in ↑ Ca^{+2} & Po_4^{-3} levels

a) Kidney

- Kidney is responsible for the overall action of Parathormone
- Parathormone

  1) Increases Calcium Reabsorption from DCT (Distal convoluted tubule)

  2) Po_4^{-3} excretion in PCT (Proximal Convoluted Tubule)

↓

By inhibiting Na^+-Po_4^{-3} Cotransporter

- Overall Action of Parathormone → Increase Ca^{+2}
  Decrease Po_4^{-3}
- So, parathormone is known as Po_4^{-3} terminating hormone
- Phosphatonin → Any hormone that decreases Po_4^{-3} in the Body-Parathormone

3) GIT

- Parathormone has indirect action on GIT
- It increases Vitamin D in GIT

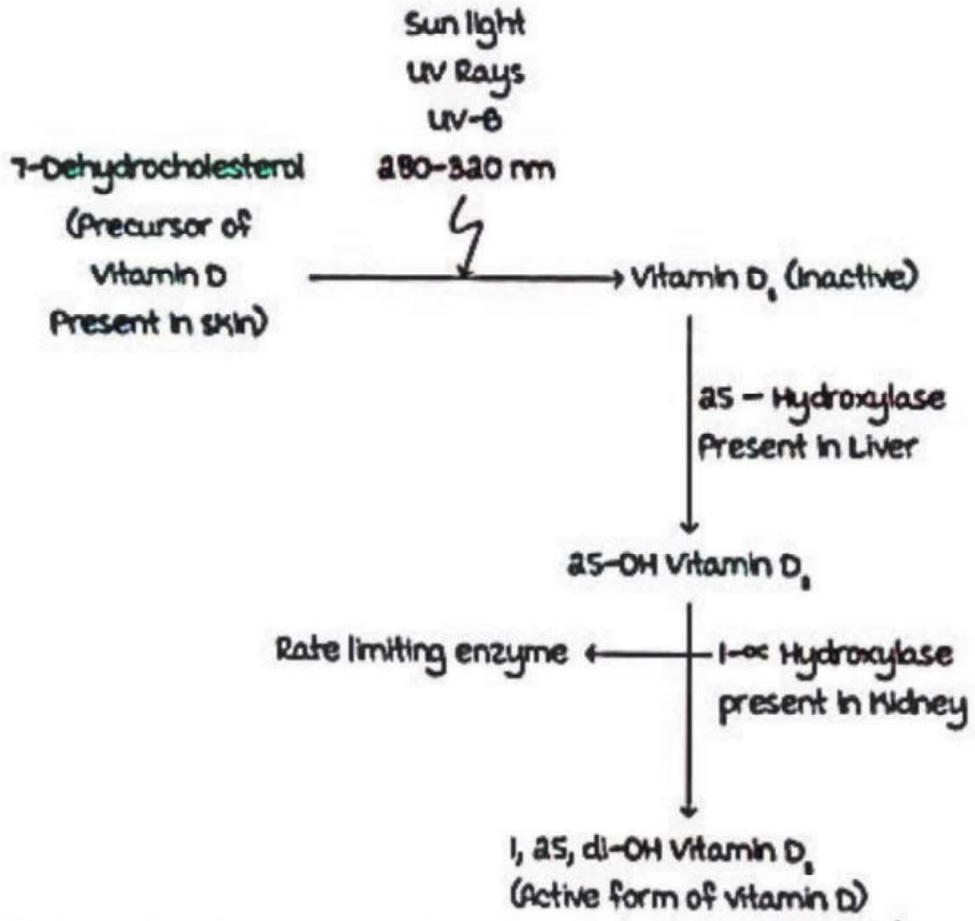
↓

Increases Calcium Absorption

- Overall action of Parathormone on GIT → Increases Calcium
  Decreases Po_4^{-3}

VITAMIN-D

00:18:36



- Lab measurement of 25-OH Vitamin D_3 is used to Assess Vitamin D Status
- 1, 25 di OH Vitamin D_3 is also known as Calcitriol

VITAMIN-D ACTIONS

00:22:45

1) GIT (Gastro Intestinal Tract)

- Calcium Absorption is influenced by Vitamin D
- Calcium Exclusively absorbed in Duodenum
- Vitamin D forms CALBINDIN

↓

Increases Ca^{++} absorption from Diet in Duodenum

2) Bone

- Vitamin D action on Bone similar to Parathormone

Vitamin D Receptors are present on osteoblast

↓

Osteoblast produces RANK ligand

↓

Induces osteoclast Differentiation

↓

Cause Bone Resorption (↑Ca^{+2}, ↑PO_4^{-3})

3) Kidney

- Vitamin D action is similar to Parathormone

↓

Increases Ca^{+2} Reabsorption from DCT (Distal Convoluted tubule)

- But Vitamin-D can also Increases PO_4^{-3} Reabsorption
- Overall Action of Vitamin-D

  1) Increase Ca^{+2} levels

  2) Increase PO_4^{-3} levels

CALCITONIN

00:27:34

- Calcitonin is produced from the Parafollicular 'C' cells of Thyroid Gland
- Drug form of Calcitonin → Salcatonin (Source is from Salmon fish)

Action → On Bone

↓

Calcitonin Receptors are present on Osteoclast

↓

Calcitonin is Inhibitory to osteoclast

↓

Thereby prevents Resorption

→ On Kidney

↓

Increases Calcium Excretion

Medullary Carcinoma Thyroid → Tumor of Parafollicular 'C' cells

→ Secretes Calcitonin in excess

↓

Used as a Tumor marker

→ Rickets →

Dz affecting young children

Causes →

① Vit D deficiency

↓

(i) Dietary deficiency of Vit D.

(ii) Inadequate exposure to sunlight which can produce Vit D from its precursor

② Chronic renal failure

↓

α-1-hydroxylase defi.

↓

non-conversion of 25-hydroxy cholecalciferol to 1,25-Dehydrocholecalciferol or Calcitriol

↓

defi. of Vit D_3.

③ Defect in Vit D receptors.

Features →

① Bones become soft due to defective mineralization

↓

Bones are bent by body wt.

↓

Knock knee and bow-leg.

② Prominent costochondral Jxn.

↓

Rickety rosary

③ Frontal bossing

④ Delayed closure of ant. fontanalle

⑤ Harrison's sulcus → depressed area of the ribs due to attachment of the diaphragm

Osteomalacia →

c/d Adult rickets.

Mainly occur in adult women

Causes →

(I) Steatorrhea → defect in fat absorption
↓
Vit D as fat soluble
cannot be absorbed by intestine
in Steatorrhea
↓
Vit D defi.
↓
leads to defective mineralization

(II) Renal dis. → defi. of 1α-1-hydroxylase
↓
Vit D_3 or calcitriol not syn.
↓
Vit D deficiency
↓
Renal rickets

Features →

(I) Bone pain
(II) Pathological fracture.
(III) Deformity of pelvic bones.

Describe physiological effects of thyroid hormones. what is thyroid storm? (10+2) (2012)(2017)

Ans → 1st part = answer of question 6. (2010)

- Thyroid storm :- A severe form of hyperthyroidism may appear in untreated or inadequately treated hyperthyroidism complicated by illness, surgery or radioactive therapy.
- The condition may be present with delirium, fever, arrhythmia, cardiac failure and hyperthermia. It has high fatality rate and should be treated vigorously.
- Treatment constitutes administration of drugs blocking thyroid hormone synthesis such as propylthiouracil and iodides. Propranolol is also useful.

5. Name the various layers of adrenal cortex and the hormones secreted from them. What are the effects of glucocorticoids? Describe cushing's syndrome [2+7+3] (2011)

Ans:- • There are three layers of adrenal cortex. These are —

i) Zona glomerulosa
ii) Zona fasiculata
iii) Zona reticularis

- Zona glomerulosa secretes ~~glucocorticoids~~ mineralocorticoid aldosterone.
- Zona fasiculata secretes glucocorticoids cortisol and corticosterone.
- Zona reticularis secretes androgenic hormones dehydro-epiandrosterone and androstenedione.

