

Q. Glucocorticoids? / corticosteroids.

Mineralocorticoids

- Adrenal gland $\left\{ \begin{array}{l} \text{cortex} \rightarrow \text{steroidal hormones} \\ \text{medulla} \rightarrow \text{adrenaline, nor-adrenaline} \end{array} \right.$

- Mineralocorticoid \rightarrow Zona glomerulosa

Glucocorticoid \rightarrow fasciculata

Adrenaline \rightarrow reticularis

- Rate of secretion $\left. \begin{array}{l} \text{1 mg daily} \rightarrow \text{Hydrocortisone} \\ 0.125 \text{ mg daily} \rightarrow \text{Aldosterone} \end{array} \right\} \begin{array}{l} 3 \text{ AM} - 8 \text{ PM} \\ \text{Sleep time} \end{array}$

Pharmacology actions

Glucocorticoid actions.

1. CARB MET \rightarrow \uparrow uptake & utilisation of glucose
 \uparrow G. neogenesis

MOA: Translocation of GLUT4 to deeper sites.

\uparrow Induction of gluconeogenic enzymes

Effect: Hyperglycemia - resistant to insulin

2. PROTEIN METABOLISM \rightarrow protein breakdown
- AminoAc mobilization
- Excess urea produced - Negative N₂ balance
- loss of bone matrix (osteoporosis)

Clinical effect: \uparrow catabolism
 \downarrow anabolism.

3. FAT METABOLISM

- Lipolysis occurs → redistribution of body fat that is deposited over face, neck, shoulder → moon face, buffalo hump, fish mouth, thin limbs → Cushing syndrome.

4. CALCIUM MET

- Inhibition of Ca metabolism
 - Enhancement of Ca⁺ excretion
- } neg cal balance
- Effected : osteoporosis

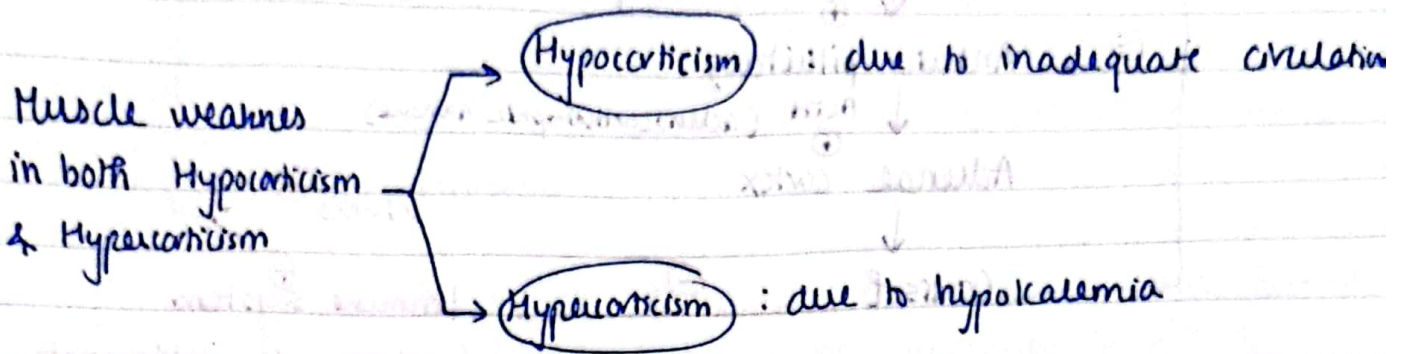
5. H₂O EXCRETION

- Enhances secretory activity of renal tubules
- Glucocorticoids have weak mineralocorticoid action, causes Na⁺ & H₂O retention, ↑ K⁺ excretion
- Thus prolonged use can cause edema & H.T.

• CVS •

- Glucocorticoids have Na⁺ & H₂O retention property, exert a permissive effect on pressor action of adrenaline & angiotensin.
- On chronic administration, these drugs may cause CHF worsening & H.T. (↑ tone of muscle ↑ contraction ✓ H.T.)

