* الغدد الكظرية *

PATHOLOGY OF THE ADRENAL GLAND: CORTEX

Hypercortisolism = Cushing syndrome (Csy) (F20-35)

Exogenous administration of steroids is the most common cause of **Csy.

تذكرها جيداً ، لأنه يستخدم على نطاق واسع بالعلاجات و بالتالي هو سبب الاشيع

Endogenous **Csy is : → ((داخل الجسم أو بسبب عوامل زائية

(I) Most often due to ***Cushing disease*** **=(Primary hypothalamic-pituitary disease,** mostly resulting from ACTH-producing pituitary micro-adenoma), accounts for **> 50% cases** of spontaneous endogenous **Csy**.

* أعتبر من 50% منطقة ← endogenous و بالتالي هو أشيع سبب

* يؤدي إلى ← Micropituitary adenoma وأهم شيء هو وجود

1ry Hypothalamic -pituitary disease

* زيادة في ← Hyperplasia يصير فيها ← both Adrenal يشتغل على ← excessive secretion of ACTH

Cortisol

↳ Hypercortilism

● Rarely, the anterior pituitary contains areas of ***corticotroph cell hyperplasia*** without a discrete adenoma.

* يعني حالات نادرة يكون عنا فرط نمو ← Adenoma وليس Ant. pituitary

(Hyperplasia)

** طب شنو findings ؟

● The ***elevated levels of ACTH*** in Cushion disease **cause** *secondary bilateral adrenal nodular cortical hyperplasia, resulting in* hypercortisolism.

* يعني يكونوا اثنين مرتفعين ↑ Cortisol + ↑ ACTH

لأنه سبب Secondary

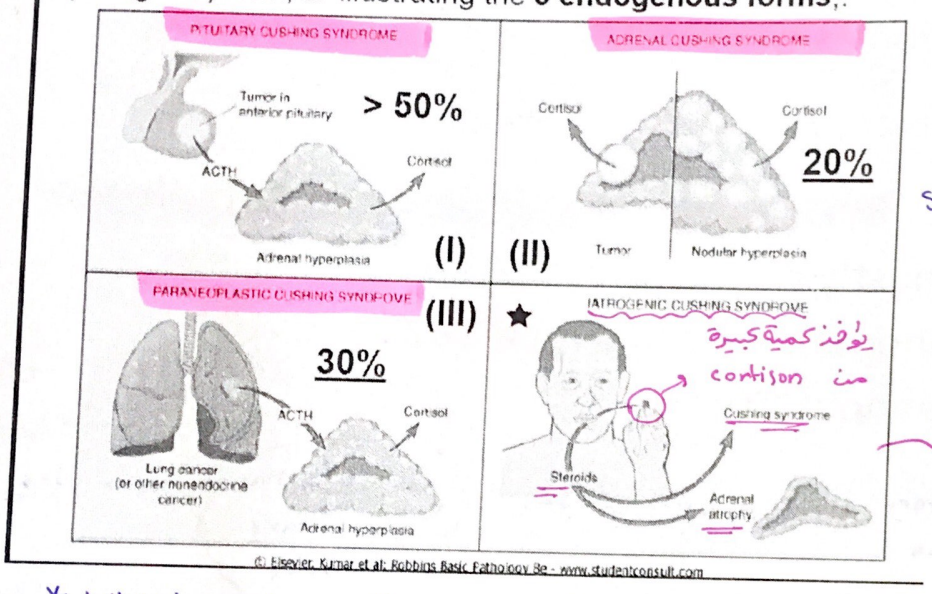
هاي صفاها العلامة المسجلة « بالفرنسي »

☼Therefore, the biochemical sine qua non of **Cushing disease** is **elevated serum levels of both cortisol and ACTH.**

عادها هرمونية

*

F 20-35: Schematic representation of the various forms of **Cushing syndrome**, showing the most common ★ exogenous (iatrogenic) form, & illustrating the **3 endogenous forms**,.