- **Effects of glucocorticoids :-**

i) **on carbohydrate metabolism** – • promotes glycogenesis in liver and skeletal muscle
• ↑ neoglucogenesis ↓ peripheral utilization of glucose and ↑ absorption of glucose from gut.

ii) **on protein metabolism** –
• ↑ protein breakdown to amino acids → neoglucogenesis → ↓ glycogenesis in liver

iii) **on fat metabolism** –
• helps in fat mobilization by GH, adrenaline
• causes redistribution of fat → truncal obesity

iv) Stimulates Na^+ reabsorption and K^+ secretion promotes Ca^{++} excretion in urine.

v) Inhibits bone formation because –
• reduces synthesis of type-I collagen
• decreases number of active osteoblasts
• Reduces Ca^{++} ion absorption from gut
• Enhances bone resorption

vi) on vascular system –

- maintains normal BP and cardiac function
- permissive effect on vasoconstrictor action of catecholamines
- Decrease permeability of vascular endothelium

vii) on kidney –

- Increases GFR
- Required for rapid excretion of water load

viii) ↓REM sleep, ↑NREM sleep

ix) Increases neutrophil, RBC and platelet count

x) ↓ growth of fibroblasts → ↓ wound healing

xi) on Inflammation and immune response –

- Inhibits Phospholipase A_2 → prevents synthesis and release of prostaglandins, thromboxane A_2
- Stabilizes lysosomes
- Inhibits growth of fibroblasts and deposition of fibrils
- Reduces number of T_4 lymphocytes and inhibits their migration to site of antigen.
- Suppresses fever by decreasing production of IL-1.

Cushing's Syndrome :–

- It is characterized by secretion of excess glucocorticoids.

It may be causes due to –

i) Exogenous administration of excess glucocorticoids
ii) Glucocorticoid secreting adrenal tumour
iii) ACTH dependent conditions include
  - pituitary tumours
  - secondary to CRH hypersecretion

Clinical features -

- Protein metabolism - As a result of enhanced gluconeogenesis there is increased conversion of protein into glucose. This results in protein depletion at various sites of body. Wound healing is delayed due to impaired collagen synthesis.

- Fat metabolism - Accumulation of fat occurs in the trunk. Deposition of fat on the back results in buffalo hump while the rounded fat filled face is called moon facies.

- Carbohydrate metabolism - In cushing's syndroome diabetes mellitus may be caused by -
  - increased gluconeogenesis from the amino acids liberated by increased protein catabolism
  - Decreased peripheral utilization of glucose

- patients also suffer from hypertension caused by -
  a. salt and water retention due to the significant mineralocorticoid effect of the excess cortisol
  b. permissive effect of cortisol ~~due~~ to the action of catecholamines on blood vessels.

Mental symptoms may vary from euphoria to restlessness, insomnia, psychoses.

write the hormones secreted from thyroid gland. Describe the functions of thyroxine. write a brief note on cretinism. [2+7+3] (2010)

There are three

Ans:- ^ Hormones secreted from thyroid gland.

These are —

- Thyroxine [Tetraiodothyronine or T_4]
- Triiodothyronine (T_3)
- Calcitonin

T_4 is secreted in higher proportions, it is a prohormone.

■ Functions of thyroxine :-

i) Calorigenic action - It increases oxygen consumption and heat production in tissues. Due to —

- Increased activity of $Na^+ - K^+$ ATPase
- ↑ activity of thermogenic uncoupling proteins
- Futile cycles of contradictory metabolic activity

ii) on Central Nervous System - Stimulates mentation, alertness, wakefulness, hearing function, neuronal development of cerebral cortex, basal ganglia and cochlea.

iii) Effects on heart - • Rise in number and affinity of β adrenargic receptors → positive ionotropic and chronotropic action via catecholamines

• Rise in MHC with higher ATPase activity → ↑ force of contraction

iv) on circulation -

a. calorigenic effect → ↑ body temperature → cutaneous vasodilation → ↓ peripheral resistance

b. Stimulates heart → ↑ cardiac output ↑ heart rate, ↑ pulse pressure, ↑ pulse volume and hyperdynamic circulation

vi) on Respiration — a. ↑ O_2 consumption, ↑ O_2 delivery to tissues, stimulation of respiration ↑ respiratory rate, ↑ minute ventilation and ↑ ventilatory response to hypoxia and hypercapnia.

b.

vi) on skin — inhibits synthesis of mucopolysaccharide s In hypothyroidism, myxomatous tissue composed of hyaluronic acid, chondroitin sulphate and protein which retain water.

vii) Thyroxine is required for conversion of carotene to vitamin A.

viii) Thyroxine increases absorption of carbohydrate from gut. It also stimulates glycolysis, neoglucogenesis and glucose utilization by tissues.

ix) Thyroxine lowers blood cholesterol.

x) It causes both lipolysis and lipogenesis.

xi) Epiphyseal closure of bones and rate of bone growth is dependent on T_4.

xii) small dose of T_4 → stimulates growth in young children but in large dose, causes weight loss due to protein catabolism

xiii) • stimulates milk secretion
• permissive effect on normal reproductive function in both sexes.

xiv) Lowers blood cholesterol due to increased number of LDL receptors → ↑ uptake of cholesterol from blood.

- When there is deficiency of thyroid hormone secretion, it is called hypothyroidism.

Established hypothyroidism in children is known as cretinism and affected children are known as cretins.

Features:- i) short in stature (dwarfed)

ii) Deficiency of thyroid hormone leads to mental retardation

iii) Large, protruding tongue with pot belly. This is because soft tissue growth is unchanged whereas skeletal growth is stunted.

iv) Dry, rough skin

v) Deaf-mutism and rigidity may be present.

vi) Delayed milestones of development

vii) Infantile body proportion is retained even in adulthood.

Enumerate the hormones of anterior pituitary gland. Describe the functions of thyroxin. Mention the cells from where the hormones are secreted. Describe the features of gigantism and acromegaly. What are somatomedians [2+2+3+3+2] 2007

⇒

- The hormones of anterior pituitary are -
  - (i) Growth hormone (GH) or Somatotrophin
  - (ii) Prolactin
  - (iii) Thyroid stimulating hormone (TSH) or Thyrotropin.
  - (iv) Adrenocorticotrophic hormone (ACTH) or corticotrophin.
  - (v) Luteinizing hormone (LH)
  - (vi) Follicle-stimulating hormone. (FSH)

- The functions of thyroxin are:-

(1) Increased calorigenic action due to (i) increased activity of $Na^+ - K^+$ - ATPase. (ii) Used activity of thermogenic uncoupling proteins (iii) Futile cycles of contradictory metabolic activity.

(2) Effects on the CNS - Stimulates mentation, Wakefullness (through reticular formation), myelination, neuronal development, reaction time of reflexes.

(3) Reaction with catecholamines - (i) Number and affinity of β-adrenergic receptors increased. (ii) Sympathectomy / Sympatholytic drugs relive symptoms of hyperthyroidism.

(4) Inhibit mucopolysaccharide synthesis

(5) Converts carotene into vitamin A

- Place of Secretion : Thyroid ~~follicular~~ acinar cells.

Features of gigantism

→ Hypersecretion of GH before epiphyseal closure causes ↑ in lenght of Long bone.

→ Visceral enlargement, increased muscle mass but lacking in strength.

→ Persistant hyperglycemia induces insulin secretion

Features of Acromegaly

→ Increase in width of fingers, toes, hands and feet.

→ Prominent ridges above the eyes with prostruded lower jaw

→ Coarse facial features with enlarged nose and tongue due to soft tissue overgrowth.

- **Somatomedians** - They are a family of polypeptide intermediaries, similar to insulin in structure and function (action on growth), through which growth hormones act. These are called insulin-like growth factor (IGF). They are of two types - IGF-I and IGF-II

They have a structure similar to insulin and a molecular weight about 7000 KDa. These are straight chain peptide having a distinct C-chain.

