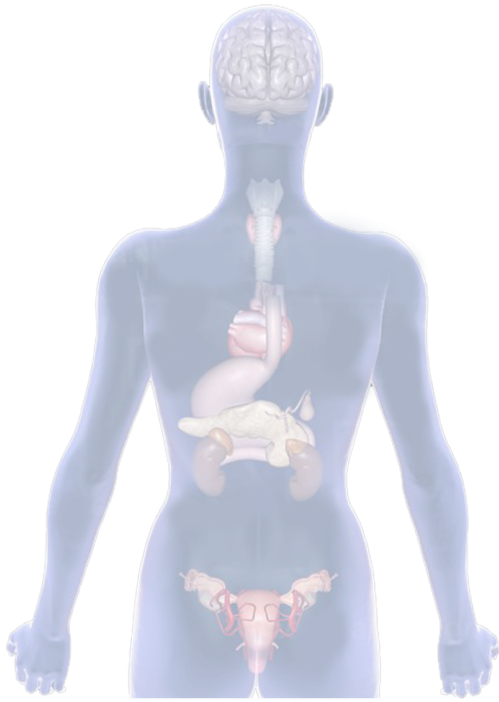
Physiology 435 team

#11 Adrenal gland hormones(Glucocorticoids)

Objectives:

- Describe the metabolism and physiological effects of glucocorticoids.
- Describe the mechanisms that regulate secretion of glucocorticoids
- Describe the main features of the diseases caused by excess or deficiency of each of the hormones of the adrenal gland.

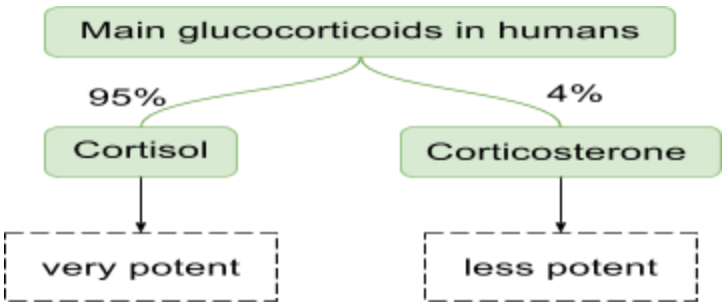


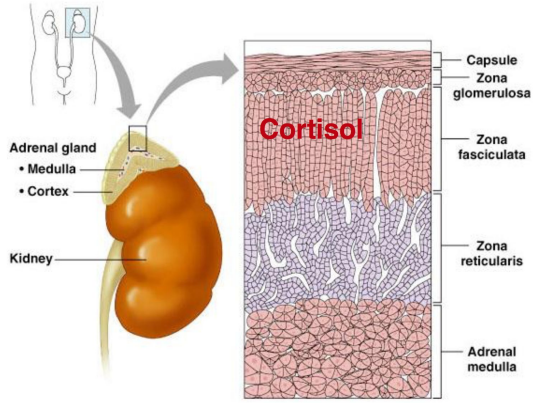
Important
Male's notes
Female's notes
Extra

Resources: 435 male's & female's slides + guyton
Editing file: click Here

Revised by
خولة العماري & هشام الغفيلي

Adrenal cortex: Glucocorticoids

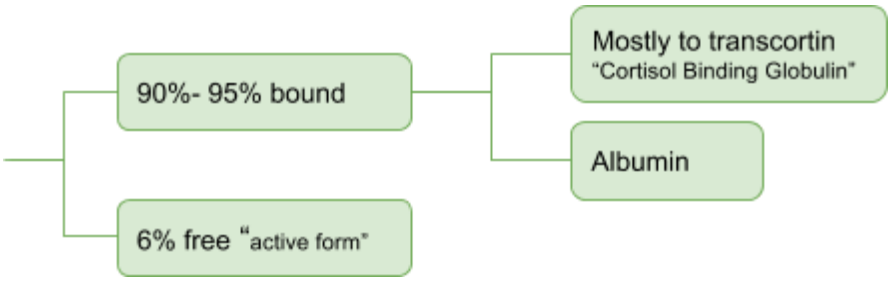




Cortisol:corticosterone produced in humans **in a ratio of 10:1**

Cortisol production : mainly by zona fasciculata and small amount by zona reticularis

Cortisol transport:



Cortisol metabolism:

- Half life =60-90 minutes
- Metabolized in liver by reductases & conjugated to glucuronides and excreted via kidney.
- Free cortisol is excreted into urine.