Very ⊛ important

انتبه انه عنا Syndrome وعنا Disease يلي pituitary فيه adenoma

شرح هاي صورة

* ⁂ Which is the most common ~~boyar~~ of cause of (form)
* cushing syndrome ? exogenous cortison
* يعني ← iatrogenic : توفد علاج يؤدي لمشكلة
* * ليش يوفد Steriods ← بالفم ← cortison راح يكون أكثر من
* طبيعيا بالدم ← بسوي ← feed back Mechanism على ← Both adrenal ← بخليها atrophic
* ضامرة ← لأنه ما في داعي لشغلها ← Bilateral atrophy of Adrenal cortex

مع هيك بنفس الوقت !! بكون عنده علامات cushing syndrome

صورة (1)

* تمثل اشيع سبب لـ endogenous Cushing Syndrome

cushing disease يلي هو

* الذي يمثل سبب لأكثر من 50٪ endogenous syndrome من حالات

* there's a tumor in Ant. pituitary ←

↑↑ ACTH → Bilateral hyperatrophy of adrenal cortex → ↑↑ cortison → Hypercortilism

صورة (3)

* هاي: 2nd most common cause of endogenous cushing syndrome

* هي عبارة عن: Paraneoplastic cushing syndrome

* طب شو يعني؟!:

cancer in lung, pancreas, any other non-endocrine organ → كان بنتج ACTH

ectopic ACTH

بهاي الحالة بصير

بأنه طلع من مكان غير مكانه ... المفروض يطلع من pituitary

* مسؤولة عن 30٪ من حالات ← تشكل نفسها نتيجة هاي

* قبل 20٪ من حالات endogenous cushing Syndrome

مين المسؤول عنها؟!

صورة رقم (2)

