ADRENAL FUNCTION TESTS

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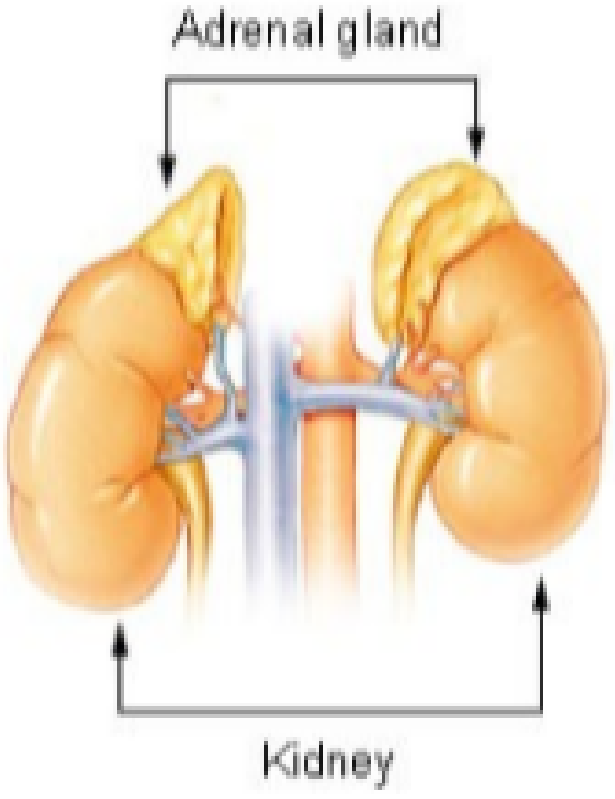
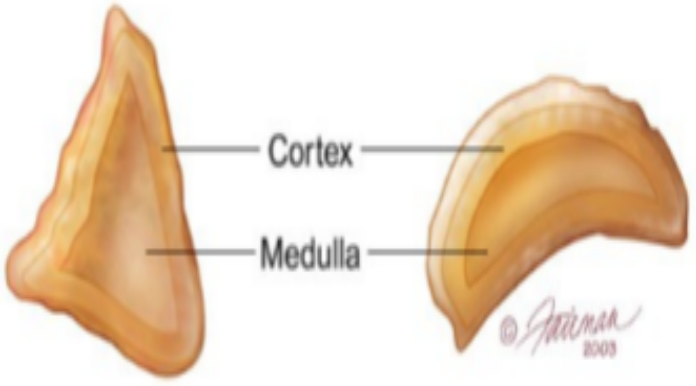
Adrenal Glands

SUPRARENAL GLANDS or ADRENAL GLANDS

- Paired organ each weight about 4 grams, pyramidal in shape, located on the top of the kidneys, one on each side at the level of T12
- It is enclosed by fibro elastic connective tissue - capsule



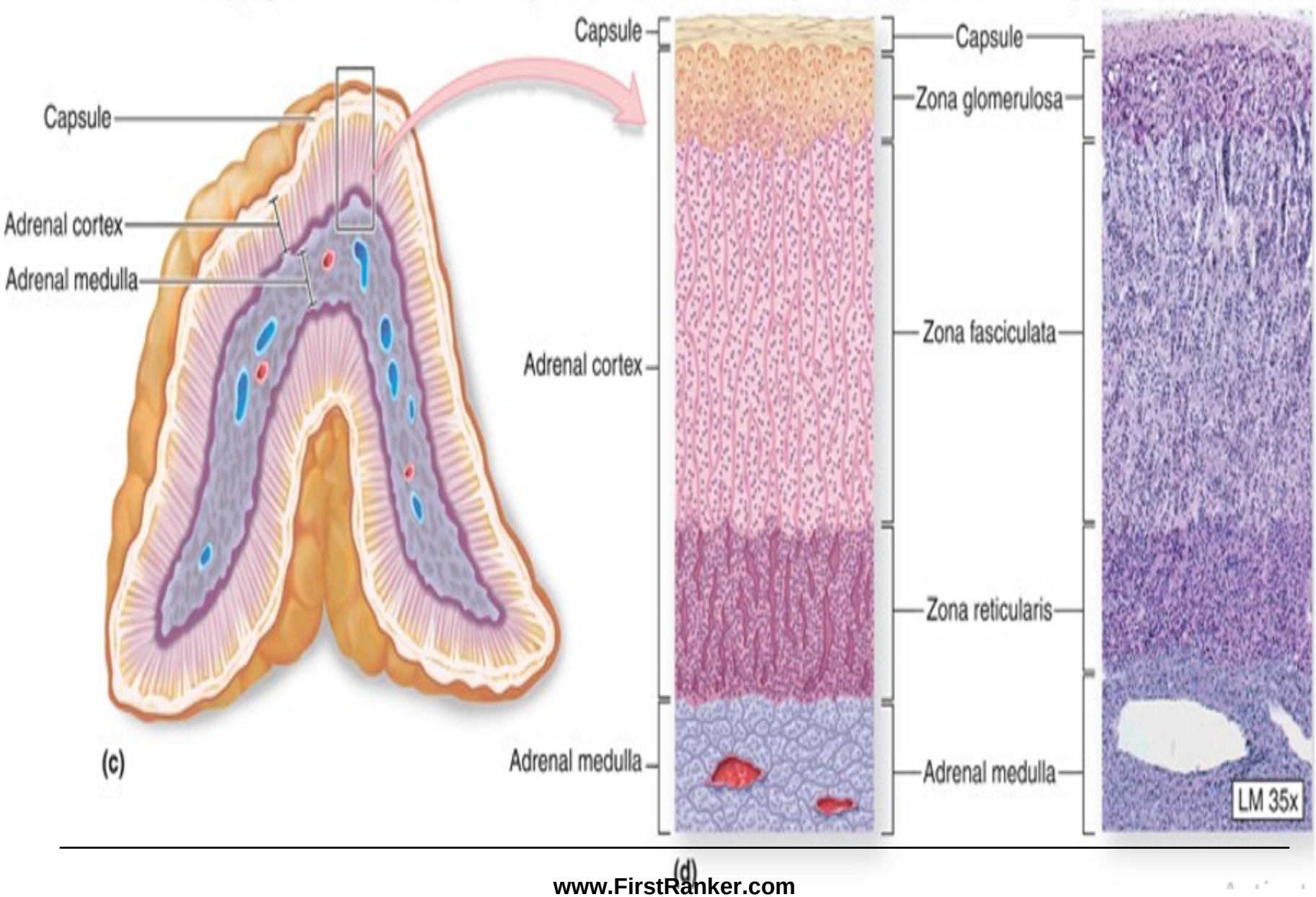
Adrenal Glands



Each gland is divided into two parts

- Cortex
  - – outer part of gland
  - – Part of hypothalamus – pituitary – adrenal axis
  - – Secrete a variety of steroid hormones
- Medulla
  - – inner part of gland, (20% of gland)
  - – Part of sympathetic nervous system
  - – Secrete catecholamines
- Both parts are structurally and functionally different