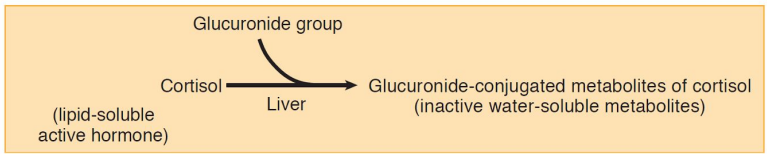


Figure X-4-3. Metabolism of Cortisol

circadian rhythm of cortisol secretion

- The secretory rates of CRF[1],ACTH, and cortisol :
  - **high in the early morning** ~ ranges between a high of about 20 µg/dl an hour before arising in the morning.
  - **low in the late evening(11-12PM)** ~ about 5 µg/dl around midnight.
- this effect results from a 24-hour cyclical alteration in the signals from the hypothalamus that cause cortisol secretion.
- When a person changes daily sleeping habits, the cycle changes correspondingly. Therefore, measurements of blood cortisol levels are meaningful only when expressed in terms of the time in the cycle at which the measurements are made. يعني لو واحد ينام الصبح ويصحى الليل بيتغير عنده تركيز الكوتيزول ويصير عالي بالليل :|

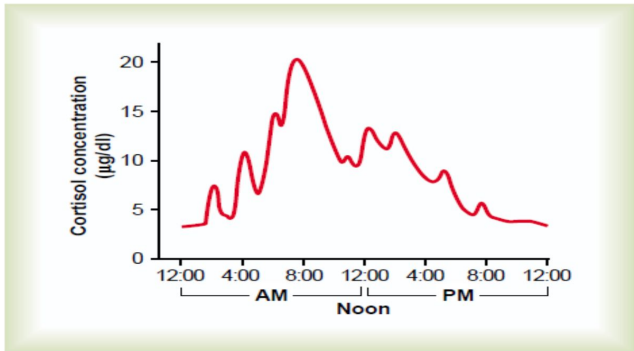


Figure 77–7

Typical pattern of cortisol concentration during the day. Note the oscillations in secretion as well as a daily secretory surge an hour or so after awaking in the morning.

Cortisol , highest in the early morning 8:00am , lowest at night 12:00pm .

والسبب ؟ لأن الصباح نكون بحالة stress بسبب العمل والدراسة والاختبارات فـ رب العالمين يقوينا بالكورتيزول ولازم مايزيد عن حده لأن بيكون ضار لذلك يقل في الليل

[1] Corticotropin-releasing hormone (CRH) also known as **corticotropin-releasing factor**

Physiological actions of cortisol

physiological actions of cortisol

discussed in details

metabolism | anti-allergic | anti-inflammatory | RBCs | stress | in circulation

On metabolism :

carbohydrates

- ↑↑ glucose level in blood
- ↑ Stimulates gluconeogenesis and glycogen synthesis by the liver.
- ↓ glucose utilization by the cells .

" adrenal diabetes "

proteins

Has catabolic effect on extrahepatic cells:(decrease protein stores,decrease protein synthesis & decrease amino acids transport into extra hepatic cells)

↓

Increase amino acids level in the blood.