* يلي هي Adrenal cushing Syndrome ←

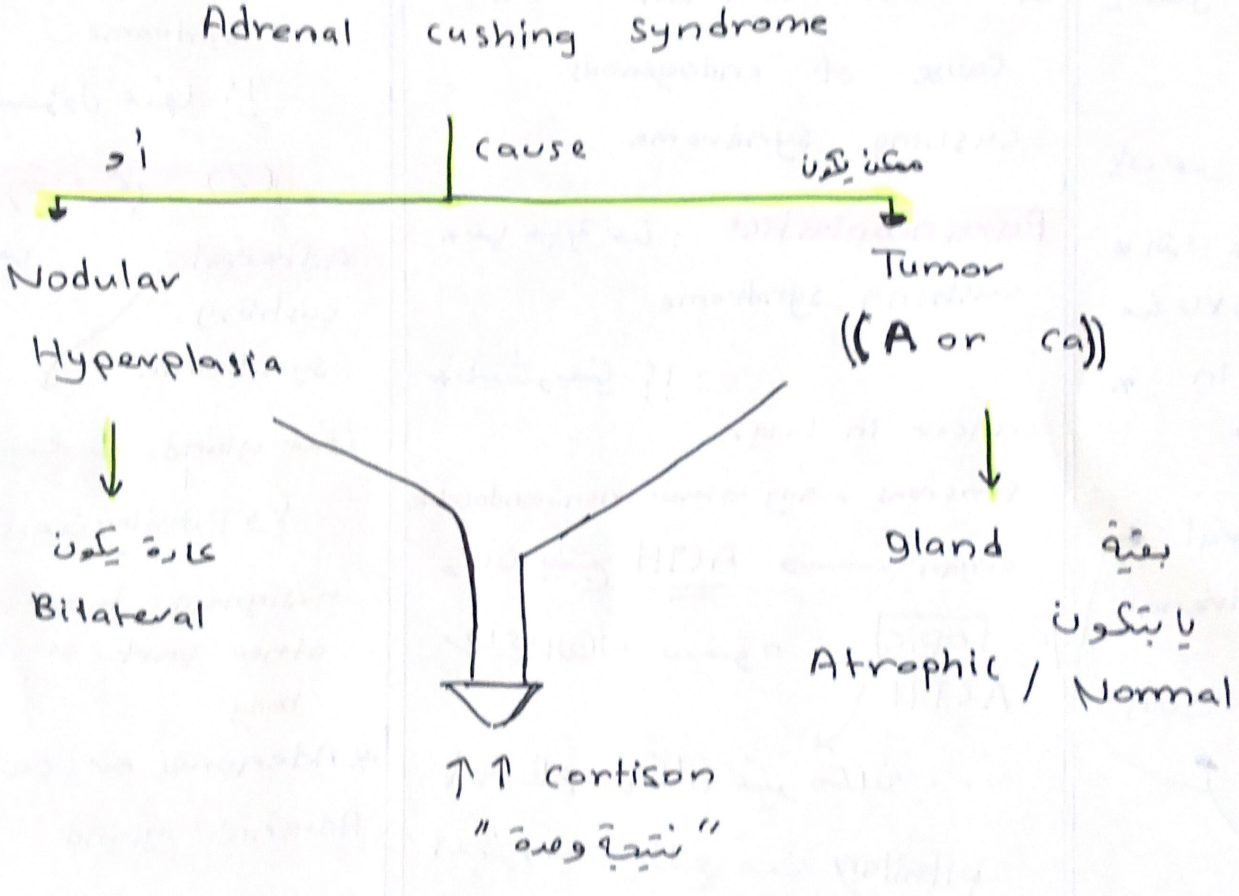
يعني سبب بـ gland نفسها

لا هي جاي من Pituitary ولا من malignant tumor in other part of the body

* Adenoma or Ca in Adrenal gland

or Nodular Hyperplasia

* تكملة شرح صورة (2)



~~exogenous ACTH~~

(II) *Primary adrenal T,*

*this form of **Csy** is also designated ***ACTH-independent Csy*** **or (adrenal Csy)** because the adrenals function **autonomously**.

It is responsible for up **20% of cases of endogenous Csy, & caused by a **unilateral** adrenocortical T, which may be either (1) **Adenoma** or (2) **Carcinoma**, or rarely by (3) **primary bilateral adrenal cortices hyperplasia.**

☼ The biochemical sine qua non of **adrenal Csy** is ***elevated levels of cortiso*** with ***low*** serum levels of ACTH.

*

*

*

(III) Paraneoplastic *secretion of ectopic ACTH by nonendocrine T* accounts for most of the remaining cases of endogenous **Csy (30%)**, by causing adrenal nodular cortical hyperplasia.

*

*

*

Commonest responsible T is a ***small cell carcinoma of the lung (SCCL)***, but others, including ***carcinoid T, thyroid medullary ca.,*** & ***pancreatic islet cell T,*** have also been associated with **Csy.**

~~* CT~~

* cushing disease :

↑↑ cortison

↑↑ ACTH

* Aderenal tumor :

↑↑ cortison

↓↓ ACTH

* paraneoplastic - -

↑↑ cortison , ↑↑ ACTH

شوف يصير فيها Adrenal gland

#The morphologic features in the adrenal include:

(1) In exogenous steroid-induced disease there is **Bilateral cortical atrophy** (F 8.17).

* ← Hypercortilism ← الدم راح يصير فيه ← من الخارج cortison * واحد يوخذ

* ليس هنا لك فائدة لـ gland إنها تشتغل ← يصير فيها ضمور

*

(2) **Bilateral diffuse or nodular hyperplasia**

(most common finding in endogenous **Csy). ← ليش؟

It is found in **60% to 70% of cases of endogenous Csy.

The adrenal cortex is **diffusely thickened & yellow, as a result of an h in the size & number of lipid-rich cells in the zonae *fasciculata & reticularis*.

Some degree of nodularity is common but is pronounced in **nodular hyperplasia (**F20-36 & 8.18**).

* شاملة منتظمة : diffuse
عُقدي : nodular ← قد تكون Hyperplasia

This takes the form of bilateral, 0.5- to 2.0-cm, yellow nodules scattered throughout the cortex, separated by i ntervening areas of widened cortex.

