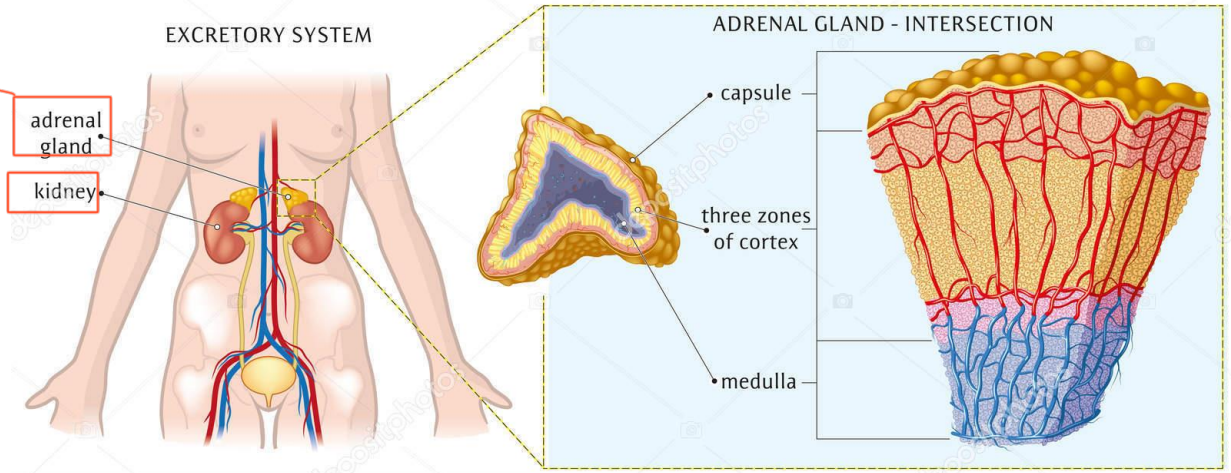
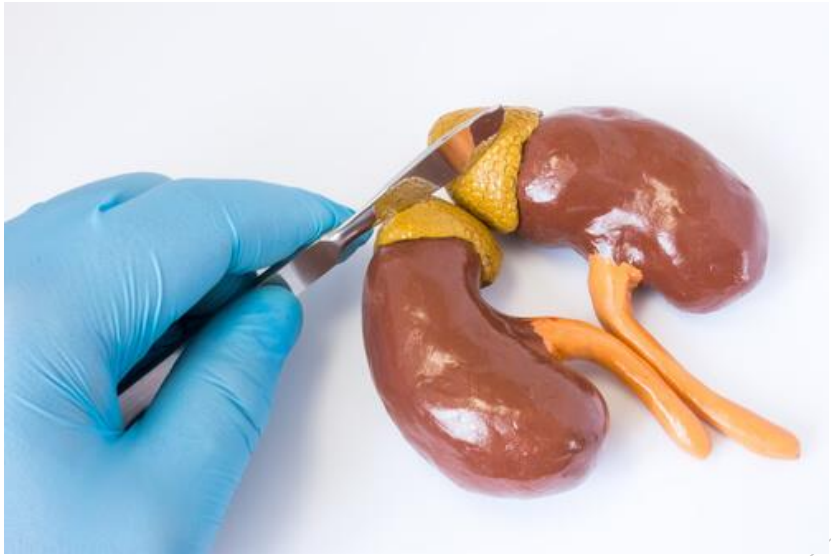
# Endocrine system pathology- ADRENAL GLAND

Dr.Eman Kreishan, M.D.

16-5-2024.

# Anatomy


retroperitoneal
EXCRETORY SYSTEM
adrenal gland
kidney
ADRENAL GLAND - INTERSECTION
capsule
three zones of cortex
medulla



Cortex subdivided into 3 functional layer

= G.F.R (1 2 3)

