The Adrenal Glands

two glands in one structure (cortex, medulla)

A paired endocrine organs; the cortex & medulla

Ghadeer Hayel, M.D.
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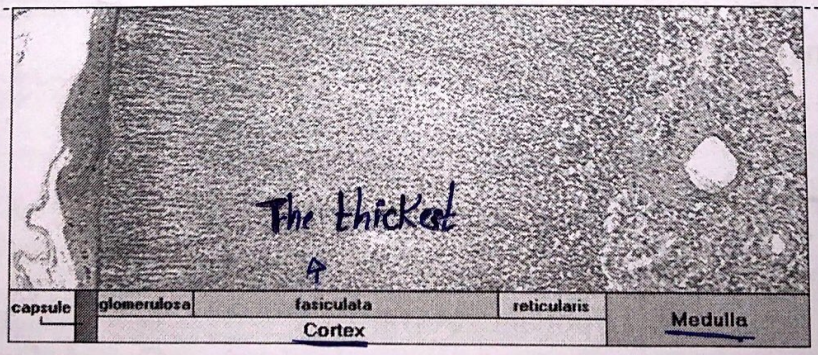


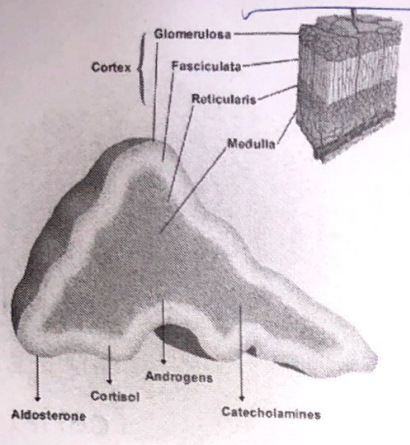
Adrenal Cortex

Synthesizes three different types of steroids: fat base hormone

- **Glucocorticoids (cortisol), zona fasciculata, zona reticularis (small contribution)**
- **Mineralocorticoids (aldosterone) zona glomerulosa**
- **Sex steroids (estrogens and androgens), zona reticularis**

the thinest

ADRENOCORTICAL HYPERFUNCTION



three distinctive hyperadrenal clinical syndromes:

- *Cushing syndrome:* an excess of cortisol.
- *Hyperaldosteronism: an* excess of mineralocorticoid. (aldosterone)
- *Adrenogenital* or *virilizing syndromes:* an excess of androgens.

Sura

الغاطق اللي تخضع لتأثير الكورتيزون هي كبيرة جدًا لكن اذا زاد بعمل مشاكل على مختلف الاعضاء لذلك سميت syndrome

I. Exogenous (The vast majority of cases): administration of glucocorticoids (iatrogenic). معظم الحالات يأخذها كدواء

any illness caused by Medical prosesures, drugs ...

II. Endogenous, the three most common disorders are:

1. Primary hypothalamic-pituitary diseases, ass with hypersecretion of ACTH
2. Secretion of ectopic ACTH by nonpituitary neoplasms
3. Primary adrenocortical neoplasms (adenoma or carcinoma) &, rarely, primary cortical hyperplasia.

01

Cushing Syndrome

Hypercortisolism: ↑↑↑glucocorticoid levels.

* adrenal تتحكم بال pituitary عن طريق ACTH

1. Primary hypothalamic-pituitary disease ass/w hypersecretion of ACTH (Cushing disease)

→ specifically related to hypothalamus and pituitary gland

70%

of spontaneous, endogenous Cushing syndrome.

women

are affected four times higher than men.

Young adults

20s & 30s are most frequently affected.

Pituitary gland

ACTH-producing microadenoma is the cause in the vast majority

Cushing disease

- Mostly there is a microadenoma & rarely, the anterior pituitary contains areas of corticotroph cell hyperplasia without a discrete adenoma.

most common

- Hyperplasia may be primary or, much less commonly, secondary to hypothalamic corticotropin releasing hormone (CRH)-producing tumor.
- Secondary to the elevated levels of ACTH ("ACTH dependent" Cushing syndrome). ☐ Adrenal cortical hyperplasia ☐ hypercortisolism.

abnormal location

2. Secretion of ectopic ACTH by nonpituitary tumors (Paraneoplastic syndrome)

- 10% of cases of Cushing syndrome.
- Mostly the tumor is a small-cell carcinoma of the lung.
- Other neoplasms; carcinoids, medullary carcinomas of the thyroid, & PanNETs.
- Occasional neuroendocrine neoplasms produce ectopic CRH □ causes ACTH secretion □ hypercortisolism.

