

بالمعدل العادة للمرضى (1)

**\*\*90% of cases** are due to either autoimmune adrenalitis, TB, AIDS or metastatic cancers (Table 20-7).

**(1) Autoimmune adrenalitis** accounts for up to **70% of cases** & is the most common cause of primary adrenal insufficiency in developed countries.

تذكر المجموعة الكبيرة من autoimmune diseases

**\*\*There is autoimmune destruction of steroid-producing cells, & autoantibodies to several key steroidogenic enzymes** have been detected in these patients.

يعني هاد المرض عنده Abs ضد الستيرويدات أو enzymes يلى تيدخل بتعنينها

**\*\*In 50% of patients** the autoimmune disease is restricted to the adrenal glands (**isolated autoimmune Addison disease**);

نتيجة نهائية تدمير ذاتي للغدة الكظرية

\* **in the remaining 50%**, other autoimmune diseases, such as Hashimoto disease, pernicious anemia, type I DM, & idiopathic hypoparathyroidism, **coexist (autoimmune polyendocrinopathy syndrome)**.

بنها المرضي يكون Autoimmune isolated addison disease معناها لوحدة

\* **in the remaining 50%**, other autoimmune diseases, such as Hashimoto disease, pernicious anemia, type I DM, & idiopathic hypoparathyroidism, **coexist (autoimmune polyendocrinopathy syndrome)**.

المتلازمة المناعية ضد عدة غدد صنم (polyendocrinopathy)

\* **thyroid** Hashimoto's thyroiditis  
\* **absorb vit. B12** / autoimmune gastritis & pernicious anemia

وغيره  
\* **absorb vit. B12** / autoimmune gastritis & pernicious anemia

**(2) Infections:** particularly **tuberculous adrenalitis (F 8.16)**,

which in the past accounted for 90% of cases of Addison disease, has become **less common** with the advent of anti-TB therapy.

كان TB هو the most common cause لمرض Addison disease

لأنه endemic وموجود بمناطق محددة ومعروف ولكن بوجود vaccination وعلاجات

\* **تصبح يصير فيه ؟**  
chronic granulomatous

توجد و tuberculin test قل صدوته

\* تَسْوَرِحٌ بِصَيْرٍ فِيهِ ؟ !

TB: chronic granulomatous  
caseating tuberculosis affecting  
and destroying the gland  
extensively

\*\*Among fungi, disseminated infections caused by *Histoplasma capsulatum* & *Coccidioides immitis* may also result in chronic adrenocortical insufficiency

\* <sup>the most imp. infection → TB</sup> / immunosuppressed patient | فاي حالات قليلة ونادرة وعادة تصت بـ

صورة 8-16 :

TB adenitis ← و سبب هو Addison disease ← primary chronic Hypoadrenalism هار \*

\*\*Patients with **AIDS** are at risk for developing adrenal insufficiency from several infectious (**cytomegalovirus, *Mycobacterium avium-intracellulare* (atypical tuberculosis)**) & noninfectious (Kaposi sarcoma) complications of their disease.  
in the adrenals

**(3) Metastatic neoplasms** are a fairly common (?) in persons with disseminated carcinomas (F 8-24).

\* ليش ال Adrenal بصير فيها Secondaries من breast , lung --  
بها ما عرف هي ليش Favorable site

\*\*Carcinomas of the lung & breast are the source of a majority of metastases in the adrenals.

\*\*Although adrenal function is preserved in most such patients, the metastatic growths sometimes destroy sufficient adrenal cortex to produce a degree of adrenal insufficiency.

\* \* أغلب الحالات الي بصير فيها سرطانات = adrenal وحدة 2  
مدلك أغلب Gland ولكنها لاتزال تشتغل لأنه بيها احتياطي استراتيجي  
ولكن إذا تدمرت gland عما ما = adrenal insufficiency بصير

### (III) Secondary Adrenocortical Insufficiency

Any disorder of the hypothalamus & pituitary, such as metastatic cancer, infection, infarction, or irradiation, that **reduces the output of ACTH** leads to a syndrome of hypoadrenalism having many similarities to Addison disease.

