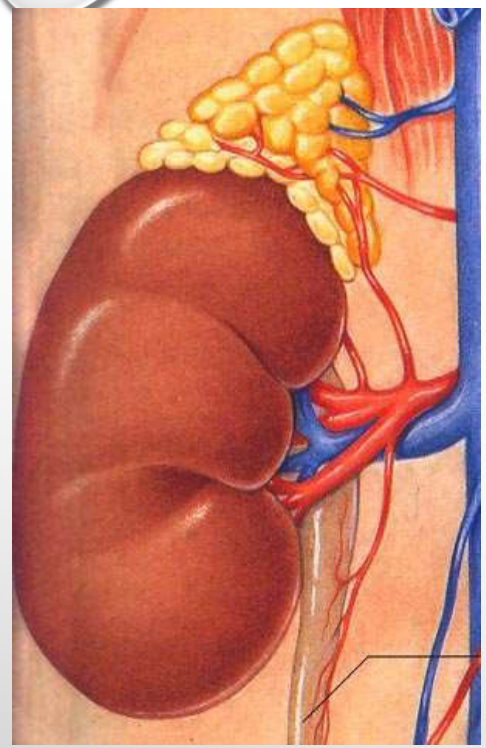
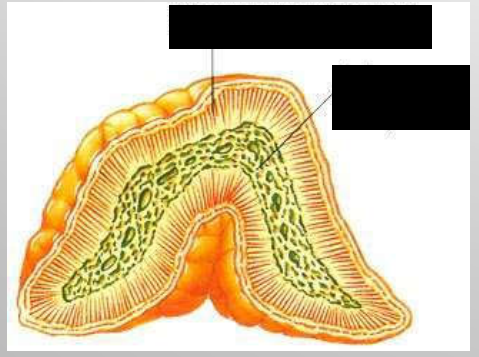
# Adrenal gland

AHMED ELSHARAWY .MD



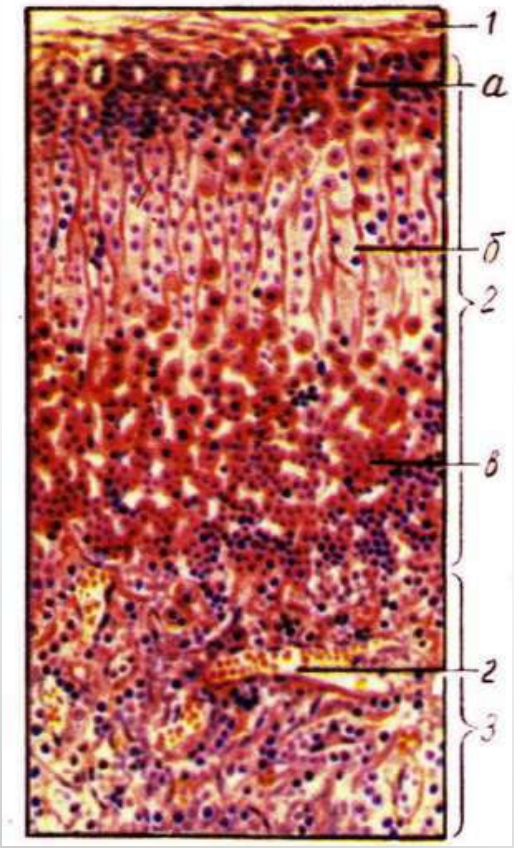


The *adrenal glands* are the pair endocrine gland, located above the superior kidneys' poles. They are against the interspace between the first lumbar vertebra and eleventh thoracic vertebra. They have triangular form.

The weight of both adrenal glands is 6 to 12 g, the length is 4-6 cm, the width is 2-3 cm, and the thickness is to 1 cm.

The external portion of the adrenal gland is surrounded by the connective tissue capsule.

The adrenal gland consists of outer *cortex* and an inner *adrenal medulla*.




1 capsule,
2 cortical substance
(а- **zona glomerulosa**,
б- **zona fasciculata**, в- **zona reticularis**),
3- medullary substance.

THE ADRENAL CORTEX FORMS THREE LAYERS:

-THE *ZONA GLOMERULOSA*

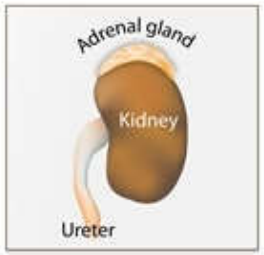
(external),

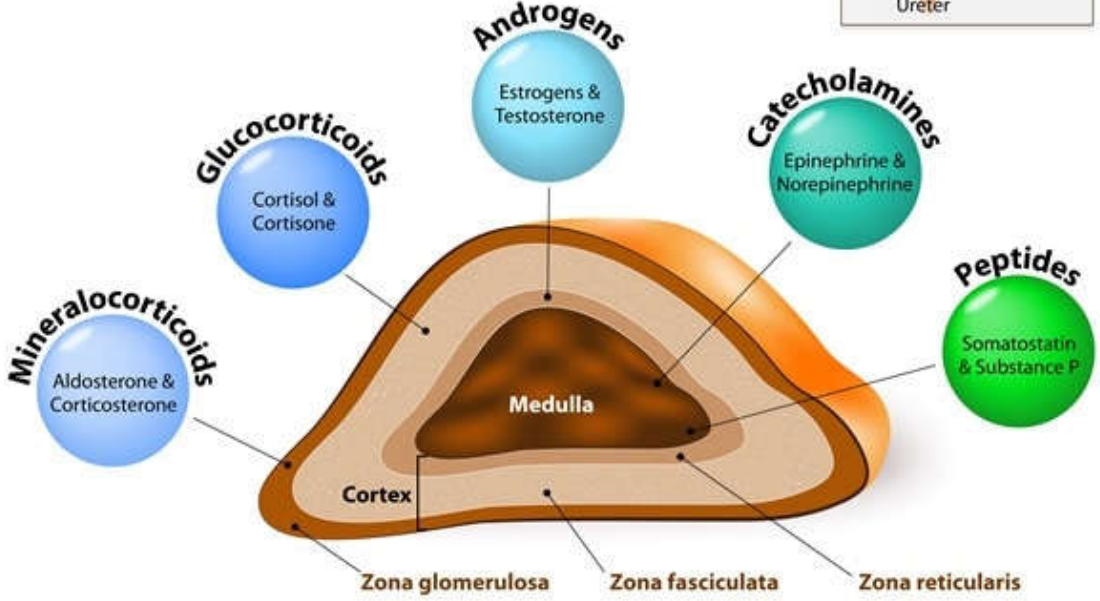
-*zona fasciculata*, located in the middle of these layers,

-*zona reticularis*, adjoining to the adrenal medulla.

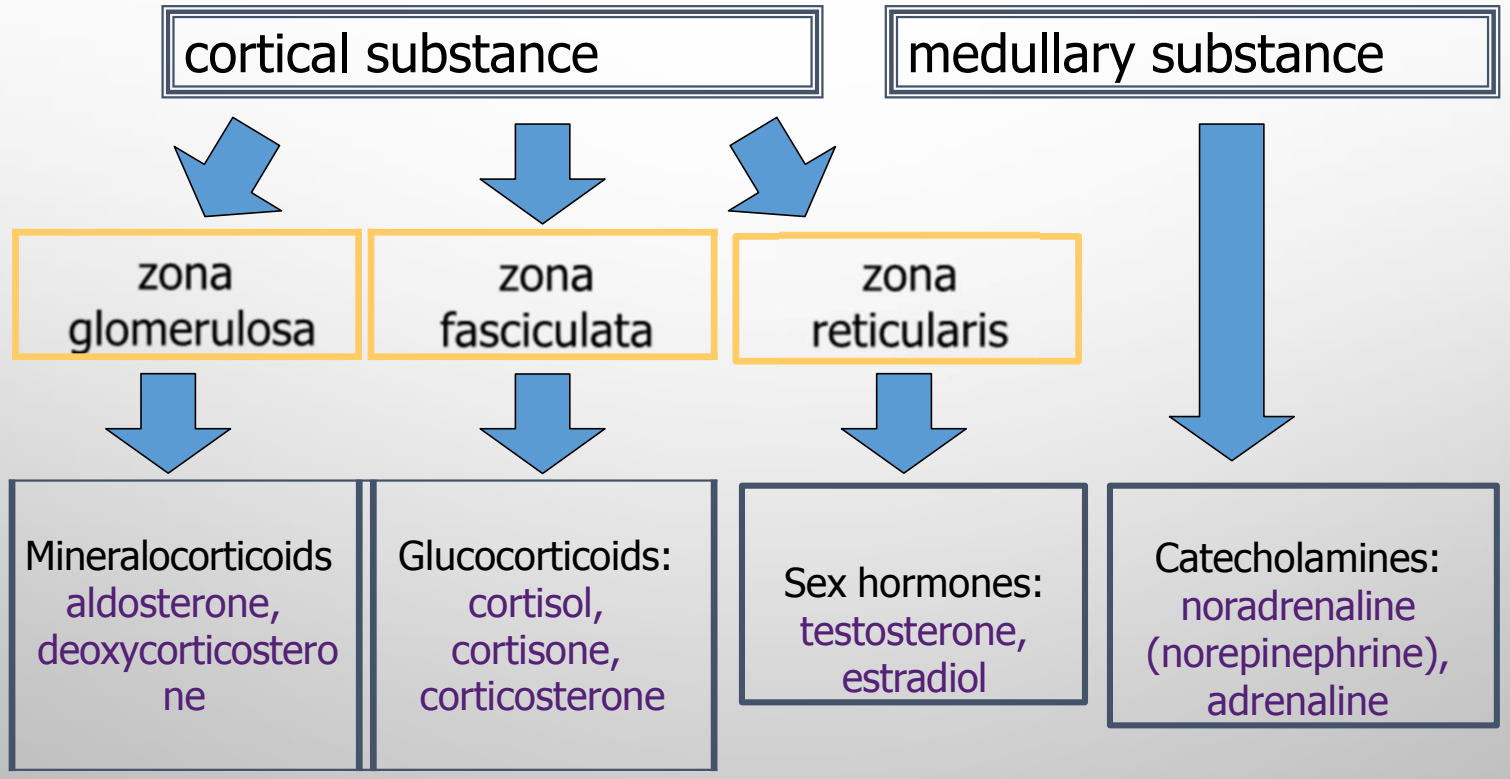
# ADRENAL GLAND

(hormones)

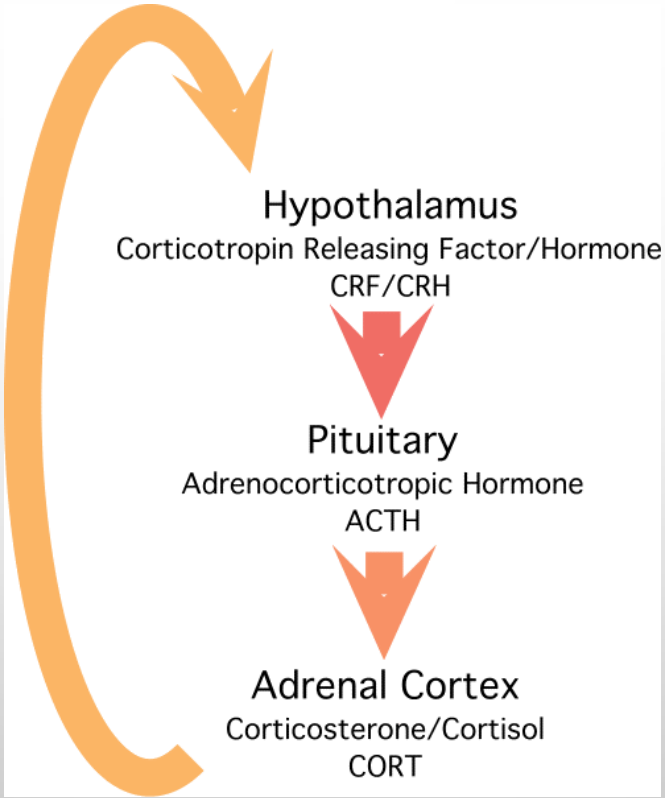


# ADRENAL GLANDS



# HPA AXIS


Hypothalamus
Corticotropin Releasing Factor/Hormone
CRF/CRH
Pituitary
Adrenocorticotropic Hormone
ACTH
Adrenal Cortex
Corticosterone/Cortisol
CORT

