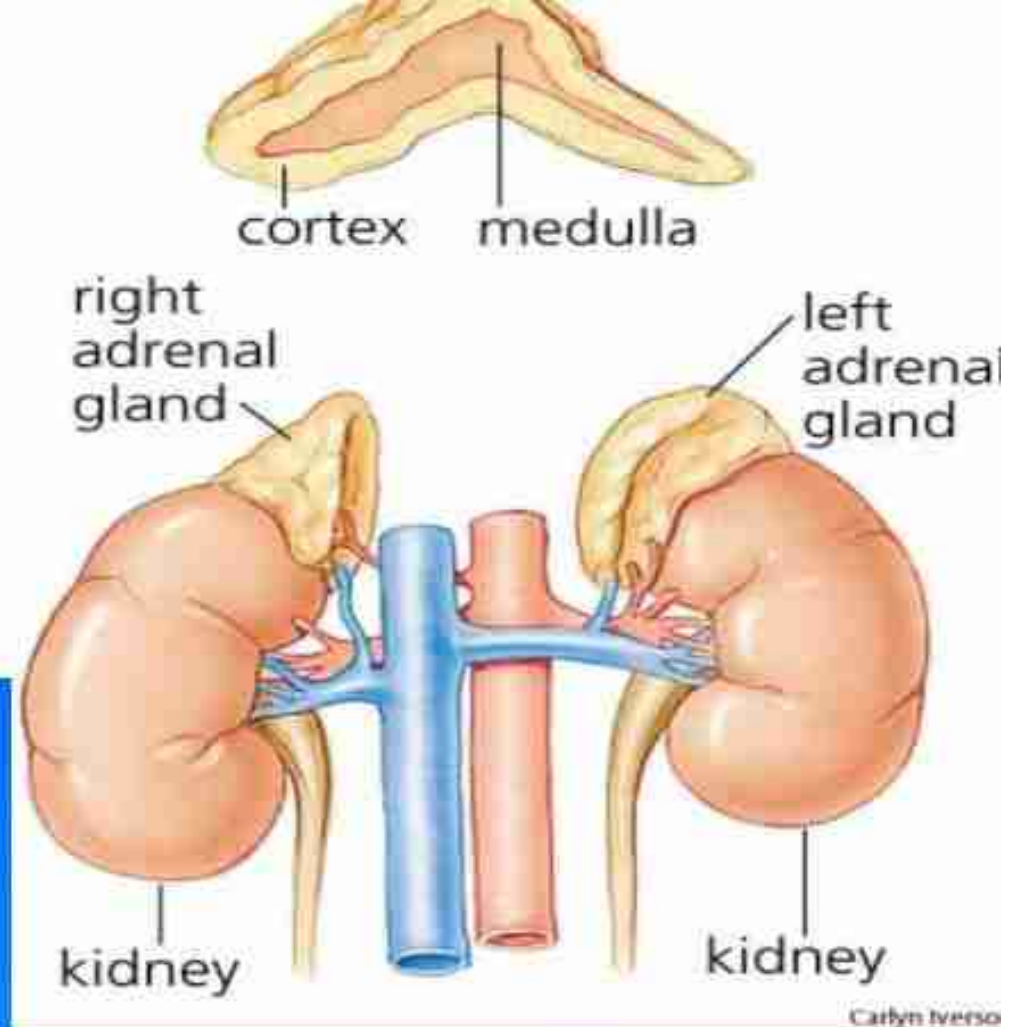


PATHOLOGY OF ADRENAL GLANDS

- Paired endocrine organ
- 4 gm each
- Cortex & medulla

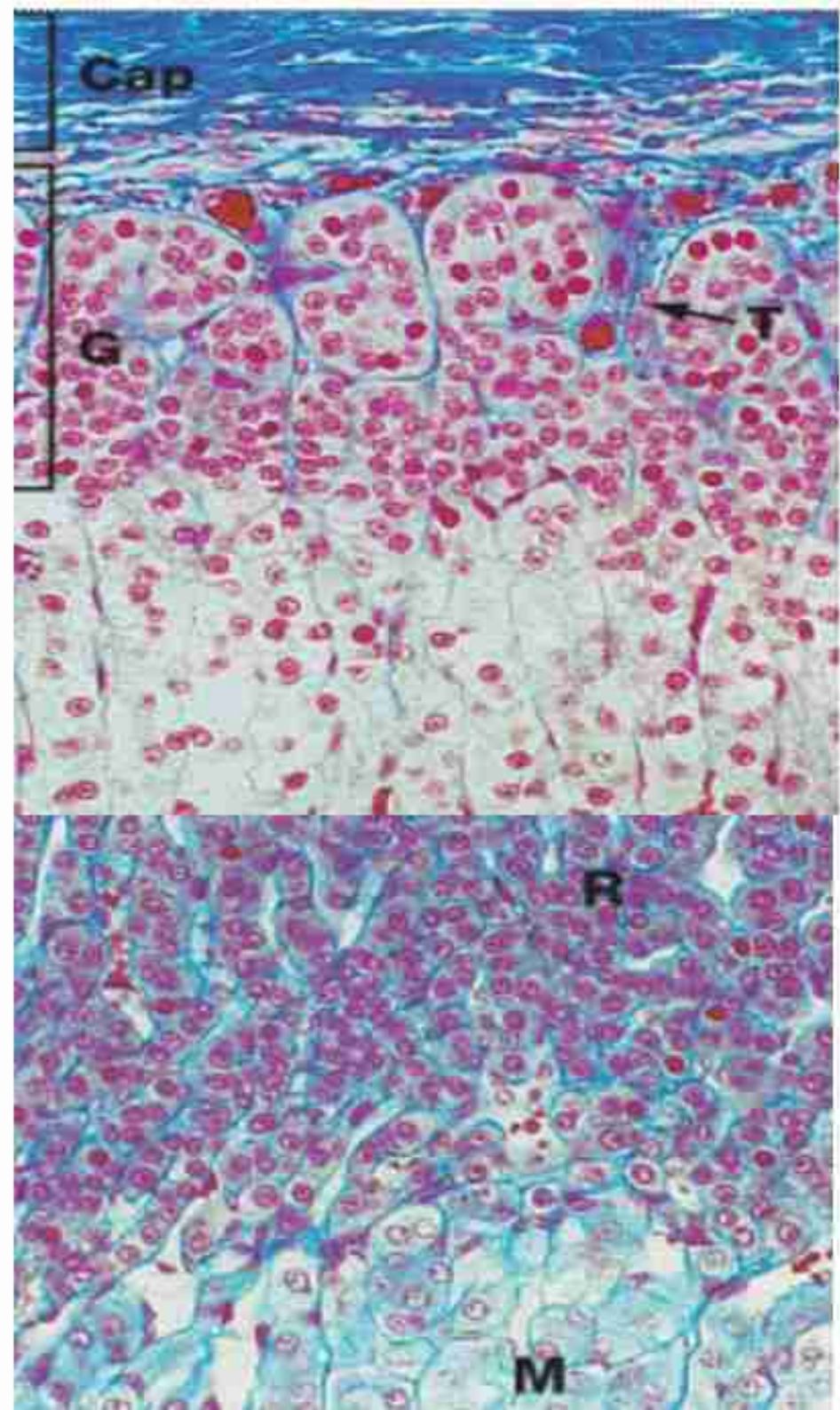


Adrenal Cortex

- Zona Glomerulosa
 - Mineralocorticoids
- Zona Fasciculata
 - Glucocorticoids
- Zona Reticularis
 - Sex steroids

