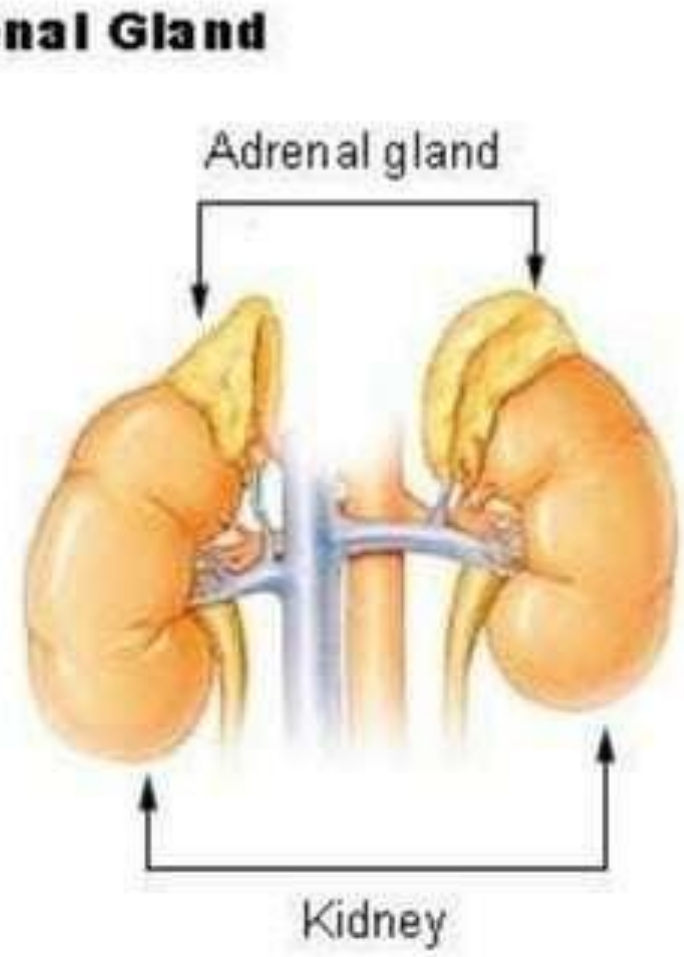
Adrenal Function Tests

Adrenal Glands

Suprarenal 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 the T12

- It 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

Adrenal cortex

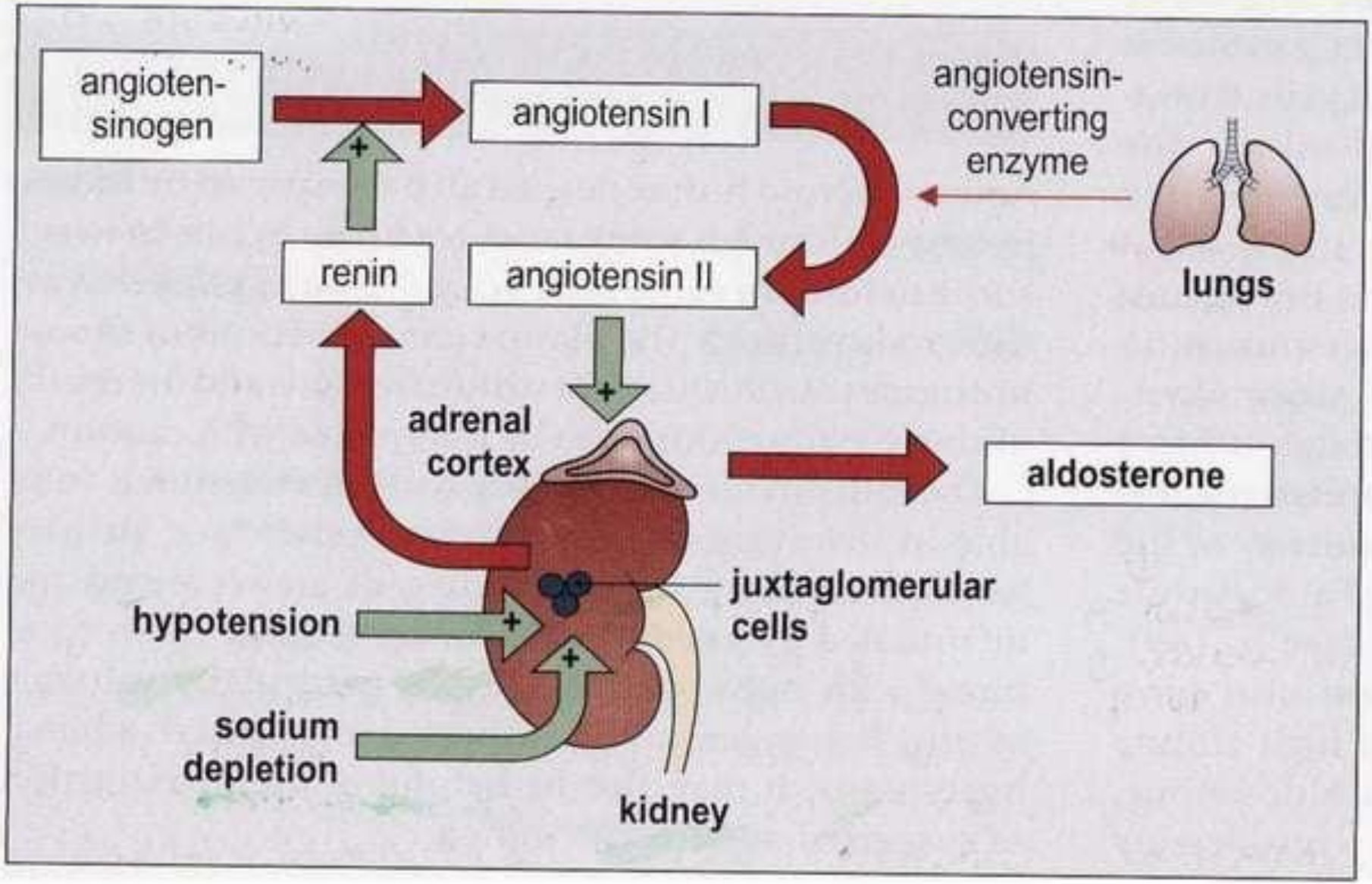
- **The large cortical cells are arranged into three layers or zones :**
  - **zona glomerulosa,**
  - **zona fasciculata,**
  - **zona reticularis**