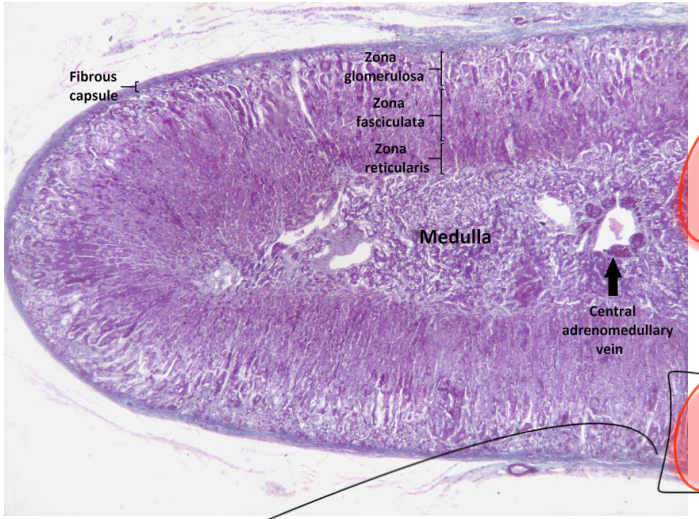
زيادة aldosteron يسبب tumor ← وظيفة aldosteronال:
- regulation of Blood pressure
- electrolyte balance

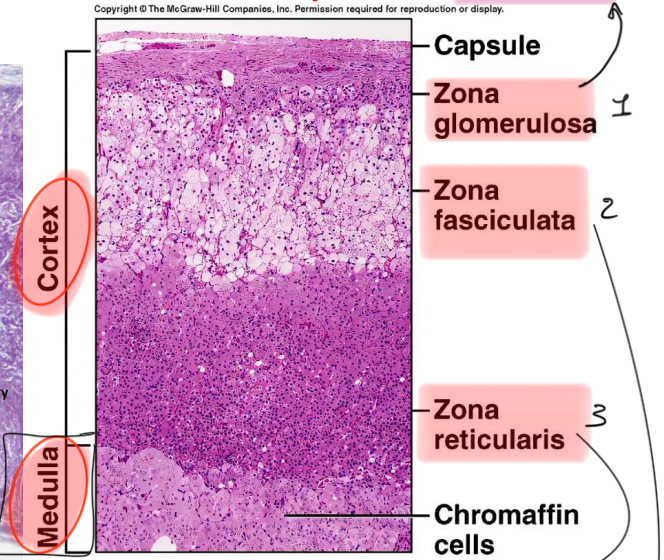
يسبب خلل في الelectrolyte balance
(↑ BP) hypertension
increase $Na^+$
(↓ potassium) hypokalemia

جغ RF ز

hormone = aldosterone

# Histology

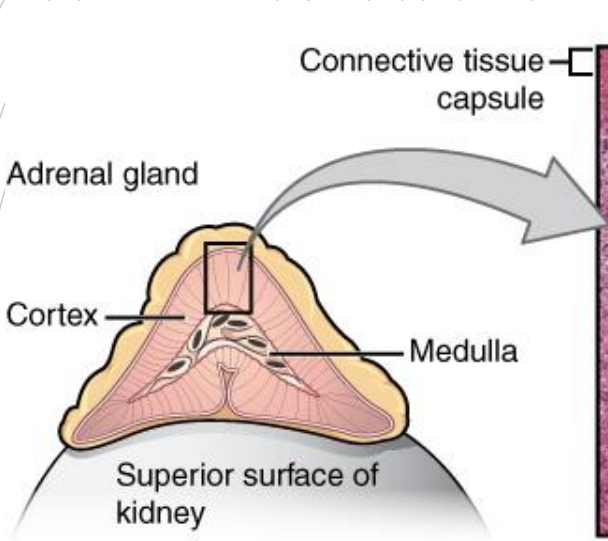


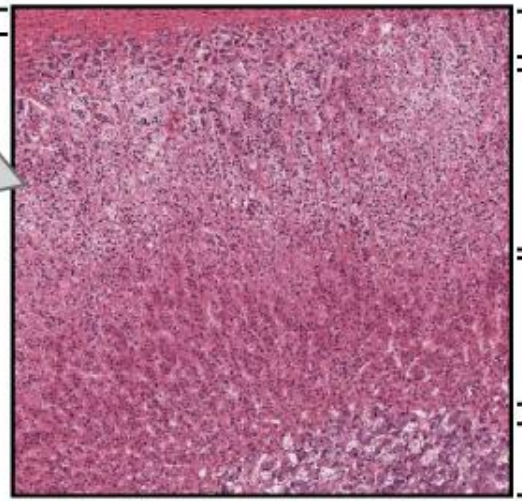




hormone = androgen
وظيفة: responsible of characteristic feature female or male (الصفة الجنسية)