3. Primary adrenal neoplasms

- Adrenal adenoma, carcinoma, and rarely, primary cortical hyperplasia responsible for 15-20% of endogenous Cushing syndromes.
- Designated ACTH-independent Cushing syndrome, because the adrenals function autonomously. → secretion cortisol without ACTH
- Adrenal Cushing syndrome: ↑↑ cortisol levels & ↓↓serum levels of ACTH. cause by feedback -
- Caused by a unilateral adrenocortical neoplasm.

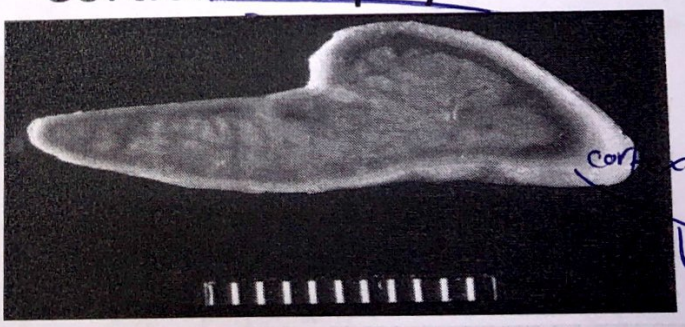
Morphology

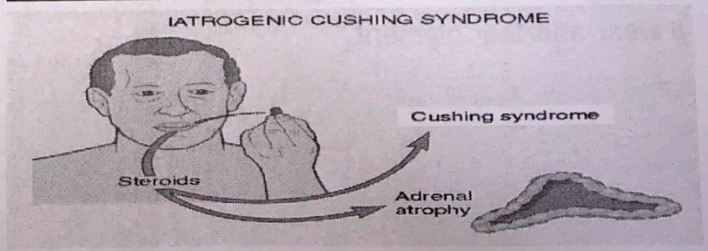
- Morphologic changes in the adrenal glands also depend on the cause of the hypercortisolism and include:

(1) Cortical atrophy,
(2) Diffuse hyperplasia,
(3) Macronodular or micronodular hyperplasia,
(4) An adenoma or carcinoma.

Morphology - Cortical atrophy

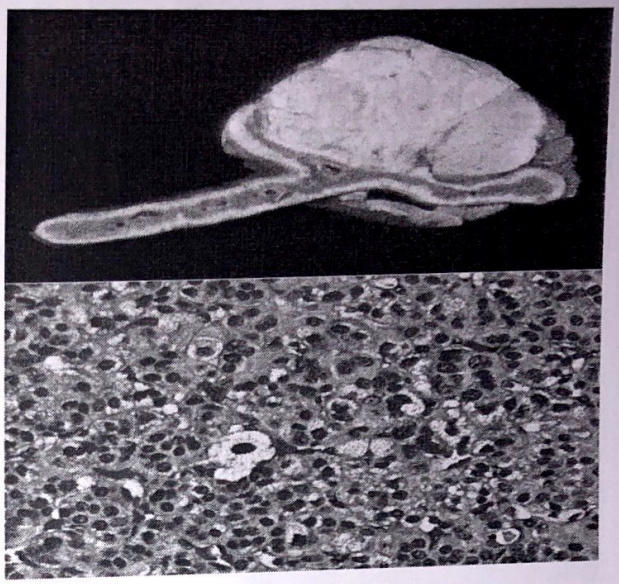
- Syndrome results from exogenous glucocorticoids → suppression of endogenous ACTH → bilateral **cortical atrophy,** due to a lack of stimulation of zona fasciculata and zona reticularis by ACTH





Morphology - Adenoma or carcinoma

- Both are more common in women in their 30s -50s.
- Only definitive criteria for malignancy are distant metastasis or local Invasion.
- Functioning tumors, both benign & malignant, causes adjacent adrenal cortex & contralateral adrenal gland are atrophic.



filled

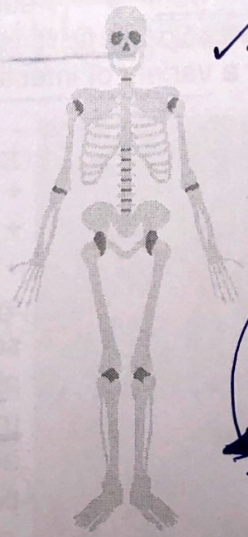
gradually

Clinical Features

+ an exaggeration of glucocorticoids known actions.