# CLASSIFICATION

## Adrenocortical hyperfunction

There are 3 basic types of corticosteroids elaborated by the adrenal cortex *"glucocorticoids, mineralocorticoids,* and *sex hormone"* and 3 distinctive hyperadrenal clinical sydromes:

- Cushing syndrome "excess cortisol"
- Hyperaldosteronism
- Adrenogenital syndromes "excess androgen"


## Adrenal Hypofunction

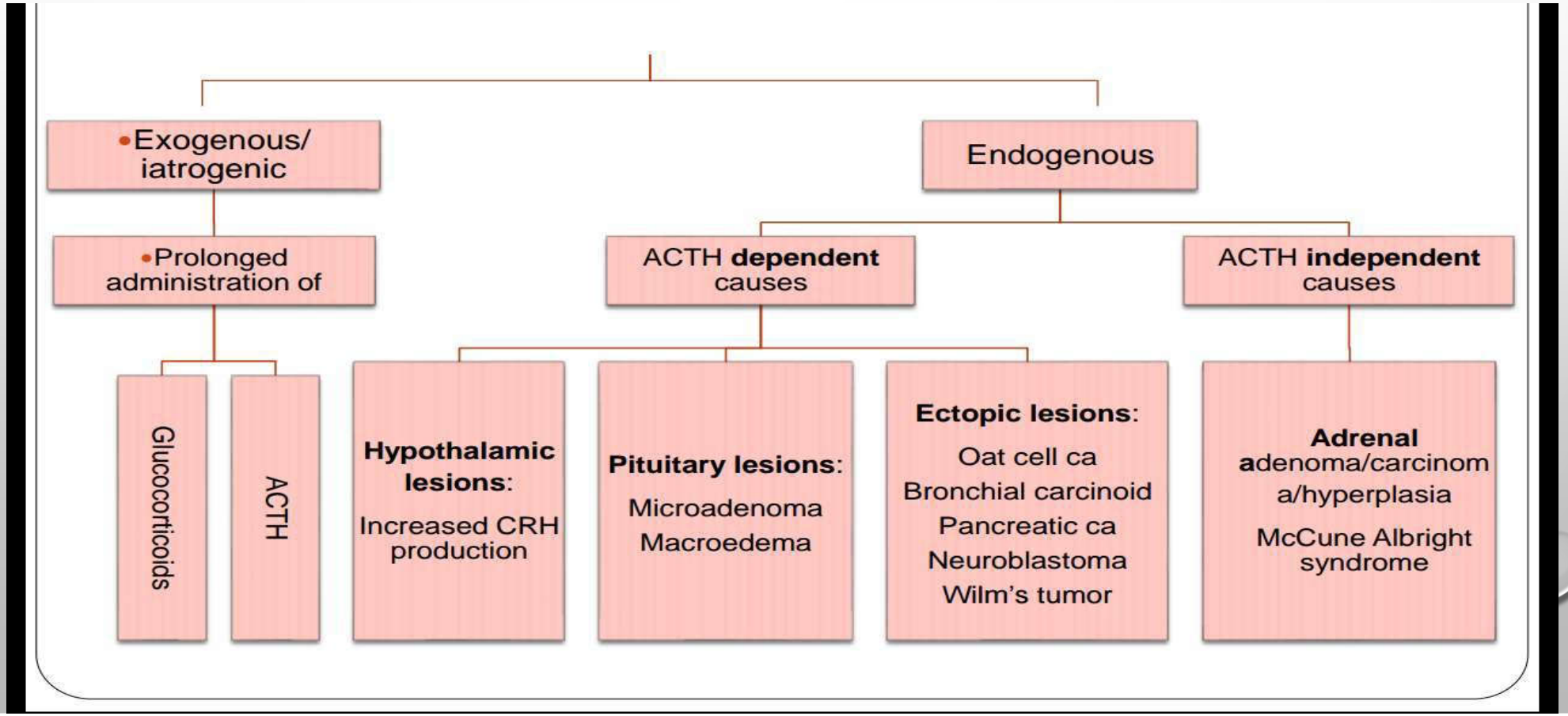
- Adrenal insufficiency leads to a reduction in the output of adrenal hormones
  - glucocorticoids and/or mineralocorticoids
- Two types of adrenal insufficiency
  - **Primary insufficiency**
    - inability of the adrenal glands to produce enough steroid hormones
  - **Secondary insufficiency**
    - inadequate pituitary or hypothalamic stimulation of the adrenal glands

# CUSHING SYNDROME

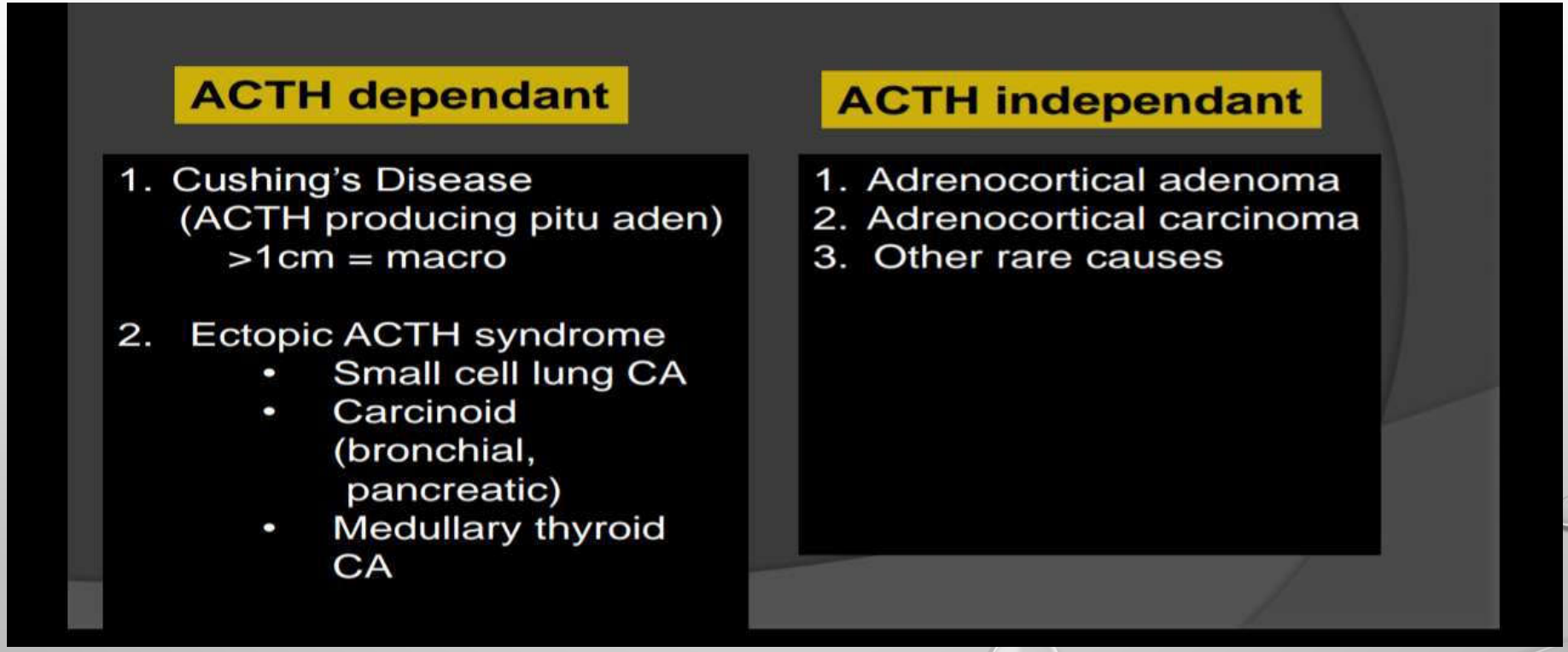
# DEFINITION

- Cushing’s syndrome: constellation of symptoms associated with cortisol excess.
- Cushing's syndrome develops when the level of a glucocorticoid in the body is too high over a long period of time.
- Too much glucocorticoid can occur from an exogenous or endogenous source
- described by Harvey Cushing in 1932

# ETIOLOGY


•Exogenous/ iatrogenic
Endogenous
•Prolonged administration of
ACTH dependent causes
ACTH independent causes
Glucocorticoids
ACTH
Hypothalamic lesions:
Increased CRH production
Pituitary lesions:
Microadenoma
Macroedema
Ectopic lesions:
Oat cell ca
Bronchial carcinoid
Pancreatic ca
Neuroblastoma
Wilm's tumor
Adrenal adenoma/carcinoma/hyperplasia
McCune Albright syndrome

# ETIOLOGY


ACTH dependant
1. Cushing's Disease
(ACTH producing pitu aden)
>1cm = macro
2. Ectopic ACTH syndrome
• Small cell lung CA
• Carcinoid
(bronchial,
pancreatic)
• Medullary thyroid
CA
ACTH independant
1. Adrenocortical adenoma
2. Adrenocortical carcinoma
3. Other rare causes

# DIFFERENTIAL DIAGNOSIS

- Pseudo-Cushingoid:
  - Chronic severe anxiety and/or depression
  - Prolonged excess alcohol consumption
  - Obesity
  - Poorly controlled diabetes
  - HIV infection
  - Malnutrition
  - Anorexia nervosa

# CLINICAL PRESENTATIONS

*Findings are more obvious in infants*

- *Children with adrenal tumors*

  *Signs of abnormal masculinization*

- *Growth impairment*

  *Short stature*

- Decreased collagen cause purplish striae on soft tissues of the body
- They are prone to infections due to compromised immune system
- Decreased linear growth

# CLINICAL FEATURE

Lipid mobilization

Lipid catabolism

Lipid redistribution

Moon-face

buffalo hump

truncal obesity

Violaceous striae

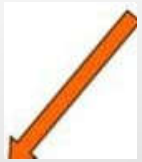
Hepatic glucose production

Insulin resistance

Glucose intolerance

protein metabolism negative nitrogen balance

disruption of water and electrolytes metabolism



Proximal muscle weakness

Dependent edema

Hypertension

Hypokalemic metabolic alkalosis

# CLINICAL FEATURES

- Body fat: Weight gain
  central obesity
  moon facies
  buffalo hump
- Skin: Purple abdominal striae
  easy bruising
  Plethoric appearance
- Bone: Osteopenia
  Osteoporosis (vertebral fracture)