hormone = cortisone
وظيفة:
- glocouse metabolism
- immunosuppression

hormone = catecolamine (sympathetic)
وظيفة: regulate our response under stressful conditions



| Tissue area | Hormones released | Examples |
|---|---|---|
| Zona glomerulosa (adrenal cortex) | Mineralcorticoids (regulate mineral balance) | Aldosterone |
| Zona fasciculata (adrenal cortex) | Glucocorticoids (regulate glucose metabolism) | Cortisol<br>Corticosterone<br>Cortisone |
| Zona reticularis (adrenal cortex) | Androgens (stimulate masculinization) | Dehydroepian-drosterone |
| Adrenal medulla | Stress hormones (stimulate sympathetic ANS) | Epinephrine<br>Norepinephrine |

or steroid

# Adrenal disorders

- **Non-neoplastic:**
  - Adrenal insufficiency:
    - Acute Adrenocortical Insufficiency.
    - Chronic Adrenocortical Insufficiency: Addison Disease.
  - Adrenal hyperfunction:
    - Cushing Syndrome.
    - Hyperaldosteronism.
    - Adrenogenital Syndromes

- **Neoplastic:**
  - Adrenalcortical tumors.
  - Adrenal medulla tumor

# Cushing syndrome.

- Hypercortisolism (Cushing syndrome) is caused by elevated glucocorticoid levels.

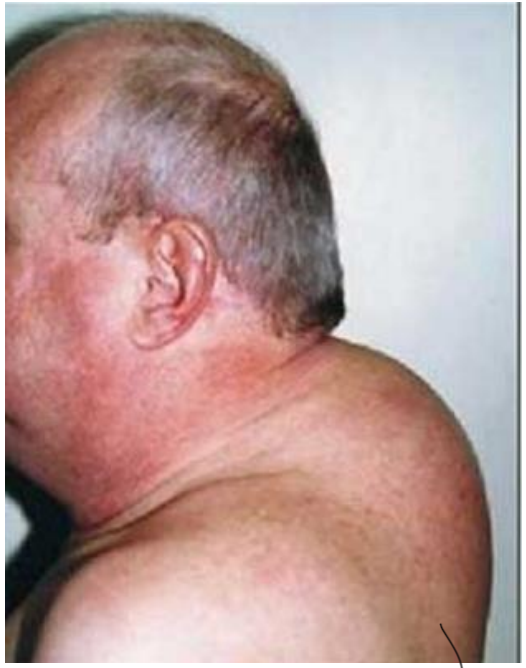
- Endogenous causes :
  - Hypothalamic/ pituitary hypersecretion ACTH.
  - Paraneoplastic syndrome ( lung CA ).
  - Adrenal tumor or hyperplasia .

- Exogenous cause :
  - Steroid Therapy.

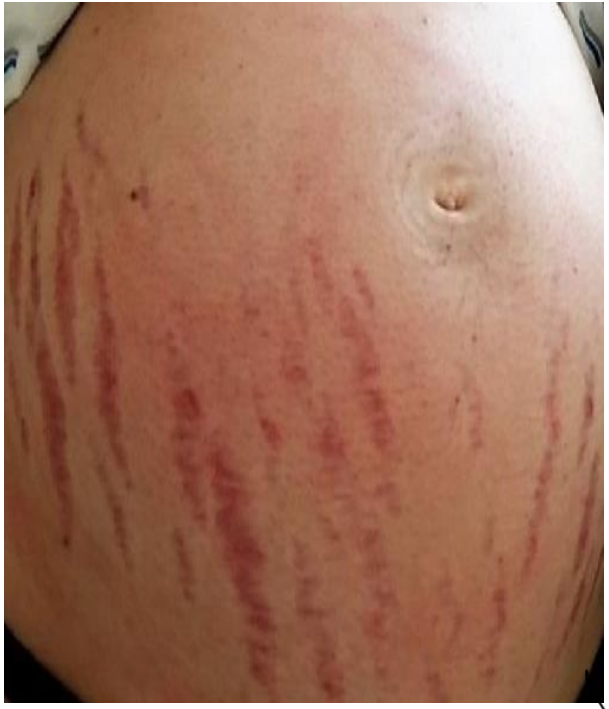
# Signs and symptoms

- high blood pressure. hypertension
- abdominal obesity but with thin arms and legs.
- reddish stretch marks. (stria)
- round red face.
- fat lump between the shoulders.
- weak muscles and weak bones.
- acne and fragile skin