+ Develops gradually & may be subtle in early stages.

+ A major exception is Cushing syndrome ass/w lung small cell Carcinoma.



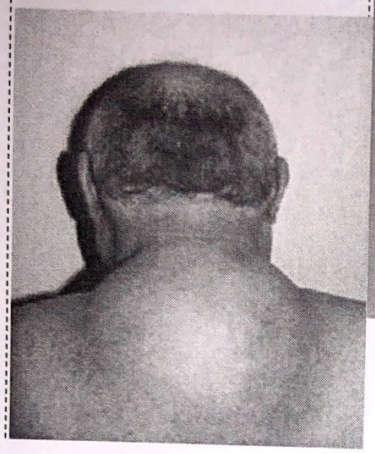
- Hypertension. ↑ HR
- Selective atrophy of fast-twitch (type II) myofibers→ ↓↓ muscle mass→ proximal limb weakness.
- Induce gluconeogenesis + inhibit glucose uptake by cells → secondary DM (hyperglycemia,glucosuria & polydipsia.)

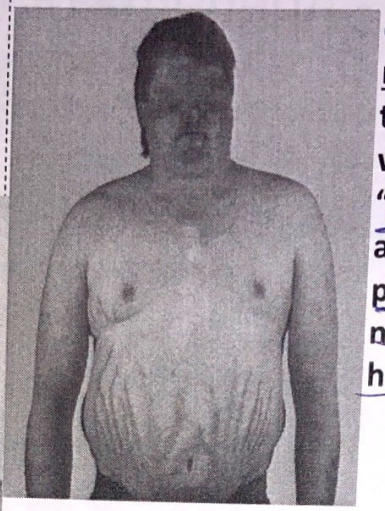
يزيد الجلوكوز بالدم

Diabetes

لما يزيد السكر في الدم يحوله الجسم الى Fat

Clinical Features- weight gain





characteristic centripetal redistribution of adipose tissue becomes apparent with time → truncal obesity, "moon facies" & accumulation of fat in the posterior neck & back "buffalo hump".

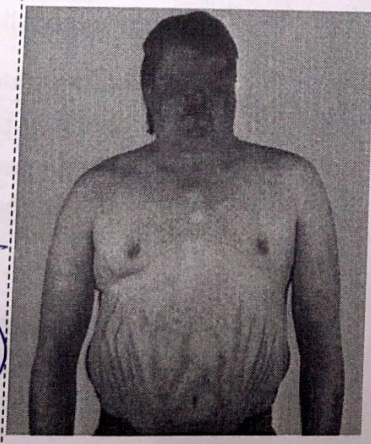
كل الأجهزة تأثر بسبب مقاومة الانسولين

Clinical Features:

+ Catabolic effects of insulin resistance on proteins→ loss of collagen→ skin is thin, fragile, & easily bruised cutaneous **striae** (common in abdominal area)

تشققات

+ Cortisol → resorption of bone → development of **Osteoporosis** → ↑↑ susceptibility to fractures.
+ Glucocorticoids **suppress** immune response→ ↑↑ risk for a variety of infections



+ hirsutism
+ menstrual abnormalities.
+ psychiatric symptoms
+ In pituitary Cushing syndrome or ectopic ACTH secretion ass+-/ w skin pigmentation 2ndary to melanocyte-stimulating activity in the ACTH precursor molecule.

syndrome involved all the body

دليل على اهمية الكورتيزون بالجسم

الألدوستيرون يتحكم بامتصاص الماء والملح
وضغط الدم

02

Hyperaldosteronism

A group of conditions characterized by chronic ↑↑↑ aldosterone secretion.

- Hyperaldosteronism may be primary, or secondary to an extraadrenal cause:

- Primary: Autonomous overproduction of aldosterone with resultant suppression of the renin-angiotensin system & decreased plasma renin activity.