Their mechanism of action is similar to that of insulin and other growth factors, involving intrinsic tyrosine kinase activity of their receptors and tyrosine kinase mediated phosphorylation of intracellular protein.

(8) Outline the steps of thyroid hormone synthesis. List the main actions of thyroid hormone. Mention the features of clinical conditions related to hypo-functioning of the gland. [2006]

Ans:- • Steps of Synthesis of Thyroid hormones:-

(i) Iodine trapping →

- Iodide present in plasma is actively taken through the basal surface into thyroid gland against electrical & chemical gradient.

(Against electrical gradient because RMP of acinar cells is -50 mV, So when $I^{\ominus}$ is taken into these cells, it has to be done against electrical gradient).

(Against conc^{n} gradient because Normal Thyroid : Serum iodide conc^{n} is 25-50 : 1, So uptake of iodides has to be against conc^{n} gradient)

- Transport of iodide affected by secondary active transport involving $Na^{+}-I^{-}$ co-transporter & $Na^{+}-K^{+}$ ATPase pump.

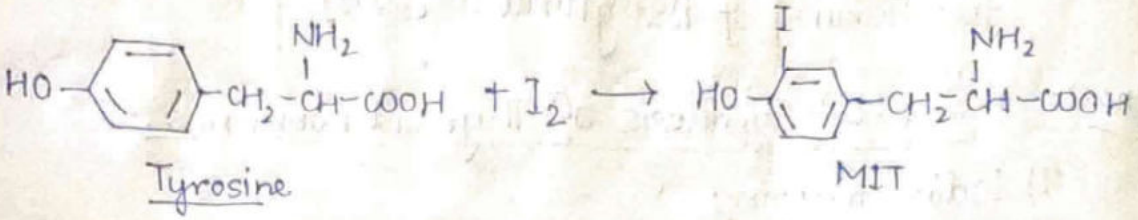
(ii) Oxidation →

- absorbed iodide migrates to the luminal or apical membrane of cell.
- At the apical membrane, enters into the lumen containing colloid through transporter protein called "pendrin."
- There oxidised by thyroid peroxidase into iodine atoms.

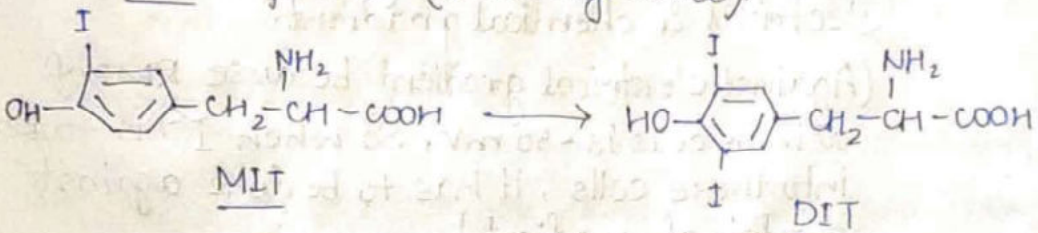
(iii) Organification →

- Process by which MIT & DIT are formed is called organification.
- Inhibited by thiouracil compounds.

- When Iodine binds to tyrosine at 3 posⁿ. attached to thyroglobulin, then resultant compound is MIT (Monoiodotyrosine).

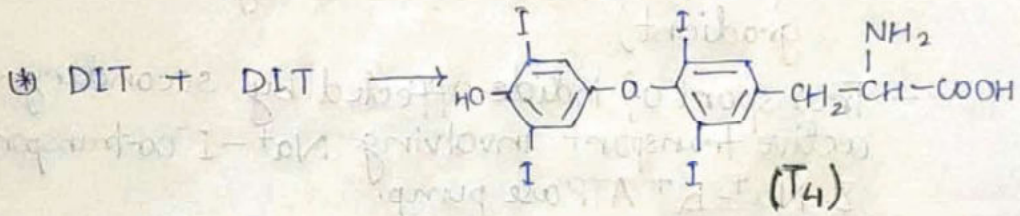


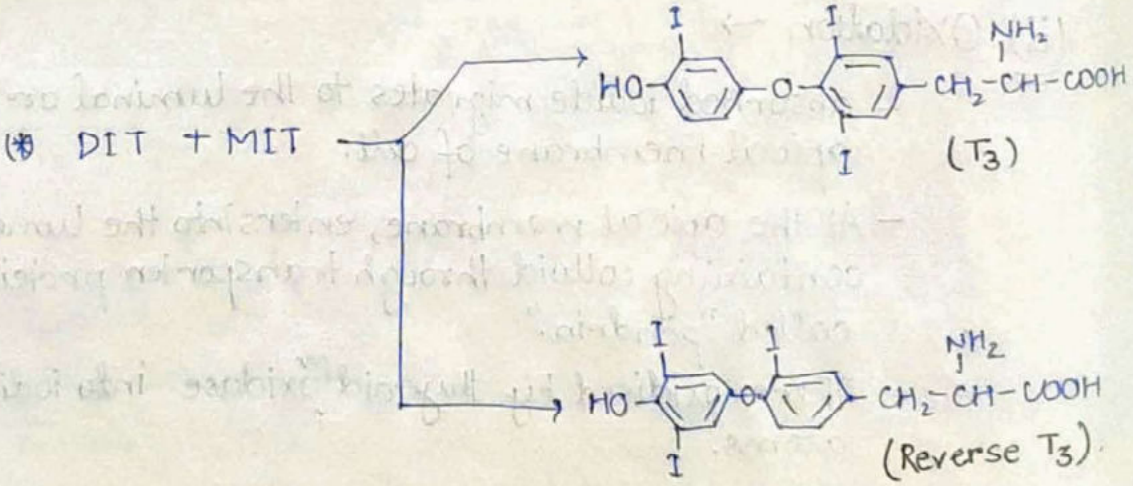
- When another Iodine binds to MIT at 5 posⁿ. then DIT is formed (Diiodotyrosine).



(iv) Coupling →

- Enzyme involved = Thyroid peroxidase





(v) Release of thyroid hormones →

- Proteolytic enzymes in lysosome breakdown the peptide bonds b/w thyroglobulin & attached iodinated residues releasing MIT, DIT, T_3 & T_4.

play a role in release of thyroid hormones.

- Action of Thyroid Hormones →

(a) Calorigenic action due to:
- ↑ activity of Na^+ K^+ ATPase.
- ↑ activity of thermogenic uncoupling proteins.

(b) Effect on CNS :
- Stimulates mentation, alertness, wakefulness, hearing funct., neuronal development of cerebral cortex, basal ganglia & cochlea & reaction time of reflexes.

(c) Effect on Heart :
- ↑ in no. & affinity of β- adrenergic receptors → (+)ve ionotropic & chronotropic action via catecholamines.
- ↑ in α-MHC (myosin heavy chain) with higher ATPase activity → ↑ force of contraction.

(d) Effect on circulation :
- calorigenic effect → ↑ body temp. → cutaneous vasodialation → ↓ peripheral resistance
- stimulates heart → ↑ cardiac output, ↑ heart rate, ↑ pulse pressure, ↑ pulse vol. & hyperdynamic circulation.

(e) Effect on Respiration →
- ↑ O_2 consumption, ↑ O_2 delivery to tissues, ↑ respiratory rate, ↑ minute ventilation & ↑ ventilatory response to hypoxia & hypercapnia.
- All these keep pO_2 & pCO_2 normal inspite of ↑ O_2 utilization & CO_2 production.

(f) Converts carotene into Vit. A.

(g) ↑ absorption of carbohydrates.
causes ↑ glycolysis, ↑ gluconeogenesis, ↑
↑ peripheral utilisation of glucose.

(h) Lower blood cholesterol :- due to ↑ no. of LDL receptors
= ↑ uptake of cholesterol from blood.