Pathological



excess fat between shoulder



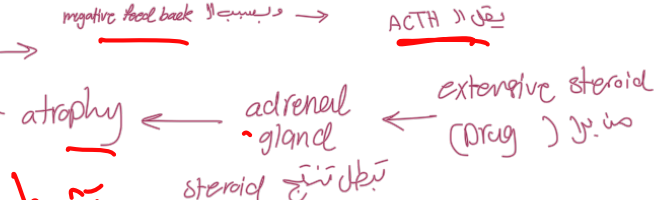
reddish stretch marks (stria)

[steroid or glucocorticoids]

# Morphology

- Morphologic changes in the adrenal glands depend on the cause of the hypercortisolism and include:

(1) cortical atrophy:




(Drug) exogenous glucocorticoids, suppression of endogenous ACTH.

(2) diffuse hyperplasia:

ACTH dependent Cushing syndrome From Pituitary & hypothalamus.

(3) macronodular or micronodular hyperplasia:

primary cortical hyperplasia.

(4) an adenoma or carcinoma.

# Hyperaldosteronism.

- Hyperaldosteronism is the generic term for a group of closely related conditions characterized by chronic excess aldosterone secretion.

- **A-primary hyperaldosteronism** are:
  - Bilateral idiopathic hyperaldosteronism, characterized by bilateral nodular hyperplasia of the adrenal glands.
  - Adrenocortical neoplasm, either an aldosterone-producing adenoma (the most common cause) or, rarely, an adrenocortical carcinoma.
  - familial hyperaldosteronism may result from a genetic defect that leads to overactivity of the aldosterone synthase gene, CYP11B2.

- B- **Secondary causes** :
  - Due to decreased renal perfusion ( heart failure ), activation of the renin - angiotensin system .

Angiotersion convert enzyme

# Adrenogenital syndromes

- Adrenogenital syndromes refer to a group of disorders caused by androgen excess, which may stem from a number of etiologies, including primary gonadal disorders and several primary adrenal disorder.

❑Could be caused by :