Has Proteoanabolic effect in the liver:(enhanced liver proteins ,increased plasma proteins & increase amino acids transport into hepatic cells)

fat

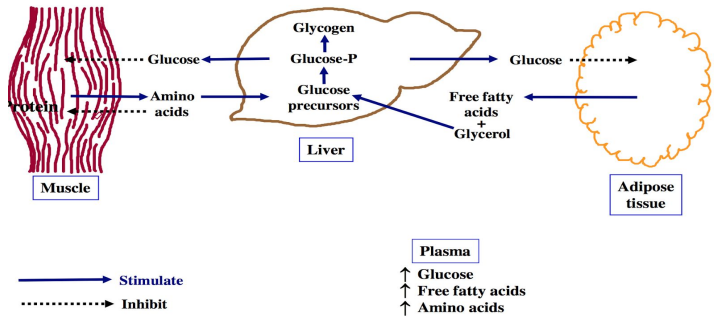
lipolytic effect

mobilization of fatty acid from adipose tissue .

↑↑ The concentration of free fatty acids in the blood.

↑↑ Their utilization for energy.

- Cortisol ↑glucose in the blood like GH and opposite action of insulin.
- Normal Glucose from 90-100 or 110.
- Role of cortisol on carbohydrate : ↑glucose in the blood.
- Role of cortisol on protein(Extra-Hepatic) : ↑ Catabolism ↓ Anabolism .
- Role of cortisol on protein(Hepatic): ↑Anabolism.
- Role of cortisol on Fat : lipolytic.
- Glucocorticoids save glucose , so we use another source which is free fatty acids .



Metabolic response to fasting: Boy's slides only

- Gluconeogenesis from amino acids (increased expression of the enzymes)
- Mobilization of stored fat (activation of HSL[2]) and its use in β -oxidation and the production of ketone bodies

[2] Hormone-sensitive lipase

Anti inflammatory &Anti-allergic effect:

Reduces all aspects of the inflammatory process:

- Stabilizes lysosomal membrane→ more difficult for these membranes to rupture → less release of proteolytic enzymes that cause inflammation.
- Reduces degree of vasodilatation.
- Decreases permeability of capillaries.
- Decreases migration of white blood cells.
- Suppresses immune system.
- Cortisol Blocks the inflammatory response to allergic reactions by:

•Inhibits histamine release
•It decreases fibroblastic activity and local swelling
•phospholipase A2
•Inhibits collagenase from breaking down proteins.
, So cortisol prevent shock and death.

1-Block the early stages of the inflammation process before inflammation even begin

2- If inflammation begun: It cause rapid resolution of the inflammation and increase rapidity of healing.

3-Resolution of inflammation

اهم خطوة بالانفلاميشن والي يصير بسببها البلاوي الي هي مرحلة release of chemical substances

Effect on circulation :

Cortisol has mineralocorticoid effect(Not as potent as aldosterone):

- Na+ reabsorption and K+secretion.
- Maintains body fluid volumes & vascular integrity →Extreme water retention hypertension.

BP regulation & cardiovascular function:

- Sensitizes arterioles to action of noradrenaline **(Permissive effect)**.
- Decreased capillary permeability.
- Maintains normal renal function.

Effect On stress :

•Stress include (trauma, infection, surgery, any debilitating disease, increase heat or cold).
•cortisol is important in resisting stress and inflammation.
•prevents stress induced reaction from becoming excessive.
Without Glucocorticoids , the body cannot cope with even mild stressors.=السترس مثال: في شجرة وعليها عصفور وصار فيه صاعقة قوية راح نلاقي العصفور مات لأنه ما قاوم" الجهد " بعكس الإنسان لو كان جنب العصفور انسان وتعرض للصاعقه ما راح يموت لأن يقدر يتحمل السترس .
مثال اخر : لو شخص اصابه حادث ، راح ينصدم لكن ما مات لأنه يقدر يتحمل السترس.
ليش يتحمل الإنسان ؟ لان عنده كورتيزول وهو الهرمون الذي يتأثر ضد السترس.

Cortisol in stress causes : يوفر طاقة للجسم لمواجهة السترس

- rapid mobilization of amino acids and FFA from their cellular stores, making them immediately available both for energy & synthesis of other compounds, including glucose, needed by the different tissues in the body.