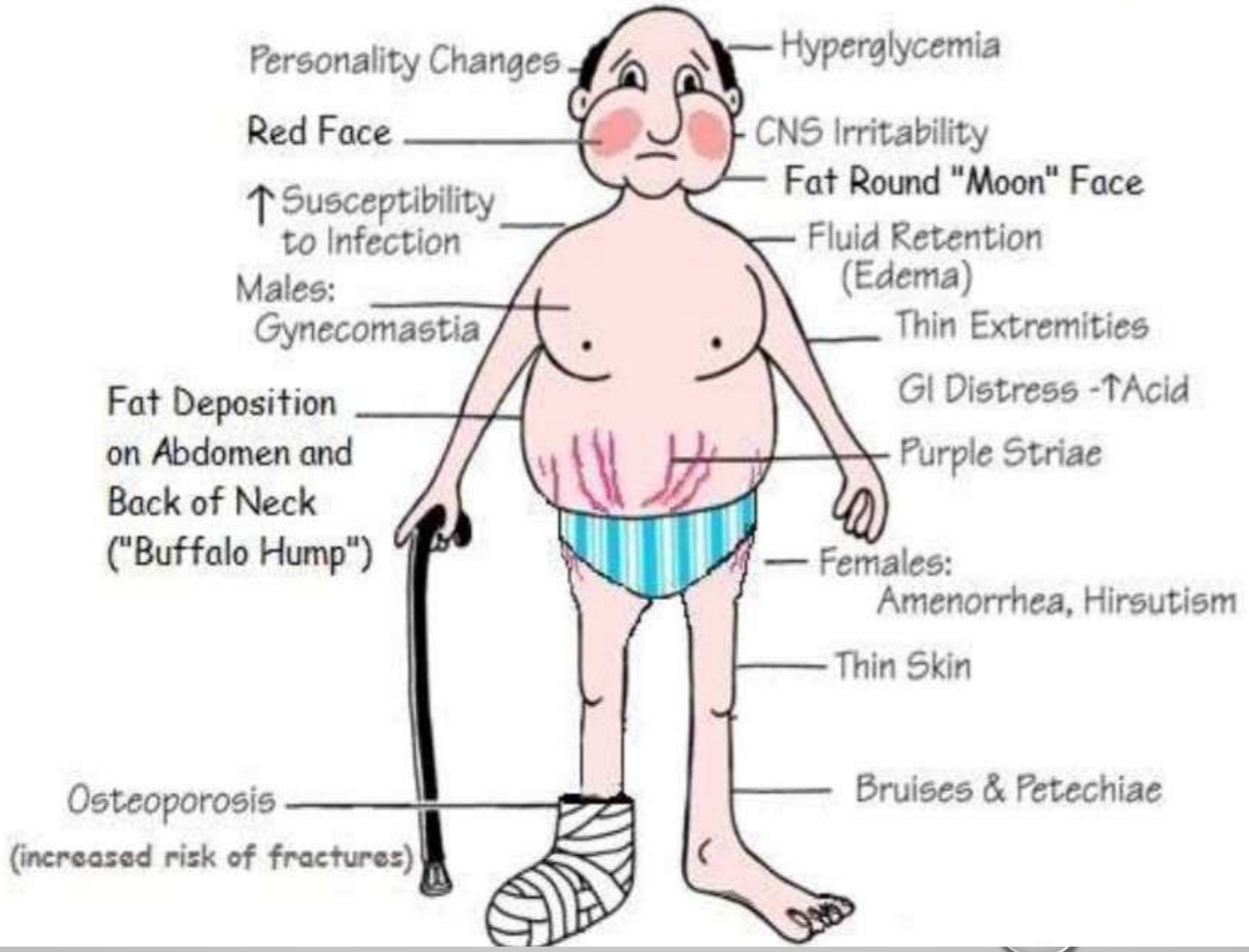
- Muscle: proximal myopathy
- CVS: diastolic hypertension
  hypokalemia
  oedema
  atherosclerosis

  Cortisol can stimulate mineralocorticoid receptors but an enzyme 11B HSD2 rapidly converts it to inactive cortisone without mineralocorticoid activity.

  In cushing's, excess cortisol overcomes the ability of 11b hsd2 to breakdown cortisol, hence mineralocorticoid effect seen- BP & K
- Reproductive sys: amenorrhea, ↓ libido
- CNS: irritability, emotional liability, paranoid psycosis

- Blood: increased susceptibility to infections
  - ↑ WBC
  - hypercoagulation- DVT, P emboism
- Metabolism: impaired glucose tolerance
  - dyslipidemia

# Cushing's Disease or Syndrome Symptoms



# DIAGNOSIS OF CUSHING'S SYNDROME

- Obtain a careful history to exclude exogenous glucocorticoid use.
- Perform at least **two first-line biochemical tests** to obtain the diagnosis:
  - Urine free cortisol (UFC) (at least two measurements)
  - Late-night salivary cortisol (two measurements)
- In $_{+ve}$ tests Morning and midnight plasma cortisol levels are elevated
- Serum ACTH level
- Bloods tests – which and why?
  - FBC
  - U/E – low K

# DIAGNOSIS

- Cortisol levels in blood are normally elevated at 8 A.M. and decrease to less than 50% by midnight except in infants and young children in whom a diurnal rhythm is not always established.
- In patients with Cushing syndrome this circadian rhythm is lost, and cortisol levels at midnight and 8 A.M. are usually comparable.
- Urinary excretion of free cortisol is increased. This is best measured in a 24-hr urine sample and is expressed as a ratio of micrograms of cortisol excreted per gram of creatinine

# DEXAMETHASONE SUPPRESSION TEST

- Dexamethasone is an exogenous steroid that provides negative feedback to the pituitary to suppress the secretion of ACTH.
- This steroid is unable to pass the blood brain barrier which allows this test to assess a specific part of the hypothalamicpituitary-adrenal axis. Specifically, dexamethasone binds to glucocorticoid receptors in the pituitary gland, which lies outside the blood brain barrier, resulting in regulatory modulation
- A single-dose dexamethasone suppression test is often helpful a dose of 25–30 μg/kg (maximum of 2 mg) given at 11 P.M. results in a plasma cortisol level of less than 5 μg/dL at 8 A.M. the next morning in normal individuals but not in patients with Cushing syndrome.
- " A low dose dexamethasone suppresses cortisol in individuals with no pathology in endogenous cortisol production. A high dose dexamethasone exerts negative feedback on pituitary ACTH producing cells but not on ectopic ACTH producing cells or adrenal adenoma.

**Low-dose**

- A normal result is decrease in cortisol levels upon administration of low-dose dexamethasone.
- Cushing's disease involve no change in cortisol on low-dose dexamethasone, but inhibition of cortisol on high-dose dexamethasone

**Large dose DX suppression test**

•D.X 2mg q6h P.O 2 days Urinary free cortisol reduced 50%: Cushing’s disease (Pituitary adenoma)

- Urinary free cortisol NOT reduced 50%:Adrenal tumor, carcinoma, ectopic ACTH Syndrome

# ALGORITHM FOR TESTING

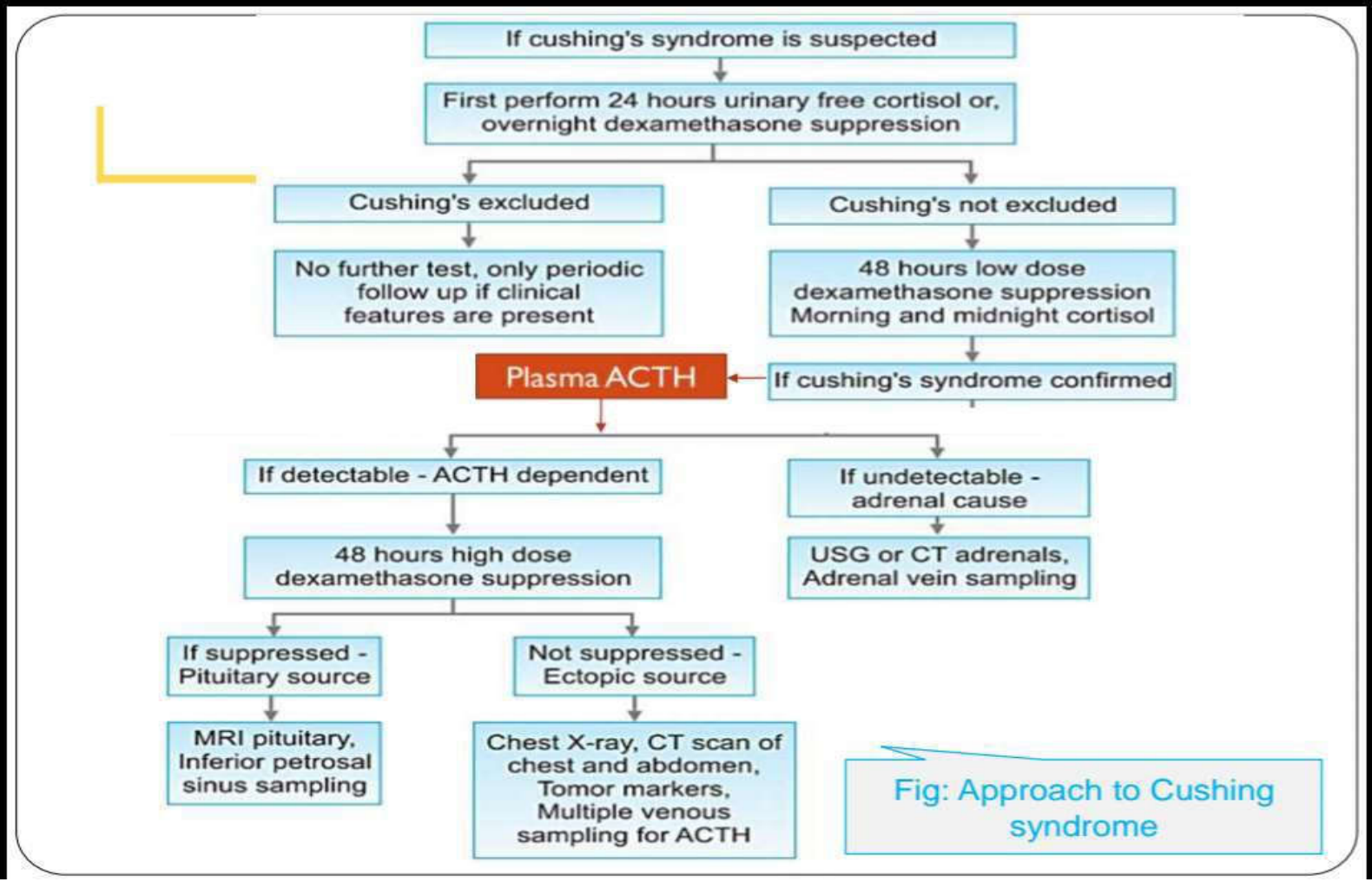



Fig: Approach to Cushing syndrome

- Dx of Cushing syndrome has been established then,the next step is to find out the cause

↓

**Serum ACTH level**

- If low or undetectable– ACTH independent cause [Adrenal cause likely]
- If high– Cushing's disease or Ectopic ACTH syndrome
- Two differentiate between these two: High dose DST is to be done

**High dose DST**

- 2 mg 6 hrly for 2 days
- Cortisol level measured at 8 AM on Day 0 and Day 2
- Partial suppression of cortisol (>50%) confirms Pituitary cause (Cushing disease)
- Failure to suppress suggest Ectopic ACTH syndrome

| | | | |
|---|---|---|---|
| **Pituitary Cushings** | | | |
| Pituitary Adenoma | most common pathogenic cause (70%), the majority of adenomas are benign. | high ACTH | Cortisol responds to dexamethasone supression test |
| **Ectopic Cushings** | | | |
| Small cell carcinoma of the lung. | ectopic ACTH secretion | extremely high ACTH | Cortisol does not respond to dexamethasone supression test |
| **Adrenal Cushings** | | | |
| Adrenal adenoma | | low ACTH | |
| Bilateral hyperplasia | | low ACTH | |
| Adrenal Carcinoma | | low ACTH | |

# OTHERS TESTS;

Effects of hypercortisolism include:

- Hyperglycemia
- Hyperlipidemia
- Hypokalemia(excrete K+)
- Metabolic alkalosis(excrete H+)

# Other Investigations

Other tests (to see the effect):
- Electrolytes (hypokalemia).
- Blood sugar
- Bone mass density to see osteoporosis

- Adrenal cause
  - USG abdomen
  - CT/MRI abdomen

  → Looking for Adrenal adenoma or carcinoma

- Cushing disease
  - CT/MRI head
    - ↓ No mass seen
  - Bilateral inferior petrosal blood sampling for ACTH level

  → Looking for Pituitary micro/ macroadenoma

- Ectopic ACTH syndrome
  - CXR
  - CT chest, abdomen

  → Looking for Oat cell ca, Bronchial carcinoid, Ca panc or Wilms tumour

# TREATMENT

## MEDICAL THERAPY

Purpose

- Correct metabolic abnormalities before attempted surgical cure
- Palliate surgically non curable disease
- Achieve remission in patients for whom surgery is unlikely to achieve satisfactory long term results