- Secondary: Aldosterone release occurs in response to activation of the renin-angiotensin system.

both adrenal affect

Primary hyperaldosteronism : Bilateral idiopathic hyperaldosteronism

not fully understood

→ genetic mutation

- Bilateral nodular hyperplasia of the adrenal glands.
- The most common underlying cause of primary hyperaldosteronism, 60% of cases.
- The pathogenesis is unclear (idiopathic), a subset harbors germline mutations in the KCNJ5 gene □ encodes a potassium channel protein that is expressed in the adrenal gland.

→ over activation of zona glumerulosa

Primary hyperaldosteronism : Familial hyperaldosteronism

- Rare, genetic defect that leads to overactivity of the aldosterone synthase gene, CYP11B2.

over activated

Born with problem in aldosterone secretion

Primary hyperaldosteronism : Secondary hyperaldosteronism

- Activation of the renin-angiotensin system ☐ aldosterone release.
- Characterized by ↑↑ levels of plasma renin, in ass/with:

1. Decreased renal perfusion (arteriolar nephrosclerosis, renal artery stenosis)
2. Arterial hypovolemia & edema (congestive heart failure, cirrhosis, nephrotic syndrome)
3. Pregnancy (caused by estrogen-induced increases in plasma renin substrate)

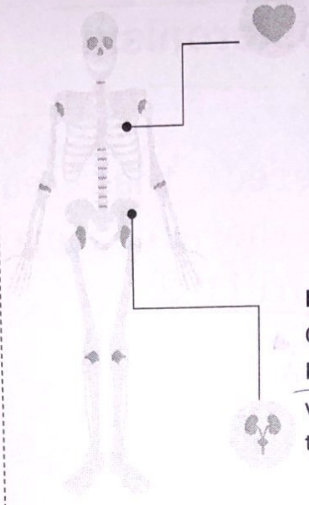
اغلاق شرايين الكلية

problem in venous return

loss of protein

↑ aldosterone but it's minor

Clinical Features



Hypertintion & its long-term effects; left ventricular hypertrophy, & an increase in the prevalence of adverse events (stroke & myocardial infarction

complication

↳ increase demand on heart

The most important clinical consequence of hyperaldosteronism is hypertension.

يزيد حجم السائل عن طريق اعادة امتصاص الماء والاملاح

Primary hyperaldosteronism may be the most common cause of 2ndary hypertension.

Hypokalemia due to renal K+ wasting. Can cause neuro-muscular Manifestations; weakness, paresthesias, visual disturbances, & occasionally frank tetany.

تشنجات

ضياع K اثناء اعادة امتصاص Na والماء وهم مهم للعضلات والأعصاب

adrenal

(ovary, testis) gonadal

sexual hormones مصادر ال **

اذا كان الخلل gonadal يكون له علاقة بال pituitary

. may stem from
(1) Primary gonadal disorders
(2) primary adrenal disorders.

. Unlike gonadal androgens, adrenal androgen is regulated by ACTH excessive secretion can present as an isolated syndrome or in combination with Cushing disease features.

. The adrenal causes of androgen excess:
(1) Adrenocortical neoplasms and an
(2) Congenital adrenal hyperplasia (CAH), uncommon group.

03

Adrenogenital Syndromes

Disorders of sexual differentiation caused by androgen excess,

• ياخذ features للذكر او للانثى

Congenital adrenal hyperplasia (CAH).

from birth

- AR disorders, characterized by a hereditary defect in an enzyme involved in adrenal steroid biosynthesis (cortisol).
- ↓↓↓cortisol ☐ compensatory ↑↑↑ ACTH due to absence of feedback inhibition ☐ adrenal hyperplasia ☐ ↑↑↑ production of cortisol precursor steroids ☐ channeled into synthesis of androgens ☐ virilizing activity (more sexual characteristic male)

excess

- Certain enzyme defects also may impair aldosterone secretion, adding salt loss to the virilizing syndrome.
- The most common enzymatic defect is 21-hydroxylase deficiency (> 90% of cases) مسؤول عن انتاج الكورتيزول

mutation affect final steps that lead to production cortisol (defective enzyme)

Congenital adrenal hyperplasia (CAH):
21-hydroxylase deficiency

- Deficiency may range from a total lack to a mild loss, depending on the nature of the mutation.

presentation

- In the adrenal glands cortisol, aldosterone & sex steroids are synthesized from cholesterol through various intermediates.
- 21-hydroxylase is required for synthesis of cortisol & aldosterone but not sex steroids. مش بتاخد طريق
- So, a deficiency of it will (1) reduces cortisol & aldosterone synthesis & (2) shunts the common precursors into the sex steroid pathway.