Histology of adrenal glands



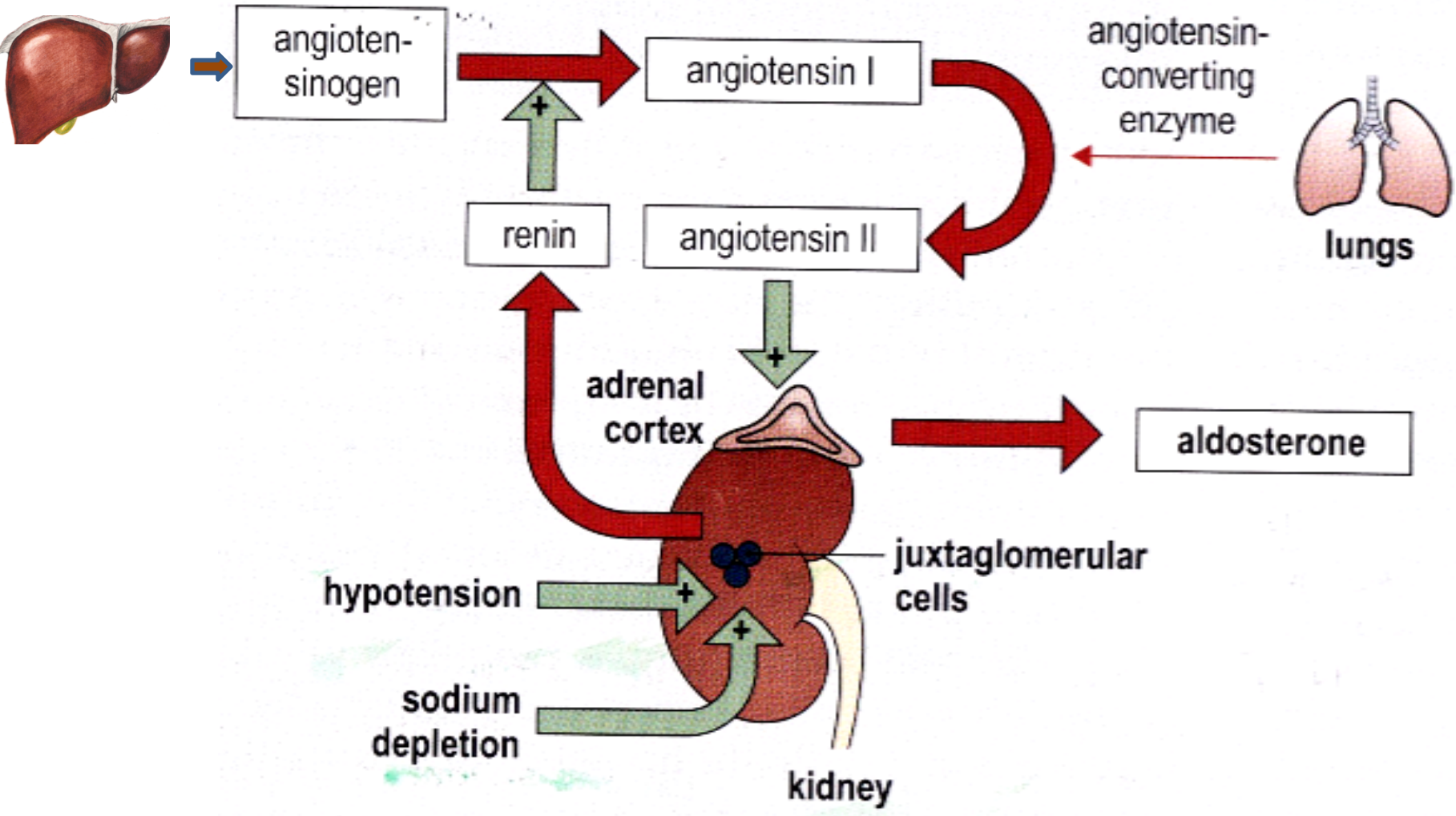
Adrenal cortex

- Zona glomerulosa:
  - Produce mineralocorticods
  - Mainly aldosterone (because it contain enzyme aldosterone synthase)

Hormones that help control the balance of minerals (Na+ and K+) and water in the blood

Adrenal cortex

ALDOSTERONE SECRETION



Adrenal cortex

Zona fasciculata

- Produce glucocorticods
  - Mainly cortisol and corticosterone
  - The human adrenal glands produce the equivalent of 35–40 mg of cortisone acetate per day

Hormone that play a major role in glucose metabolism as well as in protein and lipid metabolism

- The secretion of these cells is controlled by hypothalamic-pituitary axis via ACTH

Adrenal cortex

Zona reticularis

- The innermost layer of the adrenal cortex, lying deep to the zona fasciculata and superficial to the medulla
- These cells produce androgens

Adrenal cortex

Zona reticularis

–The androgens produced includes

. Dehydroepiandrosterone (DHEA) .