* * هاي الحالة ~~حتى~~ وين بتصير؟! مع paraneoplastic و disease Cushing Disease

* * احنا طا نفحص بـ postmortum بنشيل ~~الغدة~~ 2glands بنظفها من شحم و بنوزنها

The combined adrenals weigh (which in the J normal adult should not exceed **6 grams** for either sex), may as **much as 30 to 50 gm).** شو يعني

* توفد 2 adrenal Glands وتنظفها من شحم وتوزنها

Nodular او diffuse بس في حالة / 6gm بالميزان لازم مايزيد وزنها عن

30 - 50 يصل وزنها لـ ← Hyperplasia

... يدين موالي (8 - 5) أضعاف

**This macronodularity appears to be an extension of the diffuse hyperplasia, because the cortex between the nodules exactly resembles that found in the diffuse form of this condition.

* ما رح يختلف الوزن بين Nodular , Diffuse و ثنين رح تؤصل gland فيها إلى (3-5) أضعافها

(3) **Adrenocortical neoplasms** (see later F8.20+21& 20-37)

* هاي رح نذكرها بتوسع بعدين

*صورة 8.17: انتبه جداً بـ Adrenal gland مهم جداً توزنها

صورة 20-36 : النورمال الحلوة مسفطة بسمولها القبعة الثلاثية

صورة 8-18 : الـ Gland الـ Brown تبعها center yellowish تبعها periphery

The most common morphologic changes in the **pituitary gland in **Csy**, regardless of the cause, **resulting from high levels of endogenous or exogenous glucocorticoids, are termed "Crooke hyaline change",**

exogenous
endogenous

* مهما كانت الحالة تبعت cushing , cortison سواء كان مصدره

* الـ Hypercorticism رح يؤدي إلى تغير بالغدة النخامية بنسبة

crooke hyline change ---- طب شو هو ؟!

in which the normal granular, basophilic cytoplasm of the ACTH-producing cells in the anterior pituitary is replaced by homogeneous, lightly basophilic material, as a result of cytoplasmic accumulation of intermediate keratin filaments.

Hyperaldosteronism

**Excessive levels of aldosterone cause *Na retention* & *K excretion, with resultant hypertension & hypokalemia.*

**It can be a primary (Rare) or, secondary (Common):

► ***Secondary hyperaldosteronism***, in response to activation of the renin-angiotensin system. It is characterized by ↑ ***levels of plasma renin*** in conditions associated with:

(1) ↓ **renal perfusion** (arteriolar nephrosclerosis [A], renal artery stenosis [B]),

*

(2) **Arterial hypovolemia & edema** (CHF, cirrhosis, & nephrotic syndrome).

(3) **Pregnancy** (caused by estrogen-induced ↑ in plasma renin substrate)

*

► ***Primary hyperaldosteronism*** indicates a **primary, autonomous overproduction of aldosterone,** caused either by

(1) an aldosterone-producing **adenoma (A)** in **80%** of cases, or

(2) by primary adrenocortical **hyperplasia** in **15%** of cases,

with resultant suppression of the renin angiotensin system & ↓ ***plasma renin activity.*** → 2ry عكس

▶ **Aldosterone-secreting A,** are mostly **solitary** (F8-21), socalled **Conn syndrome.** 1ry Hyper-aldosteronism والتي هي سبب بـ 80٪ من حالات

A are **small (<2 cm in Ø), encapsulated, with **bright yellow** C/S & A are composed of lipid-laden cortical cells of uniform size & shape; with occasional nuclear & cellular **pleomorphism** (F20-38). * يعني الخلايا غالباً بتكون منتظمة الشكل والحجم ولكن أحياناً بصير تغيرات وهاي ما إلها أي قيمة nuclear + cellular pleomorphism ليست

* يلي سميناها «endocrine atypia»

A characteristic feature of such **A is the presence of eosinophilic, laminated cytoplasmic inclusions, known as **"spironolactone" bodies (similar to Psammoma bodies),** typically found after treatment with the anti-hypertensive drug **spironolactone,** which is the **drug of choice** in primary hyperaldosteronism.