Clinical Features

Depending on the nature & severity of the defect clinical symptoms may be:

+perinatal period, later childhood, or (less commonly) in adulthood.
+Be with or without aldosterone & glucocorticoid def.

- In 21-hydroxylase deficiency, excessive androgenic activity causes:

1. Masculinization in females: clitoral hypertrophy & pseudohermaphroditism in infants to oligomenorrhea, hirsutism, & acne in postpubertal girls.
2. In males, androgen excess is ass/w enlargement of the external genitalia & other evidence of precocious puberty in young patients. Most men with CAH are fertile but some have oligospermia.

- one-third has aldosterone deficiency,
- CAH should be suspected in any neonate with ambiguous genitalia

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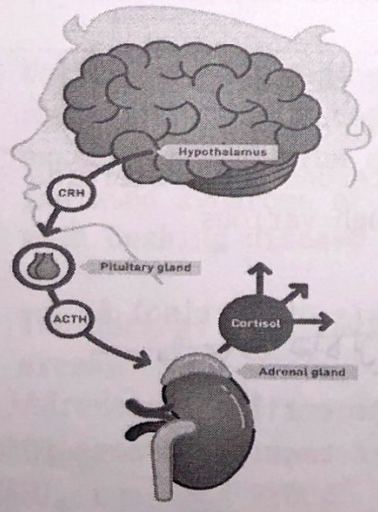
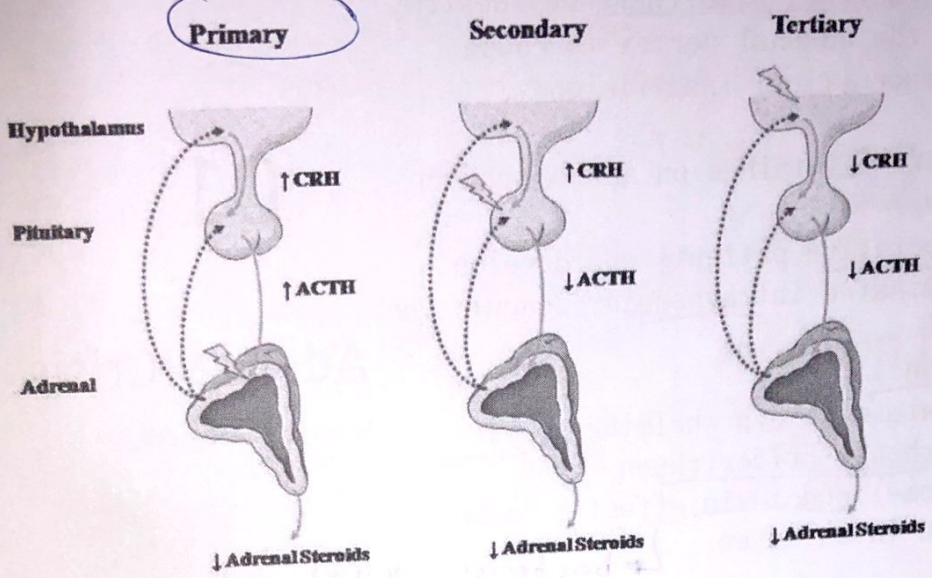
ADRENOCORTICAL ...FICIENCY



- Caused by either primary adrenal disease (primary hypoadrenalism) or decreased stimulation resulting from ACTH deficiency (secondary hypoadrenalism).
- Primary adrenocortical insufficiency may be:

1. *Acute* (called *adrenal crisis*)
2. *chronic (Addison disease)*

problem affected adrenal gland directly



Acute already take supply for cortisol

Acute
Waterhouse-Friderichsen syndrome
Sudden withdrawal of long-term corticosteroid therapy
Stress in patients with underlying chronic adrenal insufficiency

هو عنده نقص كورتيزول يدخل فجأة بوضع يتطلب تركيز أعلى من الكورتيزون واستهلاك الكمية الموجودة

01

Adrenal Crisis

Acute adrenocortical Insufficiency (sudden)

Three clinical settings:

1. Individuals with chronic adrenocortical insufficiency may develop an acute crisis after stress that taxes their limited physiologic reserves.