Permissive Actions of Cortisol enhances the capacity of glucagon and catecholamines,

- Increases BP and glycogen.
- Maintenance of the vascular response to norepinephrine.
  Vasoconstriction that's why ↑ BP
- Effects on CNS.

Effect On RBCs :

•Increases RBCs count , platelets and neutrophils .
•Decreases **lymphocyte, eosinophils,** basophils count.they r prone to infection
•Suppresses lymphoid tissue systemically therefore decrease T cell and antibody production decreasing immunity ,This effect is useful in transplantation surgery in reducing organ rejection.
And fatal in tuberculosis.

Boy's slides only:

CNS	Mineral metabolism	GIT
- Negative feedback control on release of ACTH - Modulates perception & emotion	**Anti-vitamin D effect :** ↓ Intestinal absorption & ↑ Renal excretion	Increase HCL secretion SO INCREASES THE ACIDITY

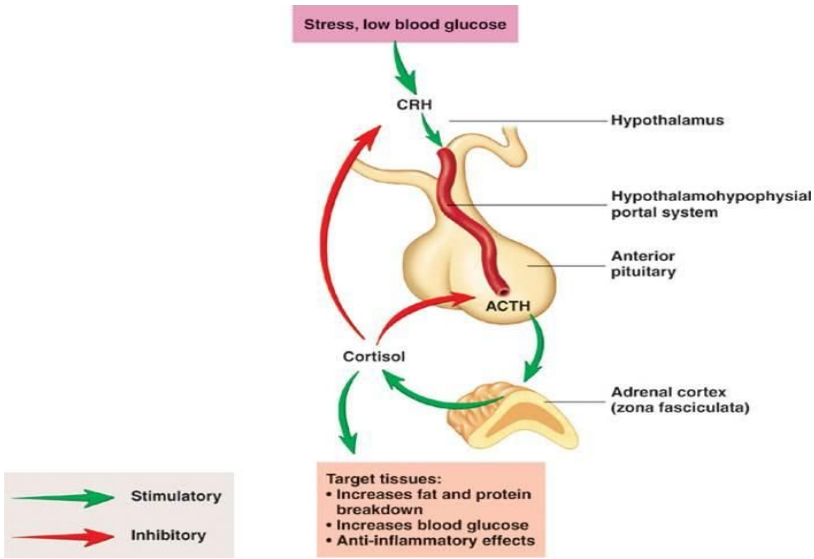
Developmental

- Permissive regulation of fetal organ maturation
- Surfactant synthesis (phospholipid that maintains alveolar surface tension).
- Inhibition of linear growth in children due to direct effects on bone & connective tissue

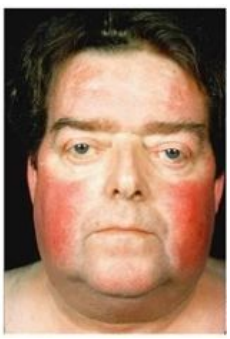
THE MOST IMP Side Effects of cortisol ? 1- immunosuppressant. 2- osteoporosis. 3- diabetics. 4- Hypertension because water retention .

Regulation of Cortisol Secretion

- Stress stimulates CRH secretion by the hypothalamus. Mental stress can cause an equally rapid increase in ACTH secretion. This is believed to result from increased activity in the limbic system, especially in the region of the amygdala and hippocampus, both of which then transmit signals to hypothalamus.
- Cortisol has a **direct negative feedback** effect on both the hypothalamus and ant. pituitary.