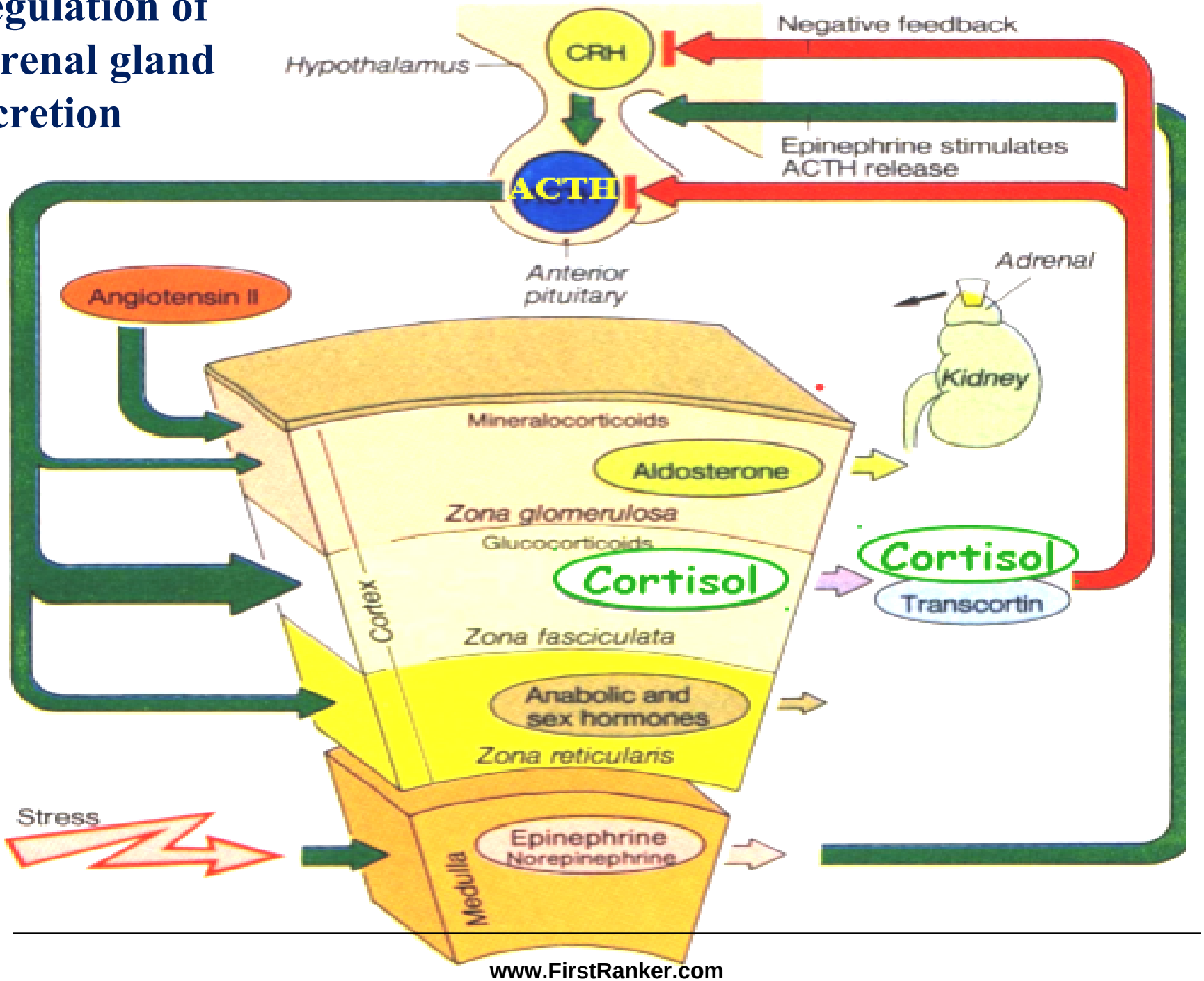
. Androstenedione

– Synthesized from cholesterol

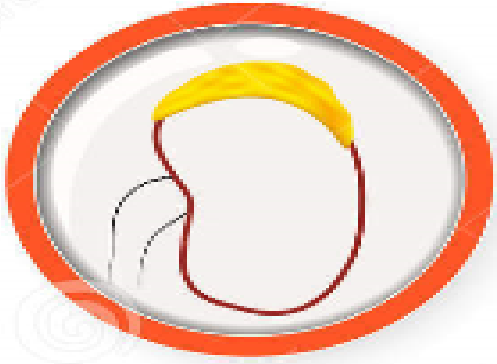
– DHEA is further converted to DHEA-sulfate via a sulfotransferase

– The androgens produced are released into the blood stream and taken up in the testis and ovaries to produce testosterone and the estrogens respectively

Regulation of adrenal gland secretion



ADDISON'S DISEASE



Adrenal glands not produce sufficient steroid hormones

Adrenal crisis:
- fever;
- syncope;
- convulsions;
- hypoglycemia;
- hyponatremia;
- severe vomiting and diarrhea.