- أي مرض أي آفة تصيب الـ Hypothalamus أو ant. pituitary مثل
- \* عليهم فقط ← تقل إنتاج ACTH ← معناه ته بطّل عنا
  - \* stimulation من pituitary لـ both adrenal glands حتى تشغل
  - \* Adrenal gland بالأي ← تغد صافية ما بسوي secretion لـ cortisol

\*\*With **secondary adrenocortical insufficiency**, the

hyperpigmentation of primary Addison disease is lacking

because melanotropic hormone levels are low

~~\*\* كيف نفرق بين 1<sup>ry</sup> و 2<sup>ry</sup> \*~~

صورة 8-24 : دبع الاعلان

⚙ At necropsy, 40% of lung ca cases & 25% of breast ca cases give rise to adrenal metastases, often bilateral

--- هـ و لـ بنلافـ فيهم كارهـ مرتين

gland can compensate and survive

مغير

2<sup>ry</sup> tumor

\* إذا كان

بسا إذا كان

gland بهاي اطة الـ

Very extensive

+ Massive

تدمر بصورة كاملة و بصير

Chronic 1<sup>ry</sup> Insufficiency → Addison disease

\* سهم الأصفر : يوشرعان ما يتقر من gland ، و باقي gland مدمرة

\* كيف نفرق بين 1<sup>ry</sup>, 2<sup>ry</sup> من آخر جملة بالسلايد بل يجب!!

مهم  
ويعني  
بالاضمان

**\*\*How you can differentiate the primary from secondary?**

<p>In patients with <b>primary adrenocortical insufficiency</b></p> <p>1<sup>ry</sup> ← يعني gland مدمرة *</p>	<p>By contrast, <b>secondary adrenocortical insufficiency</b> due to reduced ACTH levels is characterized by</p>
<p><b>the</b></p> <p>(A) serum ACTH levels may be <u>normal</u>, but ?</p> <p>(B) the destruction of the adrenal cortex <b>does not permit</b> a response to exogenously administered ACTH, in the form of ↑ plasma levels of cortisol (Diagnostic test).</p> <p>* أماحون إذا أعطيت ACTH مارح * يصير عننا Response من Gland * ومارح يرتفع ار cortisol --- لأنه * أصلاً ACTH موجود بين Gland * مدمرة وما يتطلع cortisol</p>	<p>(A) <b>low serum ACTH &amp;</b></p> <p>* hypothalamus lesion * pituitary</p> <p>(B) a <u>positive diagnostic test</u> of prompt rise in plasma cortisol levels in response to <u>ACTH administration</u>.</p> <p>* exogenous ACTH * إذا أعطيت المريض * cortisol gland اشتغلة وطلعت * معناه 2<sup>ry</sup></p>

metastatic cancers / Infections / autoimmune ← سبب

**Morphology:** varies with the cause;

**\*\*primary:** مدمرة

غير صلب  
Hyperpigmentation ← 1<sup>ry</sup>  
Pallor ← 2<sup>ry</sup>

► **Primary autoimmune adrenalitis** characterized by irregularly **shrunken glands**, which may be **exceedingly difficult to identify** within the suprarenal adipose tissue.

\* من اسمها ار يصير extensive lymphocytic Infiltration ودمير ل Gland

\* gland يتكون مدمرة بصورة كبيرة ويتكون Atrophic ضامرة وصغيرة حتى

انك ماتقدر تميز وجودها بالانسجة الشحمية الموجودة في مكانها

cortical cells

\* عدد قليل جداً من

□ H, the cortex contains **scattered residual cortical cells** in a collapsed network of connective tissue, with variable **lymphoid infiltrate** which may extend into the subjacent medulla (F 20-40). **The medulla is intact.**

تبضع طبيعية وعاري بيسوري

Nor epinephrin + epinephrin

\*

\* المرض يلي بصير - cortex عبارة ماله علاقة ب Medulla

\*

\* في حالة autoimmune adrenalitis  
عبار الشفلات يلي بالأصفر

\*

\*

صورة 20-40 : لم يضيف شيء

\*

▶ In **TB or fungal diseases**, there is a **granulomatous inflammatory** reaction to the responsible organism, & the demonstration of which may require the use of special stains.