Abnormalities



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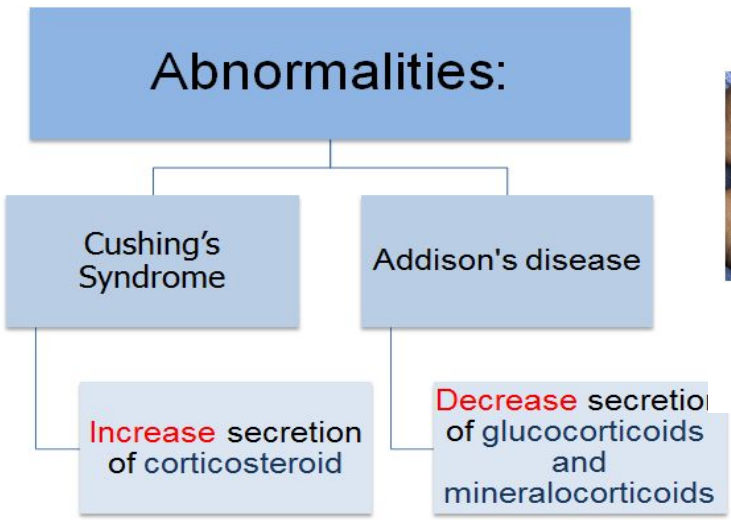
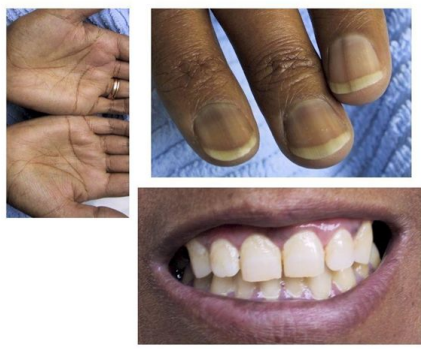




Addison's Disease vs Cushing's Syndrome (Duration: 20 min)

Cushing's Syndrome (Hypercortisolism)

Causes:

ACTH independent	ACTH dependent
Could be due to: **adenomas of the adrenal cortex.**	Could be due to: **adenomas of the anterior pituitary** → increase ACTH. *When Cushing's syndrome is secondary to increased ACTH by the anterior pituitary = Cushing's disease. Cushing's disease means increase ACTH. لازم ماتخلطون بين الكوشنق سندرم والكوشنق ديزيز : الكوشنق سندروم هو لفظ عام لمجموعة من الأمراض اللي كلها تشترك بنفس السبب "افراز الكروتيزول بكميات كبيرة" . الكوشنق ديزيز هو مرض يندرج تحت السندروم "افراز كميات كبيرة من الكوتيزول" وسبب هالزيادة هو الاي سي تي اتش من البتوتاري.(شكرا تيم البايو ^^) OR **abnormal function of the hypothalamus** → increase CRH. OR **"ectopic secretion"** of ACTH by a tumor elsewhere in the body, such as an abdominal carcinoma. And pulmonary small cell carcinoma.
Cushing's syndrome may occur when large amounts of glucocorticoids are administered over prolonged periods for therapeutic purposes. (like prednisone) e.g. patients with chronic inflammation associated with diseases such as rheumatoid arthritis :'((	

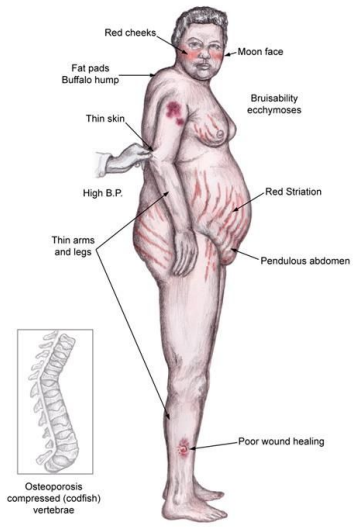
Signs and symptoms:

On Carbohydrate Metabolism:

- High blood glucose level. Due to increased gluconeogenesis and decreased glucose utilization by the tissues.

On Protein Metabolism:

- Decreases tissue proteins. Almost everywhere in the body (except liver).
- Severe weakness, Due to protein loss from the muscles.
- Thinning of the skin.**Striae.** What is the pathophysiology of striae?Breakdown of protein → Breakdown of collagen → striae.
- Loss of connective tissue. Due to protein collagen fibers in the S.C.
- Severe osteoporosis. Due to severely low protein deposition in the bones.
- Suppressed immune.