① تكون ② ③ يلي درسناها papillary ca of thyroid

* ↓ renin-angiotensin يكون 1ry Hyperaldosterism * المرضى يلي عندهم

* يبدأ تعطي المريض Laparotomy tests و CT-Scan بس تشخص هاي الحالة بـ

* Spironolacton الذي هو هاي الحالة drug of choice و drug

* 1ry Aldosteronism يستخدم بعلاج

Hypertension

* في هذه الحالة بعد العلاج ، إذا عملت Adrenalectomy وشفت المقطع تبعها رح تلقى فيها

**Carcinomas resulting in hyperaldosteronism are rare.

* produce mostly cushing , Low feminizing ,
هرمونات ذكرية أو أنثوية

صورة 8-21 :

* ↑ Aldosteron / ↓ K^+ / Hypertensive / CT scan و بكون فيه واضح ورم Adrenal cortex =

*

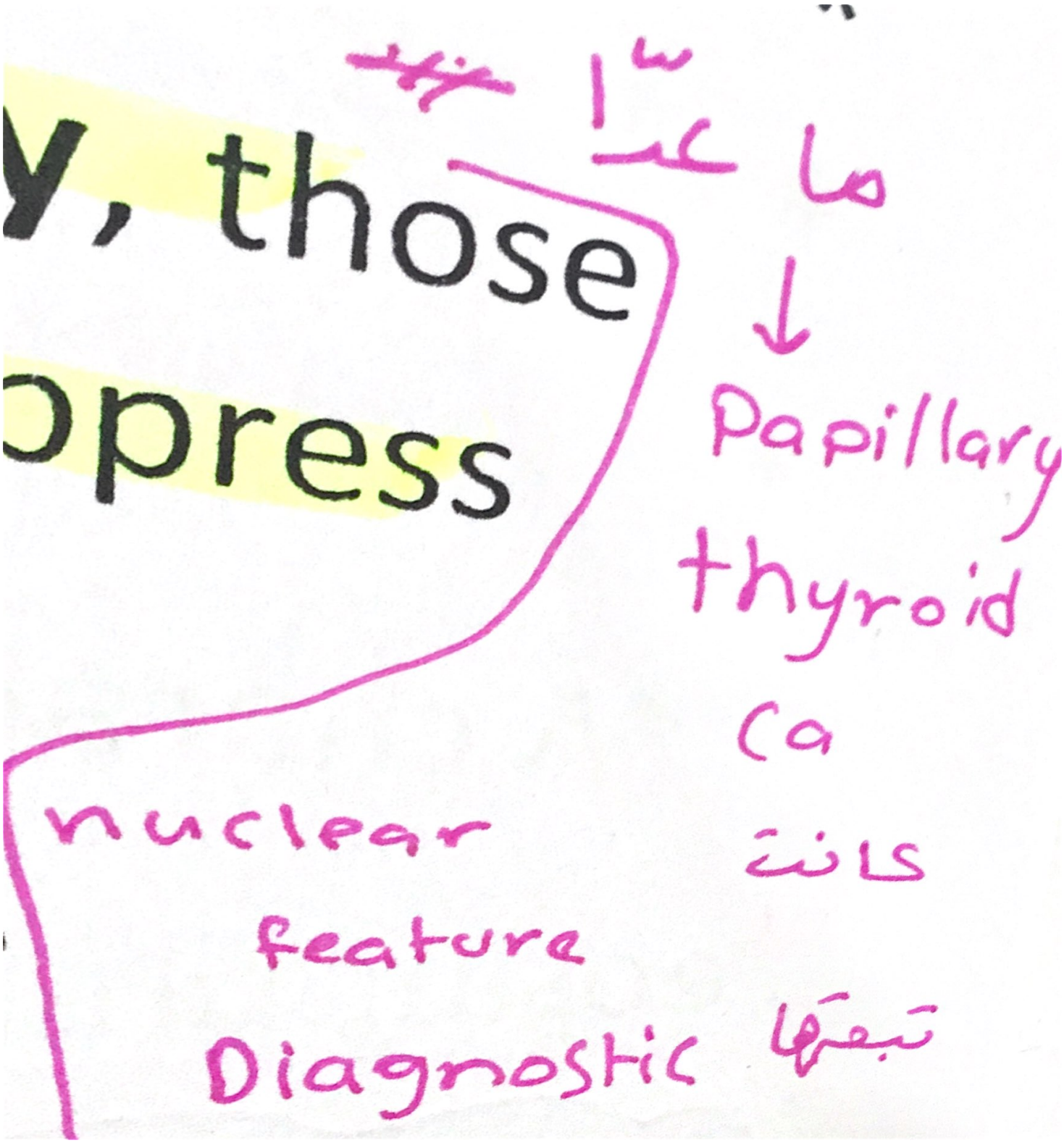
صورة 20-38 :

