



Endocrine



Title: Adrenal Gland Diseases.

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Today we'll start our lecture talking about the **Adrenal (suprarenal) gland**...

As we know the Adrenal gland is a paired endocrine organ consisting of two regions which differ in their development, structure, and function:

- Outer Cortex: which is formed by 3 layers of distinct cell types...
 - Zona glomerulosa (the outer most layer).
 - Zona fasciculata (the middle layer).
 - Zona reticularis (the inner layer).
- Inner Medulla.

The Adrenal **CORTEX** synthesizes three different types of steroid hormones:

- **glucocorticoids** (principally CORTISOL), synthesized primarily in the zona fasciculata with a small contribution from the zona reticularis.
- **Mineralocorticoids**, the most important being ALDOSTERONE, secreted from zona glomerulosa.
- **Sex steroids** (ESTROGENS and ANDROGENS), produced largely in the zona reticularis. Examples on these androgens include DHEA (dehydroepiandrosterone) and androstenedione.

The adrenal **MEDULLA** is composed of **chromaffin cells**, which synthesize and secrete catecholamines, mainly epinephrine (adrenaline).

Diseases of the Adrenal cortex 04:08.

They're of three categories represented by mass effects & hormonal abnormalities.

- 1- Hyperadrenalism: includes ->*Hypercortisolism, *hyperaldosteronism, *adrenogenital syndromes (will not be discussed here).
- 2- Hypoadrenalism: includes->*acute adrenal-cortical insufficiency, *chronic adrenal-cortical insufficiency (Addison disease), *secondary adrenal-cortical insufficiency.
- 3- Masses=Neoplasms, includes-> * adenoma, *carcinoma.

Hypercortisolism (Cushing Syndrome) 05:04.

A group of conditions that have many variable causes; mostly classified into exogenous & endogenous causes.

-Exogenous causes: They are the most common causes of Cushing syndrome. These causes are represented by the administration of cortisol containing iatrogenic drugs (glucocorticoids).

-Endogenous causes: They're of three types..

- ACTH pituitary adenoma (Cushing DISEASE): Hypothalamic-pituitary diseases causing hypersecretion of ACTH resulting in hypercortisolism. It is the most common endogenous cause as it arises 70% of etiology to cause the syndrome among other endogenous causes.
- Primary adrenal hyperplasia and neoplasms: they could be benign (adenoma=10%), or malignant (carcinoma=5%).
- Ectopic production of ACTH (10% etiology): which means secretion of the adrenocorticotrophic hormone from a non-pituitary neoplasm. Usually caused by small cell carcinoma of the lung.

The cause	The effect on the Adrenal gland
Administration of glucocorticoids drugs.	Cortisol will cause feedback inhibition on ACTH; the decreased ACTH concentration will cause Adrenal atrophy.
Cushing disease (pituitary adenoma).	The increased ACTH concentration will cause diffuse hyperplasia of the Adrenal gland, which will cause overproduction of cortisol.
The primary adrenal hyperplasia (nodular form).	These hyperplastic cells will cause overproduction of cortisol.
Ectopic production of ACTH.	It causes diffuse bilateral hyperplasia of the gland resulting in increased cortisol concentration.