Adrenal Medulla

- Chromaffin cells
 - Catecholamines



-
- Functional disorders
 - Hyperfunction
 - Hypofunction
 - Neoplasms

Hyperfunction

- Hypercortisolism (Cushing syndrome)
- Hyperaldosteronism (Conn syndrome)
- Adrenogenital (Virilising) syndrome

Hypofunction

- Adrenocortical insufficiency

Adrenal neoplasms

- Cortex-
 - Adenoma
 - Carcinoma
- Medulla
 - Pheochromocytoma
 - Neuroblastoma

HYPERCORTICOLISM (Cushing Syndrome)

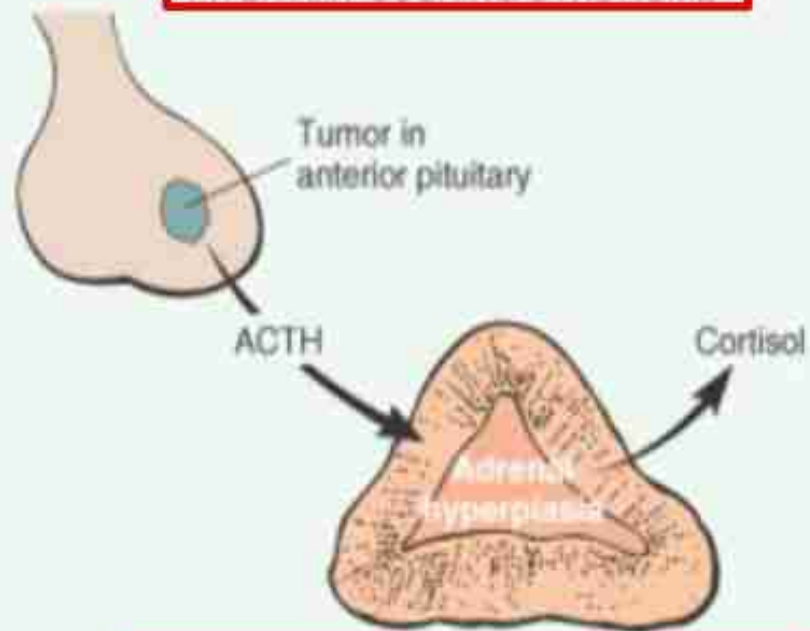
Hypercortisolism

-  Glucocorticoid levels

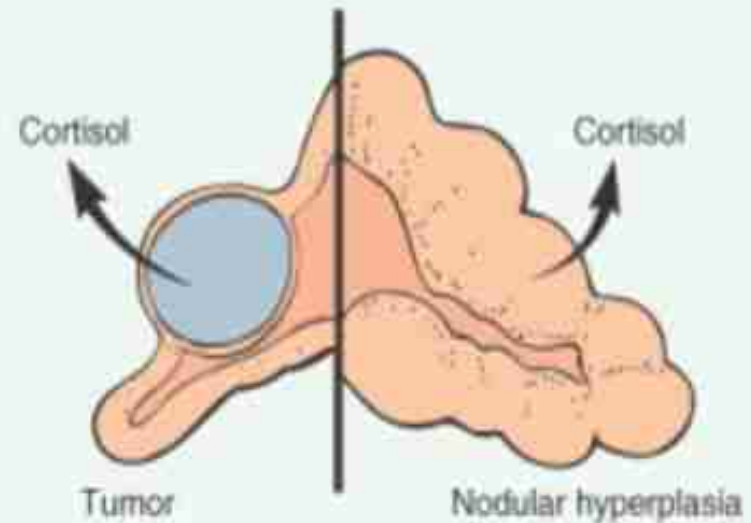
Causes

- Exogenous – iatrogenic- most common
- Endogenous
 - ACTH dependent
 - ACTH independent