## STEROIDOGENIC INHIBITION

- Mitotane
- Metyrapone
- Aminoglutethimide
- Ketoconazole

## Neuromodulatory treatment

- Bromocriptine
- Cyproheptadin
- Valproic acid
- Octreotide

## Glucocorticoid receptor antagonist

- RU486

# SURGICAL TX

**Cushing's disease**

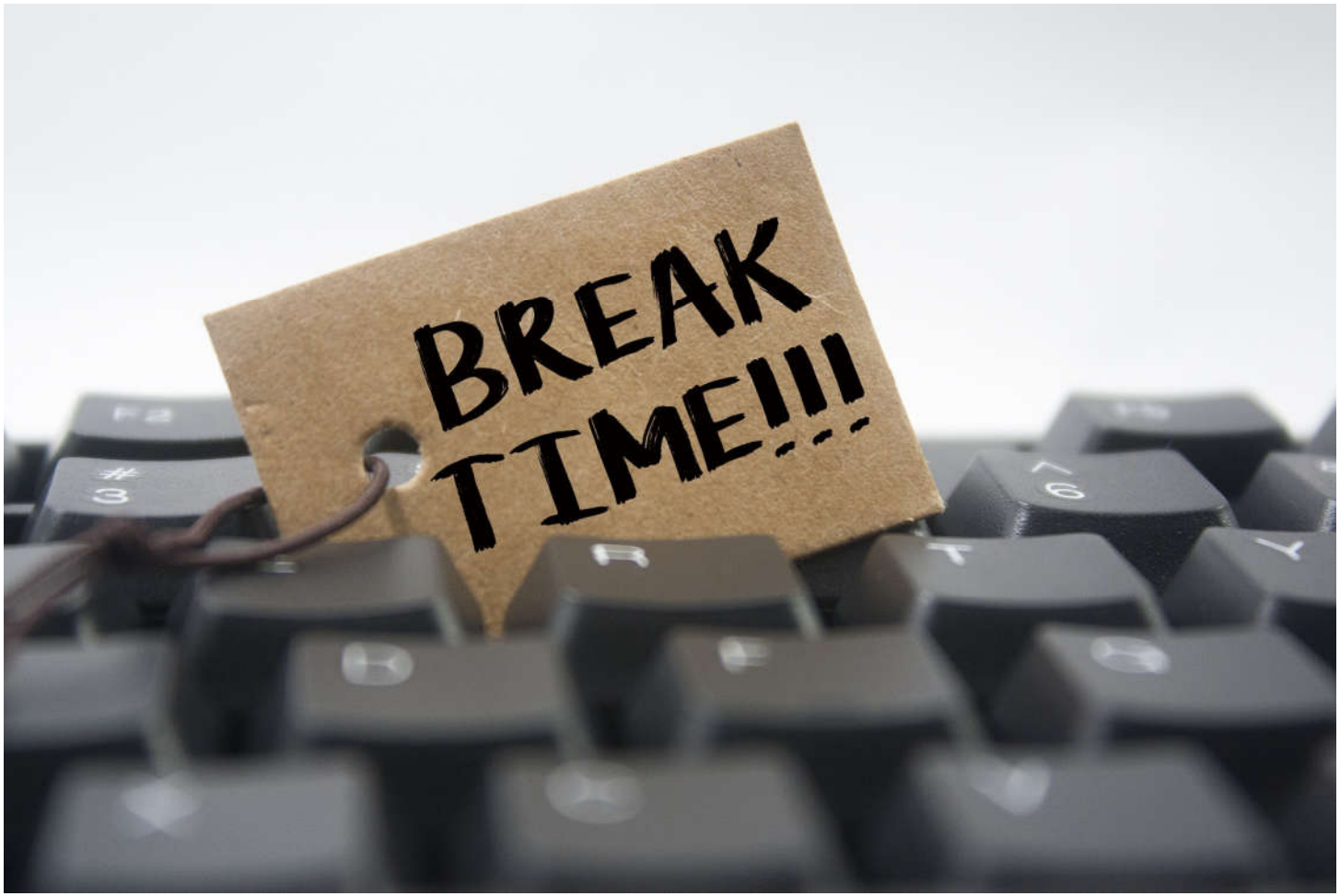
- Trans sphenoidal microadenomectomy
- Pituitary radiation
- Bilateral total adrenolectomy

**Adrenal adenoma and carcinoma**

- Surgical removal

**Ectopic ACTH Syndrome**

- Surgical removal of the ectopic tumor
- Radiotherapy

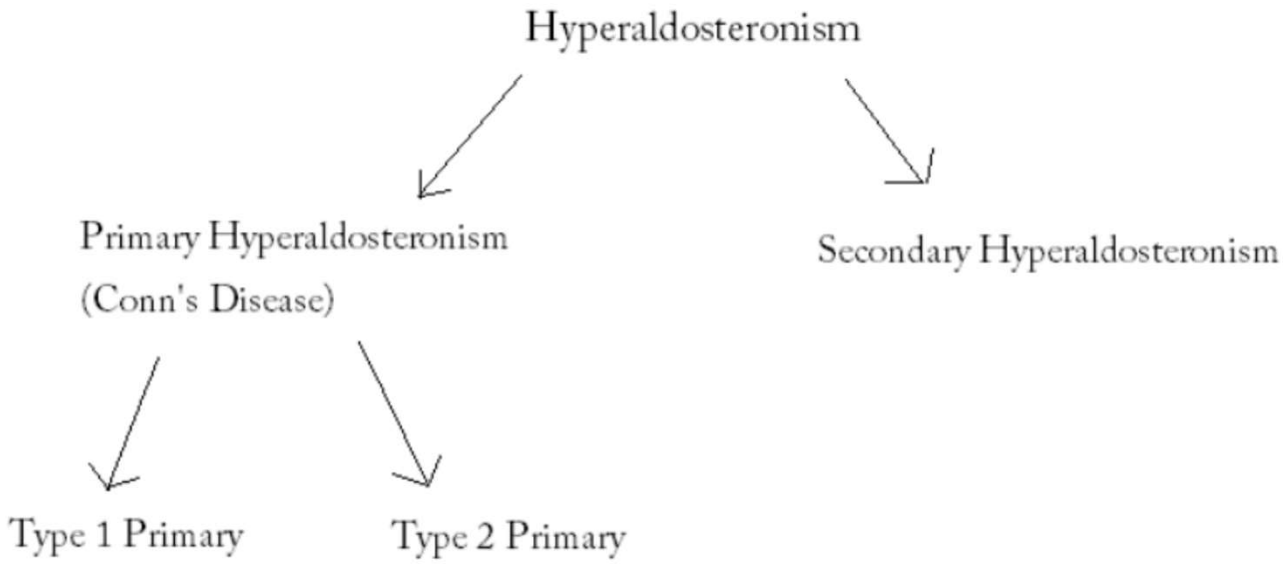

BREAK
TIME!!!

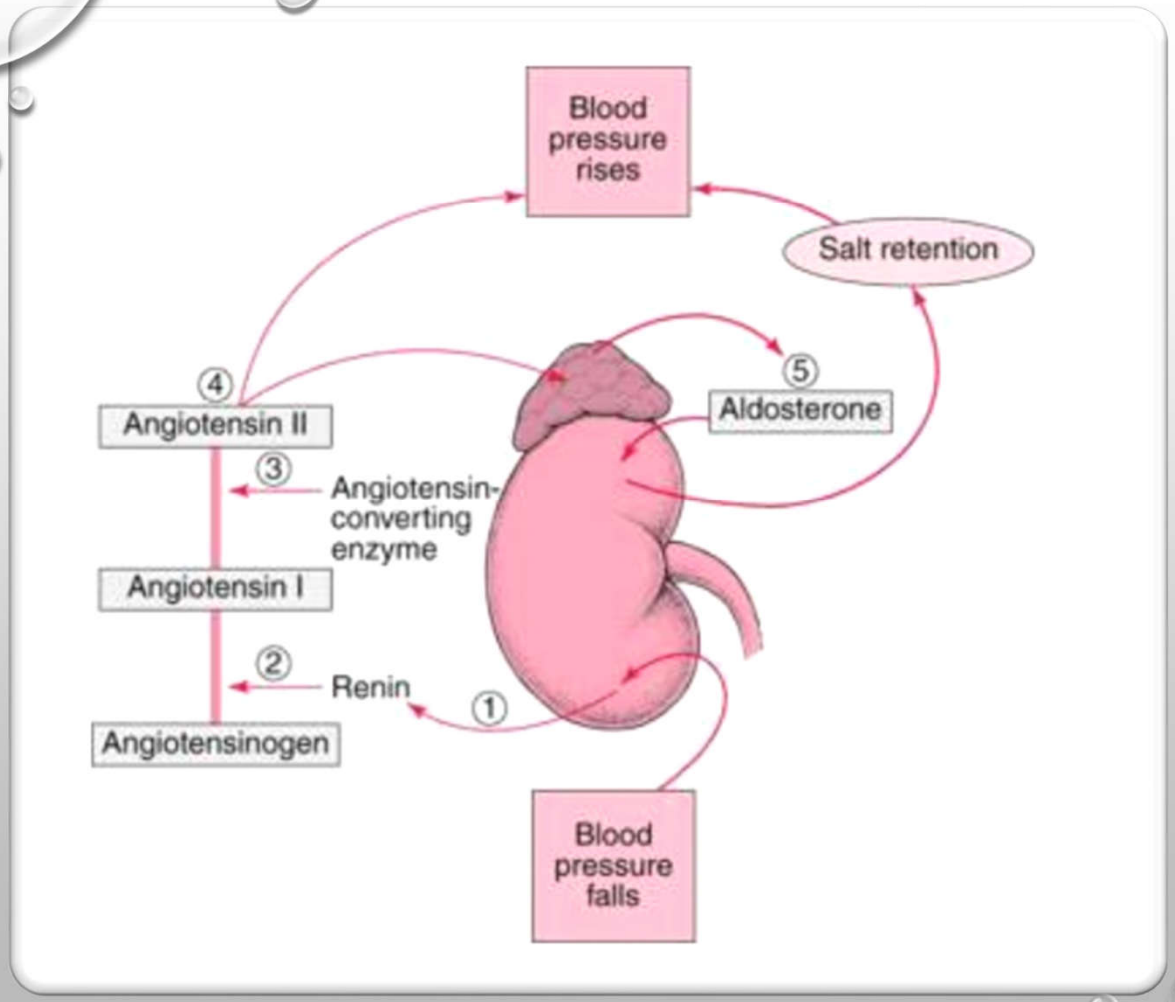
# HYPERALDOSTERONISM

# Aldosterone

Aldosterone is a hormone that controls sodium and potassium levels in the blood. Its overproduction leads to retention of salt and loss of potassium, which then leads to hypertension (high blood pressure).

# Branches of Hyperaldosteronism






# RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM

# Causes of Secondary Hyperaldosteronism

- Increased renin production, commonly caused by the ingestion of oral contraceptives and toxemia from pregnancy.
- Conditions like congestive heart failure, liver failure, kidney disease, cirrhosis, and dehydration
- Certain medicines like diuretics and fludrocortisone.
- Anything that decreases blood flow to the kidneys, lowers blood pressure, or lowers sodium levels.

*Renin - An enzyme secreted by and stored in the kidney area that stimulates aldosterone and therefore, raises blood pressure

# Symptoms of Secondary Hypertension

- Symptoms are similar to those of Primary Hyperaldosteronism
- Moderate hypertension (high blood pressure)
- Most individuals have no other specific symptoms. However, some may have:
  - Muscle weakness
  - Fatigue
  - Temporary paralysis
  - Cramping
  - Headaches
  - Low potassium level
  - Tingling
  - Muscle spasms

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# Diagnosis of Hyperaldosteronism

- Elevated aldosterone levels can be measured in the blood or urine.
  - In a blood test, PRA (Plasma renin activity), is used to distinguish between primary (low PRA) and secondary Hyperaldosteronism (high PRA).
- Abdominal CT scans can show adrenal masses
- Electrocardiograms (ECGs) can show abnormalities in heart rhythm that are often associated with low potassium level.
- It is likely that many cases of secondary Hyperaldosteronism are never detected.