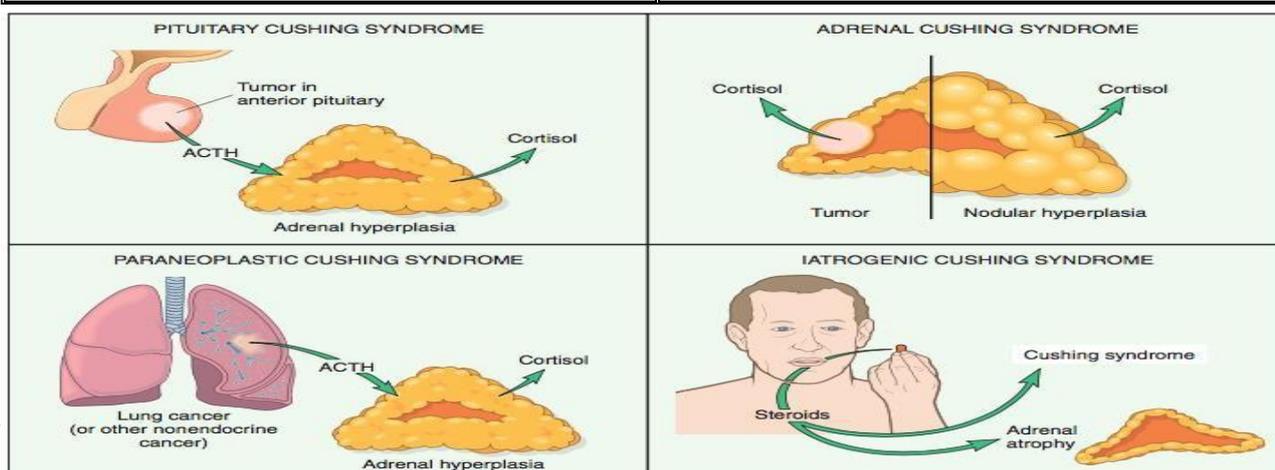


Fig. 20.34 Schematic representation of the various forms of Cushing syndrome: The three endogenous forms, as well as the more common exogenous iatrogenic form. ACTH, Adrenocorticotrophic hormone.

Now, let's have a small talk investigating more in these causes...

#-Iatrogenic Cushing syndrome [11:23](#); I guess you remember what we mean by iatrogenic: an illness caused by a medical examination/treatment. Therefore, we're surely talking about the exogenous causes of the syndrome that results from the administration of glucocorticoid drugs. Unfortunately, these drugs can cause suppression of the endogenous ACTH production resulting in bilateral cortical atrophy, due to a lack of stimulation of the zona fasciculata and zona reticularis.

NOTE: Cushing syndrome itself is caused by overdose/prolonged use of corticosteroids.

#-Cushing disease: We said that it's caused by pituitary/hypothalamic lesions. Most commonly by pituitary ACTH-producing micro-adenomas.

In the remaining cases, the anterior pituitary contains areas of corticotroph cell hyperplasia which may be primary or, less commonly, secondary to CRH (corticotrope releasing hormone) producing tumor. Please be alert that Cushing disease is a factor that can cause Cushing syndrome...they're not the exact same thing.

As a result of the increased ACTH levels the adrenal gland will undergo hyperplasia, more specifically a bilateral cortical hyperplasia. This hyperplasia is usually diffuse but can be nodular.

A nodular hyperplasia appears to show multiple nodules in the adrenal cortex. Eventually both situations (diffuse/nodular) will indicate an increased number of cells in the Adrenal cortex.

Please be alert// a bilateral hyperplasia indicates enlargement in the two Adrenal glands which might be subtle or marked enlargement with each gland weighing up to 30g.

When you have a diffuse cortical hyperplasia -no matter what the cause is- you'll see a yellow color there. This yellow color derives from the presence of lipid-rich cells, which appear vacuolated under the microscope.

In the adjacent pic YOU can see:

- Normal Adrenal gland with normal cortex thickness.
- Diffuse hyperplasia of the adrenal cortex without nodular formation.

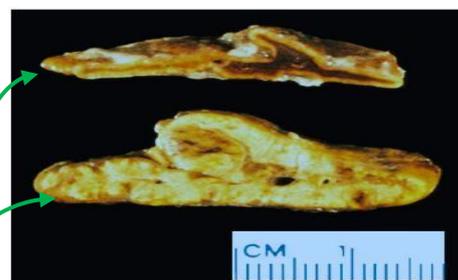


Fig. 20.35 Diffuse hyperplasia of the adrenal gland (bottom) contrasted with a normal adrenal gland (top). In a cross-section, the adrenal cortex is yellow and thickened, and a subtle nodularity is evident. The abnormal gland was from a patient with ACTH-dependent Cushing syndrome, in whom both adrenal glands were diffusely hyperplastic. ACTH, Adrenocorticotropic

Both glands in the picture do not have neither adenomas nor carcinomas.