* فقاعات البيضة الفارغة نتيجة تحضير slide نتيجة إزالة fats أثناء تحضير

* pleomorphism : variation in shape and size of nuclei

* صون Atypia ↑ تعتبر endocrine وزيها زي Atypia

by itself does not indicate Malignancy ← thyroid , pituitary


y, those
opress
ما عدا
Papillary
thyroid
Ca
كانت
nuclear
feature
Diagnostic
تبعتها

In contrast to cortical adenomas associated with **Csy, those associated with hyperaldosteronism do not usually suppress ACTH secretion.

Therefore, the adjacent adrenal cortex & that of the contralateral gland are **not atrophic.

↓ Pap thy Ca ... nuclear feature Diagnostic

* ... وقتها اخ تعمل Cortison تفرز Cortical A. ... * إذا كان في

* Atrophic اخ تكون Adrenal Gland بقية لذلك Supression of ACT Production

* ... بالتالي ما رح تقلل ~~Cortison~~ Cortical A. لا تفرز ... * هون

* Gland لبقية Atrophy ما رح تؤدي إلى ← ACTH

80 ٪ → Cortical Adenoma (Conn syndrom

▶In about 15% of cases, primary hyperaldosteronism is caused by bilateral **primary adrenocortical hyperplasia**, characterized by **bilateral nodular hyperplasia of the adrenal glands,** highly similar to those found in the nodular hyperplasia of **Csy** (F20-36 & 8.18)

* فرط نمو adrenal cortex بالجهتين

* وهاي تكون مصابة لـ adrenal Hyperplasia التي تصدّن

Adrenal cushing caused by Hyperplasia

يعني إذا شفت :

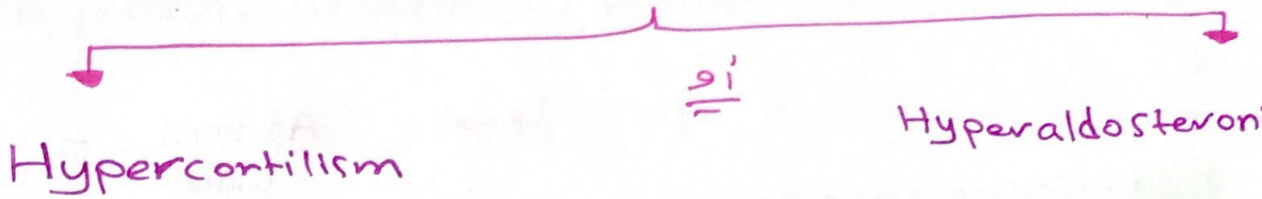
Both Adrenal glands

are diffusely hyperplastic

(30 gram – 50 gram)

وسألناهاي شو؟

ممكن تكون



طب كيف اح نحدد

النوع ؟!

further laboratary

inuestigations

هي يلي اح تحدد النوع

final diagnosis

ADRENAL INSUFFICIENCY (hypoadrenalism):

Types:

(I) **Primary *acute*** (**adrenal crisis**) hypoadrenalism,

*

(II) **Primary *chronic* (*Addison disease*)** hypoadrenalism, due to primary adrenal disease (**90% of cases** are due to *autoimmune adrenalitis, TB, AIDS or metastatic cancers*),

*

(III) **Secondary adrenocortical insufficiency** caused by a deficiency of ACTH, resulting in ↓ stimulation of the adrenals.