PITUITARY CUSHING SYNDROME

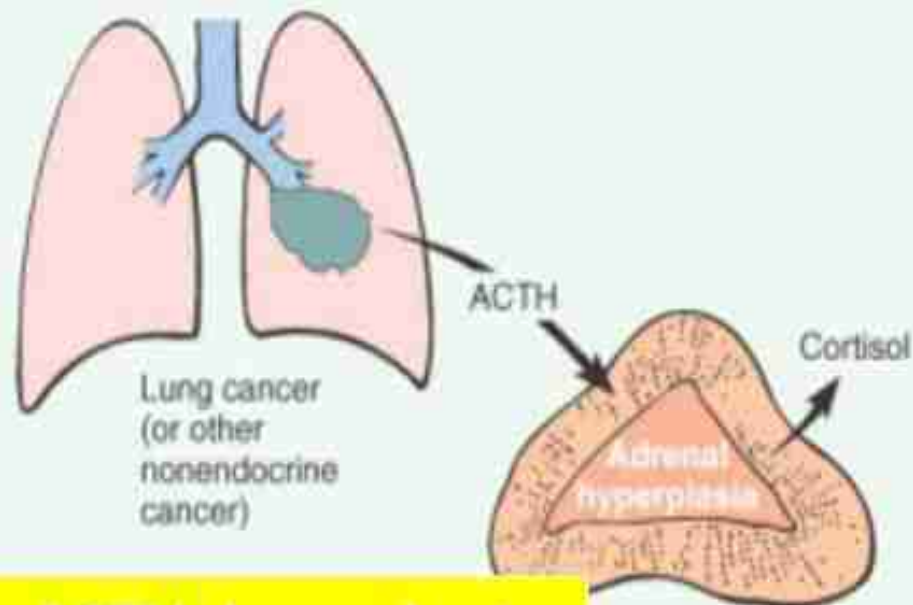


ADRENAL CUSHING SYNDROME



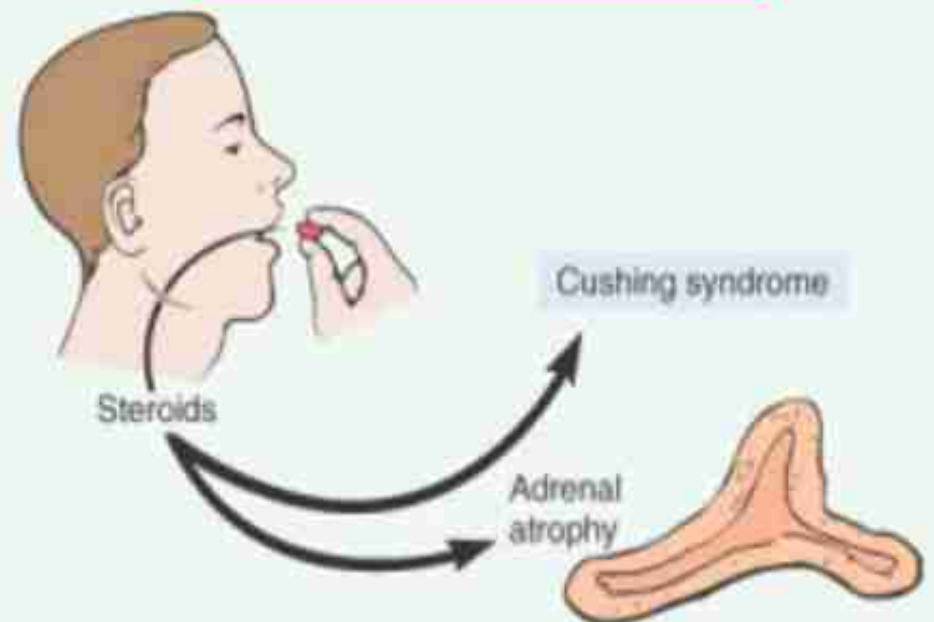
ACTH independent

PARANEOPLASTIC CUSHING SYNDROME



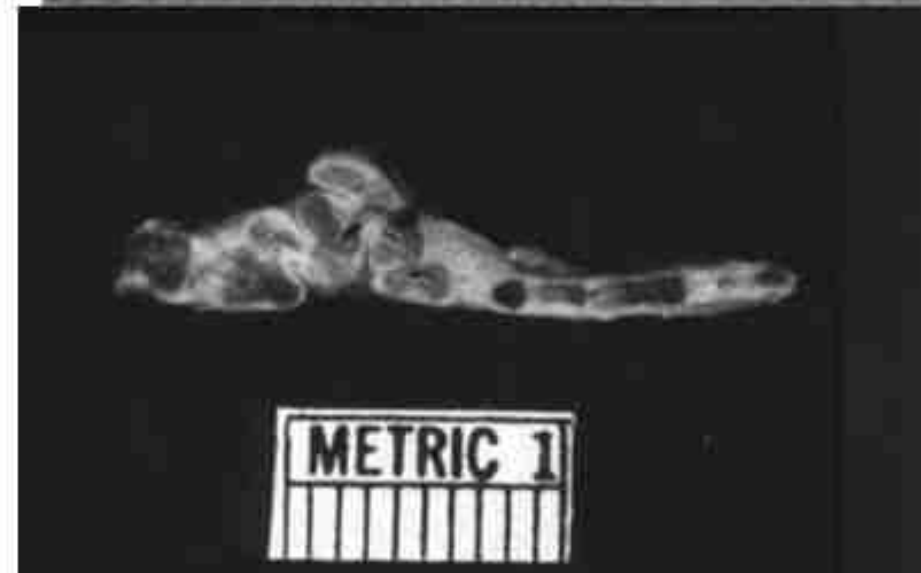
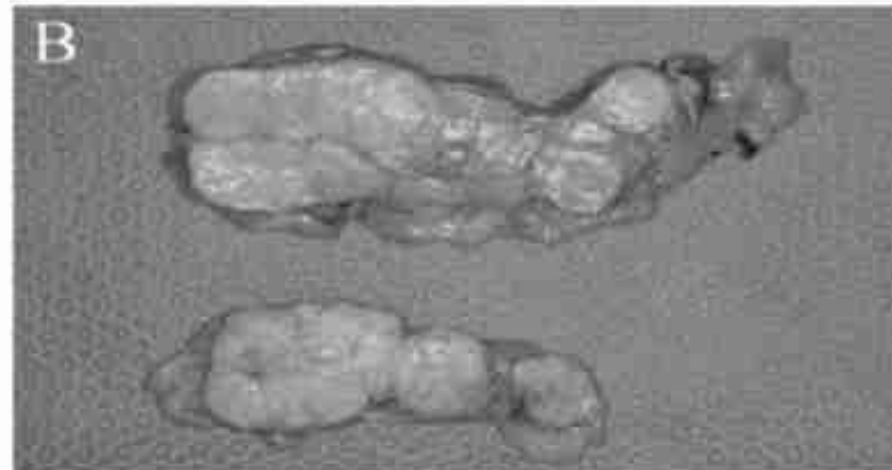
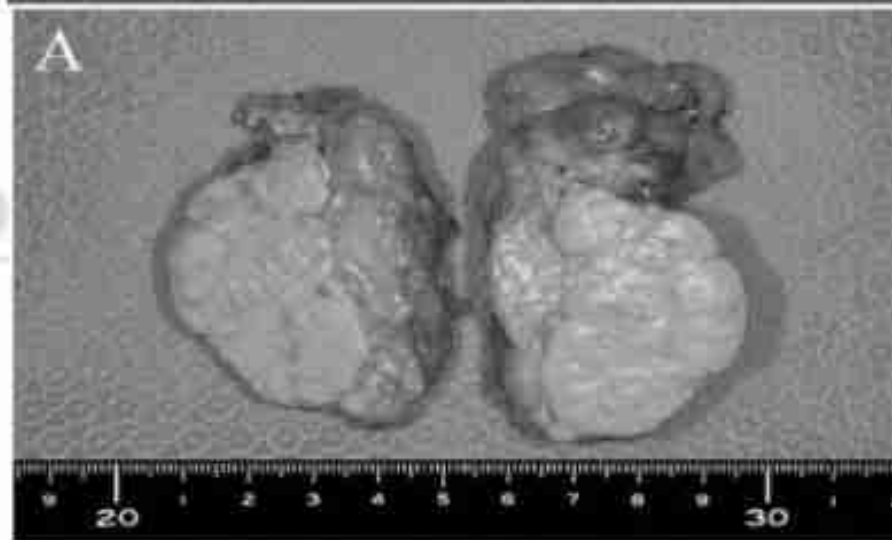
ACTH dependent