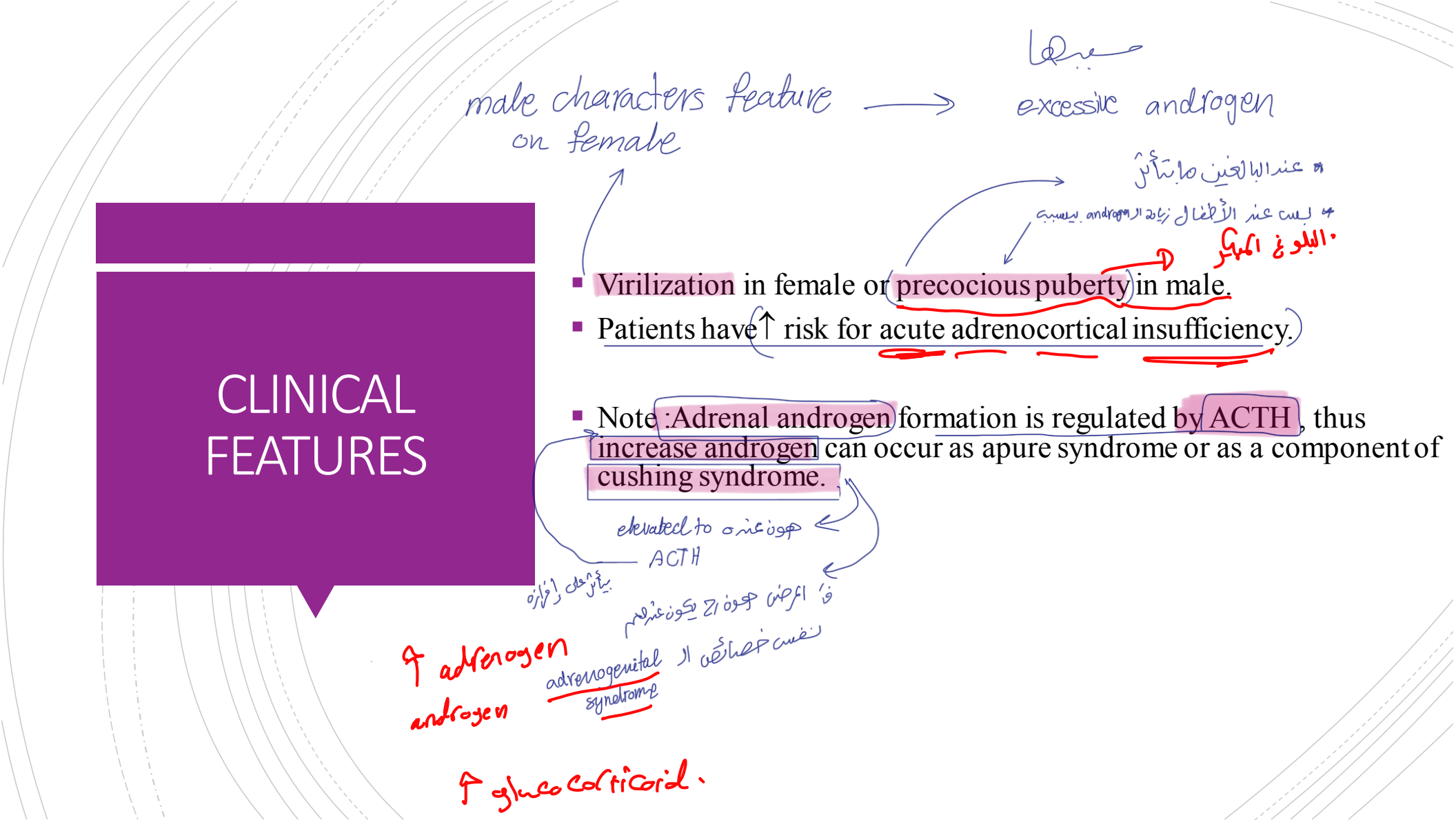
1 - Primary gonadal disorders(increase gonadal androgen).

2 -Acquired :Adrenocortical Neoplasms. can occur at any age, frequently malignant .

# CLINICAL FEATURES

- Virilization in female or precocious puberty in male.
- Patients have ↑ risk for acute adrenocortical insufficiency.

- Note :Adrenal androgen formation is regulated by ACTH , thus increase androgen can occur as apure syndrome or as a component of cushing syndrome.



# ADRENOCORTICAL INSUFFICIENCY

- **May be primary adrenal( disease affecting the adrenal gland ) :**
- **acute** (called adrenal crisis).
- **chronic** (Addison disease).
- **secondary to destruction of the pituitary as in SHEEHAN's syndrome or non functional pituitary adenoma**

Sheehan's syndrome :-

female → delivary (Labor) → excessive blood loss → قلل ال blood volume في كل الجسم

(pituitary) → necrosis → cutting blood supply

+ hypotension + shock

(hypopituitarism) قطع الدم عن الغدة النخامية وتموتها

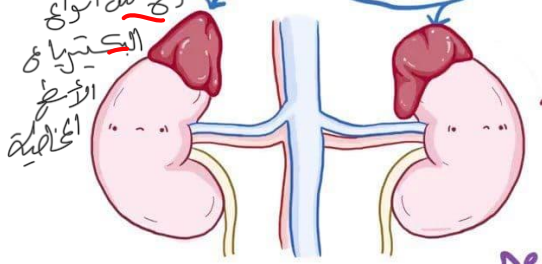
**Table 20.7 Causes of Adrenal Insufficiency**

| |
|---|
| **Acute** |
| Waterhouse-Friderichsen syndrome |
| Sudden withdrawal of long-term corticosteroid therapy |
| Stress in patients with underlying chronic adrenal insufficiency |
| **Chronic** |
| Autoimmune adrenalitis (60%–70% of cases in developed countries)—includes APS1 (*AIRE* mutations) and APS2 (polygenic) |
| Infections<br>Tuberculosis<br>Acquired immunodeficiency syndrome<br>Fungal infections |
| Hemochromatosis |
| Sarcoidosis |
| Systemic amyloidosis |
| Metastatic disease |

infant → severe infection (meisseria) → adrenal gland → hemorrhage in adrenal gland