#-Primary hyperplasia of the Adrenal gland [15:17](#): They could be adenomas, carcinomas, or nodular Adrenal hyperplasia. However, the nodular hyperplasia is rare to happen. They're more common in women in their 30s to 50s.

These factors cause an ACTH-**INDEPENDENT** Cushing syndrome because of the low serum levels of ACTH. We call it primary to differentiate it from the secondary Adrenal hyperplasia that take place in Cushing Disease.

10% to 20% of cases of endogenous Cushing syndrome are due to primary diseases in the adrenal gland.

In primary cortical hyperplasia, the hyperplasia is bilateral, where the cortex is replaced almost entirely by variably sized **macronodules** OR 1- to 3-mm **micronodules**.

- Adrenocortical adenomas: Yellow tumors surrounded by thin capsules (they do not infiltrate to adjacent tissues), mostly weigh less than 30 g. They're formed by fatty(lipid) like cells. Its microscopic examination shows cuboidal cells proliferation with eosinophilic (acidophilic) cytoplasm. Some cells would be vacuolated.
- Adrenocortical carcinomas tend to be non-capsulated masses, exceeding 200 to 300 g in weight.

CLINICAL MANIFESTATIONS OF CUSHING SYNDROME 19:10.

The clinical manifestations of the syndrome are similar regardless of the underlying etiology. These symptoms include:

- Hypertension and weight gain.
- Truncal obesity, moon facies, accumulation of fat in the posterior neck and back "buffalo hump".
- Glucocorticoids induce gluconeogenesis with resultant hyperglycemia, glucosuria, polydipsia & polyuria (manifestations of diabetes mellitus).
- The catabolic effects on proteins cause loss of collagen and resorption of bone leading to osteoporosis (decreased bone density) and susceptibility to fractures in affected patients.
- The skin is thin, fragile, and easily bruised even without traumas. Cutaneous striae are particularly common in the abdominal area.
- Patients are at increased risk for a variety of infections.
- Hirsutism (presence of hair at abnormal sites in females; ex. The face) and menstrual abnormalities in a female patient.
- Mental disturbances, mood swings, depression, psychosis.

(:PICTURES TIME:)

Moon face:-:



Buffalo hump:(()):



It was called so because it resembles the Bull's hump: fat accumulation in the neck & back.

Abdominal striae: similar to those found in the abdomen of a pregnant women.



HYPERALDOSTERONISM 22:16.

The renin–angiotensin–aldosterone system (RAAS) is a hormone system that is involved in the regulation of the plasma sodium concentration and arterial blood pressure.

We have 2 types of Hyperaldosteronism:

1-Primary hyperaldosteronism: autonomous overproduction of aldosterone with secondary suppression of renin- angiotensin system and decreased plasma renin activity. This overproduction occurs mostly because of idiopathic (unknown cause) hyperaldosteronism...We suggest that it happens due to a primary lesion in the gland, or maybe adenoma of the Adrenal gland which causes overproduction of Aldosterone.

2-Secondary hyperaldosteronism: Secondary to a systemic disease; which results in activation of renin-angiotensin system characterized by increased levels of plasma renin causing the hyperaldosteronism. Not only systemic diseases, any disease that causes activation of the Renin-Angiotensin system will result in the secondary hyperaldosteronism.

Causes of the secondary hyperaldosteronism:

- Decreased renal perfusion (renal artery stenosis).
- Arterial hypovolemia and edema; ex.heart failure.
- Pregnancy (caused by estrogen-induced increases in plasma renin substrate).

و أَيُّ الحُسَامِ لَمْ تُصِبْهُ كَهَامَةٌ
و لَهْذَمٌ رَمَحٍ لَا يُفَلُّ مِنَ الطَّعْنِ؟
فَإِنْ تَكُنِ الحَيَاةُ تَوَلَّتْ بِخَيْرِهَا
فَأَهْوَنَ بَدُنِيَا لَا تَدُومُ عَلَيَّ فَنِّ!
-محمود سامي البارودي.