Adrenal cortex

- **Zona glomerulosa:**
  - **Produce mineralocorticoids**
  - **Mainly aldosterone**

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

Aldosterone secretion



Adrenal cortex

- **Zona fasciculata:**
  - **Produce glucocorticoids**
  - **Mainly cortisol and corticosterone**

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

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

Adrenal cortex

- **Zona reticularis:**
  - **The innermost layer of the adrenal cortex, lying deep to the zona faciculata and superficial to the medulla.**
  - **These cells produce androgens**

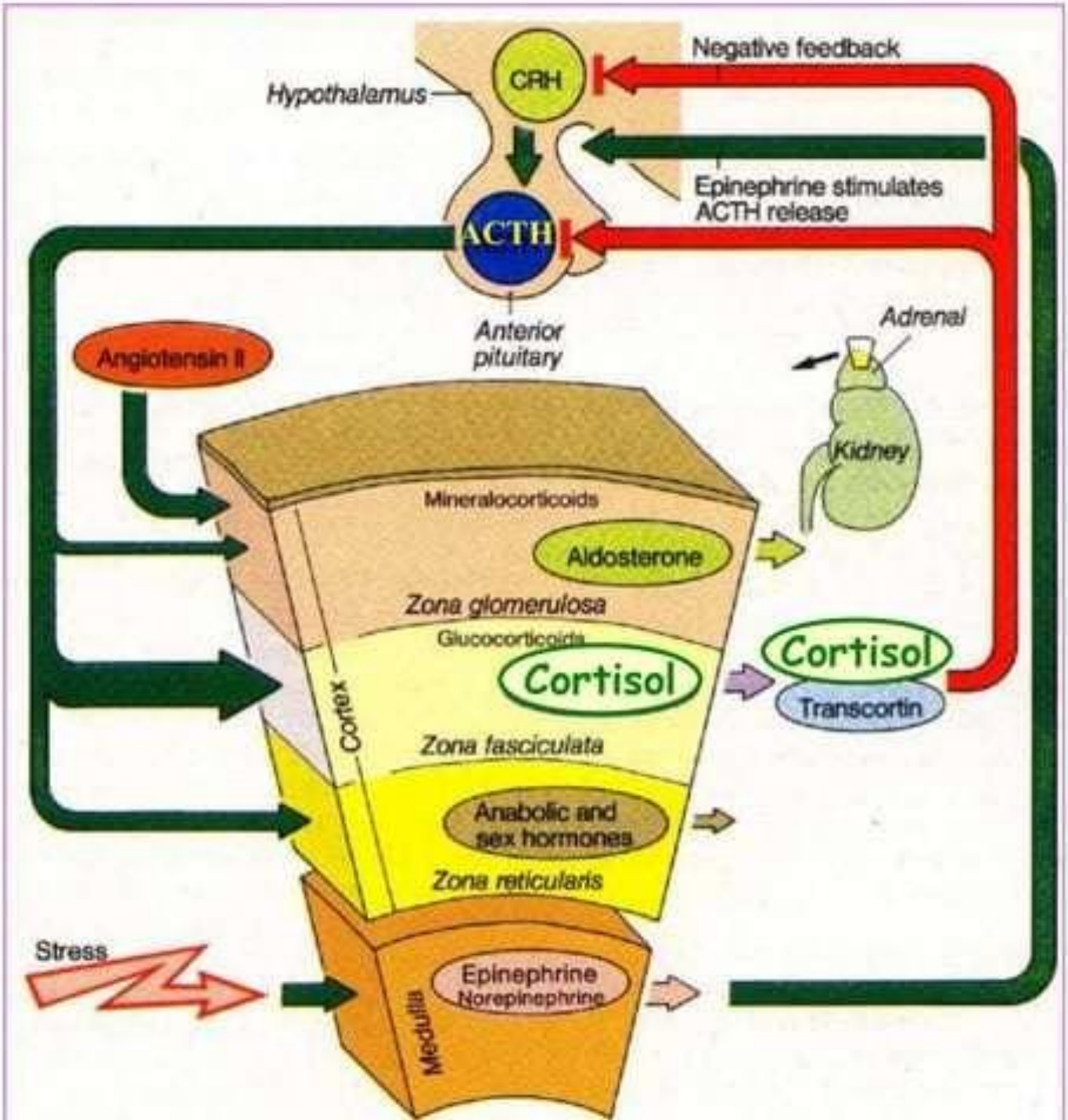
Adrenal cortex

- **The androgens produced includes**
  - **Dehydroepiandrosterone (DHEA)**
  - **Androstenedione**
    - **Synthesized from cholesterol**
  - **DHEA is further converted to DHEA-sulfate via a sulfotransferase**