7. Skeletal muscle - corticosteroids are req for normal func of skeletal muscle



8. CNS
- Mild euphoria
 - ↑ motor activity
 - insomnia
 - anxiety.

UCA

★ 2 days causes peptic ulcer

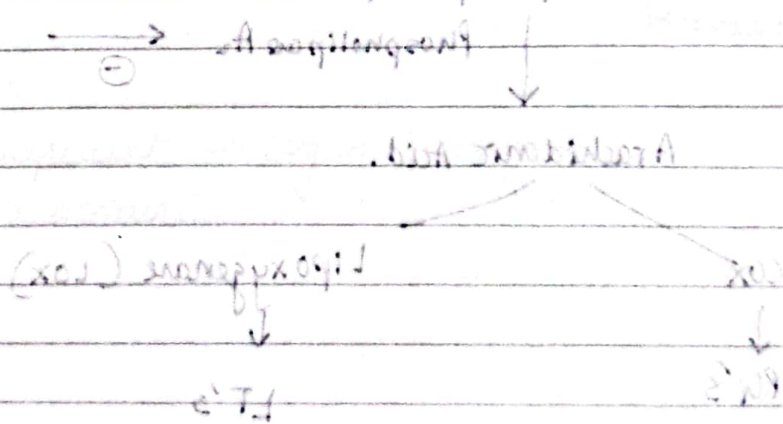
- Corticosteroids
- NSAID'S

9. GI
- ↑ gastric acid secretion & pepsin
 - peptic ulcer.

10. BLOOD CELLS

- ↓ in count of all blood cells like

- RBC
- Lymphocyte
- Eosinophils
- Basophils
- Neutrophils
- Platelets

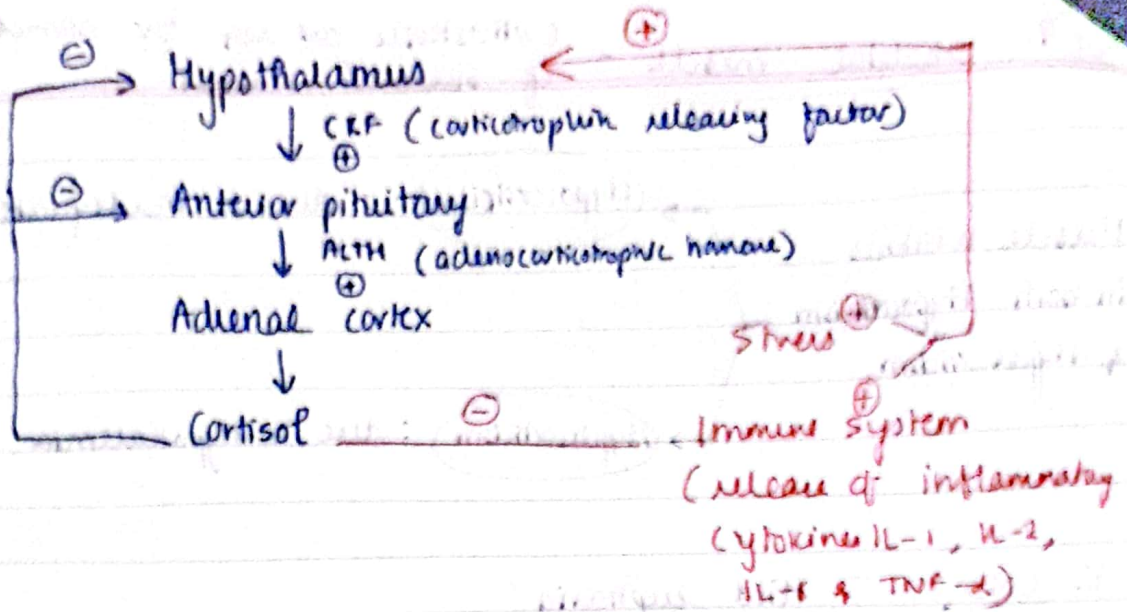


11. LYMPHOID TISSUE

- They have lytic response in malignant lymphatic cells.