(i) cause both lipolysis & lipogenesis.

(j) stimulates growth in young children but in high doses causes weight loss due to protein catabolism.

(k) Stimulates milk secretion.

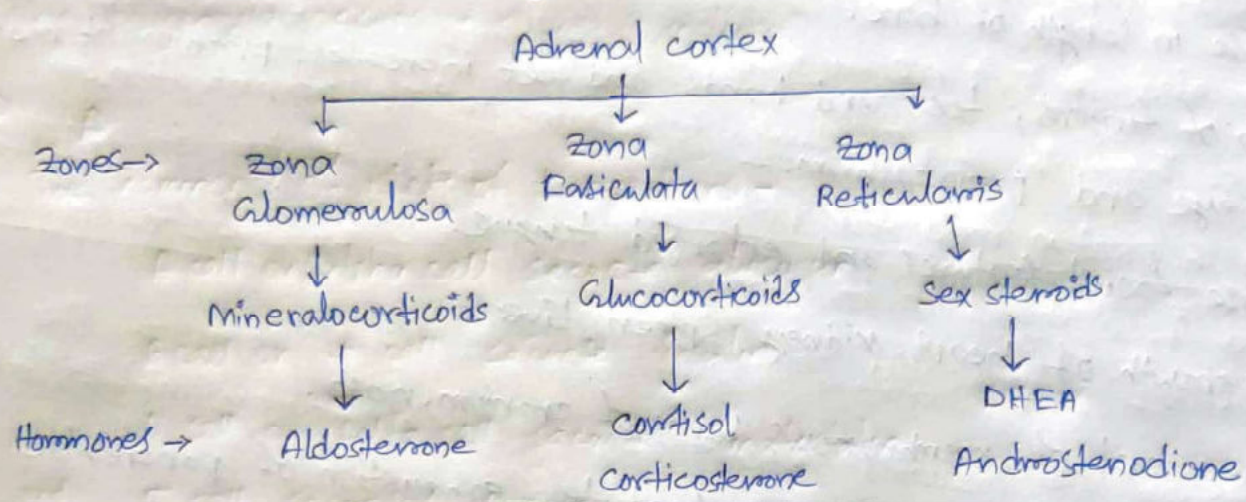
- Features of conditions related to Hypothyroidism →

① In Children : CRETINISM →
- short in stature.
- mental retardation.
- large, protuding tongue with potbelly.
- dry, rough skin.
- deaf mutism, rigidity.

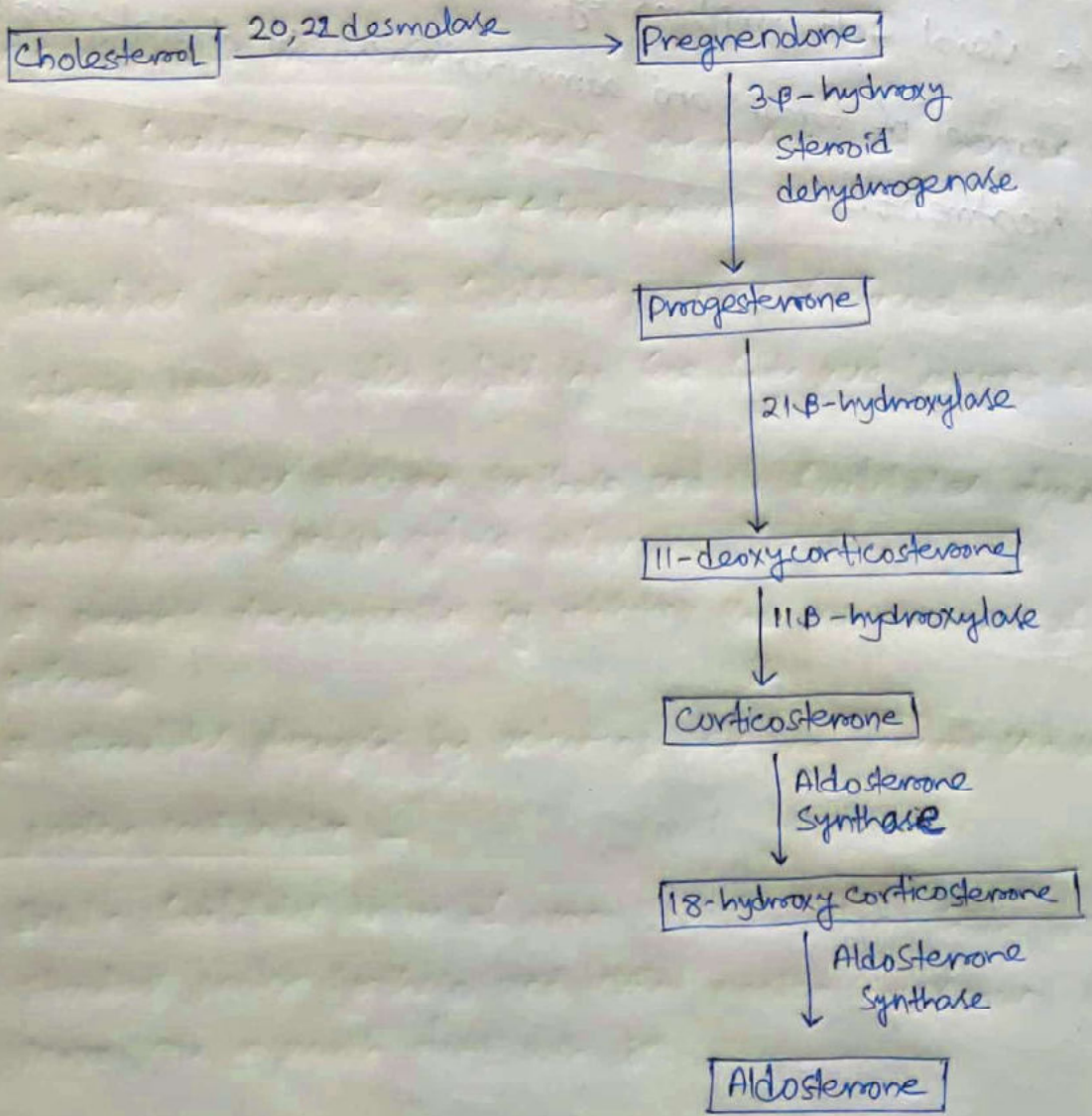
② In Adults : MYXEDEMA →
- Low BMR with sensitivity to cold & weight loss.
- dry, yellowish skin due to carotenemia.
- puffy face, enlarged tongue & stiff joints.
- poor mentation.
- Bradycardia, low cardiac output, low-voltage ECG.
- menstrual irregularities.
- Rise in blood cholesterol.

Classify the hormones of adrenal cortex. State the steps of biosynthesis and function of aldosterone. What is aldosterone escape phenomenon. [3+3+3+3]

⇒ The hormones secreted by Adrenal cortex →



- Synthesis of aldosterone



- **Functions of Aldosterone** –

1) **Reabsorption of Na^+ and secretion of K^+** –

(a) From distal tubule and cortical collecting duct

(b) From sweat gland, salivary gland and distal colon.

2) **Extracellular Fluid volume Regulation** –

By regulating the amount of Na^+ reabsorption, aldosterone plays an important role in regulating ECF volume. Increase in reabsorped Na^+ retain extra water which increases ECF volume.

3) **maintainance of Acid base balance:-**

Excess aldosterone secretion causes hypokalemic alkalosis.

mech: Excess aldosterone secretion
↓
Hypokalemia due to ↑K^+ secretion
↓
K^+ move from cell to ECF
↓
In exchange, H^+ enter the cell increasing intracellular $[H^+]$
↓
More H^+ secreted in distal tubule
↓
metabolic alkalosis.