# WATERHOUSE-FRIDERICHSEN SYNDROME (in infants)

meisseria



~ BLOOD VESSELS IN ADRENAL GLAND RUPTURE (intra-adrenal hemorrhage which obstruct the functional layer into non-functional)
- SEVERE BACTERIAL INFECTION
  - m/c is meisseria

~ ADRENAL CRISIS
- ACUTE ADRENAL INSUFFICIENCY
  - STOPS PRODUCING HORMONES

DR. WATERHOUSE & DR. FRIDERICHSEN > EARLY 1900's

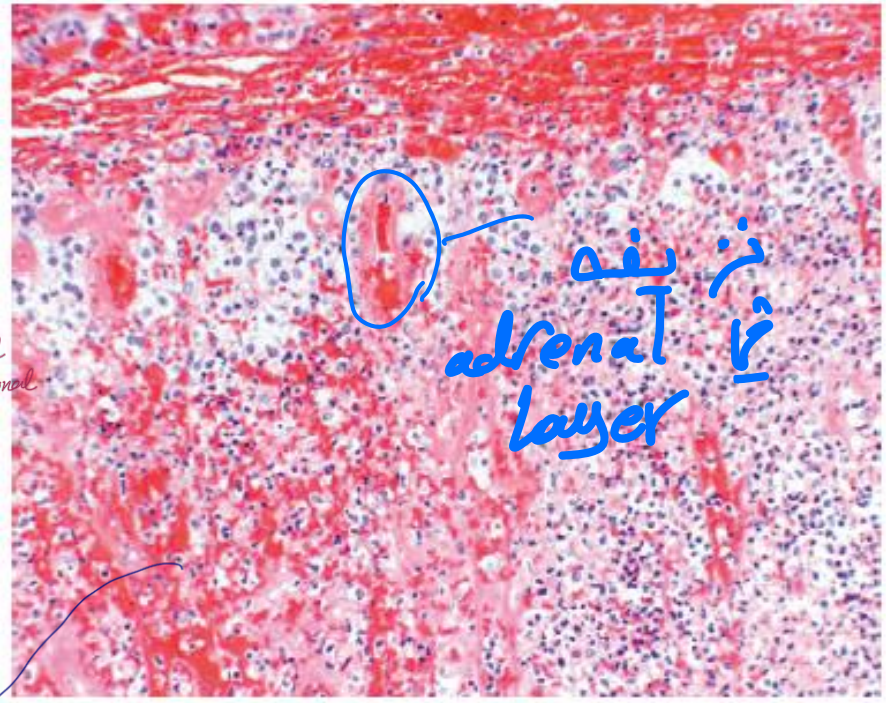



**Figure 19–39** Waterhouse-Friderichsen syndrome. Bilateral adrenal hemorrhage in an infant with overwhelming sepsis, resulting in acute adrenal insufficiency. At autopsy, the adrenals were grossly hemorrhagic and shrunken; in this photomicrograph, little residual cortical architecture is discernible.

non-functional → no hormone that released from adrenal gland → adrenal deficiency

hemmorage → functional layer

# Addison's disease.

-Chronic adrenal cortical insufficiency , required immediate therapy .

-Progressive destruction of the adrenal gland.

****Causes include:

1- Autoimmune cause: 60-70 % , may be sporadic or familial, linked to HLA-B8 or DR3 ,often multisystem involvement.

2- Infections e.g. Tuberculosis , fungi .

3- Metastatic tumors destroying adrenal e.g. lung ,breast , …others

4- AIDS.

# Morphology & Clinical features in Chronic Adrenal Insufficiency :

- Morphology depends on cause :

  Autoimmune shows irregular small glands, with cortex heavily infiltrated by lymphocytes, medulla normal.

  In T.B. → Caseating Granuloma

  In metastatic CA → Type of primary tumor

  In secondary to pituitary cause, the adrenal is shrunken

- In general, clinical manifestations of adrenocortical insufficiency do not appear until at least 90% of the adrenal destructed.