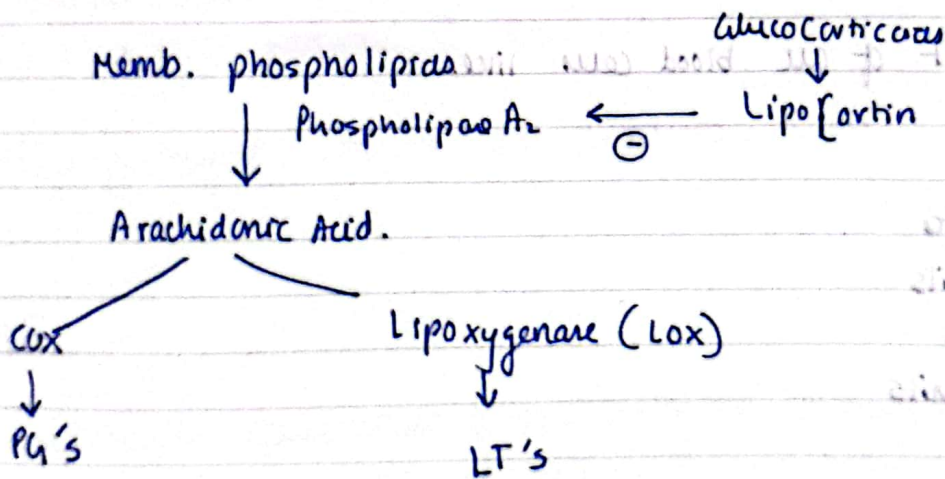
litwics: LYMPHOMA.

HYPOTHALAMO-PITUITARY AXIS



12. INFLAMMATORY RESPONSE

- They have very potent Anti-I response.
- They prevent / suppress ^{all the inflammatory mediators thus ↓} the clinical features of inflammation such as heat, redness, pain, swelling.

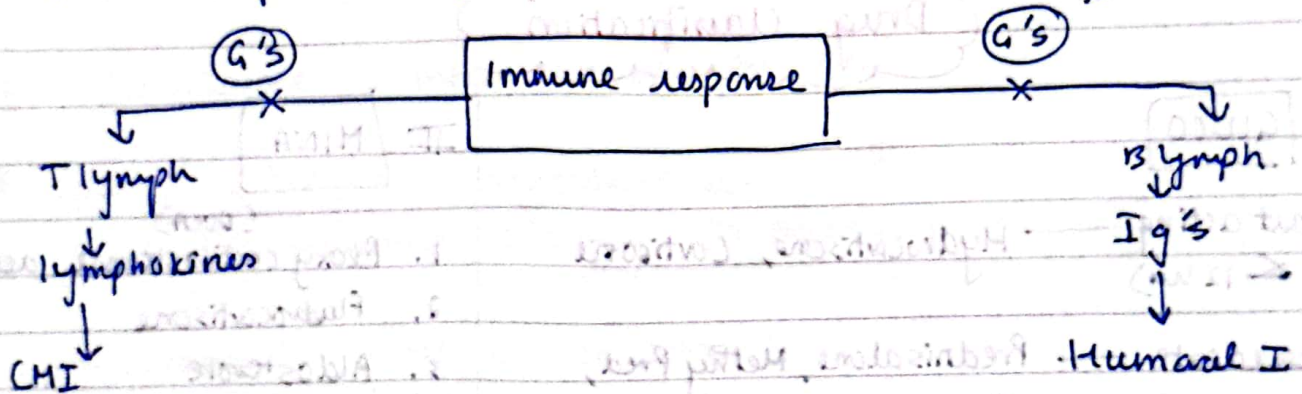


Explanation: -G's induce a protein called lipocortin which inhibits phospholipase A₂ : hence PG's & LT's

- Production of cytokines like (IL-1, IL-6, TNF- α) which is necessary for initiating inflammation is inhibited.
- Chemotaxis is suppressed.
- G's stabilize lysosomal membrane & prevent release of inflammatory mediators.
- G's inhibit expression of various molecules on endothelial cells, thus inhibiting leucocyte migration to site of injury.