*

*

*

(I) *Primary acute* adrenocortical insufficiency (adrenal crisis):

*occurs commonly in the clinical settings listed in Table 20-7.

① ▶ patients **with chronic adrenocortical insufficiency** may develop an acute crisis **after any stress,** because of the inability of the atrophic adrenals to produce more glucocorticoids hormones needed by the stress.

*

*

* بهاي الحالة شو علاجه ؟!

لازم تو فرله glucocorticoids

في حال تعرّضت لـ : surgery ,

infection , trauma ,

dehydration

2

▶ **Rapid withdrawal of steroids** or failure to ↑ steroid doses in response to an acute stress, **in patients maintained on exogenous corticosteroids may precipitate** a similar adrenal crisis, because of the inability of the atrophic adrenals to produce glucocorticoids hormones.

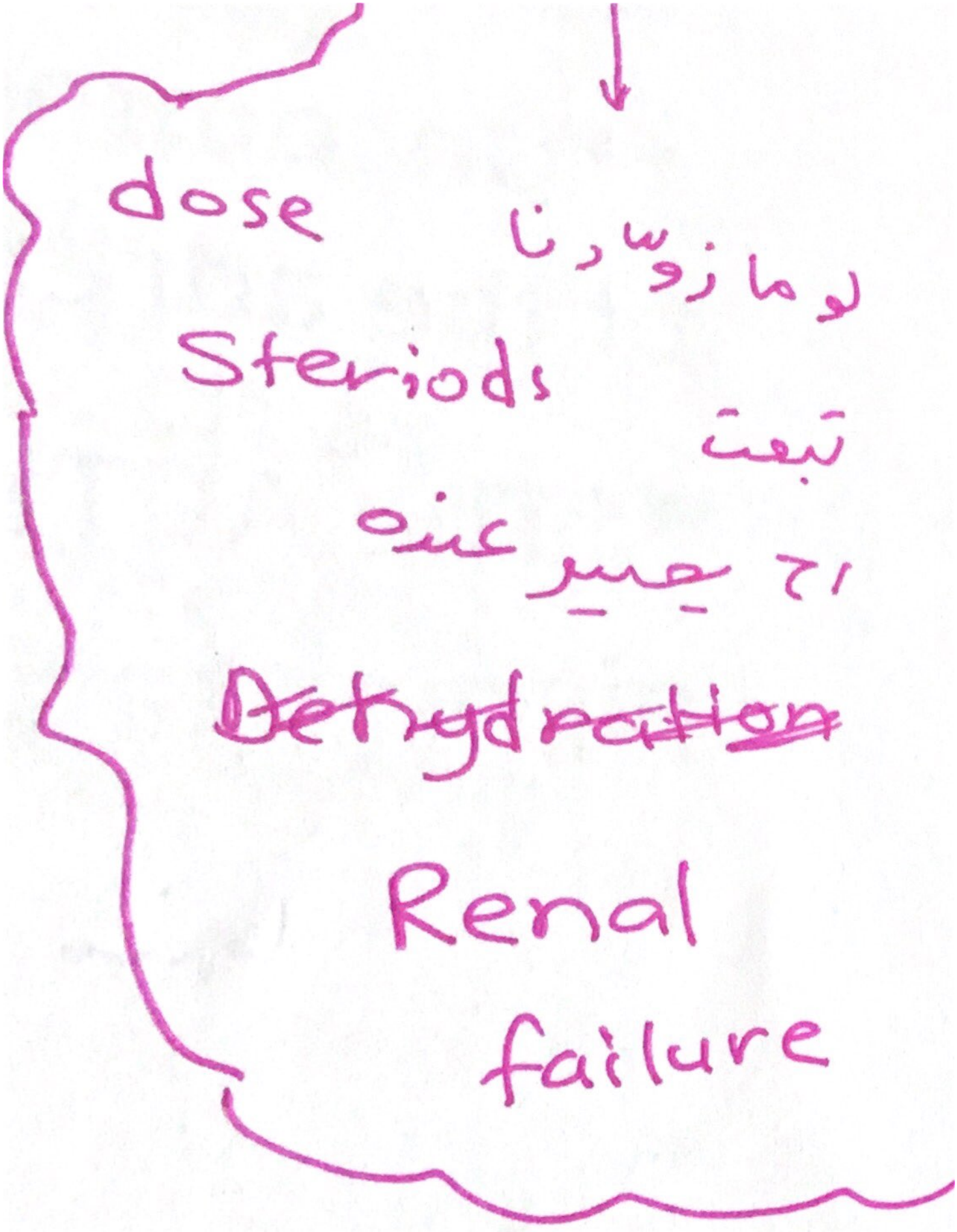
* شخص يوقف glucorticoids لعلاج chronic primary