↓ TB bacillus

▶ When hypoadrenalism is caused by **metastatic carcinoma** (F 8.24), the adrenals are enlarged, & their normal architecture is infiltrated by the **cancer**.

adrenal = cancer cells بنشون

\* lung 40% سواء أكان من

\* 25% breast أو

\*

أو أي نوع آخر

\*

\*\* In **secondary hypoadrenalism** (due to ↓ ACTH) the adrenals are **atrophic, small & flattened** usually retain their yellow color because of a small amount of residual lipid.

O/S, a uniform, thin rim of atrophic yellow  
central, intact medulla.

→ cortex = مالهها علاقه

\*

□ H, there is atrophy of cortical cells with loss of cytoplasmic lipid, particularly in the zonae fasciculata.

كانه صرئيت

\*

### ADRENOCORTICAL TUMORS (T)

عكس او pituitary  
كانت functioning  
على اقل 75%.

يجب ان تذكرها ↓

● Most adrenocortical T are Non-functioning.

● Functional adenomas (A) are most commonly associated

with hyperaldosteronism & with Csy, while virilizing T is more likely to be a carcinoma.

\* شوي يعني virilizing؟! يعني يتفرز sex hormones

\* Hyperaldosteronism! شو بسوي؟! يعني

دراكانت functioning non-functioning  
عكسها \* يعني

● Functional & nonfunctional adrenocortical T cannot be distinguished on the basis of morphologic features, & their distinction is based on clinical evaluation & measurement of the hormone or its metabolites in the lab.

\*

adrenal tumor = كيف بيدي اميزي A و C؟  
gland

\* لما يصي

\*

عن طريق Metastasis و Invasion - طب كيف بيدي اعرف اذا هي

\*

functioning ولا non-functioning؟! تشغل ولا ماشغل؟! هاد ما بنقد رجاوبه لان شوفي \*

طب على اي اساس جحيم؟! clinical evaluation؟! هل المدينه

H/E stained section

عنده Hypertension ولا؟! هل عنده Cushing؟! بانهاية ياي بتقدر عليه

بالتشخيص انها في هو قياس مستوى Hormone بالدم او metabolites

## ADRENOCORTICAL ADENOMAS (A)

\*\* Most adrenocortical A are non-functional.

\*\* They are usually encountered as **incidental** findings during abdominal imaging for an unrelated cause, so-called

"**adrenal incidentaloma**", or at the time of autopsy.

\* « Local mass effect » عرضية + موجودة بكمية صغيرة (non-functioning) أكثرها  
\* طبكف بكتشفوها؟! الاكتشافى تبعها يكون بصورة عرضية إذا عمل أشعة (imaging) لسبب آخر  
\* عند اكتشاف بصورة عرضية يعني بالصدفة أو بغيرها إذا شرفنا المريض بعد ما يموت

\*\* Usually A are small, 1 to 2 cm in, surrounded by thin or well-developed capsules, & most weigh less than 30g

(J Normal weight of both adrenals is 6 g) (F20-37 & 8.20).

\*\* C/S of A is usually yellow to yellow-brown, owing to the presence of lipid within the neoplastic cells.

\* مهما كان نوع Adenoma أو tumor يكون لونها أصفر إلى أصفر قهوهي فاتح بسبب كمية lipid الكبيرة يلي فيها

□ H, A are composed of cells similar to those populating the normal adrenal cortex. ← \* خلايا تكون مشابهة لكل طبقات

\*\* The nuclei tend to be small, although some degree of pleomorphism may be encountered even in benign lesions ("endocrine atypia") (F 20-38, see Slide no 155).