IATROGENIC CUSHING SYNDROME



Morphology

- Pituitary –
 - Crooke hyaline change
- Adrenals-
 - Atrophy, if exogenous
 - Hyperplastic-
diffuse/nodular
 - Neoplasia -
adenoma/carcinoma



Clinical features

- Central or truncal **obesity**
- **Moon facies, buffalo hump**
- Catabolic effect on bones and collagen
 - Pathological fractures, osteoporosis
 - Skin fragile, easy bruisability, **abdominal striae**



Clinical features

- Atrophy of proximal muscles --> weakness
- Secondary DM
- **Hirsutism, amenorrhea, infertility**
- Mental disorders



Diagnosis

- 24 hour urine free cortisol level

Confirmation test for cause –

- Serum ACTH
- Dexamethasone suppression test

Evaluation of cause

Pituitary cause- ACTH high

- Low dose - not suppressed
- High dose – low ACTH- low urinary steroid

Ectopic cause- High ACTH

- Insensitive to low or high dose

Adrenal cause- Low ACTH, high S. cortisol

- Insensitive to low or high dose

HYPERALDOSTERONISM

Hyperaldosteronism

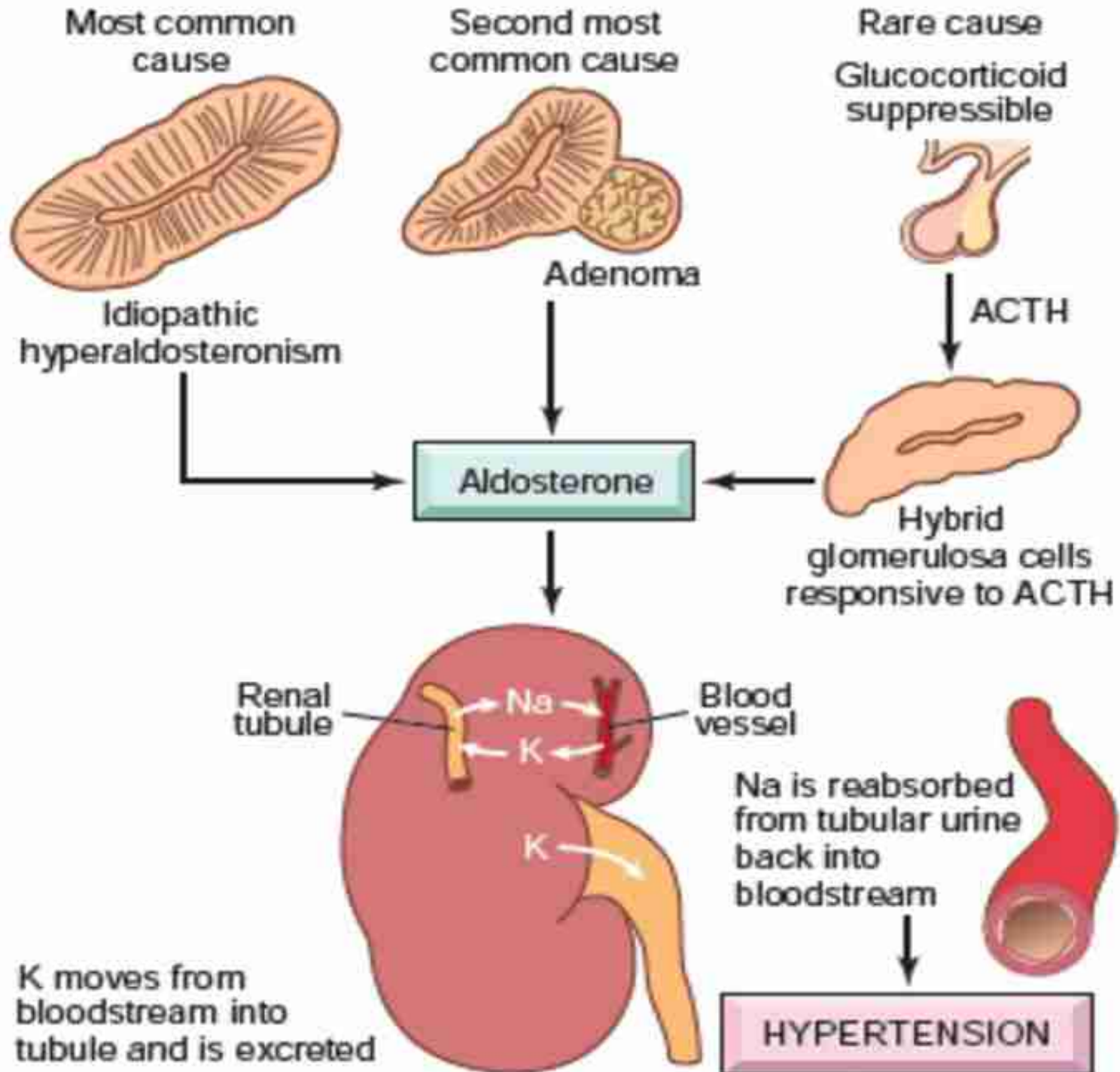
- Primary
- Secondary

Hyperaldosteronism - Primary

- Adrenocortical adenoma (80%)- Conn Syndrome
- Adrenocortical hyperplasia

“Low Plasma renin levels (Suppression)”

PRIMARY HYPERALDOSTERONISM



Hyperaldosteronism- Secondary

Extra adrenal cause

- Renal ischemia & Renal artery stenosis
 - CCF, NS
 - Pregnancy – estrogen induced
-
- High plasma renin levels