Abnormal Fat Redistribution:

- Truncal obesity. Due to mobilization of fat from the lower part of the body, with concomitant extra deposition of fat in the thoracic and upper abdominal regions, giving rise to a buffalo torso.
- Moon face.
- 80% of patients have hypertension, because of the mineralocorticoid effects of cortisol.

Treatment : Reducing corticosteroid use - Surgery - Radiation therapy - Medications

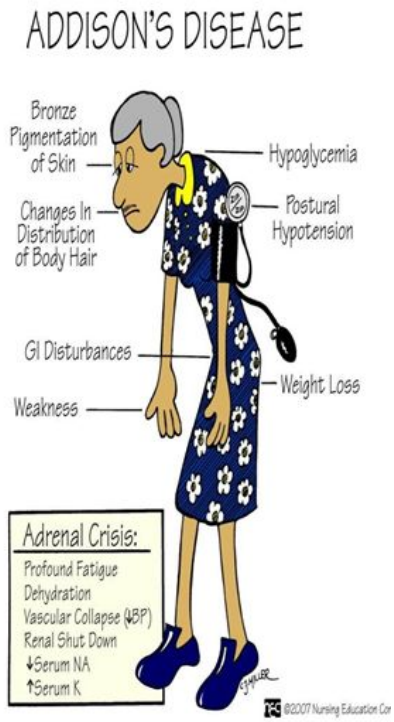
Addison's disease

Addison's disease results from an inability of the adrenal cortices to produce sufficient adrenocortical hormones ,Auto deficiency of cortisol and aldosterone.

Adrenocortical insufficiency

Primary causes, ie. Addison's disease	Secondary causes
• **Autoimmune** disease, tumors, infection (e.g. **TB**), hemorrhage, metabolic failure, ketoconazole (glucocorticoid antagonist activity)	• Hypopituitarism • Suppression by exogenous steroids. لما الشخص ياخذها لفترة طويلة بيصير للادرينال قلاند خمول تقول مايحتاج اشتغل واتعب نفسي دامه تجيني الستيرويد جاهزه فيؤدي الى ضمور للادينال

Clinical manifestation of addison's disease:



Due to Mineralocorticoid Deficiency, absence of aldosterone:

- the volume depletion(Reduction in ECF volume)may be severe.
- Increased excretion of sodium and water.↓Na→ hyponatremia / hyperkalemia. / ↓water → hypovolemia, postural hypotension , shock.
- Tendency toward low blood pressure, which falls further when standing, making the patient feel **dizzy**.
- Craving for salt, salty foods and drinks. The person is allowed to eat large amounts of salt and drink large amounts of water to balance the increased urine output of salt and water.
- Acidosis> Hypercalcemia

الالدوستيرون يطرد الهيدروجين ، لكن الالدوستيرون ابسنت مو موجود فبتالي بيزيد الهيدروجين ويصير Acidosis.

Due to Glucocorticoid Deficiency:

- Hypoglycemia.
- General weakness and becoming easily tired.indicating that glucocorticoids are necessary to maintain other metabolic functions of the tissues in addition to energy metabolism.
- Decrease appetite and weight loss
- Cramps and pains in muscles.
- Feeling sick and vomiting from time to time.
- Abdominal pains, diarrhea or constipation, which may come and go.
- Lack of adequate glucocorticoid secretion also makes a person with Addison's disease highly susceptible to the deteriorating effects of different types of stress, and even a mild respiratory infection can cause death