- **Aldosterone escape phenomenon** :-

This phenomenon is observed in hyperaldosteronism (conn's syndrome). The patient suffering from primary hyperaldosteronism, initially retain Na^+, water is also retained osmotically and this increases ECF volume. when increase in ECF volume crosses a certain Limit, Na^+ excretion is stimulated, possibly through rise in secretion of Atrial Natriuretic peptide (ANP). This keeps Na^+ concentration low and edema is not seen. This phenomenon is known as 'aldosterone escape'

10 Name the hormones of islets of Langerhans State the functions of insulin. Why polyphagia occurs in diabetes mellitus?

⟹

- The hormones of islets of Langerhans -

A cell or alpha cell secrete glucagon

B cell or β cell secrete insulin.

D cell or Delta cell secrete Somatostatin

and F cell secretes pancreatic polypeptide.

- The functions of insulin are-

A. on carbohydrate metabolism -

1. Insulin facilitates entry of glucose into muscle and adipose tissue by stimulating activity of GLUT 4 transporters.
2. Stimulates glucokinase facilitating entry of glucose into liver via GLUT 2.
3. Glucose uptake is also helped by free fatty acid lowering effect of insulin.
4. Insulin stimulates glycogen synthase and so facilitates glycogenesis. It inhibits glycogen phosphorylase responsible for glycogenolysis.
5. It prevents gluconeogenesis by inhibiting the key enzymes of the gluconeogenetic pathway.
6. It stimulates glycolysis by activating PFK and pyruvate kinase.

B. on protein metabolism -

1. Insulin facilitates entry of amino acids (branched chain) into the cells.
2. Stimulates protein synthesis and inhibit protein breakdown, so plays a major role in growth along with GH.

c. on fat metabolism –

1. Insulin inhibits hormone sensitive lipase, thus breakdown of depot fat into FFA is prevented.
2. Stimulates FFA synthesis from acetyl-coA carboxylase, thus opening up the malonyl coA pathway which prevents the ketone body formation.
3. Insulin stimulates lipoprotein lipase which breaks down triglycerides in VLDL and chylomicrons into FFA which is later converted to depot fat.
4. Net effect of insulin on fatty acid metabolism:
   (a) Storage of fatty acid is promoted.
   (b) Breakdown of triglycerides into fatty acids and their oxidation are inhibited.

D. on ion transport –

Insulin lowers plasma K^+ by stimulating K^+ entry into cell. Glucose and insulin are often used together to treat hyperkalemia.

- Polyphagia in diabetes mellitus →

In diabetes mellitus ~~due~~ insulin mediated uptake of glucose through GLUT-4 is significantly reduced in various cells of the body.

Thus, the uptake of glucose is reduced in satiety centre located in ventroposteromedian nucleus (as it requires GLUT-4 mediated uptake). This lifts the inhibition by it on the feeding centre located in the lateral part of hypothalamus, thus resulting in polyphagia.

Also due to lack of uptake of glucose there is no inhibition of nucleopeptide Y secreting neurons of hypothalamus and neuropeptide Y stimulates feeding centre resulting in polyphagia.

- Enumerate the layers of adrenal cortex and the hormones secreted from them. Explain how aldosterone controls extracellular fluid volume. what is aldosterone escape. [3+7+2]

Ans:- • Answer of 1st part is described in previous questions.

◪ Aldosterone controls extracellular fluid volume through the following pathway —

1) The fall in ECF volume is marked by lowering of BP which stretches afferent arteriole thus activating intrarenal baroreceptors activating sympathetic system.

2) Then renin secretes from JG apparatus, renin converts angiotensinogen to angiotensin-I and ACE of pulmonary capillary endothelium converts angiotensin-I to angiotensin-II which stimulates aldosterone secretion.

3) Aldosterone works in ~~two ways~~ —
   a) causes synthesis of basolateral Na^+K^+ ATPase
   b) synthesize ENa^+ channels in P cells
   c) H^+ ATPase carriers inserted in luminal membrane

4) Aldosterone increases reabsorption of Na^+ from renal tubular lumen, resulting in concomitant water reabsorption, increasing ECF volume.

5) Aldosterone stimulates Na^+ reabsorption in sweat glands and distal colon of GIT resulting in osmotic absorption of water.

6) When there is sufficient increase in ECF volume sympathetic discharge decreases thus depressing whole RAAS Pathway.

- **Aldosterone escape:—**
  - It is defined as the physiological phenomenon of absence of edema in the case of primary hyperaldosteronism.
  - The initial retention of Na^+ along with water osmotically leads to a rise in ECF volume.
  - When ECF volume crosses a sudden value there is stretch of atrial wall and this releases ANP.
  - ANP inhibits aldosterone secretion and causes loss of Na^+ and water along with it. both factors leading to loss of ECF volume. This keeps Na^+ conc. low and edema is not seen.
  - This phenomenon is aldosterone escape.

GROUP – B

LONG ANSWERS

(7 MARKS)

GROUP-B (7 MARKS)

1. List the hormones of calcium metabolism and mention the features of tetany. [4+3][2009]
2. Myxedema . [7][2004]
3. Outline the Steps of thyroid hormone synthesis. What is wolf chaikoff effect? [5+2][2018]

1) List the hormones of Ca metabolism and mention the features of tetany. [4+3] [2009]

=> The hormones involved in Ca^{2+} metabolism are as follows -

i) PTH → ⊙ Secreted from parathyroid gland from posterior surface of thyroid, hypercalcemia in nature.

① Enhances canalicular outflow of Ca^{2+} into ECF, also enhances mobilisation of Ca^{2+} from osteocytes

⊙ Enhances osteoclastic bone resorption through their activation via m-CSF secreted by osteoblasts activated by it and expression of RANKL which binds with RANK of osteoclasts and resulting in their activation.

⊙ absorption of Ca^{2+} from GIT via activation of 1α-hydroxylase.

⊙ enhances absorption of Ca^{2+} from distal nephrons and inhibits absorption of phosphates from proximal nephrons.

ii) Calcitriol / Calcitonin → ⊙ inhibits osteoclastic activity

⊙ increases Ca^{2+} excretion in urine

⊙ prevents hypercalcemia after meals

⊙ protects mothers from Ca^{2+} during pregnancy.

⊙ Important for bone growth in young individuals.

iii) Calcitriol → ⊙ Absorption of Ca^{2+} from GIT enhanced through Calbindin and $TRPV_6$ stimulation

⊙ promotes bone mineralisation

⊙ Renal absorption of Ca^{2+} & via $TRPV_5$

(1) Increased neuromuscular excitability caused by low $[Ca^{2+}]$

(2) Occurs when $[Ca^{2+}]$ is about 6-7 mg/dl

(3) Caused by ~~hypoth~~ hypoparathyroidism, alkalosis (due to formation of Ca^{2+} - protein complexes and their ~~pr~~ precipitation)

(4) Laryngeal muscles being specially ~~sensible~~ sensitive to spasm, suffers from stridor, resulting in a crowing sign called laryngeal stridor

(5) Spasm of this muscles can cause respiratory ~~obstruction~~ obstruction

(6) Generalised convulsions are seen

(6)(7) Trousseau's sign is observed which is flexion at the elbow, wrist and ~~metacarpophalangeal~~ metacarpophalangeal joint with extension at the interphalangeal joint also called as accoucheur's hand.

(8) ~~Ch~~ Chvostek's sign is observed where ~~flexion~~ facial muscles go into spasm.

(9) Peroneal sign; i.e, plantar flexion and abduction of foot.

(10) ECG with long QT segment is observed

(11) Treatment is generally intravenous calcium gluconate injection.

~~7 Marks~~ Myxedema [2004]

Ans:- If there is hypothyroidism in adults, it is called myxedema.

Because there is subcutaneous deposition of myxomatous tissues.