Secondary hyperaldosteronism

Increase in renin



Activation of renin angiotensinogen system

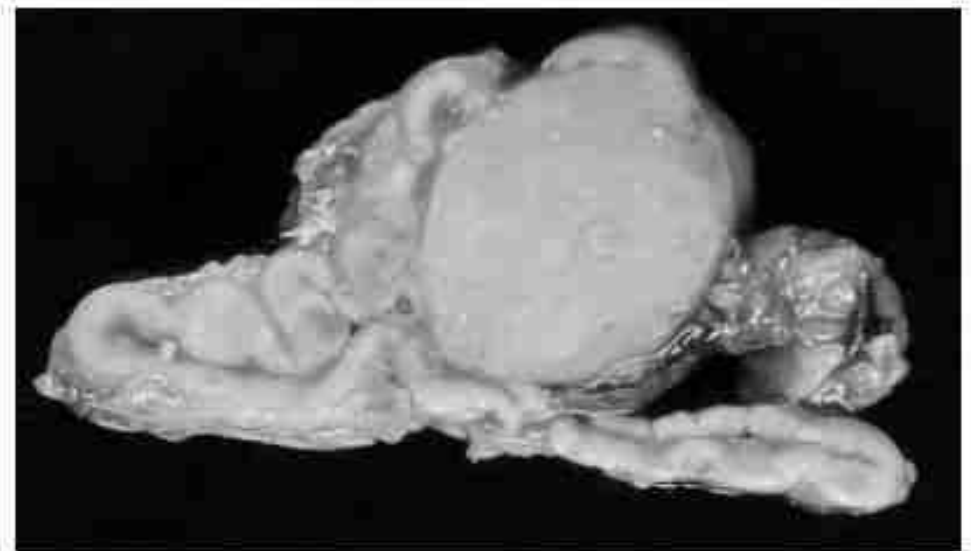


Increase in aldosterone

MORPHOLOGY - Gross

Adenoma

- Solitary, well circumscribed lesion < 2cm
- C/S- yellow



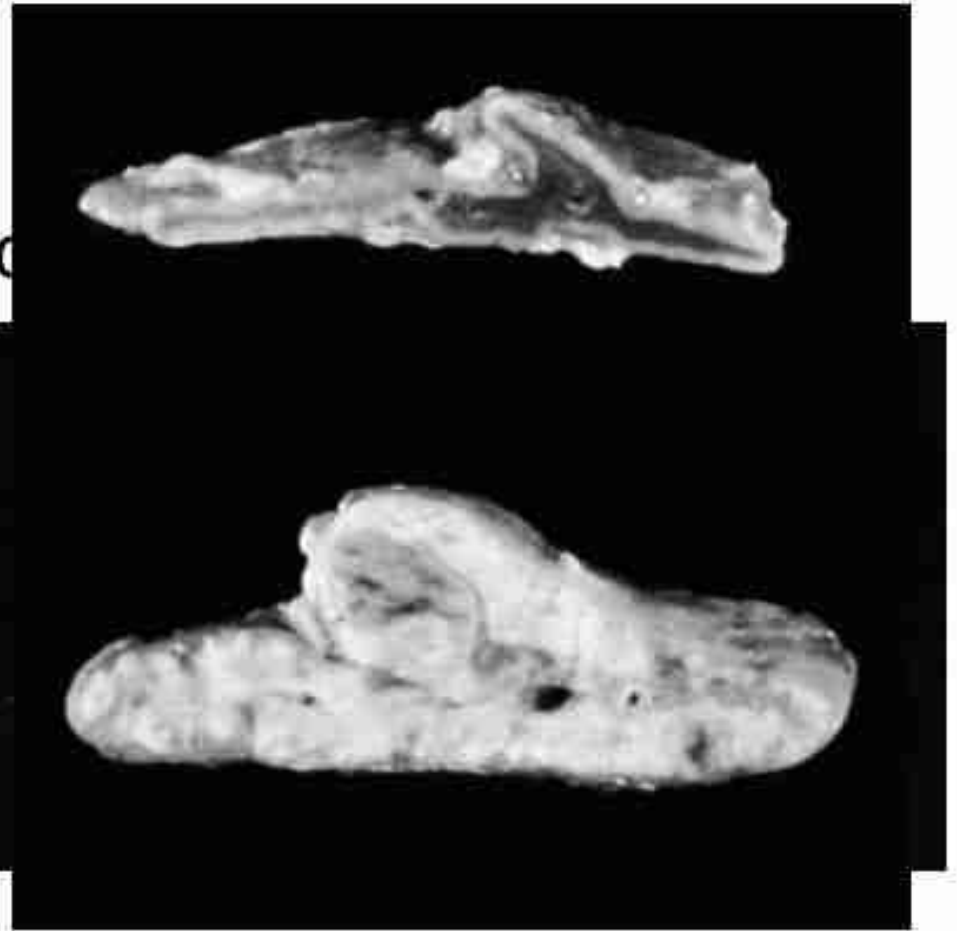
Hyperplasia

- Subtle enlargement, wedge shaped

MORPHOLOGY - Gross

Adenoma

- Solitary, well circumscribed
- C/S- yellow



Hyperplasia

- Subtle enlargement, wedge shaped

Aldosterone

Renal tubule

Na

K

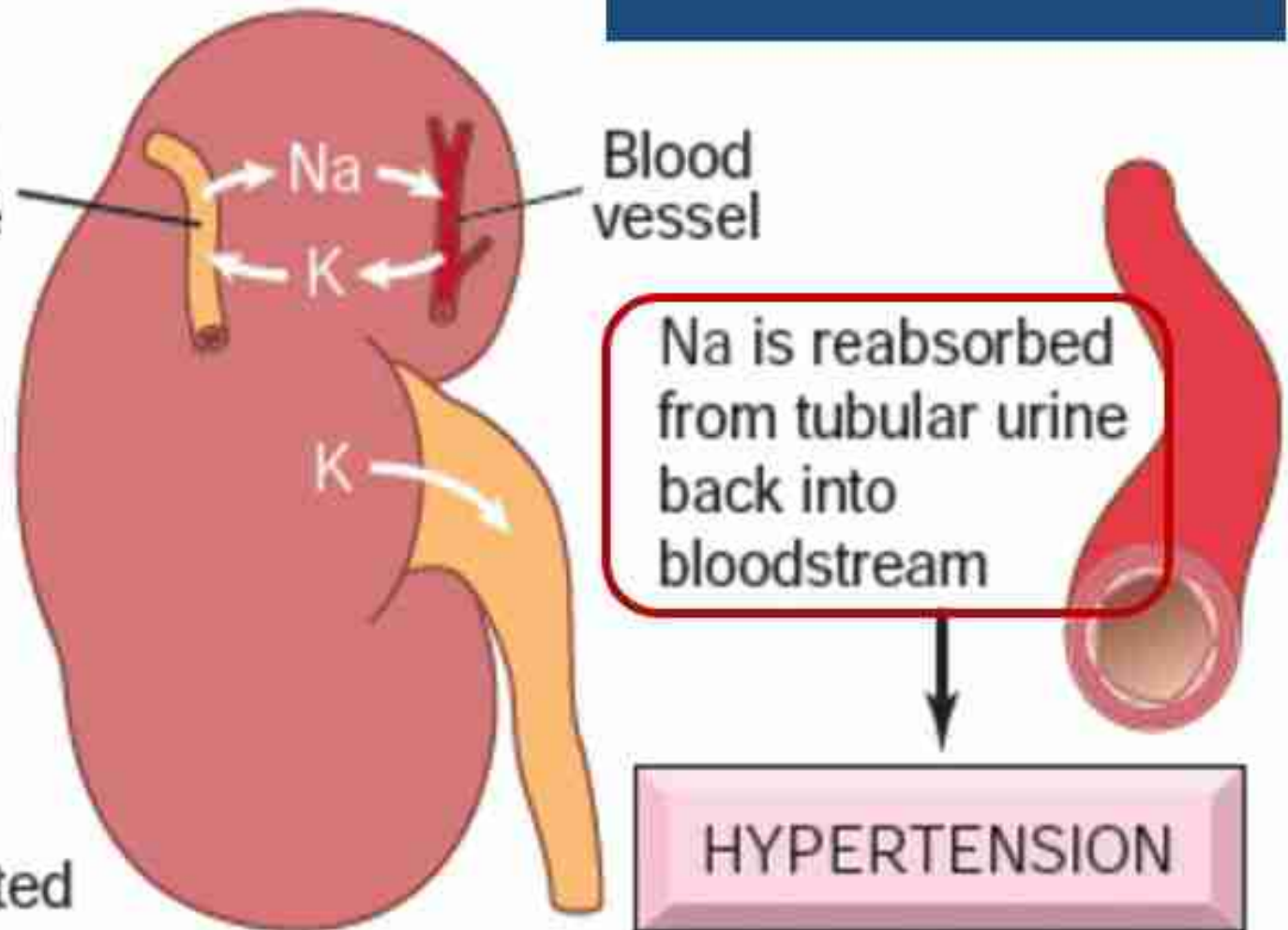
Blood vessel

K

Na is reabsorbed from tubular urine back into bloodstream

K moves from bloodstream into tubule and is excreted

HYPERTENSION



Clinical features

- Aldosterone --> Sodium retention - expansion in ECF --> increased cardiac output –**HYPERTENSION**
- **Hypokalemia** -Renal K^+ loss -- neuromuscular manifestations, weakness, paresthesias

Diagnosis

- Increased aldosterone
 - Increased ratio of aldosterone : plasma renin