Addison disease أو لأي سبب آخر ... إذا وقفت Steriods عن صيك مريض

بصورة مفاجئة أو مازيدت dose على patient في حالة ((acute stress

... حتى تعوّض عن زيادة الطلب

* لو واحد عنده Sever diarhea يعني stress وهو بتعالج بـ Steriods (مثلاً عشان hemolytic anemia)


dose
لو ما زودّت دنا
Steriods
تبعت
ز جبير عنه
Dehydration
Renal
failure

3 ▶ **Massive adrenal hemorrhage** may destroy the adrenal cortex to cause acute adrenocortical insufficiency in:

(1) Patients maintained **on anticoagulant therapy,**

(2) Postoperative patients who develop **DIC,**

(3) During **pregnancy,**

(4) Patients suffering from overwhelming **sepsis (Waterhouse-Friderichsen syndrome)** (F 8.15 & 20-39),

Classically associated with ***Neisseria meningitidis*** septicemia but can also be caused by *Pseudomonas, pneumococci*, &

Haemophilus influenzae.

The pathogenesis of this **catastrophic** syndrome probably involves endotoxin induced EC vascular injury with associated DIC.

Killer

catastrophic* : يعني كارثة وعادة ما يطلع منها المريض سالم عادة

* DIC ← endotoxin induced EC vascular injury

* هاي احنا نسوي sever bacterial infection

* Renal خاصة :

يعني Pathogenesis اله علاقة بنقطة 2 (DIC) ---

* الاسباب اللي حكيناهم تبعون primary crises .. مهمين جداً

* لأنه إذا عالجت المريض بهاي الحالة الحرجة وأعطيته glucocorticoids ممكن ينجو المريض من هاي الحالة الخطرة جداً

(II) *Primary chronic* adrenocortical insufficiency = Addison

((ACTH ↑ , cortison ↓↓)) **Disease:**

Uncommon disorder, resulting from **progressive destruction of the adrenal cortex.

تدمير متسارع لـ Adrenal cortex

The ACTH levels are elevated (Why?) & there is **skin hyper pigmentation because melanotropic hormone levels are high.

* جواب Why ؟! لأنه إذا تدمرت Adrenal cortex طارح يطلع منها ...

* cortison و glucocorticoids

* ACTH تضل تطلع ؟! Pituitary و loss of Inhibitory feedback Mechanism بالتالي ، يصير

: 8.15 صورة *

* هذا يؤدي إلى Acute Adrenal Crises (insufficiency)

Histo-pathological examination من نفس الحالة السابقة وحملنا Slide لواضدنا

: صورة **

20-39

* هاد طفل صار عنده Neisseria Meninigitis ← sepesis ← EC Vascular injury of Renal arteries

Massive Hemorhage ← DIC ←

Steriods ((هذا يؤدي إلى الوفاة لما تعطي