It may be due to —

- Iodine deficiency
- Thyroidectomy
- Hashimoto's disease
- Pituitary failure to secrete TSH
- Hypothalmic failure to secrete TRH

Main features are —

i) Low BMR with sensitivity to cold and weight gain

ii) Dry, yellowish skin due to carotenemia because in deficiency of thyroxin carotene can not be converted into vit-A, so there will be excess accumulation of carotene in body.

iii) Puffy face, enlarged tongue and stiff joints

iv) Voice is husky

v) Poor mentation, impaired memory, lethargy and somnolence

vi) Sometimes there are psychological aberrations called 'myxedema madness'.

vii) There is bradycardia, decreased cardiac output, low voltage electrocardiogram and pericardial effusion

viii) Normochromic, normocytic anemia

ix) Menstrual irregularities and reduced lactation

x) Rise in blood cholesterol because thyroid hormone lowers blood cholesterol.

☑ Thyroid hormone inhibits mucopolysaccharide synthesis. So, in hypothyroidism, myxomatous tissue composed of hyaluronic acid, chondroitin sulphate and protein is deposited under the skin. This retains water osmotically. So, it is called myxedema.

- **Wolf – Chaikoff effect →**
  - Iodides, given in high doses, inhibit organification & thus synthesis of thyroid hormone is decreased. This is known as Wolf – Chaikoff effect.
  - The above inhibitory effect is more pronounced in Thyrotoxicosis.
  - Also, iodides in high doses, reduce the vascularity of the hypertrophied gland.
  - For these reasons, iodide in the form of Lugol's iodine is routinely given during preparation of a hyperthyroid gland before surgery.

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GROUP – C

SHORT NOTES

(3 MARKS)

GROUP-C (3 MARKS) SHORT NOTES

1. ADH.[2014]
2. Cretinism. [2013]
3. Glucocorticoids. [2013]
4. Acromegaly. [2011]
5. Cushing's Syndrome. [2010]
6. Dwarfism. [2009]
7. Biological Clock. [2009]
8. Aldosterone and ANP. [2007]
9. Vit. D. [2006]
10. Hypoglycemia. [2006]
11. Tetany. [2005][2017]
12. Adission's disease. [2005][2016]
13. Adenohypophysis v/s Neurohypophysis. [2004]
14. Permissive action of hormones.[2017]

Group C - Short Notes [5 marks]

① ADH (2014)

⇒ • Produced by the supraoptic and paraventricular nuclei of the hypothalamus and secreted through the axonal terminals of posterior pituitary.

• Secreated in response to increase osmolarity and ECF volume.

• Acts through V_2 receptors, increasing cAMP concentration via G protein mediated pathway cause phosphorylation of aquaporine and their migration to luminal membrane of the collecting tubule. Resulting in increased absorption of water.

• Through V_1A mediates vasoconstriction (though it mainly inhibits fall in blood pressure during hemorrhage.)

• Through V_1B mediates release of ACTH.

② Cretinism [2013]

⇒ • It is caused by extreme hypothyroidism during fatal life, infancy or childhood, due to congenital lack of thyroid gland (congenital cretinism), from faliure of thyroid gland to produce thyroid hormones, or from lack of iodine (endemic cretinism)

• Few week after birth (as before some ammount of maternal thyroid hormones are there, though not enough) neonatal physical and mental growth become sluggish.

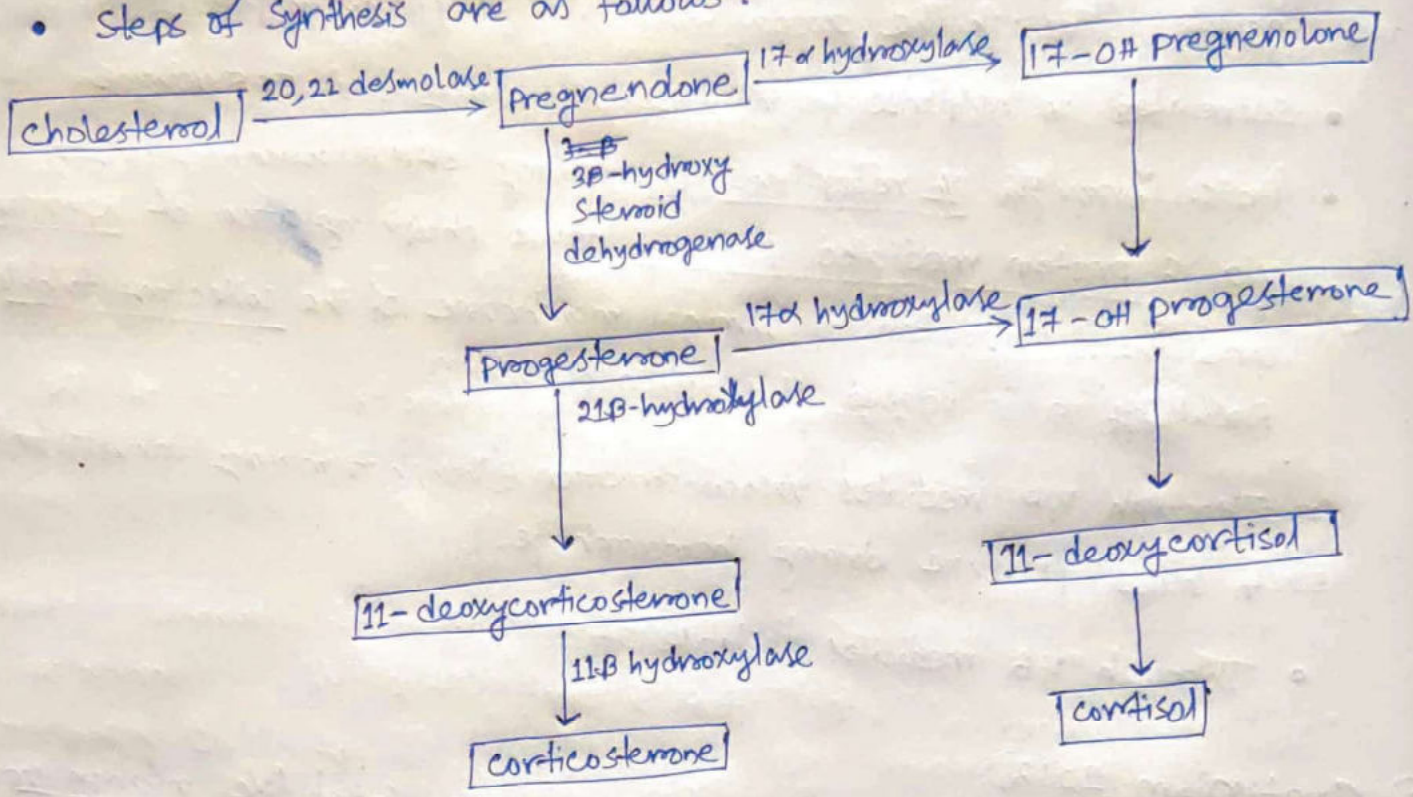
• Features include → Short stature (dwarfed)
→ mental retardation
→ Large, protruding tongue with pot belly.
→ Dry, rough skin
→ Deaf-mutism and rigidity may be present.
→ Delayed milestones of development
→ Infantile body proportion maintained till adult-hood

• Treatment of the neonate with cretinism with adequate iodine or thyroxine usually causes normal return of physical growth, but unless treated within few weeks after birth, mental growth remains permanently retarded.

(3) Glucocorticoids [2013]

⇒ • Secreated from Zona fasiculata of adrenal cortex and has 2 forms- cortisol and corticosterone.

• Steps of synthesis are as follows :-



• It is a hyperglycemic hormone (↑ses neoglycogenesis, ↑glycogenesis, ↓ses peripheral utilisation of glucose), causes breakdown of protein and lipid

• Helps in Na^+ reabsorption, Ca^{+2} excretion in urine, important for function of skeletal muscle and inhibits bone formation, also inhibits formation of connective tissue.

• Maintains Normal BP and has permissive effect on vasoconstriction, increases GFR.

• Increases Neutrophil, RBC and platelet count but decreases eosinophil and lymphocyte count.

• It has very prominent immunosuppressor role.

④ Acromegaly

⇒ • Hypersecretion of GH due to any acidophilic tumor in the anterior pituitary after epiphyseal closure leads to acromegaly.