-
- Primary - low plasma renin (Suppression of renin-angiotensin system)
 - Secondary - High plasma renin levels

Treatment

Primary

- Adenomas- surgically resectable
- Hyperplasia- medical therapy (aldosterone antagonist)

Secondary

- Treat the underlying cause

ADRENOGENITAL SYNDROME

Adrenogenital syndrome

- Disorders of sexual differentiation
 - virilisation or feminization
- Hypersecretion of sex steroids
- Primary gonadal disorders
- Primary adrenal disorders

Adrenogenital syndrome

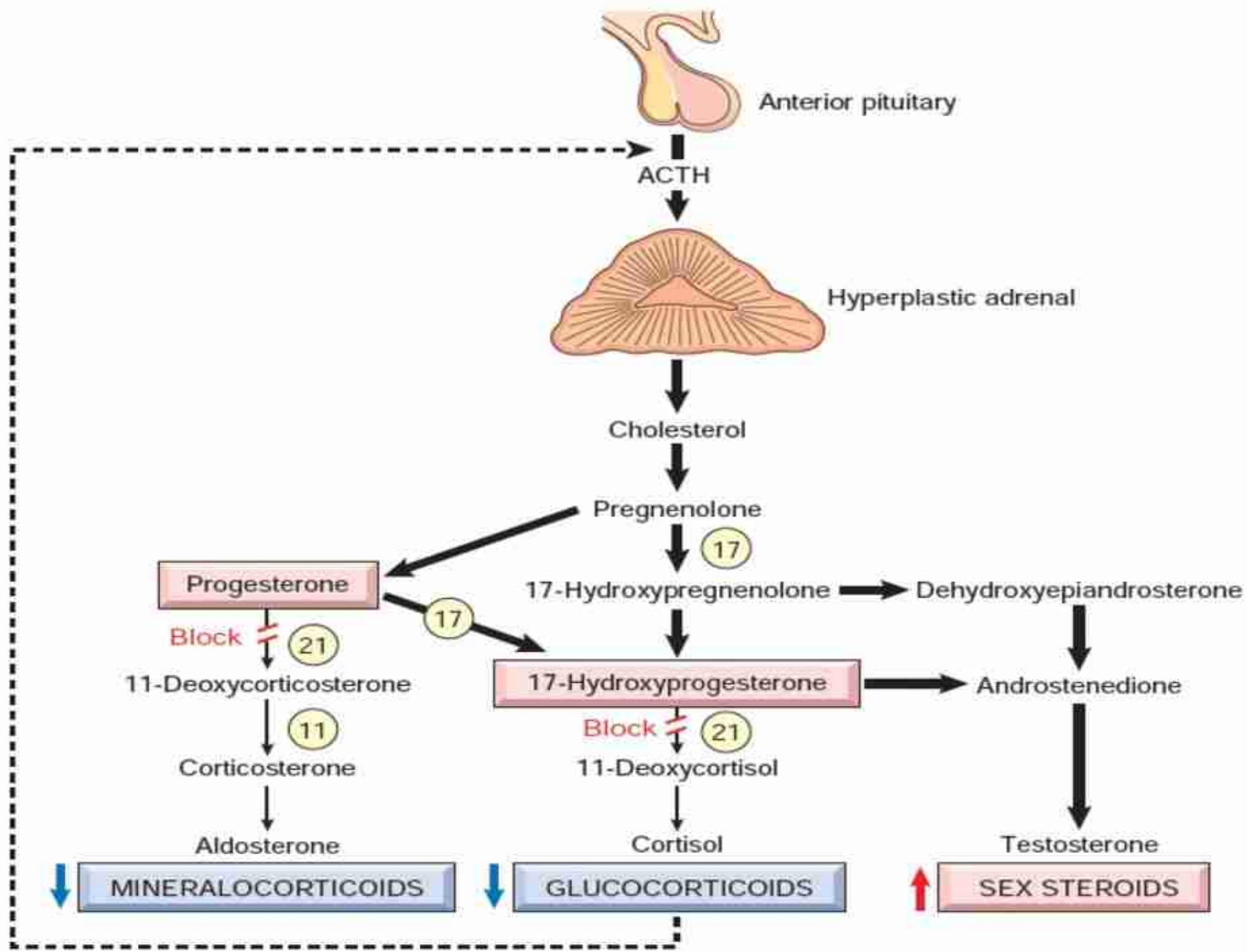
- Adrenal cortex —> DHEA & androstenedione —> testosterone in peripheral tissues

Causes –

- Children - Congenital adrenal hyperplasia (CAH)
- Adults- Adrenocortical neoplasms – Carcinoma > adenoma

Congenital adrenal hyperplasia

- Autosomal-recessive inherited metabolic error
- Children
- Deficiency or total lack of cortisol biosynthesis
- Most common cause: 21 α - hydroxylase deficiency (CYP21A2 mutations)