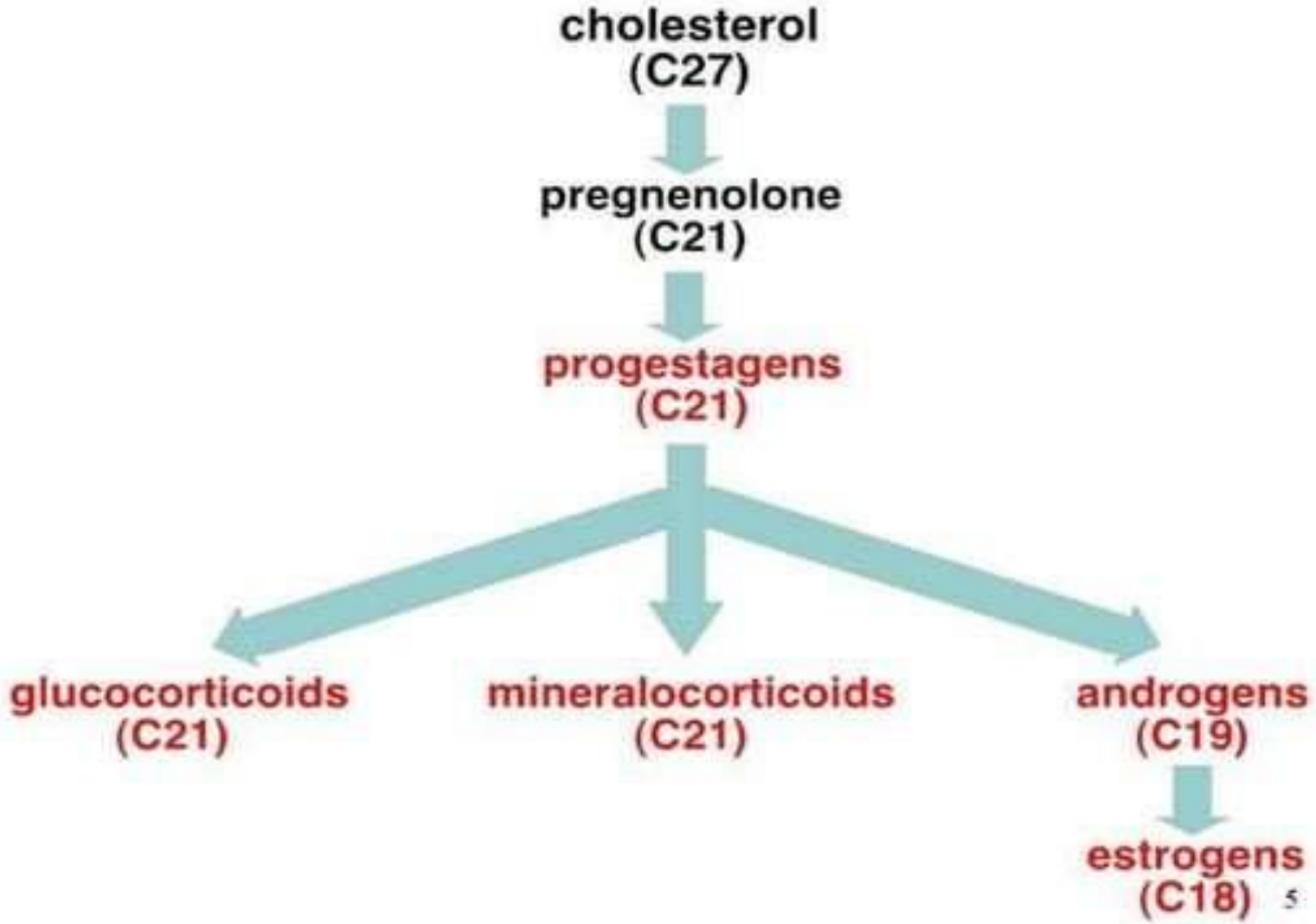
Adrenal cortex

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



Five major classes of steroid hormones derived from cholesterol



Endocrine gland		Hormone	Function	Secretion control is made by
Adrenal	Cortex	Glucocorticoids	Raises glucose levels in the blood, stimulates glucose production by cells, reduce the inflamatory response	Raised blood glucose levels
		Mineralocorticoids	Acts on the distal convoluted tubules of the renal nephrons; regulates uptake of sodium and acid/base balance	Low blood glucose levels
		Sex hormones	(Very small quantities)	_____
	Medula	Adrenaline and Noradrenaline	Fear, fight, fright syndrome	Sympathetic nervous system

Disorders of adrenal cortex

- **Patient with adrenal disorders can present with features related to:**
  - **HYPOFUNCTION OF THE GLAND**
  - **HYPERFUNCTION OF THE GLAND**

DISORDERS OF ADRENAL CORTEX

ADRENAL HYPOFUNCTION

Adrenal Hypofunction

Adrenal insufficiency leads to a reduction in the output of adrenal hormones

- **glucocorticoids and/or mineralocorticoids**

- **Two types of adrenal insufficiency**
  - **Primary insufficiency**
    - **inability of the adrenal glands to produce enough steroid hormones**
  - **Secondary insufficiency**
    - **inadequate pituitary or hypothalamic stimulation of the adrenal glands**

Adrenal Hypofunction

- Causes
  - **Glucocorticoid treatment**
  - **Autoimmune adrenalitis**
  - **Tuberculosis**

  } Common

  - **Adrenalectomy**
  - **Adrenal haemorrhage**

Adrenal Hypofunction

- **Congenital causes:**

Metabolic failure in hormone production

- **Congenital adrenal hyperplasia e.g. 21-hydroxylase deficiency**

Adrenal Hypofunction

Addison's disease:

- **Progressive destruction of entire adrenal cortex , This is usually autoimmune based.**
- Most likely the result of **cytotoxic T lymphocytes**,

Addison's disease: Clinical features

- **Tiredness, generalized weakness, lethargy**
- **Anorexia, nausea, vomiting**
- **Hyponatremia**
- **Hyperkalemia ,Hypercalcemia**

  Dizziness and postural

  hypotension
- **Pigmentation**
