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★ Imp. Point mentioned by doctor!

Interoduction:

ANATOMICALLY:

- The adrenal gland is situated on the anteriosuperior aspect of the kidney and receives its blood supply from the adrenal arteries.

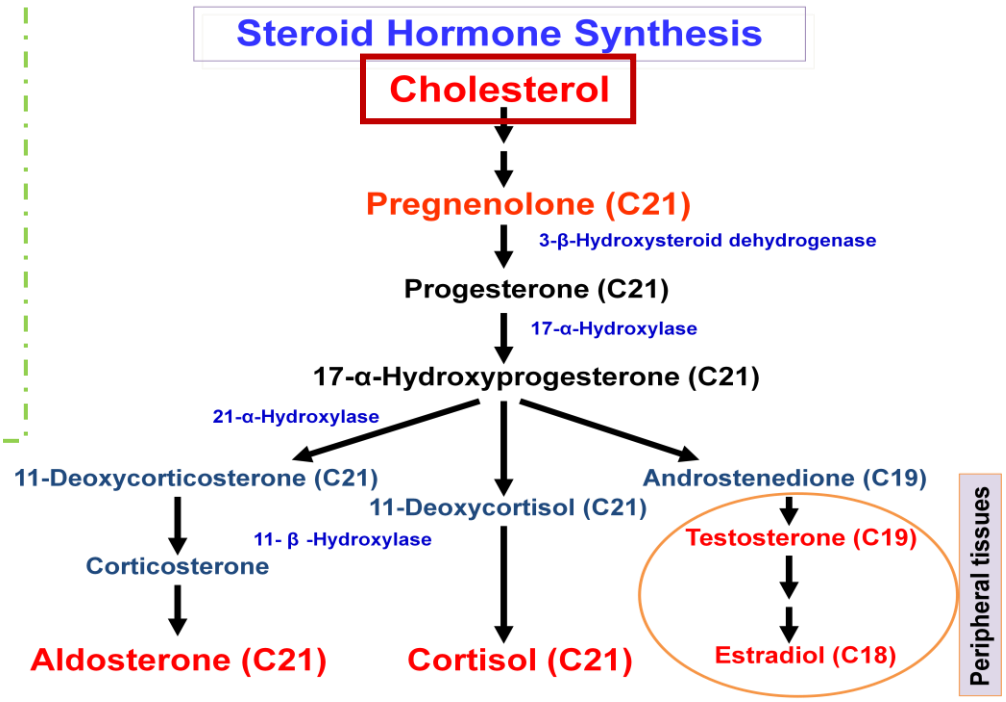
HISTOLOGICALLY:

- The adrenal gland consists of two distinct tissues of different embryological origin, the outer cortex and inner medulla.

➢ **The adrenal cortex comprises three zones based on cell type and function:**

Zona glomerulosa	• The outermost zone → aldosterone (the principal mineralocorticoid).
Zona fasciculata	• The deeper layers of the cortex → glucocorticoids – mainly cortisol (95%) is the most important in man.
Zona reticularis	• androgen production – mainly testosterone.

From this diagram you only have to know that cholesterol is the precursor of adrenal cortex hormones !



Aldosterone Hormone:

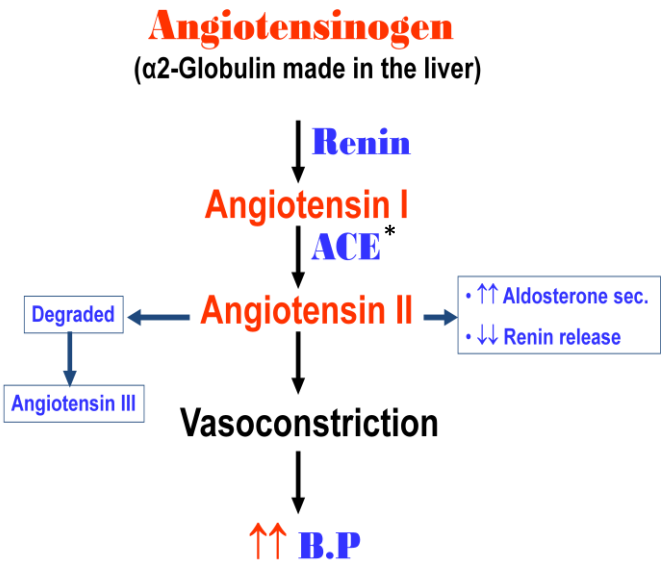
- The principal physiological function of aldosterone is to conserve Na^+, mainly by facilitating Na^+ reabsorption and reciprocal K^+ or H^+ secretion in the distal renal tubule.
- aldosterone is a major regulator of water and electrolyte balance, as well as blood pressure.
- Aldosterone, by acting on the distal convoluted tubule of kidney, leads to:
  - ✓ ↑↑ potassium excretion
  - ✓ ↑↑ sodium and water reabsorption
- Renin-Angiotensin system is the most important regulatory mechanism for aldosterone secretion

The renin - angiotensin system:

- It is the most important system controlling aldosterone secretion.
- It is involved in B.P. regulation.

Renin:

- a proteolytic enzyme produced by the juxtaglomerular cells (JGC) of the afferent renal arteriole.
- Sensitive to B.P. changes through baroreceptors
- released into the circulation in response to :
  1) a fall in circulating blood volume.
  2) a fall in renal perfusion pressure.
  3) loss of Na^+.