# Treatments for Secondary Hyperaldosteronism

- Secondary Hyperaldosteronism is treated by treating the underlying cause.
- Typically, medication and diet (but not surgery) are used
- When untreated, the disease can lead to uncontrolled hypertension (which can become a risk factor for stroke and heart disease).

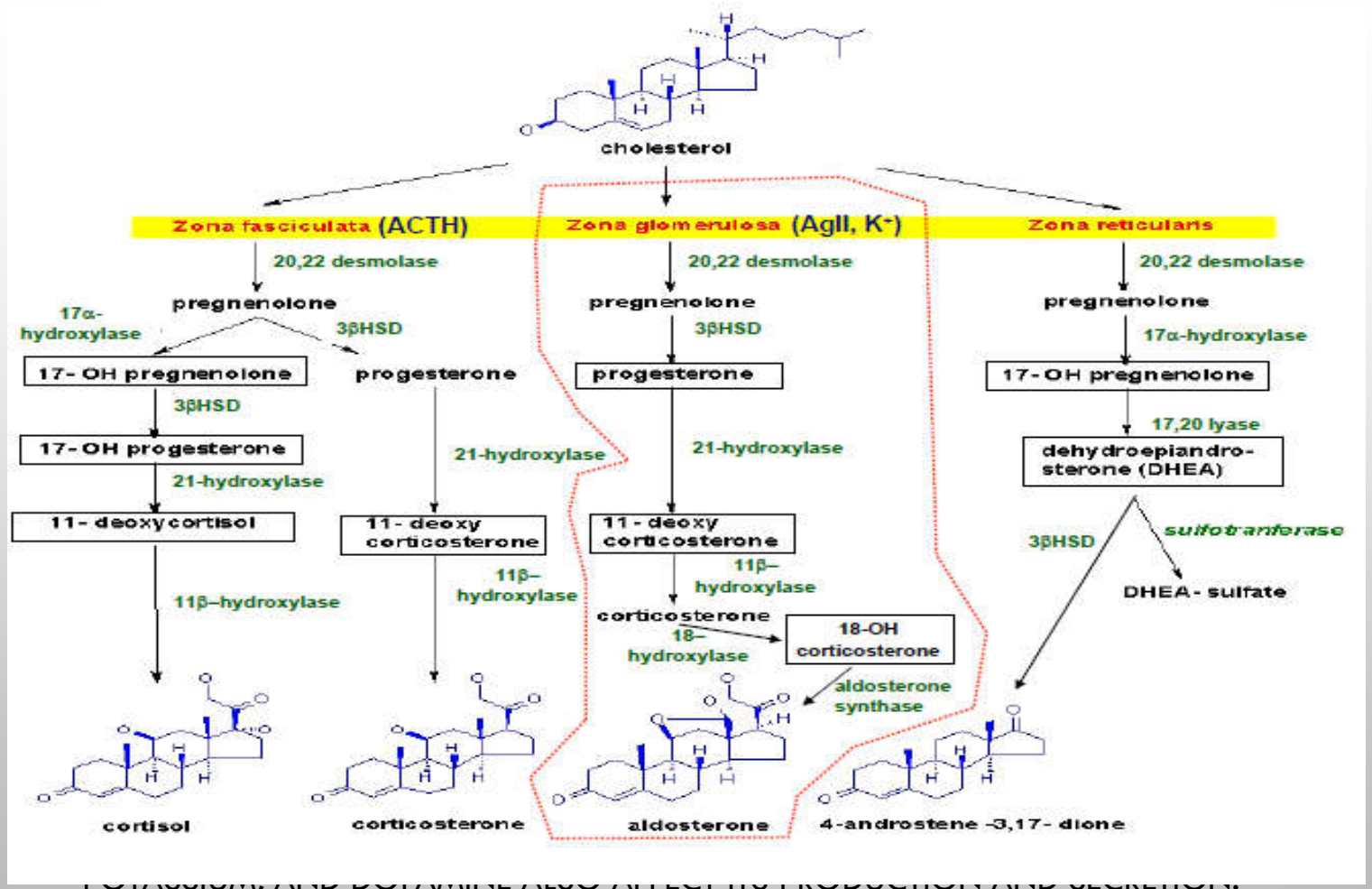
# PRIMARY ALDOSTERONISM

# PREVALENCE OF PRIMARY ALDOSTERONISM

- *COMMON FORM OF SECONDARY HYPERTENSION.*
- *HYPERTENSION ASSOCIATED WITH LOW RENIN AND INCREASED ALDOSTERONE LEVELS THAT ARE NOT SUPPRESSED BY APPROPRIATE TESTING*
- *PREVALENCE AMONG HYPERTENSIVE PATIENTS → 5% AND 13%.*
- *WITH AN ESTIMATED PREVALENCE OF 10% →* **8.5 MILLION PEOPLE** *IN THE US HAVE PRIMARY ALDOSTERONISM.*

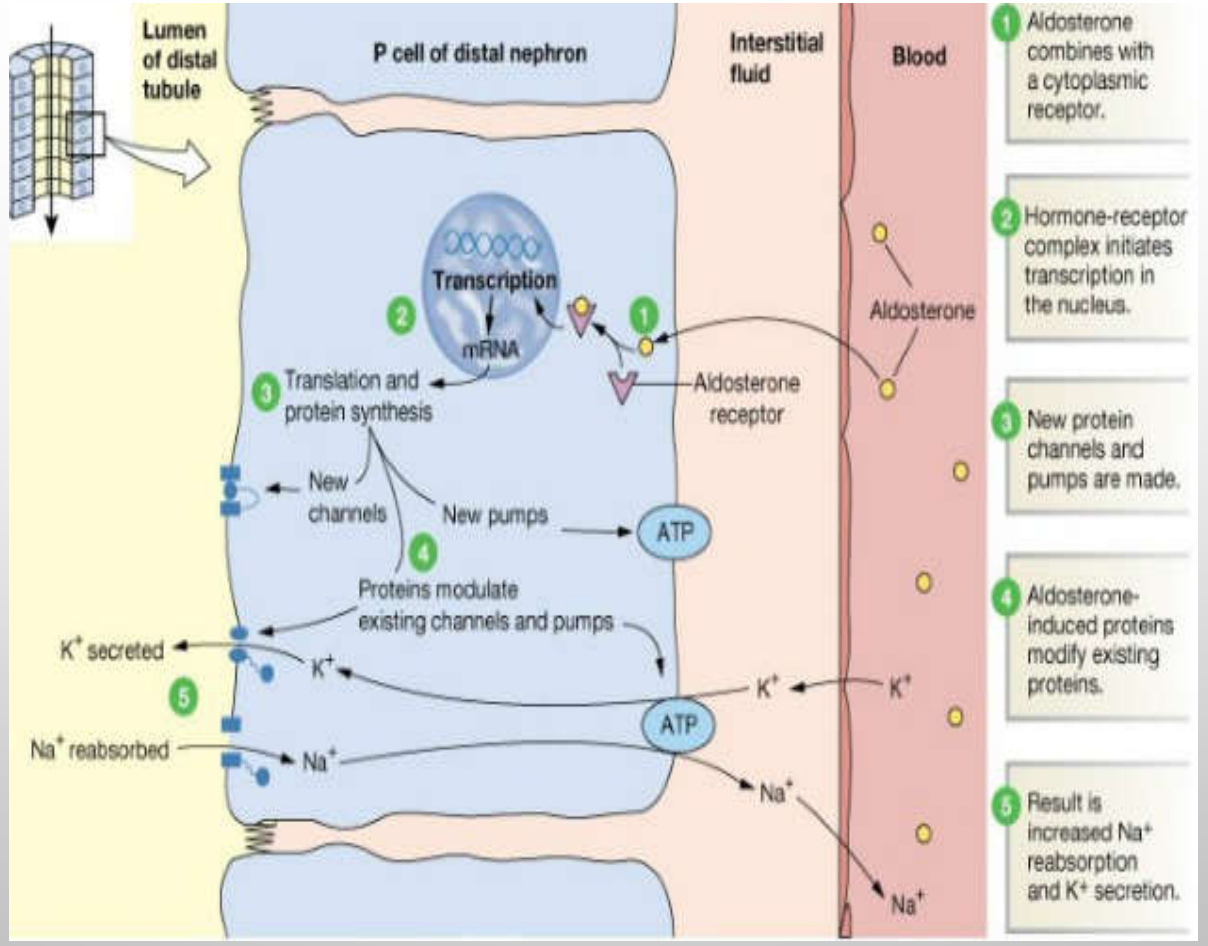
Mosso L *et al.* Primary aldosteronism and hypertensive disease. *Hypertension 2003*

# ALDOSTERONE SYNTHESIS




POTASSIUM) AND DOPAMINE ALSO AFFECT ITS PRODUCTION AND SECRETION.

# ALDOSTERONE ACTION




↑ $U_K$
↑ $U_H$
↓ $U_{Na}$
↑ Blood Vol

↑ $K^+$
↓ $Na^+$
↓ BV

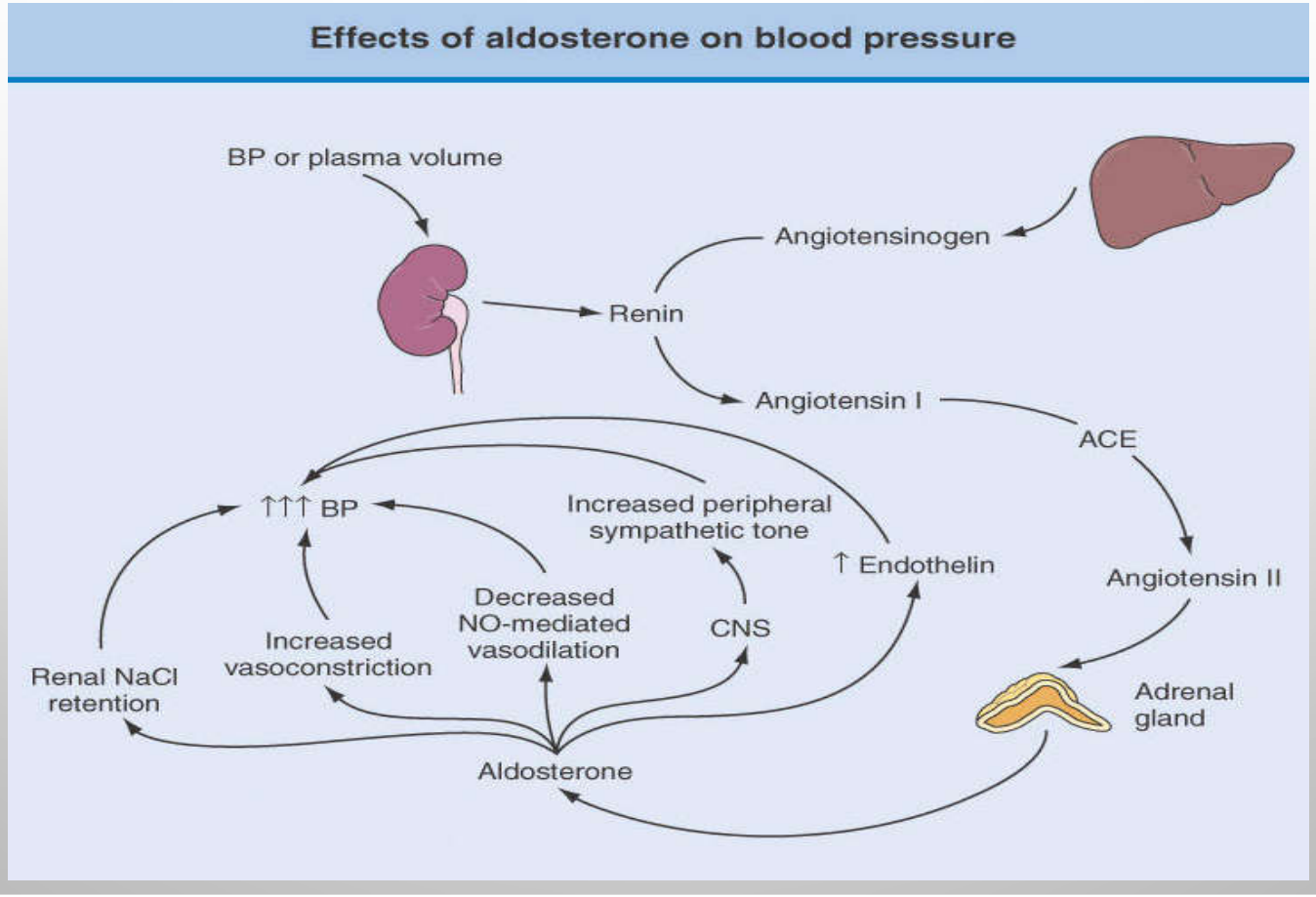
# INHIBITION AND STIMULATION

- *ALDOSTERONE IS STIMULATED BY A NUMBER OF FACTORS BUT THE MOST IMPORTANT INCLUDE ANGIOTENSIN II, HYPERKALEMIA, AND ACTH.*