- **Loss of body hair**

Addison's disease: clinical features

- hyperpigmentation

Addison's disease: clinical features

- Hyperpigmentation

INVESTIGATIONS (HORMONAL)

- **Plasma cortisol concentration**

- **ACTH stimulation test / Synacthen test**
- **Measurement of plasma ACTH**

- **CRH stimulation test**
- **Plasma renin and aldosterone levels**

PLASMA ACTH MEASUREMENT

- **To differentiate between primary and secondary adrenal failure**
  - **Primary insufficiency - ACTH increased**
  - **Secondary insufficiency - ACTH decreased**

CRH STIMULATION TEST

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

Pituitary disease – blunted or nil response

Hypothalamic lesions – positive response

PLASMA RENIN AND ALDOSTERONE

- **Adrenal insufficiency**
  - **Low aldosterone level with high renin**

Disorders of adrenal cortex

ADRENAL HYPERFUNCTION

Adrenal Hyperfunction

- Cushing syndrome : High Cortisol
- Hyperaldosteronism : High aldosterone
- Pheochromocytoma : High catecholamine

Hyperaldosteronism

A medical condition where too much aldosterone is produced by the adrenal glands, which can lead to sodium retention and potassium loss.

- **Types:**
  - **Primary hyperaldosteronism**
  - **Secondary hyperaldosteronism**

Primary hyperaldosteronism

Conn's syndrome

Primary aldosteronism

CONN'S SYNDROME

- Characterized by **autonomous** excessive production of **aldosterone** by **adrenal glands**

- Presents with hypertension, hypokalemia
- and renal K+ wasting

Conn's Syndrome

- **Causes:**
  - **Adrenal adenoma**
  - **Bilateral hypertrophy of zona glomerulosa cells**
  - **Adrenal carcinoma**

Secondary aldosteronism

Increased adrenal aldosterone production in response to non-pituitary, extra-adrenal stimuli

- **Commoner than primary aldosteronism**

Secondary aldosteronism

- **CCF**
- **Liver cirrhosis with ascitis**
- **Nephrotic Syndrome**

Conn's syndrome

- **Clinical features:**
  - **Hypertension : *aldosterone induced Na retention***
  - **Muscle weakness: *Due to decrease K+***
  - **Muscle paralysis: *severe hypokalemia***
  - **tetany and paraesthesia**