Team Notes:

✓ Low aldosterone lead to ↓ Na ,↑ K and hypotension.
✓ Aldosterone has (-ve) feedback on rennin.
✓ Renin from JGC of kidney have a baroreceptor that sense hemorrhage, hyponatremia ,cardiac problem (↓ C.O) → stimulate renin to be secreted.
✓ Proteolytic enzyme convert angiotensinogen (by removing some of the AA) to give the active form (angiotensin 1)
✓ * ACE= angiotensin converting enzyme

Remember !
In the cortisol the regulator is ACTH BUT in aldosterone the regulator is renine angiotensin system

Causes of adrenocortical hypofunction:

A. Primary destruction of adrenal gland:	B. Secondary to pituitary disease:
• Autoimmune • Infection, e.g., tuberculosis • Infiltrative lesions, e.g., amylodosis	• Pituitary tumors • Vascular lesions • Trauma • Hypothalmic diseases • Iatrogenic (surgery or radiotherapy) • sudden withdrawl of corticoids therapy

Team notes:
2ry adrenal hypofunction **not** called addison's

Remember !
In cushing's the primary disease→problem in the pituitary ?
BUT
primary addison's the →problem in the adrenal gland it self

Signs and symptoms of primary adrenal failure (Addison's disease):

The symptoms are precipitated by trauma, infection or surgery:

- Lethargy, weakness, nausea & weight loss.
- Hypotension especially on standing (postural)
- Hyperpigmentation (buccal mucosa, skin creases, scars)
- Deficiency of both glucocorticoids and mineralocorticoids
- Hypoglycemia, ↓ Na^+, ↑ K^+ and raised urea
- Life threatening and need urgent care.

Team notes:
- In cushing it is the opposite (hyperglycemia,↓K,↑Na)
- Life threatening b\c of the hypotension
- ↑urea b\c of dehydration (Na excereted & pull water with it)

MCQ! ★

Pt. with hypotension and hyperpigmentation…?

Addison's disease

Hyperpigmentation in Addison's disease:

- Hyperpigmentation occurs because melanocyte-stimulating hormone (MSH) and (ACTH) share the same precursor molecule, Pro-opiomelanocortin (POMC).
- The anterior pituitary POMC is cleaved into ACTH, γ-MSH, and β-lipotropin.
- The subunit ACTH undergoes further cleavage to produce α-MSH, the most important MSH for skin pigmentation. (hypofunction→↓cortisol→stimulate pituitary to secrete more ACTH→more α -MSH→melatonin secretion "no –ve feedback)
- In secondary adrenocortical insufficiency, skin darkening does not occur. (b\c

Investigation of Addison's disease (AD):

Team notes!

✓ primary → ↓cortisol, ↑ACTH

✓ Secondary → both ↓ (cortisol &ACTH)

- The patient should be hospitalized
- Basal measurement of:
  - Serum urea, Na^+, K^+ & glucose
  - Serum cortisol and plasma ACTH
- Definitive diagnosis and confirmatory tests should be done later after crisis.
- Simultaneous measurement of cortisol and ACTH improves the accuracy of diagnosis of primary adrenal failure(Addison):
  Low serum cortisol (<200nmol/L)
  High plasma ACTH (>200 ng/L)
  (measure them at the same time b\c of the diurnal rhythm)

Team notes!
Don't make the confirmatory test unless you treat the pt. especially from hypotension.

Confirmatory Tests:

1. Short tetracosactrin (Synacthen) test (Short ACTH stimulation test)	2. Adrenal antibodies	3. Imaging (Ultrasound/CT)
• Measure basal S. cortisol • Stimulate with I.M. synthetic ACTH (0.25 mg) • Measure S. cortisol 30 min after I/M injection • Normal: ↑ of S. cortisol to >500 nmol/L • Failure of S. cortisol to respond to stimulation, confirm AD. • Abnormal results: – emotional stress – glucocorticoid therapy – estrogen contraceptives.	• Detection of adrenal antibodies in serum of patients with autoimmune Addison's disease	• Ultrasound or CT for adrenal glands for identifying the cause of primary adrenal failure

No need to know the steps of the procedures

Team notes!
✓ (only for your information =))
Tetracosactrin: Tetra = 4 , Cosac= 20
24 active AA which is similar to the active AA of the ACTH
✓ S.= serum

Investigation of Secondary AC Insufficiency:

- Low serum cortisol with low plasma ACTH ★ !
- No response to short synacthen test: Adrenocortical cells fail to respond to short ACTH stimulation

❖ Depot (prolong) Synacthen test (confirmatory test)

1. Measure basal S. cortisol
2. Stimulate with I.M. synthetic ACTH (1.0 mg) on each of three consecutive days
3. Measure S. cortisol at 5 hours after I.M. injection on each of the three days

✓ Interpretation of results:

- Addison's disease: No rise of S. cortisol >600 nmol/L at 5 h after 3rd injection.
- Secondary AC: Stepwise increase in the S. cortisol after successive injections

Summary Very Imp! :

Investigation for	A) Addison's disease:	B) Secondary AC Insufficiency:
★ Screening	• Basal plasma ACTH and basal serum cortisol, glucose, urea and electrolytes • High ACTH and Low cortisol	• Low ACTH and Low cortisol
★ Confirmation	• Short ACTH stimulation test: No response	• Long ACTH stimulation test: Stepwise increase in S. cortisol (there is response b\c the adrenal is intact)
Others	• Adrenal autoantibodies • Ultrasound/CT adrenal glands	• Insulin-induced hypoglycemia • MRI pituitary gland