13. IMMUNE RESPONSE

- Suppress all sorts of ~~the~~ hypersensitivity reactions
- Greater suppression of CMI (cell mediated immunity)



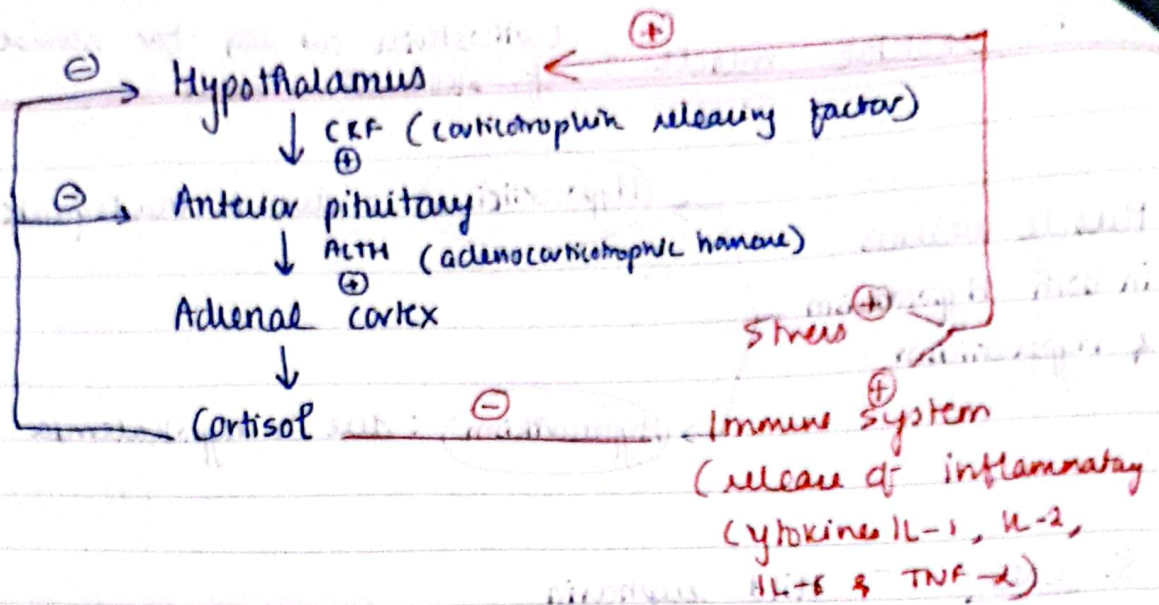
- Clinical :
- Immunosuppressant \rightarrow Organ transplant.
 - Allergic reactions.

Mineralocorticoid actions

1. Enhances sodium reabsorption in ADH
2. \uparrow K^+ excretion
3. Water retention.

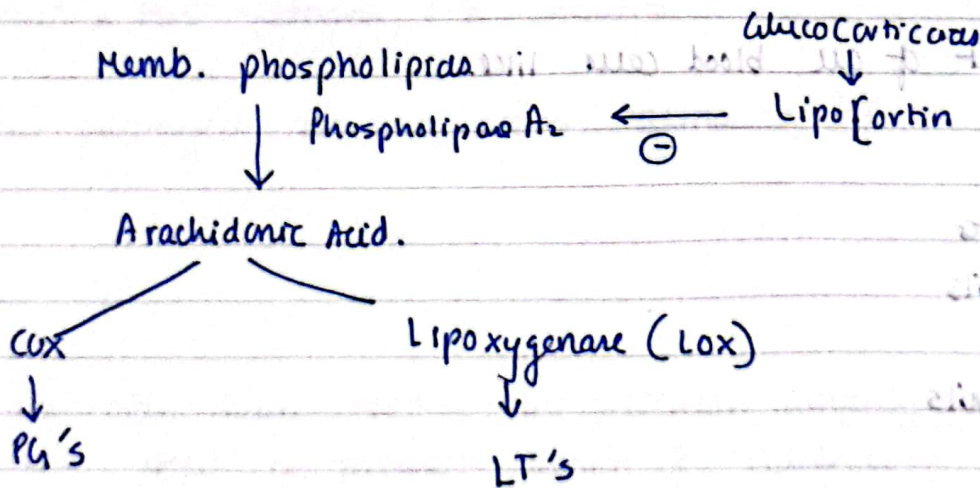
Clinical : HT & water retention.