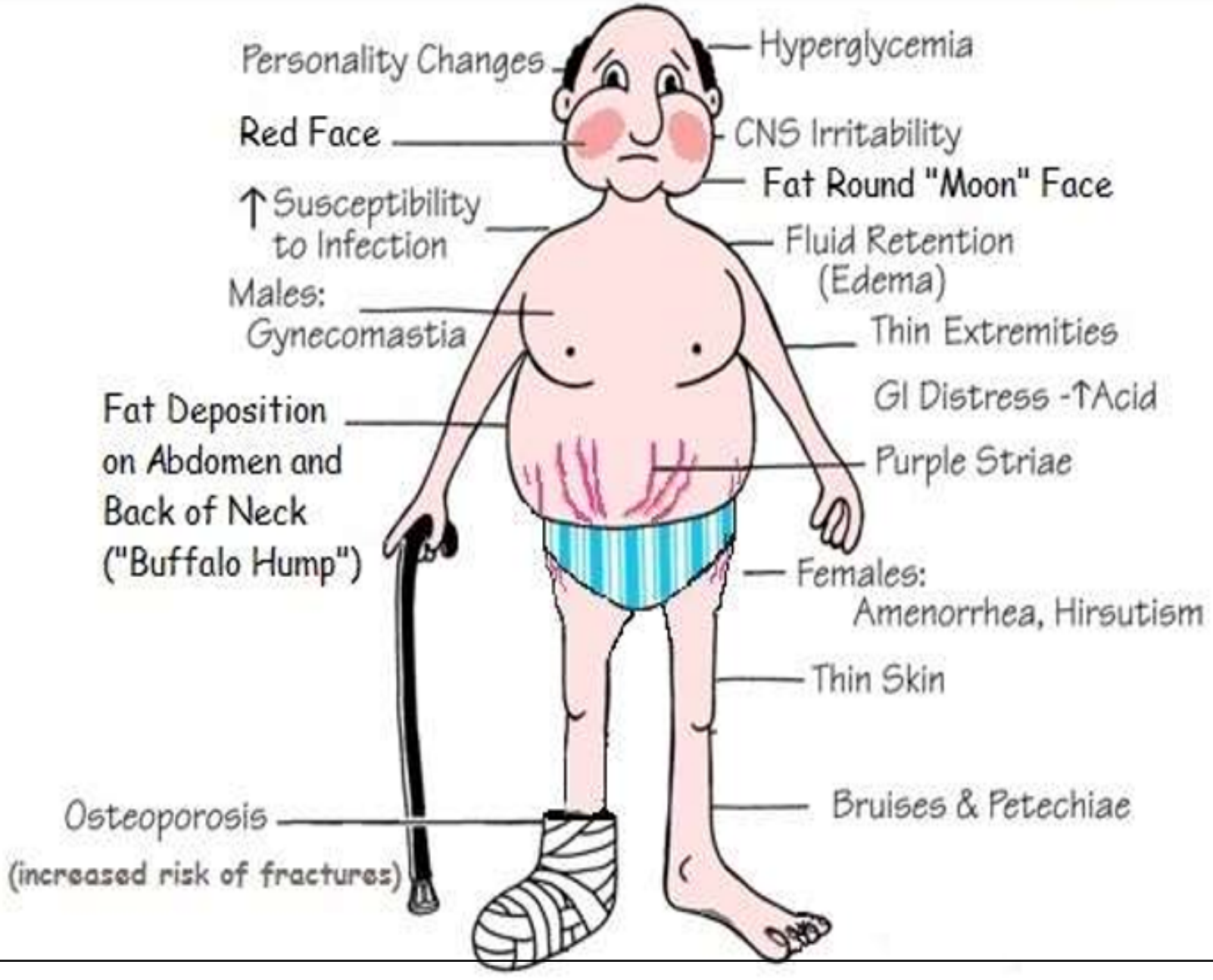
Skin
Hyperpigmentation

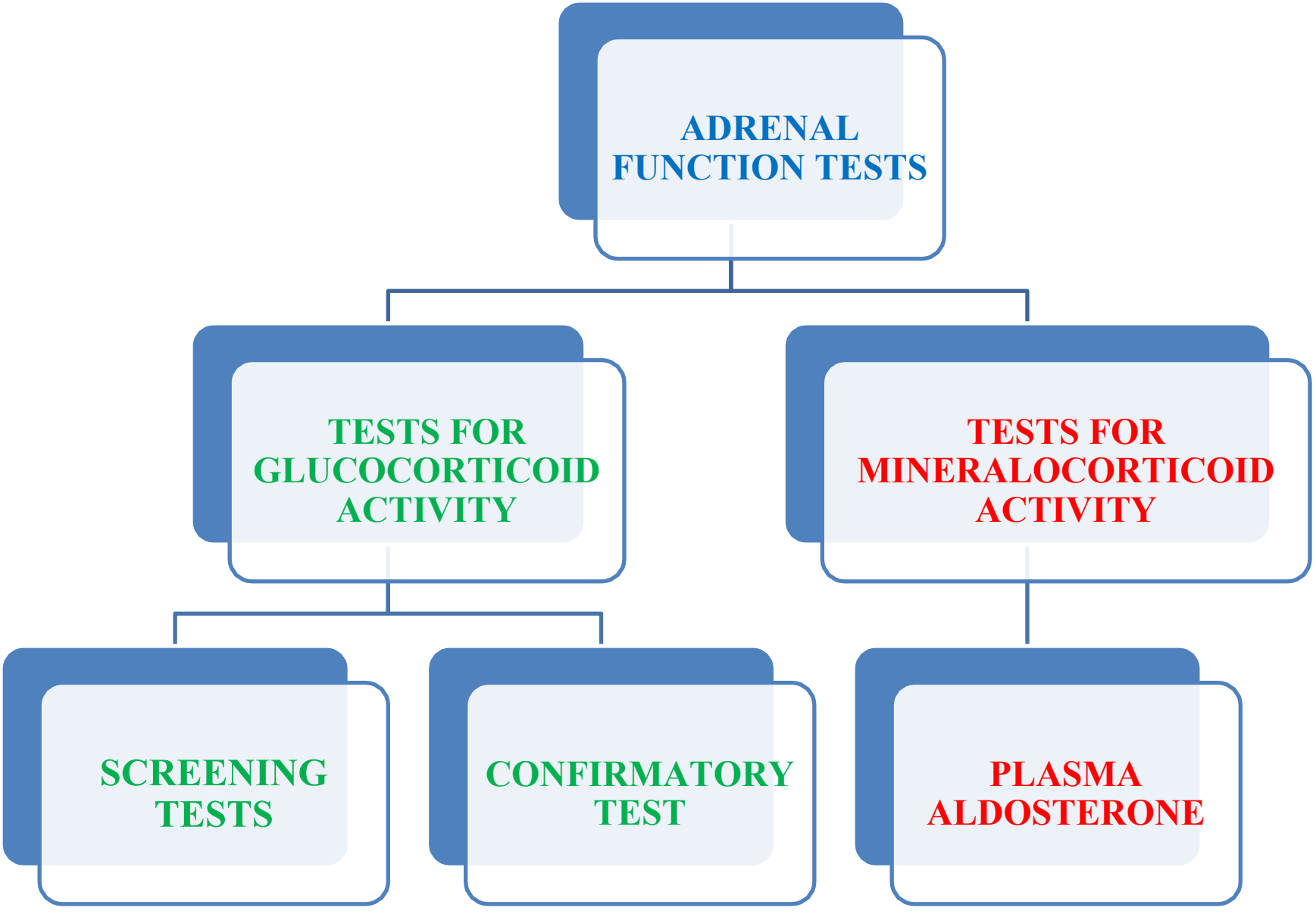
Low blood pressure
Weakness
Weight loss

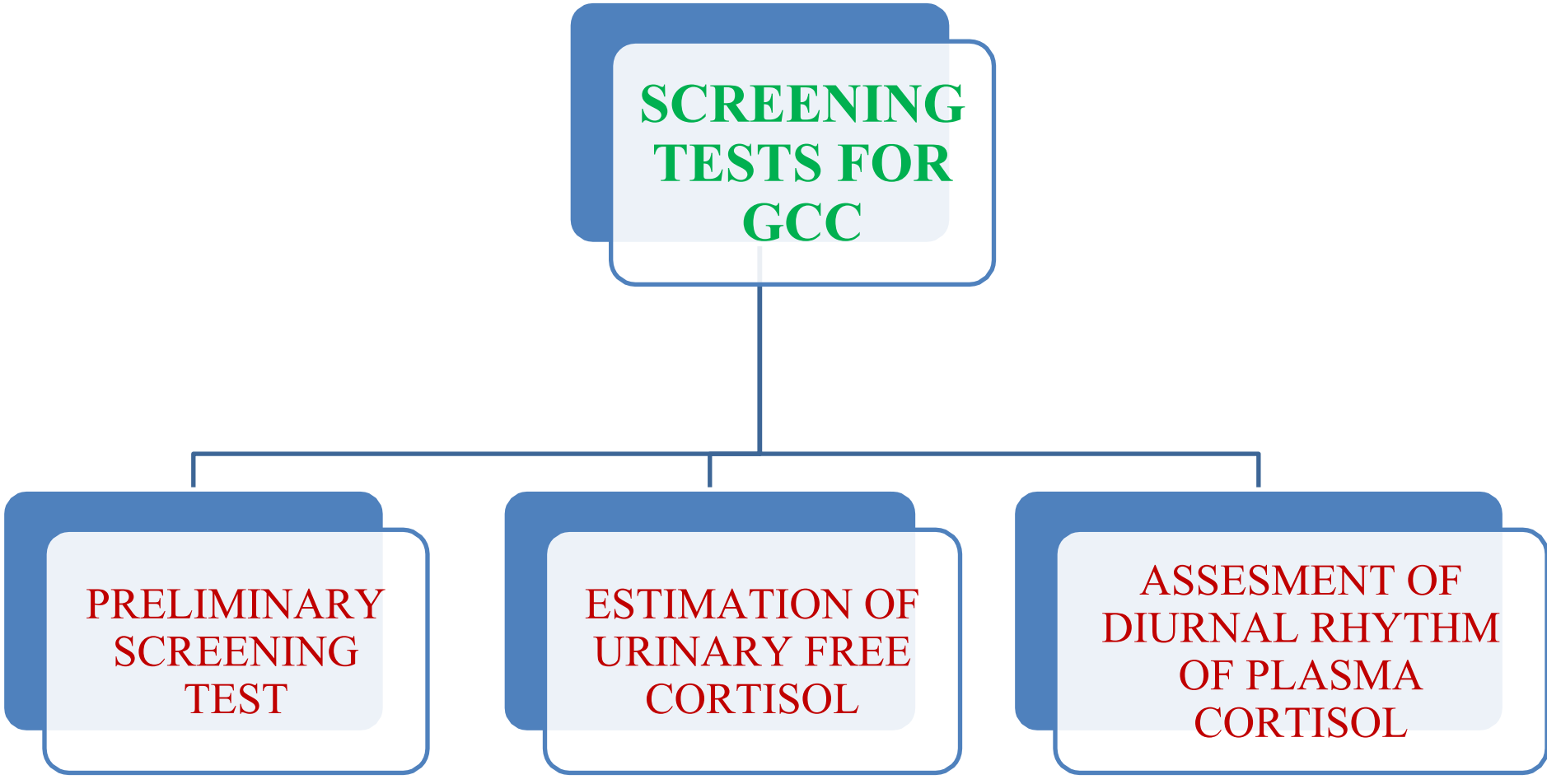
Gastrointestinal
Nausea
Diarrhea
Vomiting
Constipation
Abdominal pain