# Adrenal tumor:

- ✓ **ADRENALCORTICAL TUMORS**
- ✓ **ADRENAL MEDULLA TUMOR**

# adrenalcortical tumors

- Malignant epithelial tumor of adrenal cortical cells
- Adrenocortical carcinoma (ACC) is a rare endocrine tumor with high mortality
- More often involves left adrenal: left to right ratio = 1.2:1
- Functional adrenal cortical carcinomas have the following symptoms related to hormone production:

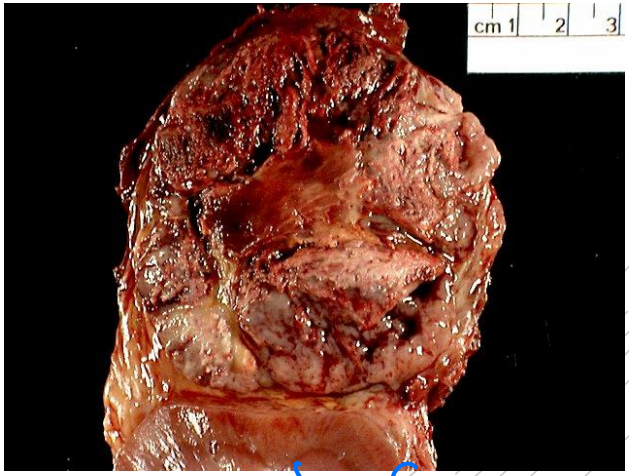
fasciculata → 50% cortisol excess (Cushing syndrome, rapid onset)

reticularis → 20% sex hormone secretion (mainly androgens causing hirsutism, virilization and menstrual irregularities)

glomerulosa → 8% aldosterone (hypertension, hypokalemia)

# Morphology

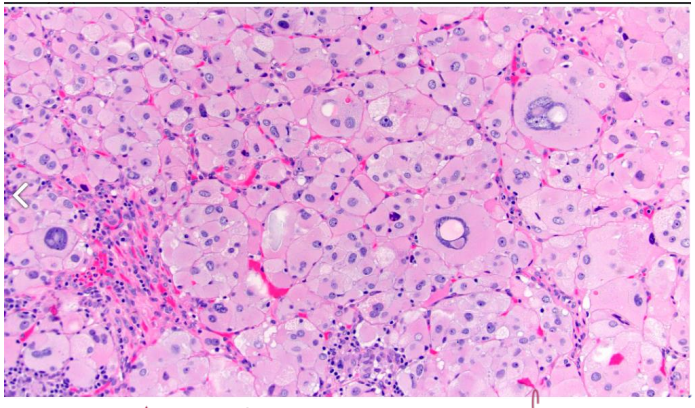
- Encapsulated, usually yellow color: single or multiple.
- Size variable 1-2 cm, up to large tumors
- Malignant tumors may show necrosis, hemorrhage and are usually larger.



adrenal cortical carcinoma → invasion → capsule or BV

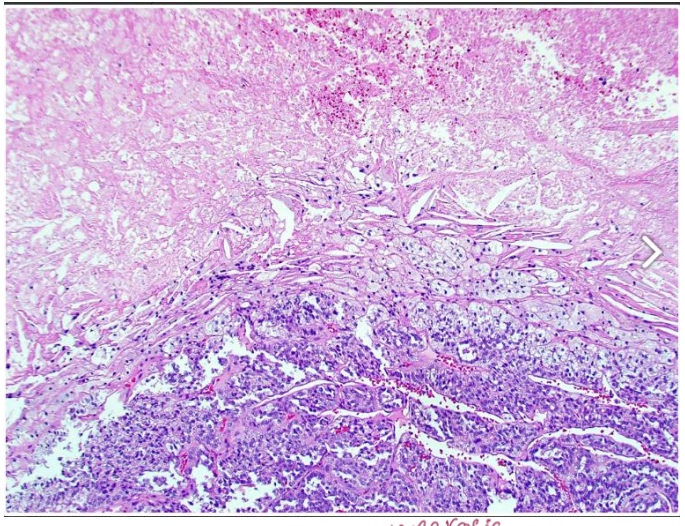
- Histology:
- Large cells with granular clear to eosinophilic cytoplasm, often pleomorphic. and hyperchromasia and inclusions
- Invasion of thick fibrous capsule
- Lymphovascular invasion.
- Areas of necrosis, hemorrhage, degeneration are common