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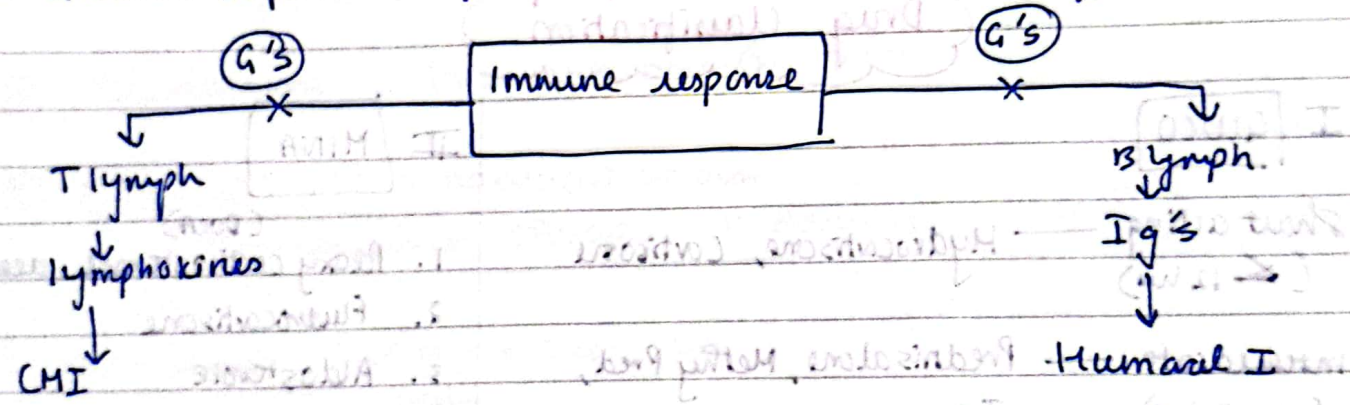
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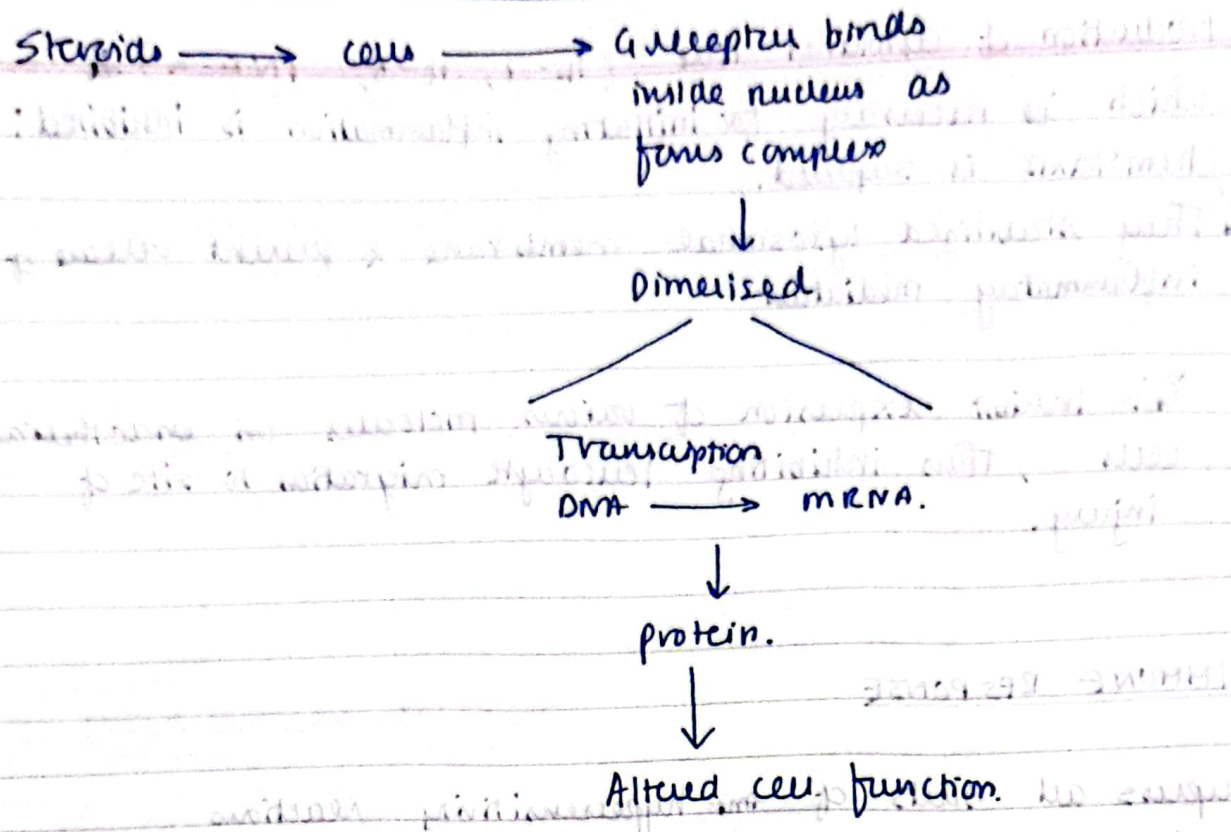
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Clinical : HT & water retention.