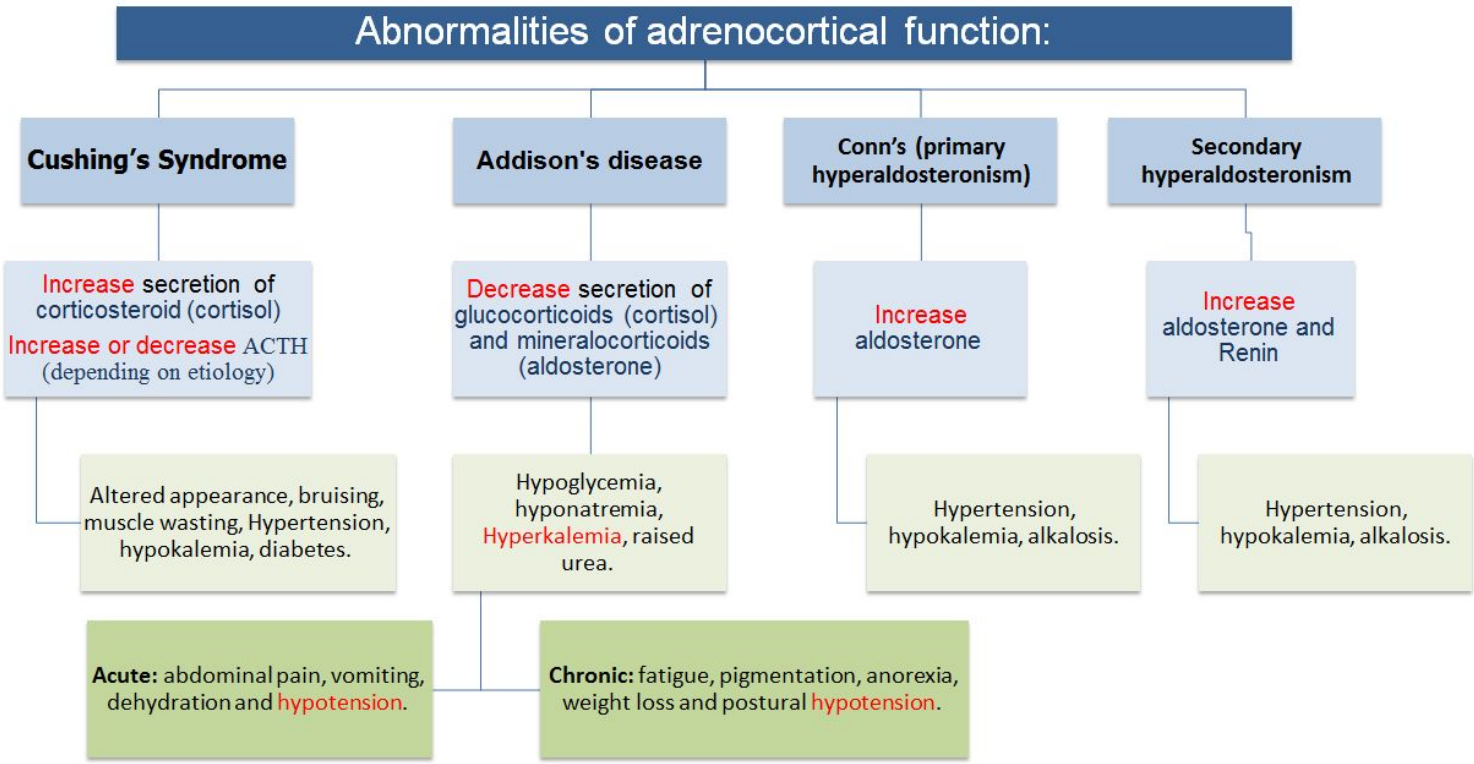
Due to ↑ ACTH :

- Darkened areas of skin (Generalized pigmentation, but especially deposition in the palmar skin creases, nails and gums).↑ ACTH will stimulate synthesis of melanin

Endocrine Images: Adrenal Insufficiency

This slide of identical twins is from Dr. Hammer's lecture and is meant to emphasize the hyperpigmentation and thin body habitus that is often seen in primary adrenal insufficiency (the woman with adrenal insufficiency is on the right). Hyperpigmentation may also be seen in the extensor surfaces of the limbs (knuckles, elbows, knees), in newly formed scars and in palmar creases and buccal mucosa. (What's the cause?)

SUMMARY OF ABNORMALITIES OF ADRENOCORTICAL FUNCTION



Physiology 435 team

Thanks to this amazing team!

روان الضويحي
لولوه الصغير
مي العقيل
منيرة السلولي
حصة المزيني

عمر آل سليمان
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عمر العتيبي
عمر الشهري