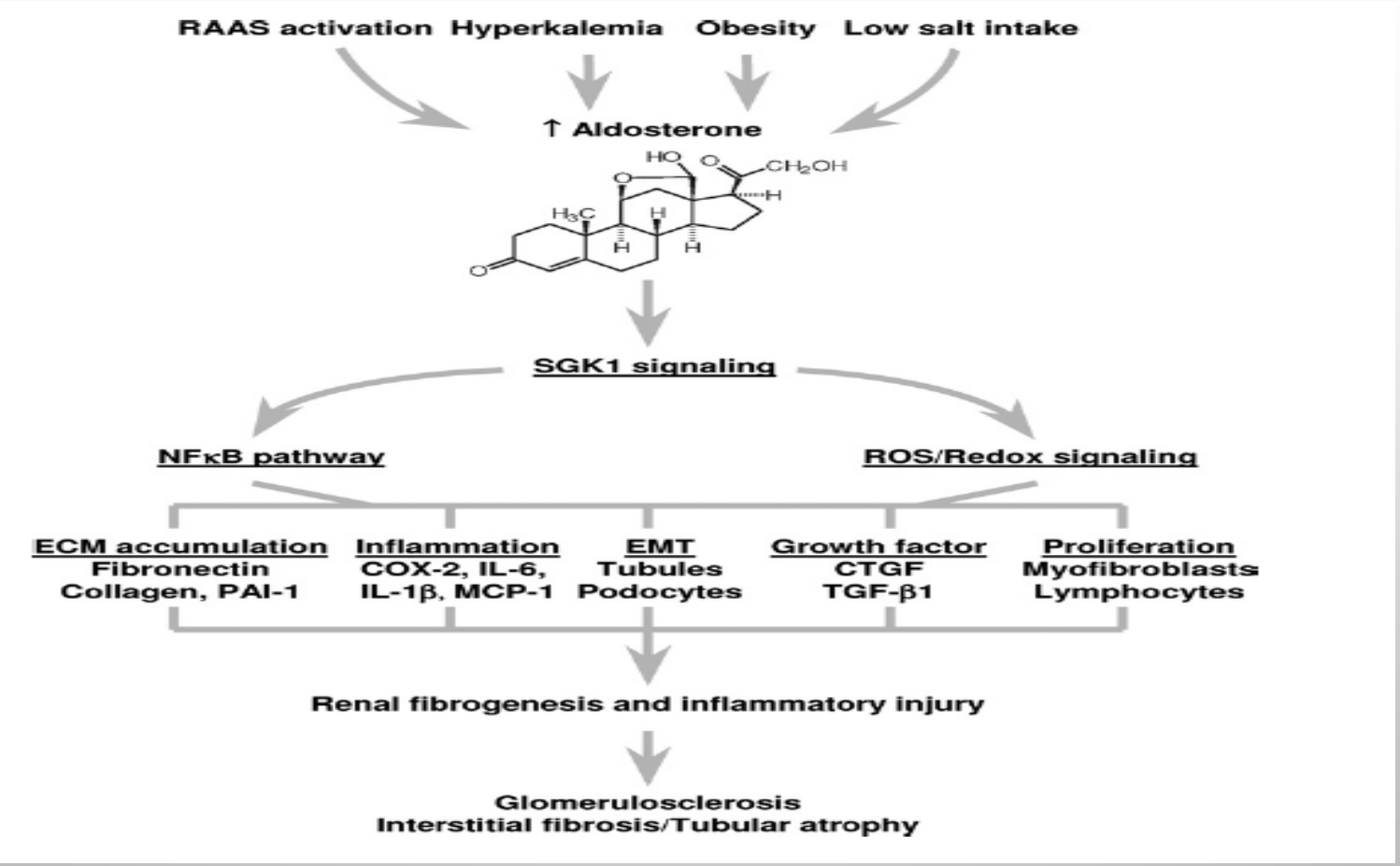
- *ANGIOTENSIN II AND HYPERKALEMIA STIMULATE BOTH THE SYNTHESIS AND STIMULATION OF ALDOSTERONE SYNTHASE IN THE ZONA GLOMERULOSA.*

- *ALDOSTERONE INHIBITION OCCURS PREDOMINANTLY BY ANP AND HYPOKALEMIA*

# ALDOSTERONE REGULATES BLOOD PRESSURE THROUGH A NUMBER OF MECHANISMS



# ALDOSTERONE AND KIDNEY FIBROSIS




Brem AS , Am J Kidney Dis. 2011

# CARDIOVASCULAR EVENTS AND PRIMARY ALDOSTERONISM

| Rate of Cardiovascular Events and Cardiac Structure in Primary Aldosteronism | | | | |
|---|---|---|---|---|
| | *Primary Aldo (n=124)* | *Essential HTN (n=465)* | *Odds ratio (95% CI)* | *p value* |
| *Stroke (%)* | *12.9* | *3.4* | *4.2 (2.0-8.6)* | *< 0.001* |
| *Myocardial infarction (%)* | *4.0* | *0.6* | *6.5 (1.5–27.4)* | *< 0.005** |
| *Atrial fibrillation* | *7.3* | *0.6* | *12.1 (3.2-45.2)* | *<0.0001** |
| *Echo LVH (%)* | *34* | *24* | *1.6 (1.1-2.5)* | *< 0.01* |
| *EKG LVH (%)* | *32* | *14* | *2.9 (1.8-4.6)* | *< 0.001* |

Cardiovascular events (stroke, myocardial infarction and atrial fibrillation) are more common in patients with primary aldosteronism than in subjects with essential hypertension, a finding that is inde pendent of blood pressure.

Milliez P et al. J Am Coll Cardiol 2005; 45(8):1243-1248

# CLINICAL FEATURES

- **HYPERTENSION**
- **HYPOKALEMIA**
- **METABOLIC ALKALOSIS**
  - DUE TO INCREASED URINARY H+ EXCRETION MEDIATED BOTH BY DIRECT STIMULATORY EFFECT OF ALDOSTERONE ON DISTAL ACIDIFICATION
- **MUSCLE WEAKNESS**
  - IT IS PRIMARILY DUE TO HYPOKALEMIA

- **LACK OF EDEMA:**
  - ALTHOUGH ALDOSTERONE INITIALLY INDUCES SODIUM AND WATER RETENTION, THIS IS FOLLOWED WITHIN A FEW DAYS BY A SPONTANEOUS DIURESIS **(CALLED ALDOSTERONE ESCAPE)** THAT RETURNS EXCRETION TO THE LEVEL OF INTAKE AND PARTIALLY LOWERS THE EXTRACELLULAR FLUID VOLUME TOWARD NORMAL .

  - THE MECHANISMS RESPONSIBLE FOR THE ESCAPE PHENOMENON ARE INCOMPLETELY UNDERSTOOD, BUT AT LEAST THREE FACTORS MAY BE IMPORTANT:

❑ **INCREASED SECRETION OF ATRIAL NATRIURETIC PEPTIDE (ANP) INDUCED BY THE HYPERVOLEMIA**

❑ **DECREASED ABUNDANCE OF THE THIAZIDE-SENSITIVE NA-CL COTRANSPORTER THAT MEDIATES SODIUM REABSORPTION IN THE DISTAL TUBULE**

❑ **PRESSURE NATRIURESIS .**

# HYPOKALEMIA: AN INCONSISTENT FINDING

- WITH INCREASING USE OF THE PLASMA ALDOSTERONE TO PLASMA RENIN ACTIVITY RATIO AS A CASE DETECTION TEST FROM PA IN HTN PATIENTS, MORE NORMOKALEMIC PATIENTS ARE BEING IDENTIFIED
- IN A MULTICENTER REVIEW USING THIS APPROACH, APPROXIMATELY 60 PERCENT OF PATIENTS WITH PRIMARY ALDOSTERONISM WERE NOT HYPOKALEMIC