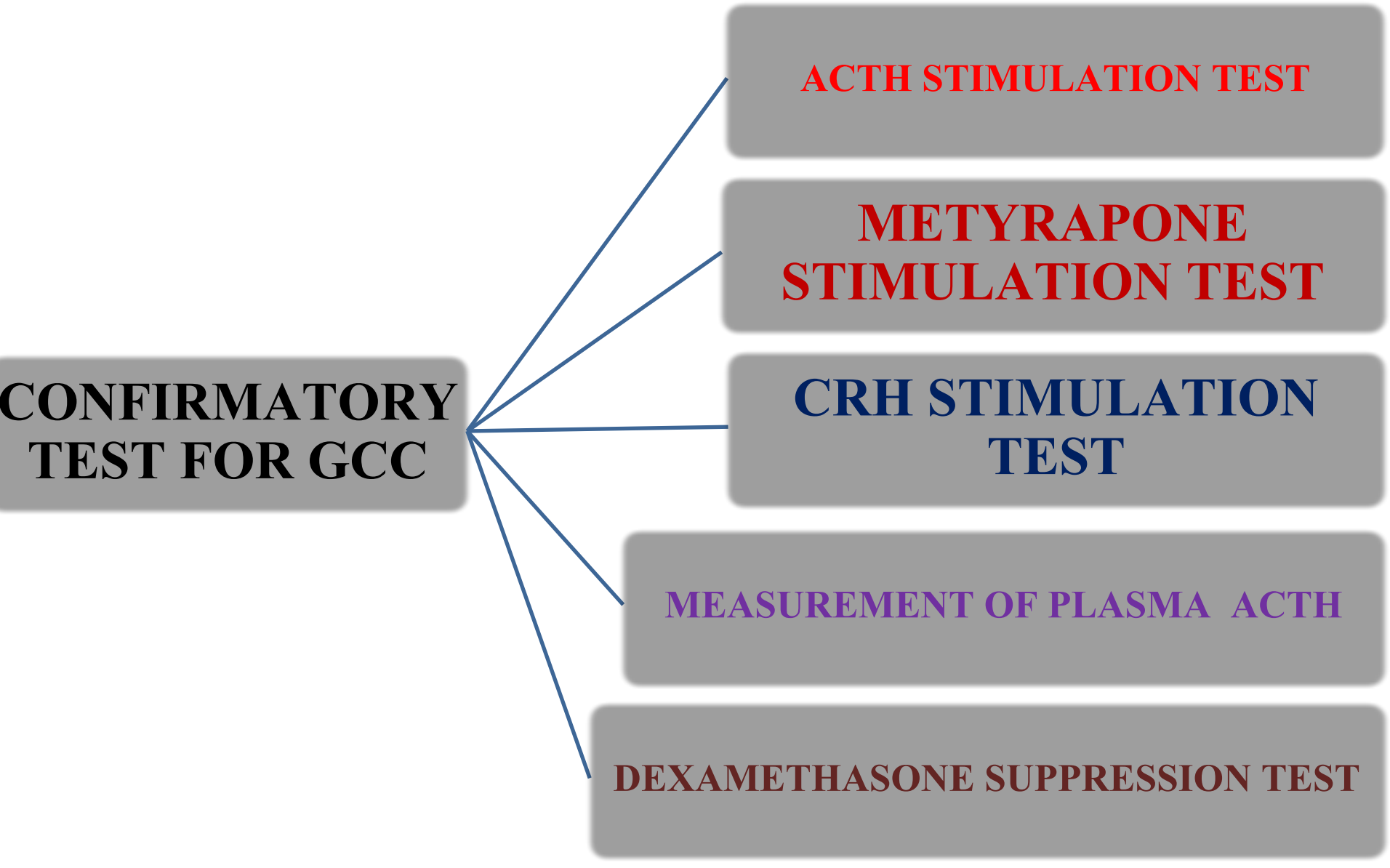
Skin
Vitiligo

CUSHING DISEASE SYMPTOMS









A. TESTS FOR GLUCOCORTICOID FUNCTIONS

SCREENING TESTS

1. PRELIMINARY SCREENING TEST

- The most potent effect of GCC is on carbohydrate metabolism.
- so evaluation of blood sugar and plasma cortisol at 8:00 AM are the initial tests.
- A high blood sugar or low sugar level along with changes in cortisol levels go in favour of adrenal cotex lesion.
- The initial screening is followed by further definite test

2. ASSESMENT OF DIURNAL RHYTHM OF PLASMA CORTISOL

- Plasma cortisol levels are about 10 times higher in the early morning hours than at midnight.
- Normal range for plasma cortisol

  At 8:00 AM – 8-26µg/dL

  At 12:00 AM - < 1µg/dL
- Loss of this diurnal rhythmicity is an early indication of a lesion at any point in the hypothalamic –pituitary –adrenal axis.
- Stress such as trauma, pain, apprehension, fever and hypoglycemia can also override this diurnal rhythm

3. Estimation of Urinary Free Cortisol

- Another useful screening test
- Urinary cortisol secretion is higher during day time (7 AM – 7 PM) than night (7 PM – 7 AM). Hence a properly collected 24 hours urine sample is required.
- Urine creatinine should also be measured to assess renal function and adequqte urine collection.
- Urine cortisol ranges from 10-100 µg/day.
- Levels of urine cortisol increases in hyperadrenalism and decrease in hypoadrenalism.