capsule لا invasion ممكن يكون عامل

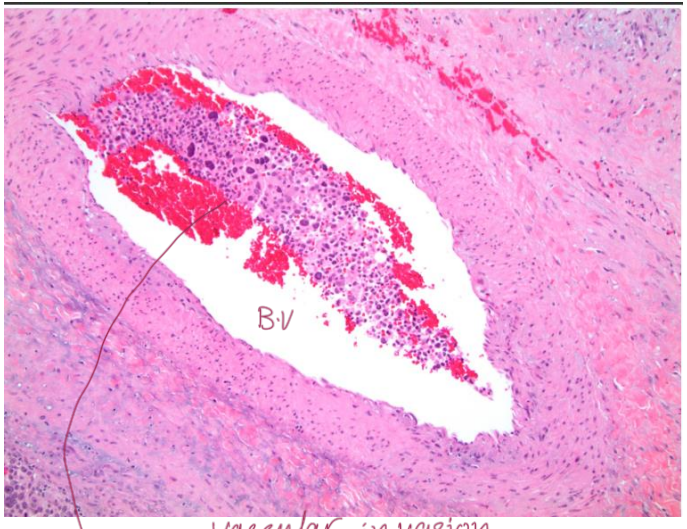


* nuclear polymorphism
* incidental inclusion
* mitotic inclusion

malignant الذي يدل على



necrosis




vascular invasion

blood vessels

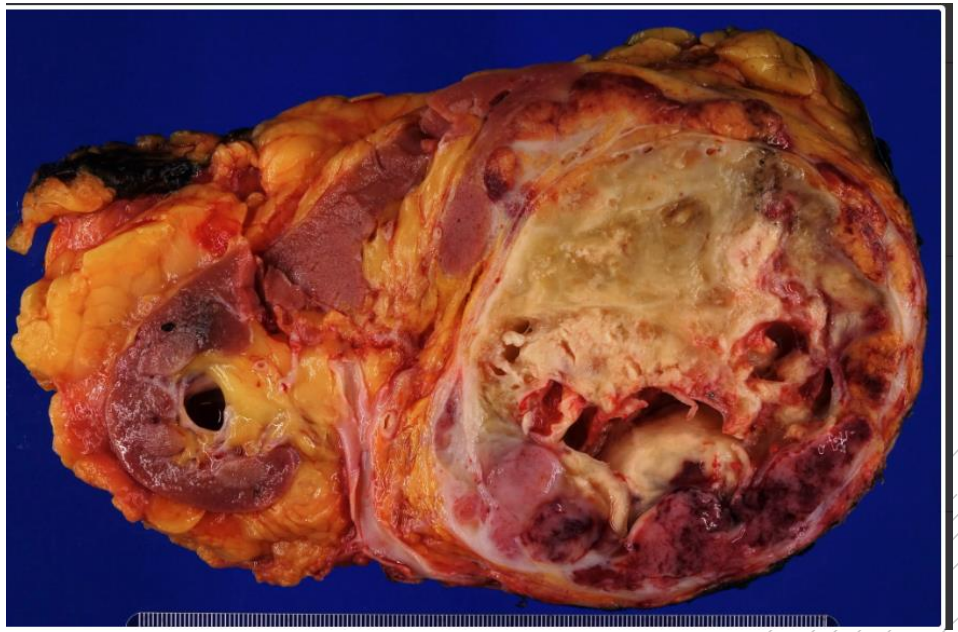
tumor

# Tumor of the adrenal medulla pheochromocytoma

- Pheochromocytomas are neoplasms composed of chromaffin cells, which, like their nonneoplastic counterparts, synthesize and release catecholamin.
- Sometimes described as Ruleof 10% Tumor because :
- * 10% bilateral.,
- 10 %multiple,
- 10% non functional
- * 10% familial, may be part of MEN syndrome.
- * 10% Malignant.
- * 10% extraadrenal site.
- *25% associated with genetic mutation.

# Morphology

- **well circumscribed, small to large in size**



# Histology

group of tumor cell

- **Nested (zellballen), trabecular patterns.**
- Nests of cells (Zellballen) with abundant cytoplasm filled with granules containing catecholamine.
- Malignancy confirmed by METASTASES

على شكل قروبات موزعين