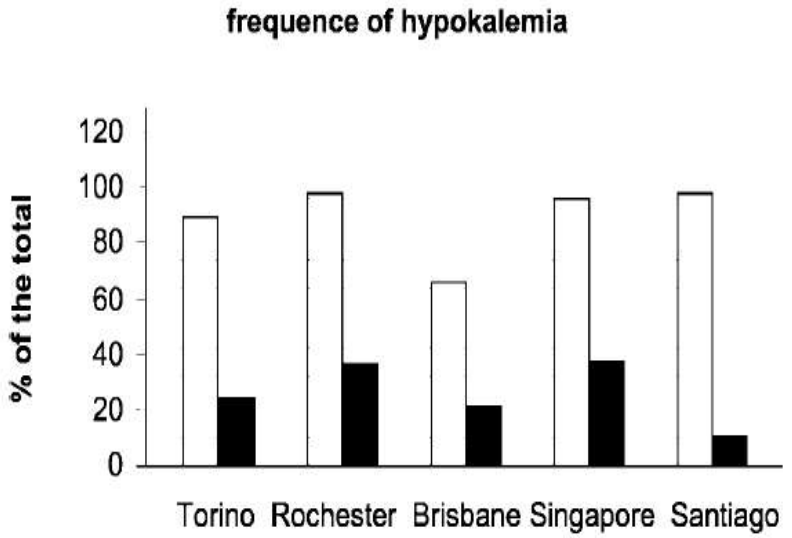


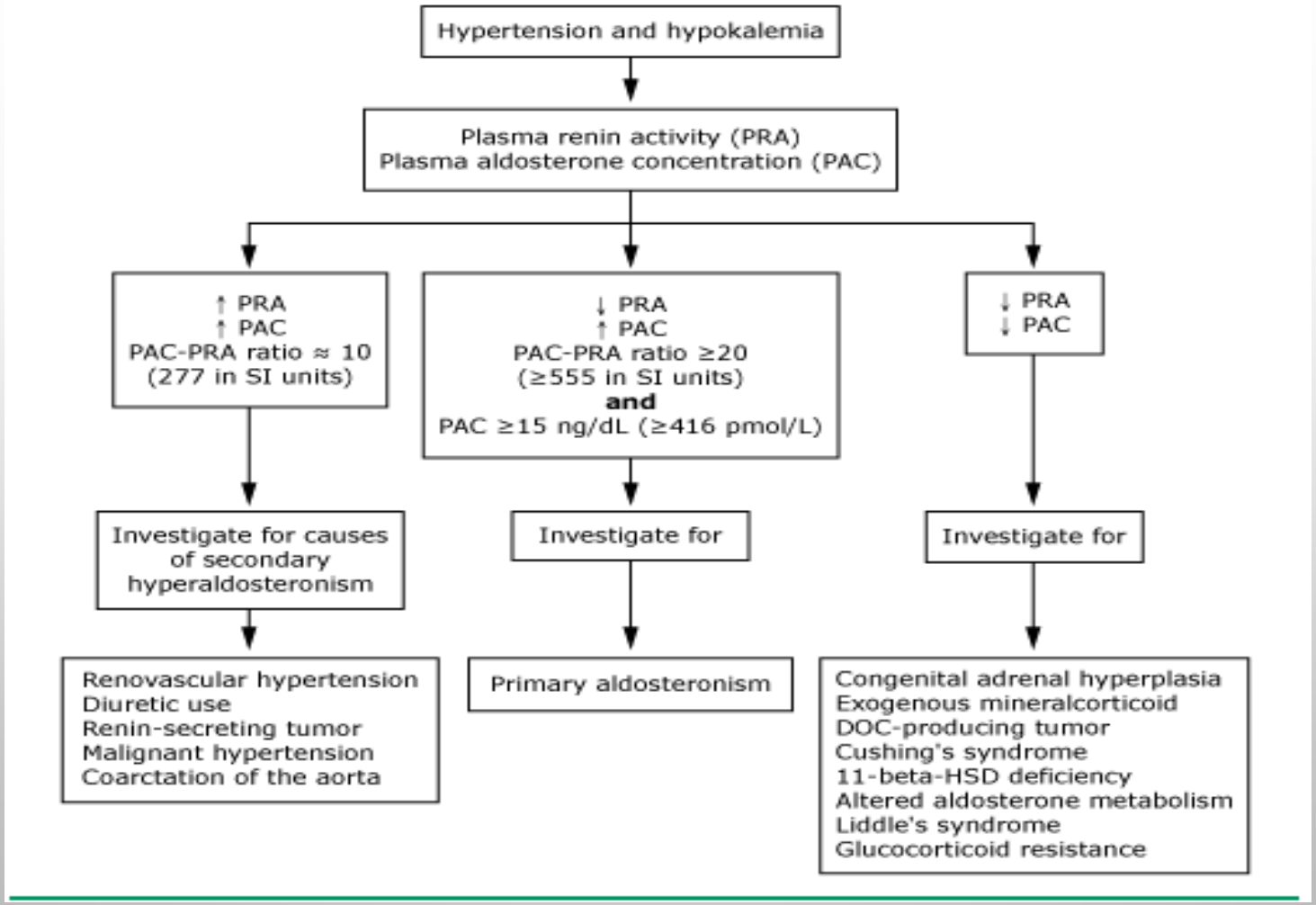

FIG. 2. Percentage of PA patients with hypokalemia. Pre-ARR (*white columns*) signifies the period before adopting the strategy of screening most of the hypertensives referred to the center. Post-ARR (*black columns*) signifies the period after the widespread use of the ARR as a screening test. Torino: pre-ARR 1988–1993, post-ARR 1994–2002; Rochester: pre-ARR 1955–1985, post-ARR 1999; Brisbane: pre-ARR 1971–1991, post-ARR 1992–2002; Singapore: pre-ARR 1990–1994, post-ARR 1995–2001

Mulatero *et al* J Clin Endocrinol Metab, March 2004

# SCREENING FOR PA : ARR

- **Aldosterone-Renin Ratio (ARR)>20 *and* Aldosterone level>15 ng/dl**
- **Morning testing**
- **K+ repletion**
- **Mineralocorticoid receptor antagonists (spironolactone and eplerenone) and high-dose amiloride (e.g. >5 mg daily) should be dis continued 6 weeks before blood sampling to avoid direct interference with the results**
- **Confirmatory testing should be performed**

# PAC/PRA ratio in hypertension and hypokalemia



# CONFIRMATORY TEST FOR PRIMARY ALDOSTERONISM

**Confirmatory Testing for Diagnosis of Primary Hyperaldosteronism**

| Test | Method | Evaluation | Limitations |
|---|---|---|---|
| Oral NaCl loading | Oral NaCl intake >200 mmol/d for 3 days, with oral KCl as needed to prevent hypokalemia, with subsequent 24–h urine aldosterone measurement | Urine aldosterone <10 μg/d, diagnosis unlikely; >12 μg/d, diagnosis likely | Avoid if severe uncontrolled hypertension, CKD, CHF, cardiac arrhythmias, or severe hypokalemia |
| Saline infusion test | Patient in recumbent position for 1 h before testing and then throughout entire test<br>Begin test between 8:00 and 9:30 am. Measure plasma aldosterone, plasma renin activity, cortisol, and potassium at beginning of test and then after infusion of 2 L/NS IV during 4 h | Plasma aldosterone at end of infusion <5 ng/dl, diagnosis unlikely; <10 ng/dl diagnosis likely; 5–10 ng/dl, indeterminate | Avoid if severe uncontrolled hypertension, CKD, CHF, cardiac arrhythmias, or severe hypokalemia |
| Fludrocortisone suppression test | Fludrocortisone, 0.1 mg PO every 6 h for 4 days, plus oral NaCl, 30 mmol 3x/d, and high-salt diet combined with sufficient KCl to avoid hypokalemia | Upright plasma aldosterone on day 4 >6 ng/dl and plasma renin activity <1 ng/ml/hr, diagnosis likely | Frequently requires hospitalization for patient monitoring of blood pressure and potassium |
| Captopril challenge test | Oral captopril, 20–50 mg, with plasma aldosterone and plasma renin activity obtained immediately before captopril and then 1–2 h afterward, with patient seated throughout test | Plasma aldosterone decrease >30%, diagnosis unlikely | Probably more false-positive and false-negative results than other tests |

# CT SCAN OF SUPRARENAL GLAND

- *INITIAL STUDY TO DETERMINE SUBTYPE (ADENOMA VERSUS HYPERPLASIA) AND EXCLUDE ADRENAL CARCINOMA*

- *THE DIAGNOSIS OF AN ADRENAL CARCINOMA SHOULD BE SUSPECTED WHEN A UNILATERAL LARGE (>4 CM) ADRENAL MASS IS FOUND ON CT*

- *AN ABNORMALITY IN BOTH GLANDS SUGGESTS ADRENAL HYPERPLASIA; HOWEVER, PATIENTS WITH HYPERPLASIA MAY ALSO HAVE NORMAL APPEARING ADRENAL GLANDS ON CT*

# LIMITATIONS

- LOTS OF FALSE POSITIVES
  - ONLY CAN IMAGE ADENOMA IF $\geq$ 1CM
  - OF THESE, 1/3 ARE INCIDENTALOMA (NO LATERALIZATION ON ADRENAL VEIN SAMPLING)
- LOTS OF FALSE NEGATIVES
  - UP TO 1/3 OF ADENOMAS ARE MISSED BECAUSE OF SMALL SIZE (LATERALIZE ON ADRENAL VEIN SAMPLING)

# ADRENAL VEIN SAMPLING

- IT IS A MEASUREMENT OF ALDOSTERONE IN SAMPLES OF ADRENAL VENOUS BLOOD, OBTAINED BY AN EXPERIENCED RADIOLOGIST
- IS THE CRITERION STANDARD TEST TO DISTINGUISH BETWEEN UNILATERAL ADENOMA AND BILATERAL HYPERPLASIA.
- UNILATERAL DISEASE IS ASSOCIATED WITH A MARKED (USUALLY FOURFOLD GREATER THAN CONTRALATERAL ADRENAL) INCREASE IN PAC ON THE SIDE OF THE TUMOR, WHEREAS THERE IS LITTLE DIFFERENCE BETWEEN THE TWO SIDES IN PATIENTS WITH BILATERAL HYPERPLASIA.

- **INDICATIONS —** THE ENDOCRINE SOCIETY RECOMMENDS AVS TO CONFIRM UNILATERAL DISEASE IN ALL PATIENTS WITH PRIMARY ALDOSTERONISM WHO WOULD LIKE TO PURSUE SURGICAL MANAGEMENT (UNILATERAL ADRENALECTOMY).

- OTHER CENTERS APPROACH IS SLIGHTLY DIFFERENT, THEY RECOMMEND AVS IN SUCH PATIENTS WHEN THE CT SCAN IS NORMAL, SHOWS BILATERAL ABNORMALITIES, OR SHOWS A UNILATERAL ABNORMALITY, BUT THE PATIENT IS OVER AGE 40.

# TREATMENT OF PRIMARY ALDOSTERONISM

- GENERAL PRINCIPLES — *ESTABLISHING THE CORRECT DIAGNOSIS IS ESSENTIAL SINCE THE TREATMENT OF PRIMARY ALDOSTERONISM IS BASED UPON WHETHER THE ADRENAL ALDOSTERONE HYPERSECRETION IS UNILATERAL (ADENOMA, UNILATERAL HYPERPLASIA, OR CARCINOMA) OR BILATERAL (IDIOPATHIC ADRENAL HYPERPLASIA OR GLUCOCORTICOID-REMEDIABLE ALDOSTERONISM).:*