- Girth of bones increases and soft tissue mass increases, but not much increase in length of bone.
- Width of fingers, toes and hands and feet increases, prominent ridges over eye and prognathism.
- Coarse facial features and enlarged tongue.
- overgrowth of heart, kidney, Spleen, Liver,
- Enlargement of membranous bones of cranium, nose.
- Its antiinsulin effect may lead to exhaustion of pancreatic insulin resulting in frank diabetes mellitus.
- can cause visual field symptoms eg. bitemporal hemianopia.
- Surgical removal of tumor and administration of somatostatin analogus are modes of treatment.

6. **Dwarfism** :-

Dwarfism or short stature is caused by -

i) Growth hormone deficiency, GHRH deficiency, or deficiency of IGF-I, all may result in dwarfism.

ii) In some cases of dwarfism the circulating GH level is normal but there is a defect in GH receptor. This results in a condition known as Laron dwarfism.

iii) Dwarfism is found in cretinism and in patients with precocious puberty.

iv) Dwarfism is also found in achondroplasia, a condition characterized by short limbs and a normal trunk. It is genetically transmitted as an autosomal dominant disorder.

v) Dwarfism may be the result of chronic neglect. It is known as Kaspar Hauser syndrome.

vi) patients having XO chromosomal pattern with gonadal dysgenesis also show dwarfism.

vii) African pygmies suffer from a dwarfism of uncertain etiology. In them, GH level is normal but pubertal increase of IGF-I level does not occur.

7> Biological clock [2009]

Ans:- • The suprachiasmatic nucleus of hypothalamus has an internal mechanism acting as an internal clock and it behaves as an internal timekeeper of the body.

• suprachiasmatic nuclei plays major roles in light dark entrainment process.

• The SCN receive information about the light dark cycle via a special neural pathway, the retinohypo-thalamic fibers. Efferent fibers from SCN initiate neural and humoral signals that entrain a wide variety of well known circadian rhythms including sleep wake cycle and melatonin release from richly vascularized pineal gland.

• SCN have two peaks of circadian activity that may correlate with the observation that exposure to bright light can either advance, delay or have no effect on the sleep wake cycle depending on the time of day

Aldosterone and ANP :-

- **Aldosterone:-**
  - It is mineralocorticoid hormone secreted from Zona glomerulosa

Mode of action – It is soluble in lipids It easily passes through cell membrane and binds with the highly specific cytoplasmic receptors Then hormone receptor complex migrates to nucleus.

Action – i) Aldosterone facilitates Na^+ reabsorption from the distal tubule and the cortical collecting duct in exchange for K^+ and H^+ ions

ii) It stimulates Na^+ reabsorption in sweat glands

iii) By regulating amount of Na^+ reabsorption, aldosterone plays an important role in regulating ECF volume.

- **ANP :-**
  - It is atrial natriuretic peptide.
  - It is secreted from walls of Cardiac atria.

function – i) It reduces extracellular fluid volume.

ii) It decreases Na^+, water reabsorption from renal tubules.

iii) It increases glomerular filtration rate and glomerular permeability

iv) It inhibits angiotensin II

v) It reduces aldosterone secretion by Zona glomerulosa.

vi) Relaxes vascular smooth muscle in arterioles and venules.

9. Vit D. (2006)

Ans:- • Vitamin D is a group of Steroid compounds produced by the action of ultraviolet rays from precursor substances.

Synthesis - i) The ultraviolet rays in sunlight rapidly convert 7-dehydrocholesterol present in the skin to previtamin D_3. Previtamin D_3 is then slowly converted into vitamin D_3 or cholecalciferol.

- Vit D is a prohormone.
- Calcitriol or $1,25(OH)_2D_2$ is the active hydroxylated form of vitamin D.
- It is hydroxylated at 25 position in liver and then at 1 position to produce calcitriol. This reaction takes place in proximal tubular cells of the kidney.

Source:- Fish, fish liver oil, butter, eggs

Function - i) calcitriol promotes the absorption of calcium and phosphorus from intestine.

ii) It increases reabsorption of calcium and phosphorus by renal tubules.

iii) calcitriol stimulates osteoclastic bone resorption, it also promotes bone mineralization.

Deficiency - In children → Ricket

In adult → Osteomalacia

(3 marks)

10. Hypoglycemia [2006]

↝ If the blood glucose level falls below 50 mg% in an individual, he complains of giddiness, confusion, palpitation, sweating, anxiety, etc. In severe untreated cases, this culminate in convulsions and coma. The symptoms arise due to two reasons -

a) The hypoglycemia leads to deficient supply of glucose to brain. This results in such symptoms as giddiness, confusion and in extreme cases coma.

b) The hypoglycemia stimulates sympathetic overactivity and secretion of epinephrine. This causes tachycardia, sweating, anxiety, etc. These symptoms are important in the sense that they warn the patient about imminent hypoglycemic coma (this is known as hypoglycemia awareness)

11. Tetany [2005, 2017]

↝ It can be defined as a clinical condition characterised by increased neuromuscular excitability caused by low Ca^{2+} in blood. Among the causes there are -

(1) Hypoparathyroidism - Cas in accidental surgical removal of parathyroid glands during thyroidectomy)

(2) Alkalosis - Part of ionized Ca^{2+} form complexes with plasma proteins

(3) Rickets / Other renal diseases - Even

(4) Other renal disease

Even a minor stimulus may lead to convulsions.

Clinical features -

(1) Trousseau's sign → flexion at the elbow, wrist

the interphalangeal joint with extension at the interphalangeal joint.

② Laryngismus stridulus → laryngeal muscles may go into spasm, producing stridor.

③ Chvotok's sign → spasms of the facial muscles when the facial nerve is tapped over the ramus

④ Cab's sign

⑤ Peroneal sign

12) Addison's disease [2005, 2016]

This disease is also known as primary adrenocortical insufficiency. There is deficient secretion of adrenal cortical hormones including aldosterone and cortisol. It mainly involves the adrenal corter. In this disease, there is destruction of adrenal corter due to -

a) Tuberculosis

b) Autoimmune disease

c) Cancer of the adrenal gland

⊙Clinical features -

a) Hyperpigmentation - caused by excess secretion of ACTH.

b) Electrolyte imbalance with hyponatremia and hyperkalemia.

c) Chronic hypotension.

d) Addinson crises

13) Adenohypophysis vs Neurohypophysis [2004]

Adenohypophysis	Neurohypophysis
⇝ Adenohypophysis is derived from an upward extension of the primitive buccal ectoderm called Rathke's pouch.	⇝ Neurohypophysis is a downward extension of neural tube from the ventral hypothalamus. It is therefore, a true extension of brain.
⇝ Adenohypophysis contain the pars distalis, pars intermedia, pars tuberalis.	⇝ Neurohypophysis contains the median eminence, infundibular stem, pars nervosa.
⇝ Adenohypophysis actually secretes hormones from the pars distalis part.	⇝ The neurohypophysis is not the site of synthesis of hormones. It transports, stores and releases the posterior pituitary hormones.

(14) Permissive action of hormone. (2017)

Def^{n} → Permissive action of hormone is the ability of a hormone to increase the sensibility of the target cell towards some other hormones.

Binding of permissive hormone to its receptors

↓ ⊕

Migrat^{n} of the receptors of another hormone / ↑es of Receptors from intracellular compartment to the cell membrane.

↓

↑ed action of the 2nd hormone as the responsiveness ↑es.

Eg.: ① Thyroxine

↓

↑es the expression of β-adrenergic receptors in heart

↓

↑ed action of epinephrine on heart in presence of Thyroxine

② Cortisol augments the action of GH.

Group-D (3 marks): Explain Why

① Exercise is good for diabetes mellitus *(2013).

Ans.:

Exercise

↓

↑es the recruitement of the GLUT-4 molecules from the intracellular compartment to the plasma membrane surface

↓

Now, ↑↑ GLUT-4 channels present on the cell mem.