CONFIRMATORY TEST FOR ADRENAL CORTEX FUNCTION

- If the preliminary test shows that the adrenal function is increased (hyperadrenalism) or decreased (hypoadrenalism) then they are confirmed by further tests
- Hyperadrenalism is confirmed by SUPPRESSION TEST
- Hypoadrenalism is confirmed by STIMULATION TEST.
- These tests evaluate the pituitary adrenal axis and also the adrenal reserve.

1.DEXAMETHASONE SUPPRESSION TEST

A. LOW DOSE DEXAMETHASONE SUPPRESSION TEST

- This test is recommended if results of urinary free cortisol test are abnormal.
- Dexamethasone is a potent suppressor of pituitary ACTH and cortisol level.
- It causes about 50% fall in serum cortisol with a dose as low as 2mg .

The patient takes 2mg of dexamethasone at night

The next morning 8:00 AM plasma cortisol level is determined.

B. HIGH DOSE DEXAMETHASONE SUPPRESSION TEST

This test is carried out with administration of 2 mg dexamethasone every 6 hours for 2 days while collecting urine for 24 hrs.

Plasma and urine cortisol is determined

There is suppression of plasma cortisol in pituitary dependent Cushing disease.

If these parameters are not suppressed , adrenal tumors producing high levels of cortisol or ectopic ACTH producing tumors are usually the aetiology

2. Measurement of plasma ACTH

- Cortisol and ACTH interact in a feedback loop.
- Low levels of plasma cortisol associated with high plasma ACTH would indicate primary adrenocortical insufficiency.
- Likewise increased plasma cortisol will be associated with suppression of ACTH in primary adrenal lesion.
- In contrast, increased cortisol due to an ACTH producing pituitary adenoma (Cushing's disease) or due to ectopic production of ACTH will be associated with increased plasma ACTH levels.

3. ACTH STIMULATION TEST

- Useful in assessing adrenal reserve capacity
- Also used for documenting the existence of hormonal deficiency state.
- The test uses a synthetic form of ACTH *(Synacthen)*
- It consists of first 24 amino acids of ACTH, which is injected IM/ IV

A. SHORT ACTH STIMULATION TEST

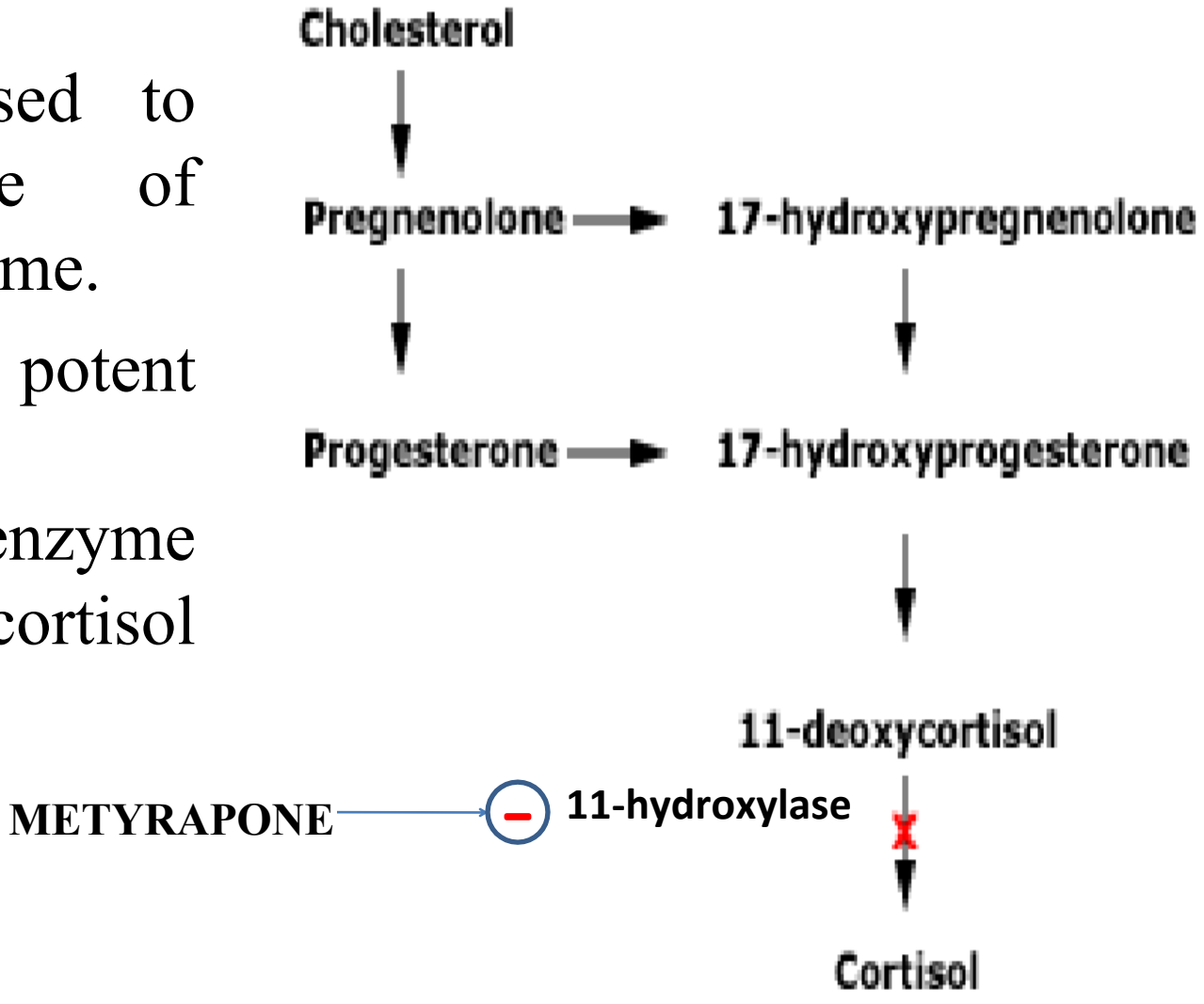
- 250 µg Synacthen is administered intramuscularly or intravenously
- Basal and post ACTH administration, cortisol measurement at 30 and 60 minutes is done.
- There should be a minimum rise of more than 7µg/dL over the basal level or plasma level should be more than 18µg/dL.
- Lower results show hypofunction of adrenal.
- Whereas a person with primary adrenal failure does not respond.