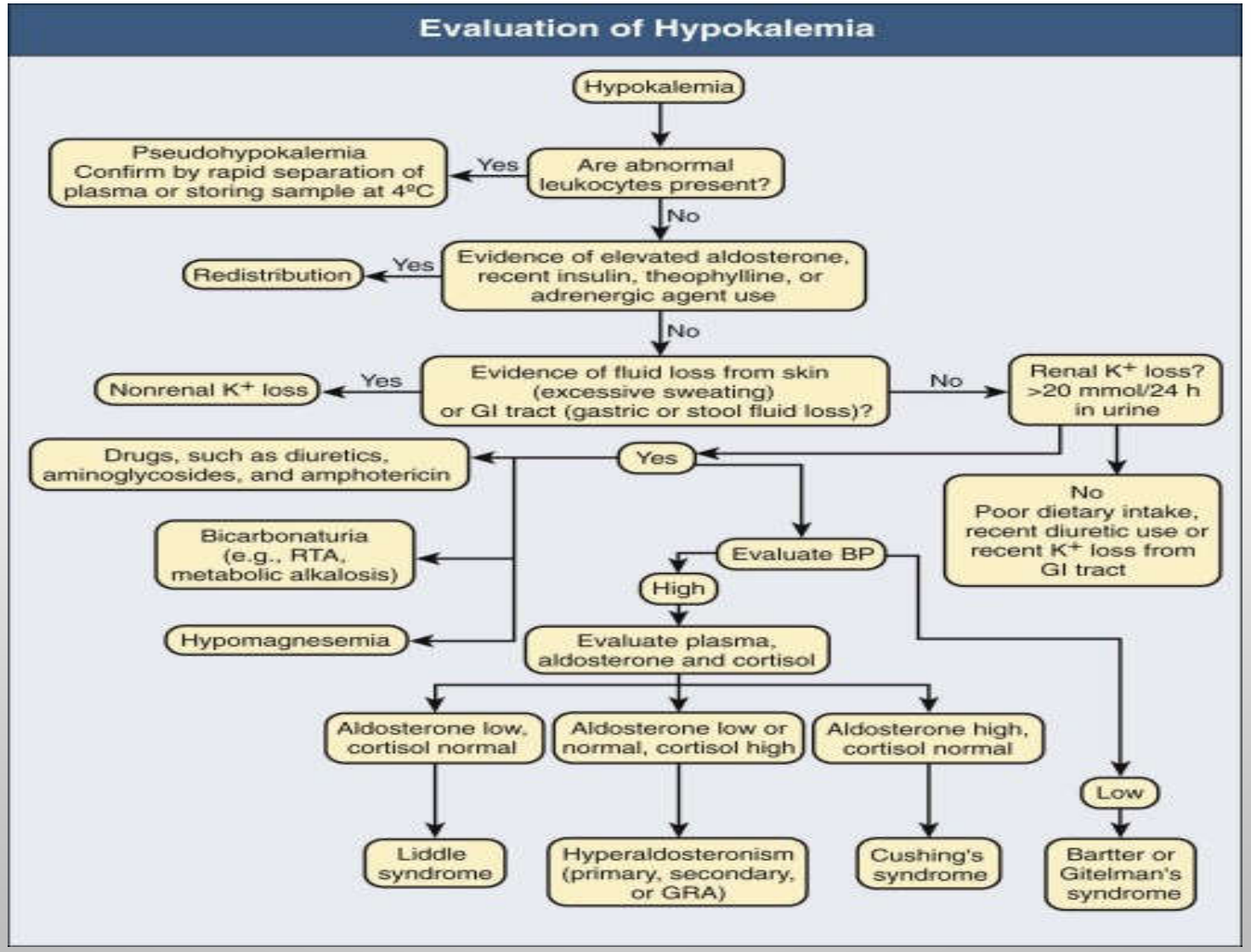
## *TWO LINES OF TREATMENTS*

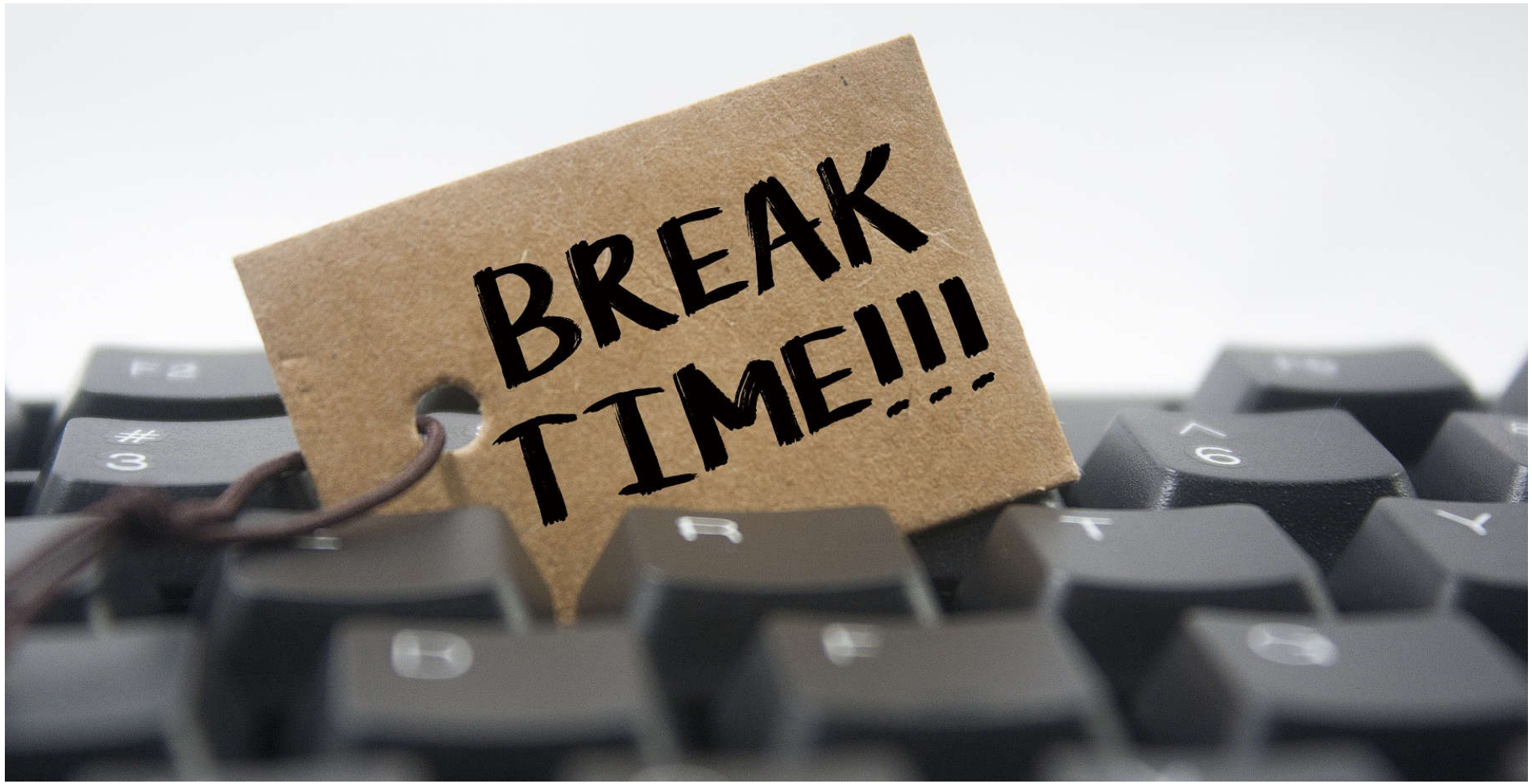
1) SURGERY IS CURATIVE ONLY IN PATIENTS WITH UNILATERAL DISEASE.

2)PATIENTS WITH BILATERAL IDIOPATHIC ADRENAL HYPERPLASIA ARE TREATED WITH A MINERALOCORTICOID ANTAGONIST.

# MEDICAL THERAPY

- *ALDOSTERONE ANTAGONISTS — ALTHOUGH LAPAROSCOPIC ADRENALECTOMY IS MORE COST-EFFECTIVE OVER TIME , THE ADMINISTRATION OF AN ALDOSTERONE (MINERALOCORTICOID RECEPTOR) ANTAGONIST* **IS AN EFFECTIVE ALTERNATIVE IN PATIENTS WHO REFUSE OR ARE NOT CANDIDATES FOR SURGERY.**


Evaluation of Hypokalemia
Hypokalemia
Are abnormal leukocytes present?
Yes
Pseudohypokalemia Confirm by rapid separation of plasma or storing sample at 4°C
No
Evidence of elevated aldosterone, recent insulin, theophylline, or adrenergic agent use
Yes
Redistribution
No
Evidence of fluid loss from skin (excessive sweating) or GI tract (gastric or stool fluid loss)?
Yes
Nonrenal K+ loss
No
Renal K+ loss? >20 mmol/24 h in urine
Yes
Drugs, such as diuretics, aminoglycosides, and amphotericin
Bicarbonaturia (e.g., RTA, metabolic alkalosis)
Hypomagnesemia
No Poor dietary intake, recent diuretic use or recent K+ loss from GI tract
Evaluate BP
High
Evaluate plasma, aldosterone and cortisol
Aldosterone low, cortisol normal
Aldosterone low or normal, cortisol high
Aldosterone high, cortisol normal
Low
Liddle syndrome
Hyperaldosteronism (primary, secondary, or GRA)
Cushing's syndrome
Bartter or Gitelman's syndrome


BREAK
TIME!!!

# Congenital Adrenal Hyperplasia

# Congenital adrenal hyperplasias(CAH)

- A group of heritable disorders with an inability /reduced ability to produce cortisol.
- The disease begins early in gestation and leads to disease that is manifest at birth/ later.
- Without cortisol, no negative feedback and so, excessive secretion of CRH from hypothal& ACTH from anterior pituitary
- Continued secretion of ACTH causes **unremitting stimulation of the adrenal cortex, leading to hyperplasia.**

# CAH

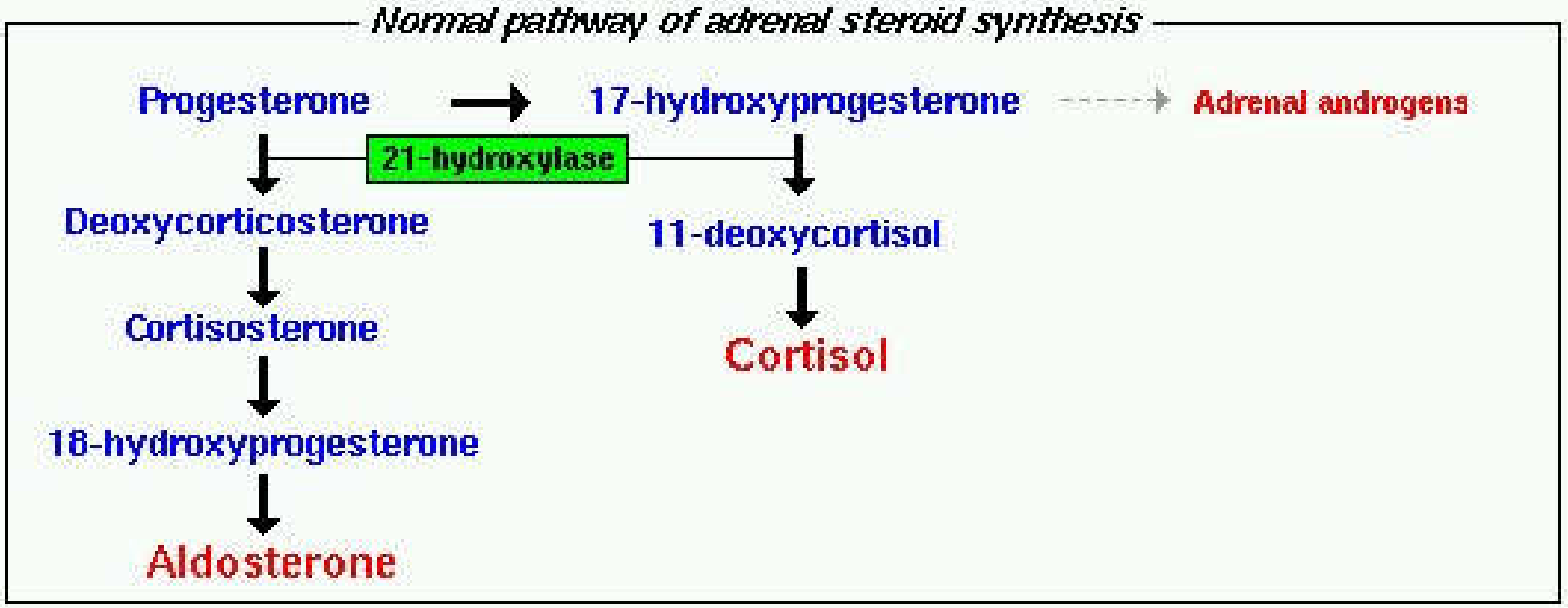
- In most cases, adrenal hyperplasia also involves a deficiency in aldosterone which results in mild to severe loss of body sodium.
- It also involves overproduction of adrenal androgens , which, in affected females, results in prenatal virilization with an ambiguous /male external genitalia at birth.

# CAH Due to 21-Hydroxylase Deficiency

•Greater than 90% of the cases of CAH are the result of deficiency in the enzyme steroid 21-hydroxylase. Absolute or partial deficiency in this enzyme leads to two problems:

*1.Deficiency in production of cortisoland aldosterone*

*2.Shunting of steroid precursors to form androgens*


Normal pathway of adrenal steroid synthesis
Progesterone
17-hydroxyprogesterone
Adrenal androgens
21-hydroxylase
Deoxycorticosterone
11-deoxycortisol
Cortisosterone
Cortisol
18-hydroxyprogesterone
Aldosterone


21-hydroxylase deficiency (absolute)
Progesterone
17-hydroxyprogesterone
Adrenal androgens

# CAH 21-hydroxylase deficiency
# Incidence and Clinical Presentation

1 of every 15,000 births. Three primary forms:

*1.Simple virilizingform*: 25%.

Excess prenatal production of androgens

- masculinizationin females -"ambiguous genitalia" or appears male.
- males are usually normal at birth.

Linear growth is accelerated, but epiphyses fuse early ⇦short stature.

# CAH 21-hydroxylase deficiency
# Incidence and Clinical Presentation

2. *Salt-wasting form*: 75%. Inadequate aldosterone. Electrolyte & water imbalance; "adrenal crisis“ at 1 -4 wks (non-specific signs-poor appetite, vomiting and failure to grow).

3. *Non-classical form**: Mild, usually manifest as androgen excess later in life.

# CAH: Diagnosis and Prenatal Screening

- 21-hydroxylase deficiency is first suspected in a newborn infant with "ambiguous genitalia".
- Elevated blood levels of 17-hydroxyprogesterone, and USG ⇧rapid diagnosis.
- DD:
  - –True hermaphorditism
  - –Pseudohermaphroditism
  - –Sex chromosome abnormalities
- None have high 17-hydroxyprogesterone.

# CAH: Treatment

- All forms-glucocorticoid replacement therapy.
  - –alleviates glucocorticoiddeficiency
  - –provides negative feedback to suppress ACTH secretion and prevent continued adrenal stimulation.
  - –As a result, excessive 17-hydroxyprogesterone is N/A as a substrate for excessive androgen production.
- Patients with the salt-wasting form –also need mineralocorticoidtherapy.

# CAH: Treatment

- Prenatal treatment of mother with glucocorticoids can prevent/reduce the virilizing effects of fetal21-hydroxylase deficiency (previous afflicted babies; AR inheritance).

- Surgical correction of genital anomalies and gender reassignment in adults.

# THANK YOU