\*\* The cytoplasm of the neoplastic cells ranges from eosinophilic to vacuolated, depending on their lipid content; mitotic activity is generally inconspicuous

تتعدى كمية lipid نحو واضحة  
بها الطلية



The functional status of an adrenocortical adenoma cannot be predicted from its gross or microscopic appearance

\* well-circumscribed \* واردة : خطوطها الخارجية واضحة  
\* Solitary \*  
\* لو سألنا هل هي هائي

\* لا نعرف لأنه  
\* clinical picture \* تعتمد على

Hormone measurement \*  
\* وهذا يلي رح تطيلك تشونوعه إذا كان  
\* زياد أو تنقص نوبال !!  
\* Aldosterone / sex Hormones  
\* cortisol

functioning  
ولا !!  
non-functioning

صورة 8.20 :

disease in lung result in Cor-pulmonale \*  
Rt side HF  
Adrenal gland cortex occupied by adenoma  
\* \* سهم الاضطر يرك على ما تبقى من  
\* \* كانه  
\* \* فصا تبقى من  
\* \* بصير على شكل  
\* \* compressed  
\* \* كضام على  
\* \* periphery  
\* \* تبعت  
\* \* adrenal

### ADRENOCORTICAL CARCINOMAS

\*

\*\*Are rare, occur at any age. Two rare inherited causes are: Li-Fraumeni & Beckwith-Wiedemann syndromes.

\*\*Large, up to 2000 gm, invasive ca that efface the adrenal gland, C/S contains areas of necrosis, hemorrhage, & cystic change (F 8.23 & 20-41).

\*\*H, may be well-differentiated, resembling cortical A or undifferentiated, difficult to be distinguish from an

undifferentiated ca metastases to the adrenal (Fig.20-42).

\* 1<sup>ry</sup> و 2<sup>ry</sup> !

\* لا قصير  
انه حكتنا انها

favorable site for  
secondary  
Metastatic tumor

إذا  
كانت  
undifferentiated

\* وقتها لازم تعدر حل هو

\*\*They have a strong tendency to invade <sup>①</sup> lymphatics, <sup>② blood</sup> adrenal vein, & vena cava, with common metastases to regional & periaortic LN, lungs & other viscera.

\*\*The median patient survival is about 2 years.

\*\*⚙️ With **functioning** benign & malignant T associated with **Cushing syndrome**, the adjacent adrenal cortex & that of the contralateral adrenal gland are **atrophic** (Why?) because of suppression of endogenous ACTH by high cortisol levels.

Malignant أو كانت Cortical Adenoma ( Benign )

\*

\* إذا كانت functioning يعني ( producing cortisol ) وقتها الح يصل

\* Suppression of feedback Mechanism على pituitary و يؤدي إلى

\* atrophic ACTH من adrenal gland الصورة 8.23 :  
 ACTH ما وصلها ACTH من adrenal gland  
 بانخفاض إنتاج ACTH  
 من adrenal gland

صغيرة

غريب لأنه A حكتنا أغلبها non-functioning

⚙️ 90% of adrenal carcinomas are functional, with 50% are associated with Cushing's, 20% with virilization & 12% with feminization (as in this case of a 66y-old women with

evidence of estrogen secretion by the tumor.

\* virilization ♂ Male sex Hormones ↑↑

\* feminization ♀ female sex Hormones ↑↑

\* دائماً تذكر Normal Size

6grams لأنه مهمة

90%  
of adrenal

ca



functioning

50%

20%

12%..

Cortison

excessive male

feminization

↓  
Cushing

Sex Hormone  
production

(excessive estrogen)

↓  
Virilization

formation

~~20%~~

\* evidence of excessive  
estrogen secretion :

|| abnormal uterine bleeding

لأنه كلما 66 سنة موهبي بصير  
عندما uterine bleeding

\* اول شي بنفكر فيه هو

Ca of endometrium

Adrenal  
Ca

\* بس صون سبب

\* شرح صورة 20-41 :

سهم الأصفر مؤشر على Kidney يلي وزنها عند أنضاعف ( 200-300 ) يعني الكلية وزنها  
متواضع Adrenal يلى موجودة فوقها ذلك سموا suprarenal أما بهي صورة تقريبا ال tumor  
gland gland  
حجم أكبر من Kidney عند انهيك مكتوب Dwarfs ( يعني بقدم kidney ) ... لأنه أصبح  
أكبر منها بالحجم