↓

↑↑ plasma glucose uptake inside the cells

↓

↓ plasma glucose level

↓

Improve the condition of diabetic patient

GROUP – D

EXPLAIN WHY QUESTIONS

(3 MARKS)

GROUP-D (3 MARKS) EXPLAIN WHY

1. Exercise is good for diabetes mellitus. [2013]
2. Metabolic acidosis may be found in diabetes mellitus. [2013]
3. Diabetes mellitus is characterized by polyphagia. [2010]
4. Food intake is increased in diabetes mellitus. [2008]
5. IN hyperthyroid state, beta 2 blocker are used. [2009]
6. Hyperglycemia after pancreatectomy is corrected by hypophysectomy in experimental animal.[2006]
7. Thyroid dwarfs are mentally retarded. [2005]
8. Hyper pigmentation of skin in Addision's disease. [2004]
9. Acromegaly may be associated with visual field defect [2019]

(1) Exercise is good for Diabetes Mellitus. [2013]

Ans :- → For uptake of plasma glucose GLUT-4 transport protein on cell surface is an utmost requirement.

→ Exercise like the insulin action causes migration of GLUT-4 molecules from cytoplasmic compartment to the cell surface.

→ Where they bind with plasma glucose & transport the glucose to the intracellular compartment.

→ In diabetes mellitus, this action helps the cells to uptake the plasma glucose & reduce its elevated level.

→ Thus, helps to reduce the effects of glucose intoxication & cellular starvation, thus helps to improve the condition of diabetic patients.

(2) Metabolic acidosis may be found in diabetes mellitus. (2013)

Ans→ a) Insulin inhibits hormone sensitive lipase

Fat —(Hormone sensitive lipase; ⊖ Insulin)→ free fatty a (FFA)

b) In, Diabetes mellitus
↓
In absence / ↓ an amount of Insulin
↓
↑ activity of Hormone sensitive lipase
↓
↑ FFA levels
↑ FFA ⟶ catabolised to acetyl coA
↓ β-oxidation
Most of the acetyl coA converted into ketone bodies in liver due to deficiency of acetyl coA carboxylase (Insulin is req. for its action)
↓
↑ Acetone, ↑ Acetoacetate, ↑ β-hydroxybutyrate
↓
Diabetic ketoacidosis
(ketone bodies are acidic)

(3) Diabetes mellitus is characterized by polyuria polyphagia. (2010)

Impaired glucose utilizat^{n} in the ventromedial nucleus of the hypothalamus due to lack of insulin

↓

↓ activity of the satiety center

↓

So, there is no longer suppression of the apetite center

↓

↑ hunger

No inhibition of the neuropeptide Y secreting neurons of the hypothalamus

↓

Neuropeptide Y stimulates feeding center

↓

Polyphagia

④ Food intake is increased in Diabetes mellitus. [2008]

Ans:→ In Diabetes Mellitus due to lack of insulin mediated uptake of glucose through GLUT-4 transporters is significantly reduced in various cells of the body.

→ Thus, the uptake of glucose is reduced in satiety center located in ventroposteromedian nucleus (as it requires GLUT-4 mediated uptake) this lifts the inhibition by it on the feeding center located in the lateral part of hypothalamus, thus resulting in the sensation of hunger (carving for meal) resulting in polyphagia.

→ Also due to lack of uptake of glucose there is no inhibition of nucleopeptide Y secreting neurons of hypothalamus & neuropeptide Y stimulates feeding center resulting in polyphagia.

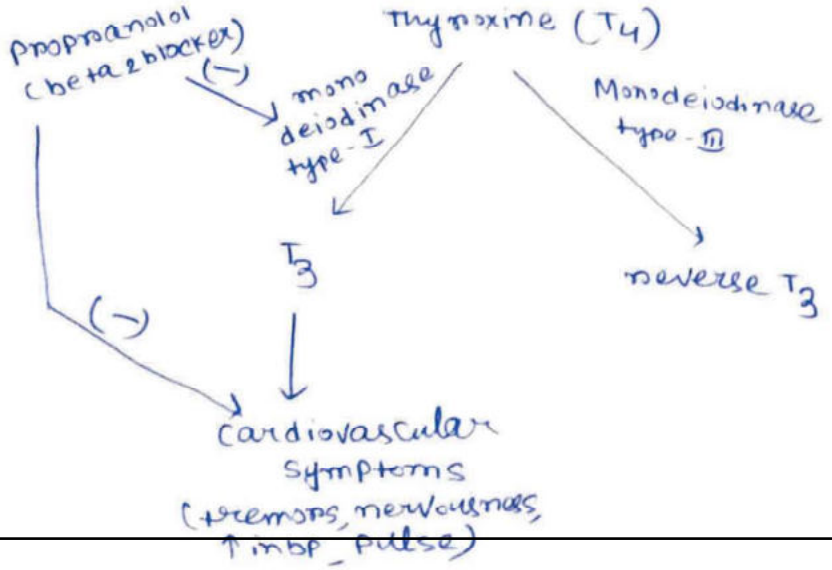
In hyperthyroid state, beta 2 blocker are used. [2009]

Ans:- In hyperthyroidism, there is an excess of thyroid hormone (T_4 & T_3) production and secretion.

- Due to this, it increases the number and affinity of β- adrenergic receptors in the heart highly.
- So, It may result in increase in heart rate, cardiac output, pulse pressure, tremors and nervousness.
- To reduce these symptoms beta 2 blocker like ~~Propa~~ propranolol is used.

- In hyperthyroidism, increase in T_3 may put the patient at risk for developing high output cardiac failure.

Propranolol will not only control tachycardia and tremors, it also inhibits conversion of T_4 to T_3 because it inhibits monodeiodinase type-I enzyme. Then, T_4 is converted into reverse T_3 which is metabolically inactive.



6. Hyperglycemia after pancreatectomy is corrected by hypophysectomy in experimental animal (2006)

Ans:- After pancreatectomy there will be deficiency of insulin. So,

- There is decrease in peripheral glucose utilization.
- Glycogenolysis and neoglucogenesis are promoted.
- So, due to actions of other antagonistic hormones blood glucose level is highly increased. So hyperglycemia is seen.

But ~~if~~ it is corrected by hypophysectomy in experimental animal because of the antagonistic effects of insulin and hormones of ant. pituitary.

- Adrenocorticotropic hormone, thyroid stimulating hormone and GH secreted from anterior pituitary all produce diabetogenic features ~~in~~ by increasing neoglucogenesis, glycogenolysis, blood glucose level in absense of insulin in a pancreatectomized animal.

So, Hypophysectomy abolishes hyperglycemia after pancreatectomy.

(7) Thyroid dwarfs are mentally retarted. [2005]

Ans. :-
- Thyroxine is essential for the development of brain & neuronal growth particularly during the period beginning from the 2nd trimester in utero to 6 months after birth.
- Deficiency of thyroid hormone in this period may lead to permanent mental retardation.

(8) Hyperpigmentation of skin in Addison's disease. [2004].

Ans. :-
- The ACTH molecule shares the same amino acid sequence as that of MSH.
- That's why, ACTH hypersecretion, as occurs in Addison's disease, causes deposition of the pigment melanin in the skin similar to action of MSH.
- This hyperpigmentation leads to darkening of skin in Addison's disease where secretion of ACTH is high due to (-)ve feedback.

Explain why

- Acromegaly may be associated with visual field defect. [3] [2019]

Ans:-

- Acromegaly occurs as a result of hypersecretion of growth hormone in adults after closure of epiphyses, for that only periosteal bone growth is increased.
- visual field defects may be bitemporal hemianopia or ~~bitemporal~~ binasal hemianopia
- Acromegaly may be caused by pituitary tumour. In this condition, also there is hypersecretion of GH.
- But in pituitary tumour, it ~~aaa~~ adds pressure on central part of optic chiasma leading to bitemporal hemianopia i.e visual field defect.

So, Acromegaly may be associated with visual field defect.