INVESTIGATION

- **Electrolyte & blood gasses:**
  - **Hypernatremia**
  - **Hypokalemia**
  - **Alkalosis: Blood p H > 7.45**

Plasma aldosterone : renin activity ratio high

Disorders of adrenal cortex

ADRENAL HYPERFUNCTION

CUSHING'S SYNDROME

- Definition
- Clinical features
- Investigations
  - Screening for Cushing's syndrome
  - Elucidation of the cause of Cushing's syndrome

- Management

CUSHING'S SYNDROME

Adrenal cortex hyperfunction

- Any condition resulting from overproduction of **primarily glucocorticoid (cortisol)**
- Mineralocorticoid and androgen may also be excessive

Pseudo-Cushing's syndrome

- Appear cushingoid and have some biochemical abnormalities of true Cushing's disease
- Causes
  - Severe depression
  - Alcoholism
  - Obesity
  - Polycystic ovarian syndrome

Etiology

- **Excessive cortisol (ACTH dependent)~75%**
  - Pituitary disease
  - Ectopic ACTH syndrome
    - Malignancy - (bronchus, thymus, pancreas, ovary)
  - Ectopic CRH syndrome
  - Exogenous ACTH administration

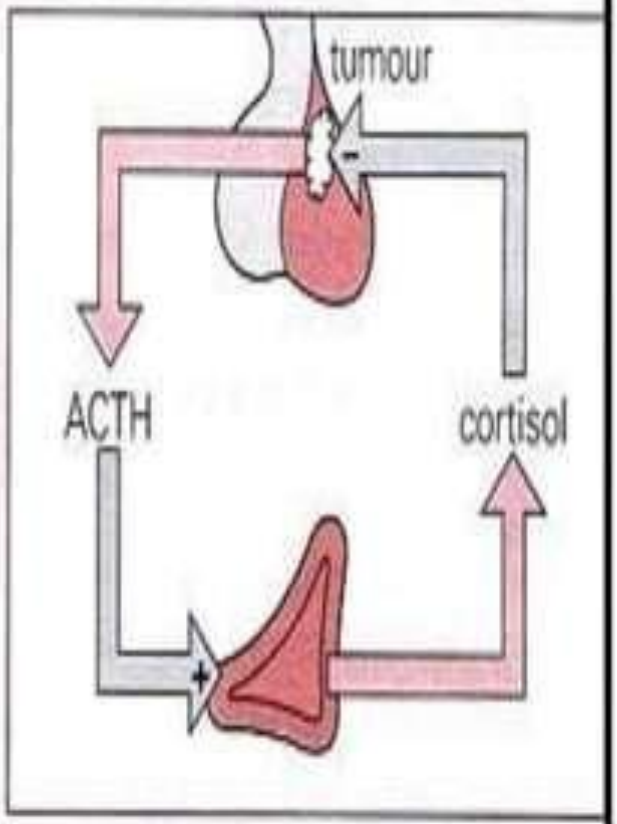
ACTH dependent causes

b. Cushing's disease

ACTH secretion increased

pituitary insensitive to feedback
by normal levels of cortisol

higher levels of cortisol required to produce
negative feedback effect on ACTH secretion

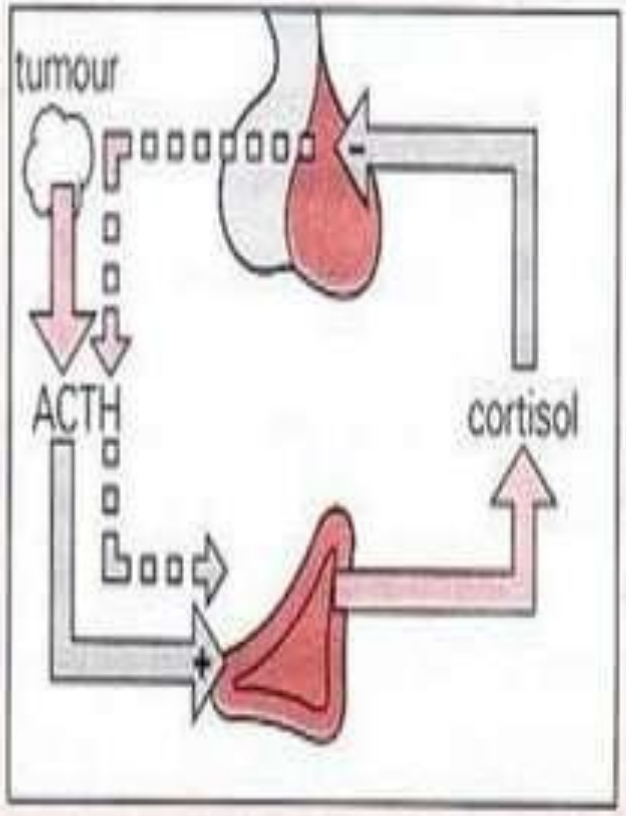


ACTH dependent causes

d. Ectopic ACTH secretion

high level of ACTH secreted by tumour
stimulates excessive cortisol production

secretion of ACTH by pituitary inhibited



*Hypersecretion of ACTH and Cortisol is greater in ectopic ACTH syndrome than Cushing Disease