Reduced Cortisol & Mineralocorticoid production



Compensatory increase in ACTH



Adrenal hyperplasia



Redirected to **High DHEA & Androstenedione** production



Testosterone synthesis in peripheral tissues

Clinical features

- **Virilizing/ masculinising effects**
 - Females : Ambiguous genitalia, oligomenorrhea, hirsutism
 - Males : Precocious puberty
- Salt (sodium) wasting --> **hypotension**

Adrenogenitalism – 3 types

- Salt wasting (Classic)
- Simple virilising without salt wasting
- Non classic/ late onset adrenal virilism

Morphology

- B/L hyperplastic
- C/S- thickened & nodular



ADRENOCORTICAL INSUFFICIENCY

Adrenocortical insufficiency

Hypofunction

- Primary adrenal disease
 - Acute (Adrenal crisis)
 - Chronic (Addison disease)
- Secondary to ACTH deficiency

Primary acute adrenal insufficiency

Causes

- **Stress induced crisis** in patients with c/c insufficiency
- Sudden **withdrawal of exogenous steroids**
- Massive adrenal haemorrhage --> damage adrenal cortex

Waterhouse-Friderichsen syndrome

- Uncommon catastrophic syndrome--> Adrenal cortical damage

Causes

- Bacterial sepsis (*Neisseria meningitidis*)
- Rapid hypotension --> shock
- DIC
- Massive bilateral adrenal hemorrhage

Clinical features

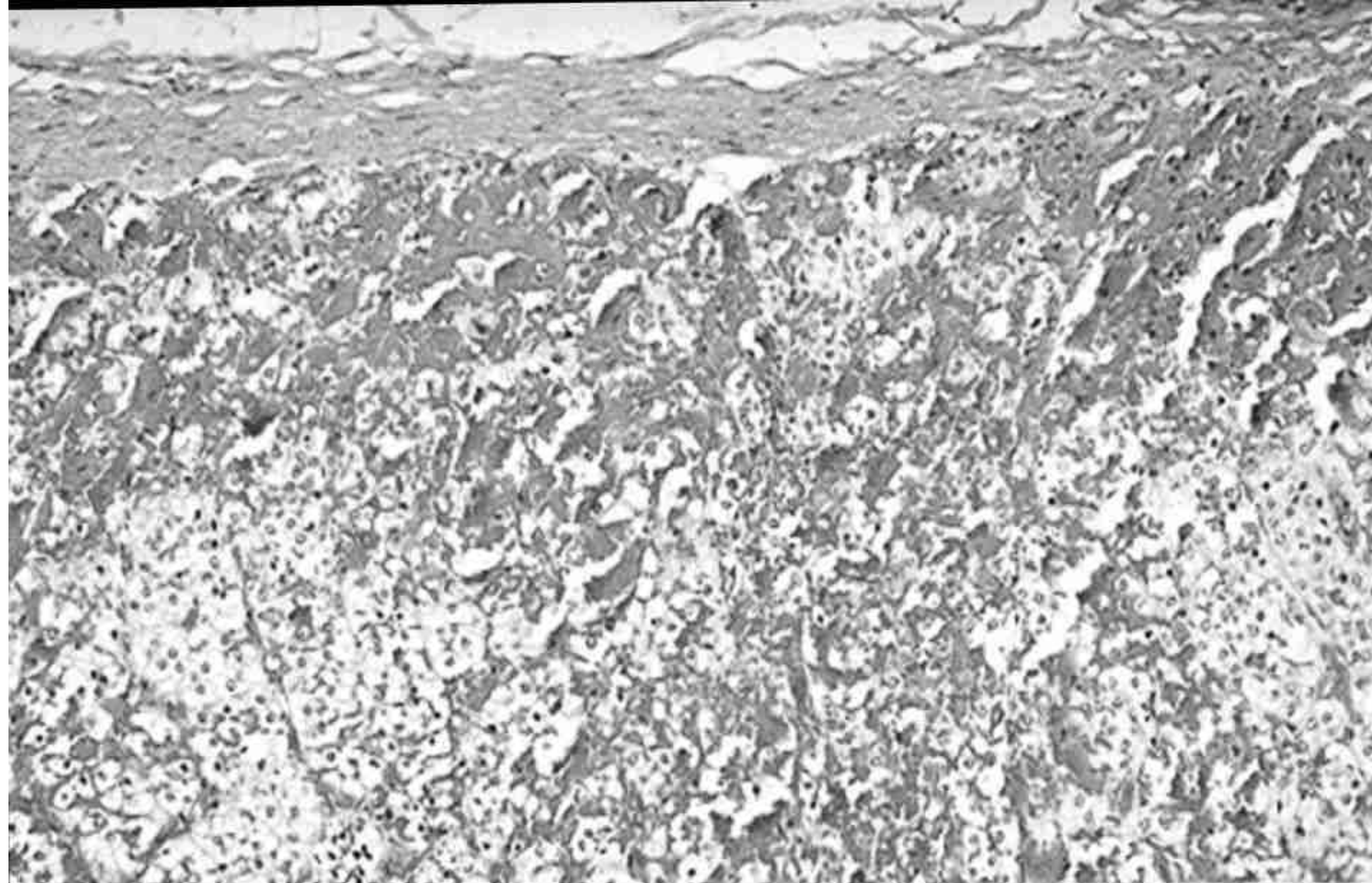
- Any age ; more common in children

Pathogenesis

- Uncertain
- Septicemia--> DIC--> endothelial injury --> adrenal hemorrhage







Extensive hemorrhage with little residual cortical architecture

Primary chronic adrenal insufficiency

Addison disease

- Progressive destruction of adrenal cortex

Causes

- Autoimmune (60-70%)
- Infections -TB, histoplasmosis
- Metastasis-Lungs, breast, GIT, Melanoma
- Congenital hypoplasia

Morphology - varies on cause

Clinical features

- Progressive fatigability
- **Hyperpigmentation** – sun exposed areas & pressure points (neck, elbows, knees, knuckles)
- Hyperkalemia, hyponatremia, hypotension

Secondary adrenal insufficiency

- ACTH deficiency

Causes

- Prolonged exogenous steroids
- Panhypopituitarism

ADRENAL NEOPLASMS

Neoplasms

Cortex

- Adrenal Adenoma
- Carcinoma

Medulla

- Pheochromocytoma
- Neuroblastoma

Adrenocortical Neoplasms

Functional

- Adenoma- Conn syndrome & Cushing syndrome
- Carcinoma – virilising

Non – functional (majority)

- Adults - Adenoma & carcinoma equally common
- Children- Carcinoma common
- Most are clinically silent **(INCIDENTALOMA)**