M.O.A of corticosteroids



Drug Classification

I GLUCO

- Short acting (≤ 12 hrs) — Hydrocortisone, Cortisone
- Intermediate (12 - 36 hrs) — Prednisalone, Methyl Pred, Triamcinolone
- Long acting (> 36 hrs) — Paramethasone, Dexamethasone, Betamethasone.

II MINA

- (DOCA)
1. Deoxy corticosterone acetate
 2. Fludrocortisone
 3. Aldosterone

*
 PK: - except DOCA all absorbed orally
 - Met by CYP450
 - Prone to DI
 - excreted in urine after being met ⁱⁿ liver by conjugation.

1) Hydrocortisone - Rapid onset.
- ⊖ equal M & G activity
- ✓ i.v, topically

2) Cortisone : - Prody of ①

3) Prednisolone - 4x, potent.
- HPA suppression
- Selective 'G' activity

4) Methylp - More selective & potent than ③
- ✓ transplantation *

5) Triamcinolone : - More potent than ③
- Selective 'G' action

6) Dexamethasone & Betamethasone - v. potent, ✓ Highly selective
- Supp of HPA
- ✗ fluid retention / ✗ HT

* used in cerebral edema & reduce intra cranial tension

7) Paramethasone - Intermediate b/w ③ & ⑥

8) DOCA : - Only mineralocorticoid
- replacement therapy in Addison's disease *

9) Fludrocortisone ✓ Min & Gluco action
✓ orally.
✓ Addison's disease.

10) Aldosterone - **(MOST)** POTENT MINERALOC
- ✗ used because ↓ bioavailability.
Difficulty in dose regulation

uses: Replacement therapy

① Acute adrenal insufficiency

- Hydrocortisone / dexamethasone + Saline / Glucose

② Chronic adrenal infus (Addison's disease)

- Hydroc + DOCA

③ Congenital Adrenal hyperplasia (Adrenogenital syndrome)

- genetic deficiency of 21-hydroxylase.
- Hydroc + Fluoroc daily.

non-endocrinal uses:

- Skin
- Intermittent
- Collagen.
- Autoimmune.
- Lung.
- Infectious
- Eye
- Cancers (ALL, Hodgkin's lymphoma)
- Rheumatoid arthritis.
- Osteoarthritis
- Gout

dream

Adverse effects:

1. HPA suppression.
2. CNS: behavioural disturbances, insomnia
3. Eye: Glaucoma, cataract.
4. GIT: peptic ulcer.
5. Cushing's habits: moon face buffalo hump
6. Met defects: Hyperglycemia.
7. water retention, Na⁺ retention.
8. hypokalemia → muscle weakness → myopathy.
9. osteoporosis.
10. Growth retardation (in Rex & ketamethasone) Children

Contraindications

1. Peptic Ulcer
2. DM.
3. HT
4. Preg
5. ~~Malabsorption~~ TB
6. Osteoporosis.
7. Epilepsy.
8. Renal failure
9. Bycosse.
10. Chronic \heartsuit failure.

general immersion in corticosteroids therapy:

- single & short dose x ramped
- long term dangerous.
- x abrupt with adrenal HPA suppression

To minimize HPA supp:

- \checkmark share \downarrow acting drug \checkmark short period.
- alternate day dose.
- local preparation \checkmark

Steroid syn inhibitors / Antagonists \star MCQ.

1. Metyrapone (int. of Cushing syn)
2. Aminoglutethimide (bust cancer, Cushing syn due to human)
3. Trilostane (Cushing, primary hyperaldosteronism)
4. ketakonazole
5. Mifepristone (anti progesterin drug)
gluco receptor antagonist