Etiology

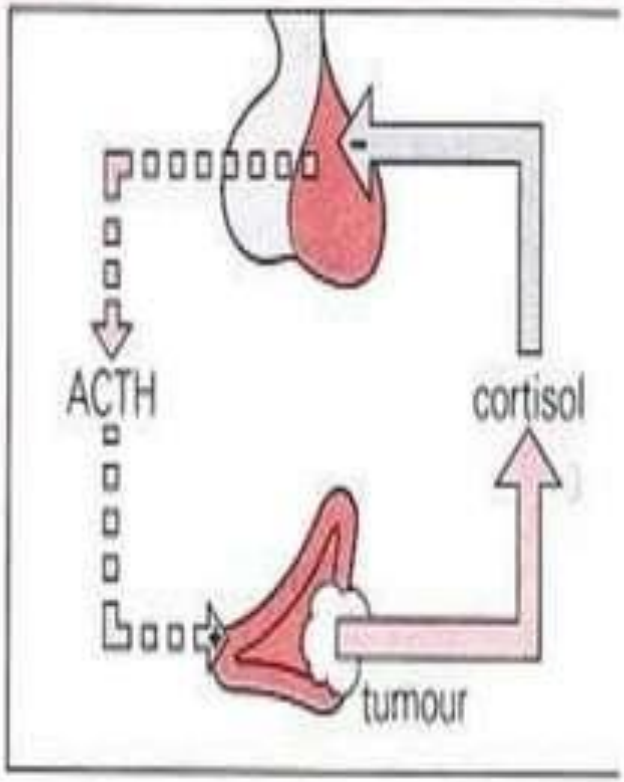
- **Excessive cortisol (ACTH independent)** ~25%
  - Adrenal tumour
    - Adenoma
    - carcinoma
  - Nodular hyperplasia
  - Exogenous glucocorticoid administration

ACTH independent causes

c. Adrenal tumours

autonomous cortisol production

high circulating cortisol inhibits ACTH secretion



Etiology

- **Excess cortisol binding globulin**
  - Estrogen therapy : Osteoporosis, OCP
  - Pregnancy

Clinical features

- **Truncal obesity** with deposition of adipose tissue in characteristic site (moon face, buffalo hump)– exact mechanism unknown
- **Thinning of skin** – catabolic response
- **Purple striae** – catabolic response
- **Excessive bruising** – catabolic response

Cont..

- **Hirsutism** (esp adrenal carcinoma) - ↑ adrenal androgen
- **Menstrual irregularities** - ↑ adrenal androgen