B. LONG ACTH STIMULATION TEST

- Here, lower dose of 1µg/day of ACTH is administered for several days to effectively stimulate adrenals than single dose of 250µg.
- This successfully assesses the adrenal insufficiency.

4. METYRAPONE STIMULATION TEST

- This test is used to delineate cause of Cushing's syndrome.
- Metyrapone is a potent inhibitor of the 11-hydroxylase enzyme so blocks cortisol synthesis.



- Measures the ability of the pituitary gland to release ACTH in response to decreased blood cortisol levels
- Hypothalmic pituitary axis responds by releasing more ACTH and so increases the concentration of 11-deoxycortisol due to inhibition of 11-hydroxylase
- Likewise the urinary excretion of 17-hydroxycorticosteroid also increases.
- In Cushing's syndrome caused by a pituitary tumor, the ACTH response remains intact and 11 deoxycortisol level show marked rise (>200 nmol/L)
- Levels of 11 deoxycortisol that are less than this are consistent with adrenal tumour or ectopic ACTH.

5. CRH STIMULATION TEST

- To differentiate between secondary adrenal insufficiency due to pituitary or hypothalamic disease.
- Results :

  Pituitary disease – blunted or nil response

  Hypothalamic lesions – positive response

B. TESTS FOR MINERALOCORTICOID ACTIVITY

A. PLASMA ALDOSTERONE

- Levels of plasma aldosterone are more in morning than in evening.
- Morning blood levels in supine position are 6 -22 µg/dL in males and 5-30 µg/dL in females.
- Levels increase in hyperaldosteronism and low in hypoaldosteronism.

A. STIMULATION TEST

- The stimulation test use volume depletion by
  - salt restriction
  - use of diuretic
  - up right posture

  These act as stimulant which increases renin activity leading to high aldosterone secretion

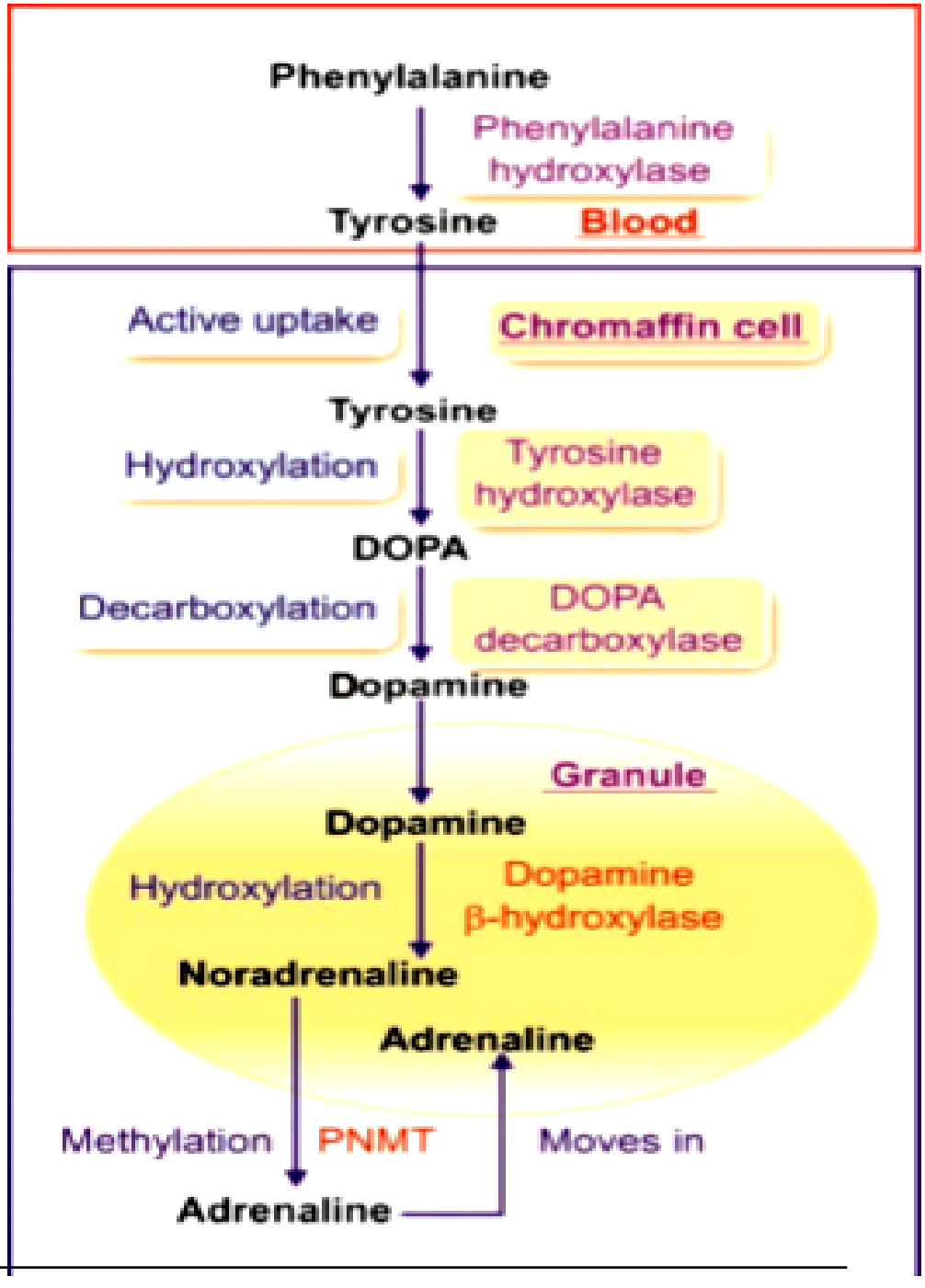
- Salt restricted diet 0.5-0.6g of dietary salt / day for 3-4 days leads to 2-3 times increase over the basal levels of aldosterone.

B. SUPPRESSION TEST

- High sodium leads to volume expansion leading to decrease in plasma renin level which in turn decreases aldosterone.
- Normal saline infusion 500 ml/hour for 4 hours should lead to a plasma aldosterone level of less than 8 µg/dL.

ADRENAL MEDULLA

Synthesis of catecholamines.