\* وصف : ~~A~~ : Ca / large / Very Huge / necrotic

فأى tumors II diagnosis تبعا صعبا و إنما present on retroperitonum و إذا ما وصلت

للحجوم الكبيرة جدا --- ليس من الممكن تشخيصها في حال كانت non-functioning

بما إذا كانت functioning مستويات

Hint ←

androgen

cortison  
virilizing  
estrogen

Suspicion of diagnosis of adrenal tumor على

صورة 20.42 :

\* anaplasia & loss of differentiation (loss of resembling the original tissue => cortical cells) \*

\* إذا جابنا أيضا بالامتحان وحكنا هل هي Ca ؟! يعني ما بنعرف \*

\* لأنه يبي يحكم انه هاي Malignant مش benign هو وجود invasion و metastasis \*

Most imp. evident (factor) in diagnosis of Ca in endocrine system

\*\*In contrast; those associated with hyperaldosteronism do not usually suppress ACTH secretion. Therefore, the adjacent adrenal cortex & that of the contralateral gland are not atrophic.

لا عدا  
Papillary  
Ca of  
thyroid  
بيك

nuclear  
feature  
هو بي يتحكم

give you  
definitive  
diagnosis  
حتى بيون  
invasion

### ADRENAL MEDULLA

Is populated by cells derived from the neural crest (chromaffin

## ADRENAL MEDULLA

Is populated by cells derived from the neural crest (**chromaffin cells**) & their supporting cells.

feature  
هو الذي يتعلم  
→ give you  
defin  
diagr  
برون  
meda

The **chromaffin cells** (so named because of their **brown-black color** after exposure to potassium dichromate)

زوي المارة الشوائبية  
إزاعرضتها (Amyloid)

Adrenalin / nor-adrenalin

\* synthesize & secrete catecholamines in response to signals from preganglionic nerve fibers in the sympathetic nervous system.

ليود  
صبح  
black

\* Similar **chromaffin** cells collections are distributed throughout the body in the extra-adrenal **paraganglion** system.

## PHEOCHROMOCYTOMA

\*\* Tumors of the adrenal medulla chromaffin cells, which synthesize & release catecholamines &, in some cases, other peptide hormones.

موشاة في  
clinical practice

ليس

\*\* 😊 Although uncommon, these T are important, because like **aldosterone-secreting adenomas (Conn Syndrome)**, they



note

→ treatable / resectable

give rise to a surgically correctable form of hypertension

\* Very severe Hypertension \* عاي بسوي noradrenalin/ adrenalin تبعل

\* ~~conn syndrome~~ صحیح مش و مہلہ جہاً؟! ایست؟! لائے صی و conn syndrome

\* ~~سائے~~ سائے و لکن مہلہ؟! لائے إذا تسلیم Surgery اح یعالجوا المریض من Hypertension

\*\*Pheochromocytoma "rule of 10s":

\*

● 10% arise in association with one of several familial

syndromes, including MEN-2A & 2B & neurofibromatosis

type 1, Von Hippel-Lindau disease and Sturge-Weber

syndromes

adrenal خارج ار

● 10% is extra-adrenal, occurring in the organ of Zuckerkanal & the carotid body, where they are called paragangliomas.

● 10% of adrenal pheochromocytomas are bilateral; & up to 50% in cases that are associated with familial syndromes.

\* bilateral Sporadic (الاعتباریة) 10% من bilateral familial 50% من

● 10% of adrenal pheochromocytomas are biologically malignant, although the associated hypertension represents

شو صناعاً

a serious & potentially lethal complication of even "benign"

tumors. Frank malignancy is somewhat more common in

tumors arising in extra-adrenal sites.

\* بعض الحالات مع انها Benign حمید ولكن ممكن يصير ارتفاع

Biologically Malignant

لضغط الدم بصورة شديدة عشان هيك حكينا

→ spread to other organs