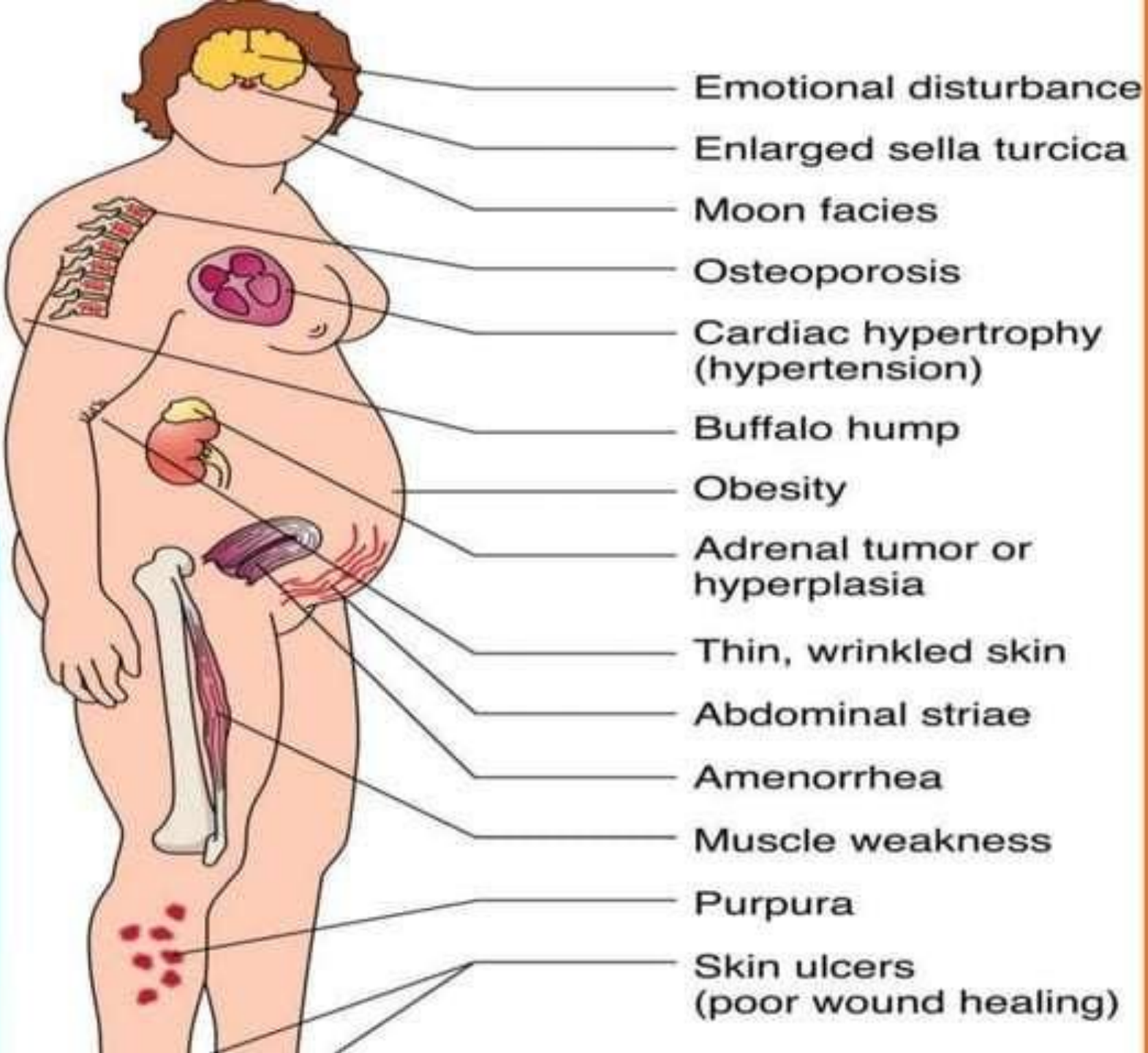
- **Skin pigmentation** (ACTH ↑) – melanocyte stimulating activity

Cont..

- **Hypertension** – mineralocorticoid effect → sodium retention
  - metabolic alkalosis
- **Glucose intolerance** - ↑ hepatic gluconeogenesis and insulin resistance
- **Muscle weakness and wasting**

Cont..

- **Back pain**
- **Psychiatric disturbances**


Emotional disturbance
Enlarged sella turcica
Moon facies
Osteoporosis
Cardiac hypertrophy (hypertension)
Buffalo hump
Obesity
Adrenal tumor or hyperplasia
Thin, wrinkled skin
Abdominal striae
Amenorrhea
Muscle weakness
Purpura
Skin ulcers (poor wound healing)

Laboratory investigations

- There are two diagnostic steps in the investigation of patient suspected of having Cushing's syndrome

  - Screening test

    for identification of Cushing's syndrome.

    the demonstration of high plasma cortisol level

  - Identification of cause

1. Demonstration of increased cortisol

- Assessment of circadian rhythm in cortisol secretion
- 24-Hour urinary free cortisol excretion
- Overnight / low dose dexamethasone suppression test

Laboratory investigations

1. **Assessment of circadian rhythm in cortisol secretion.**

- Measure 8 am and 11 pm serum cortisol level

  - Normal : Serum value at midnight is 50% less than value at 8 am
  - Cushing's syndrome : rhythm is lost
  - Pseudo-Cushing : normal circadian.

Laboratory investigations

2. Measuring 24-hour urinary free cortisol

> 100 microgram	Diagnostic of Cushing's syndrome

Laboratory investigations

3. Low dose Dexamethasone suppression test :

After injection of dexamethasone urinary and

plasma cortisol levels should fall

But in cushing's syndrome there is no fall in cortisol levels

- High dose Dexamethasone suppression test
- Normal individuals suppress plasma cortisol
- Patients with Cushing's syndrome fail to show complete suppression of plasma cortisol levels. This test is highly sensitive

2. Elucidation of the cause

- Plasma ACTH
  - Low – adrenal causes
  - Elevated
    - Slight – pituitary dependent Cushing's
    - Gross – ectopic secretion of ACTH

Elucidation of the cause

- CRH Test
  - Differentiate ectopic ACTH secretion and Cushing's disease.
  - Cushing's disease – plasma ACTH increases 50% over baseline and cortisol increase by 20%
  - Ectopic ACTH or adrenal tumour – no response

Elucidation of the cause

- Imaging
  - CT scan of adrenal gland
  - MRI of pituitary gland:
  - CT scan/MRI of thorax & abdomen: ectopic ACTH producing tumor