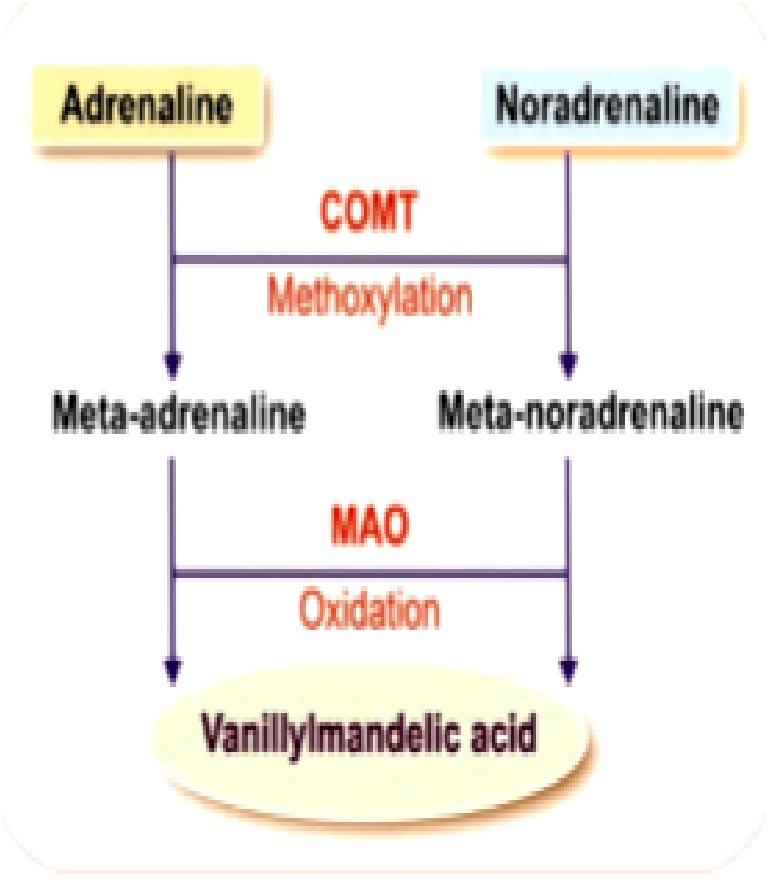
DOPA = Dihydroxyphenylalanine,

PNMT=Phenylethanolamine-

Nmethyl transferase.

ADRENAL MEDULLA

Metabolism of catecholamines



COMT = Catechol-O-methyltransferase,

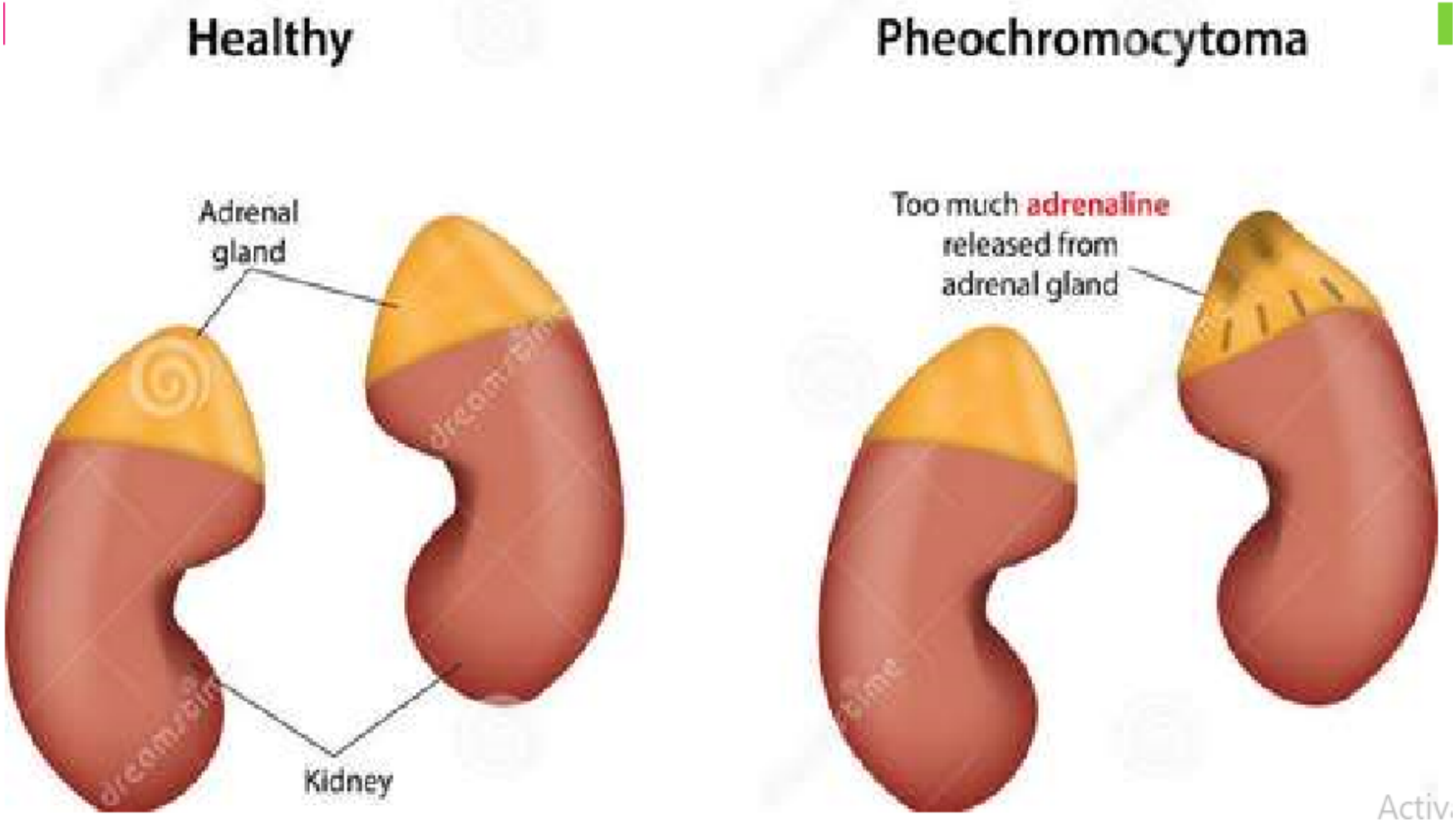
MAO = Monoamine oxidase

PHAEOCHROMOCYTOMA

- Tumour of the adrenal medulla, which is derived from chromaffin cells → catecholamines
- Occur around 4th decade, earlier in hereditary type
- Known as “10% tumor

10%
inherited
extra-adrenal
malignant
bilateral
children

Pheochromocytoma



Symptoms

Hypertension:
- Paroxysmal
- Continuous

Headache

Sweating

Palpitation

Pallor

Weight loss

Hyperglycaemia

Nausea

Psychological effects

Lab. investigation

- Urine

  -Determination of adrenaline, noradrenaline, metanephrine, normetanephrine levels in a 24hour urine collection

- Plasma

  -free metanephrine& normetanephrine