2. Patients maintained on exogenous corticosteroids after ~~rapid~~ withdrawal of steroids ☐ inability of the atrophic adrenals to produce glucocorticoids.

المريض وقف الدواء أو قلل الجرعة

حتى لو الدكتور بده يوقف الدواء لازم يكون بالتدريج

01

Adrenal Crisis

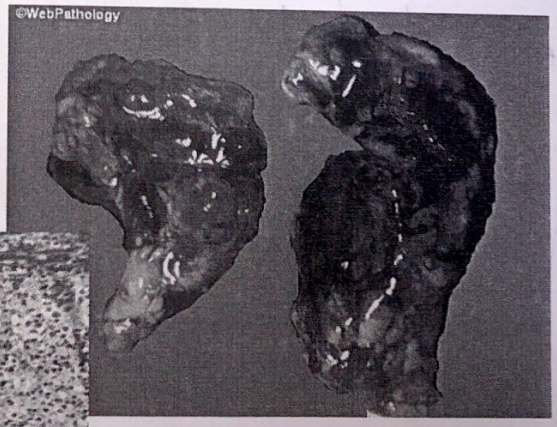
Acute adrenocortical Insufficiency

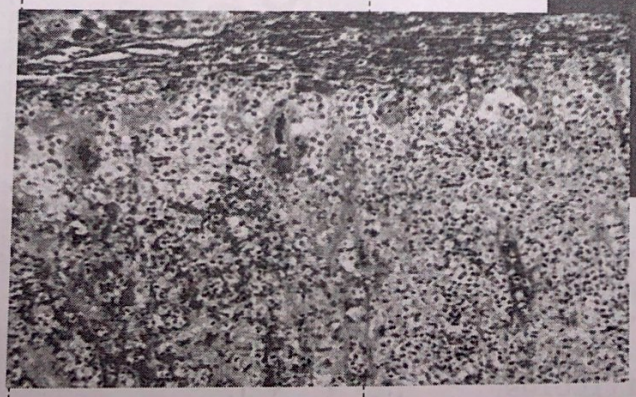
3. **Massive adrenal hemorrhage** may destroy enough of the adrenal cortex to cause acute adrenocortical insufficiency, causes:

a. Patients maintained on anti-coagulant therapy.
b. Postoperative patients who develop disseminated intravascular coagulation DIC.
c. Pregnancy.
d. Patients with overwhelming sepsis (Waterhouse-Friderichsen syndrome): endotoxin effect ?, more common in children.

↳ bacteria , virus
↓ اكثر اشي
تبعث الـ toxins الى الـ adrenal
* هذا الاشي زمان يبب وجود المضادات الحيوية

Waterhouse Friderichsen syndrome





02

Addison Disease

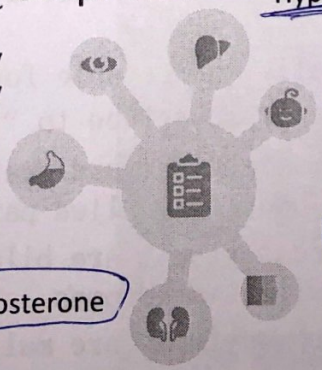
Chronic Adrenocortical Insufficiency

- An uncommon disorder resulting from progressive destruction of the adrenal cortex.
- 90% of cases are caused by four disorders:

A. Autoimmune adrenalitis.
B. Tuberculosis.
C. The acquired immune deficiency syndrome (AIDS).
D. Metastatic cancer; Most commonly carcinomas of lung & breast

* يسمى chronic لانه بالعادة تظهر الاعراض بعد 90% of distruction

Clinical Manifestation do not appear until at least 90% of the adrenal cortex has been ompromised



Initially Nonspecific

Progressive weakness & easy fatigability

GI disturbances

Anorexia, nausea, vomiting,& diarrhea.

Decreased aldosterone

Hyperkalemia, hyponatremia, volume depletion, & nhypotension
In Primary only → ACTH doesn't affect aldosterone

Hypoglycemia

A result of glucocorticoid deficiency & impaired gluconeogenesis.

Hyperpigmentation

In primary adrenal Insuff, due to increased levels of ACTH precursor hormone.
Face, axillae, nipples, areolae, & perineum

بسبب تحفيز pitutery بانه لا يوجد كورتيزون