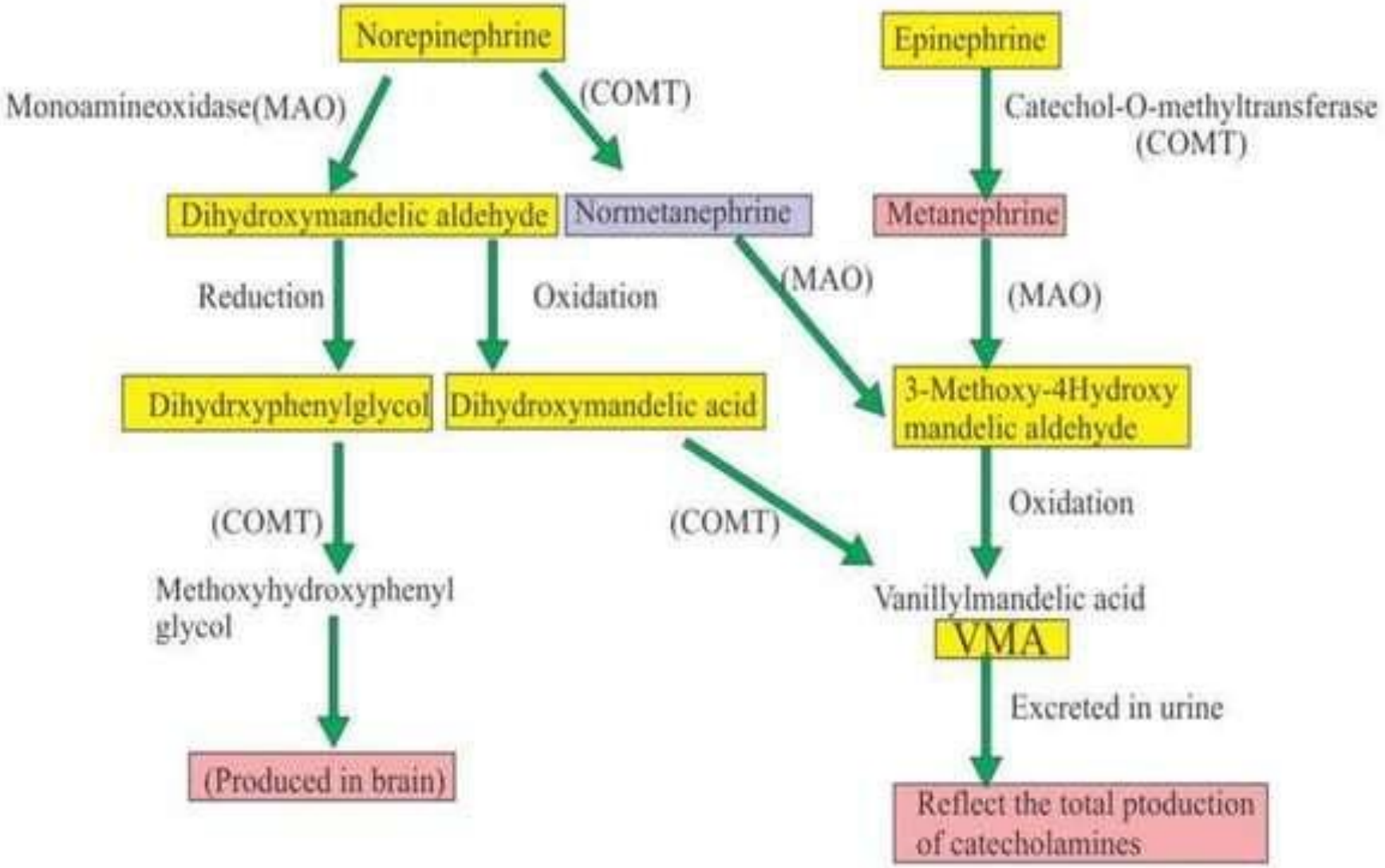
Treatment

- Depend of Cushing's syndrome depends on the etiology:
  - Adrenal adenoma
  - Adrenal Carcinoma – resection
  - Cushing's disease
  - Drug (block cortisol synthesis) - metyrapone

Phaeochromocytoma

Tumor of adrenal medulla
Excessive production of catecholamines
Hypertension, hot flushing, sweating, headache

Diagnosis done by urinary VMA estimation: excess tea, coffee, chocolates, ice creams should be avoided before VMA estimation test
Treatment is surgical removal of tumor.


Norepinephrine
Monoamineoxidase(MAO)
(COMT)
Epinephrine
Catechol-O-methyltransferase
(COMT)
Dihydroxymandelic aldehyde
Normetanephrine
Metanephrine
Reduction
Oxidation
(MAO)
(MAO)
Dihydrxyphenylglycol
Dihydroxymandelic acid
3-Methoxy-4Hydroxy
mandelic aldehyde
(COMT)
(COMT)
Oxidation
Methoxyhydroxyphenyl
glycol
Vanillylmandelic acid
VMA
Excreted in urine
(Produced in brain)
Reflect the total ptoduction
of catecholamines


thankyou