Morphology - Adenoma

Gross-

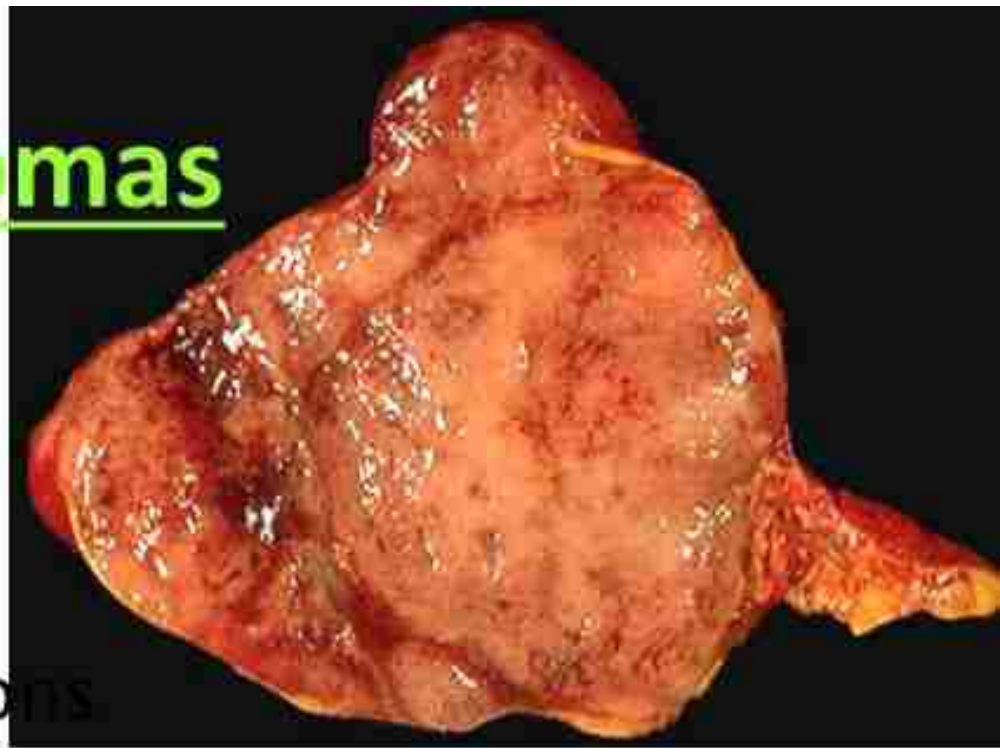
- Well circumscribed, nodular
- C/S- yellow, areas of hemorrhage, necrosis, calcification
- Functional adenoma- atrophy of



Microscopy-

- Cells similar to normal cortical cells

Adrenocortical Carcinomas



Gross

- Large (20cms) invasive lesions
- C/S- Variegated , Areas of h'ge, necrosis

Microscopy

- Moderate to marked anaplasia seen

Hematogenous & lymphatic spread --> lung & LN

Adrenal medullary neoplasms

- Phaeochromocytoma
- Neuronal tumors
 - Neuroblastoma

PHEOCHROMOCYTOMA

- Cell of Origin- **Chromaffin cells**
- **Synthesis & release catecholamines**
- **Surgically correctable HTN**

- Sporadic – 90%
- Familial syndromes- 10%

Rule of “10”- Pheochromocytoma

- 10% extra-adrenal (Paraganglioma)
- 10% bilateral
- 10% familial
- 10% malignant
- 10% not associated with HTN
- 25% assoc with germline mutations- MEN-2A & 2B, VHL, NF-1

Clinical feature & lab findings

- Paroxysmal episodes of HTN
- Assoc. with tachycardia, palpitations, headache, sweating, tremor
- Increased urinary free catecholamines & its metabolites - VMA, metanephrine

Morphology

Gross

- Well circumscribed, small/ large
- C/S: yellow, varying consistency

Dark brown colour in Potassium dichromate solution – oxidation of catecholamines -chromaffin



Microscopy

Benign/Malignant

- Definitive diagnosis of malignant phaeochromocytoma – **exclusively on -presence of metastasis**

NEUROBLASTOMA

- Malignant tumor from neural crest cells
- Most commonly in children
- Adrenal medulla/ autonomic ganglia

Clinical feature & Diagnosis

Clinical

- Abdominal distension

Imaging

- Suprarenal mass with calcification

Lab tests

- 24 hr urine test
 - Catecholamine
 - VMA & metanephrine

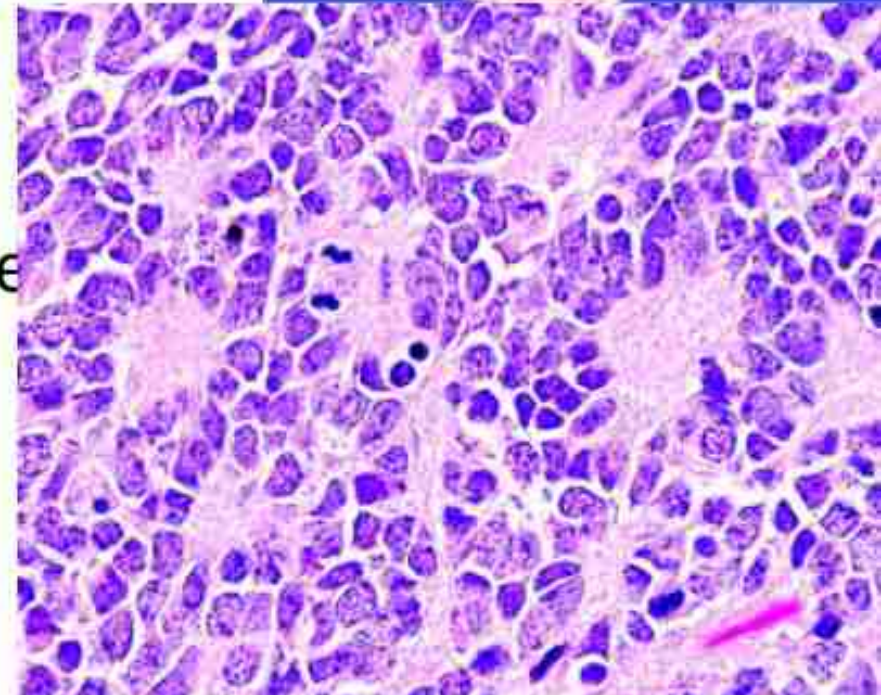
Morphology

Gross-

- Large , grey white, extensive areas of necrosis & hemorrhage, calcification

Microscopy

- Small round cells, scanty cytoplasm
- Homer- Wright rosettes (pse



Spread & Prognosis

- Metastasis –
 - Hematogenous (bone, liver, lungs)
 - Lymphatic – LNs
- Favorable if
 - Age < 2yrs
 - Extra abdominal location
 - Tumor histology showing more differentiation
 - Clinical stage –I or II