Endocrine Physiology

The Adrenal Gland
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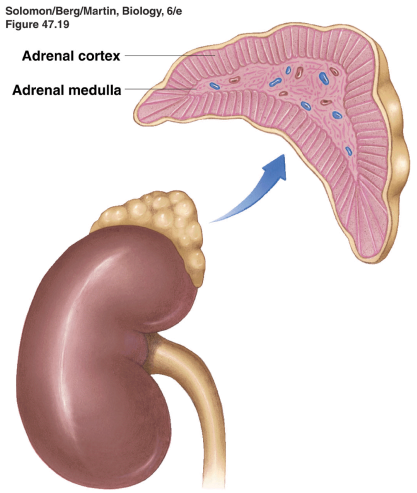


Glucocorticoids

- Produced by the **fasciculata** and reticularis layers of the adrenal cortex
- Glucocorticoids (cortisol): recognized early to increase plasma glucose levels:
  - Mobilization of amino acids from proteins
  - Enhance liver gluconeogenesis
- Target tissues: most body tissues

Glucocorticoids (cont.)

- CRH from hypothalamus is the major regulator of ACTH secretion
- ADH is also a secretagogue for ACTH
- ACTH from anterior pituitary stimulates cortisol synthesis and secretion
- CRH (and ACTH) are secreted in pulses
- The greatest ACTH secretory activity occurs in the early morning hours and diminish late in the afternoon.

Regulation of Glucocorticoid Secretion

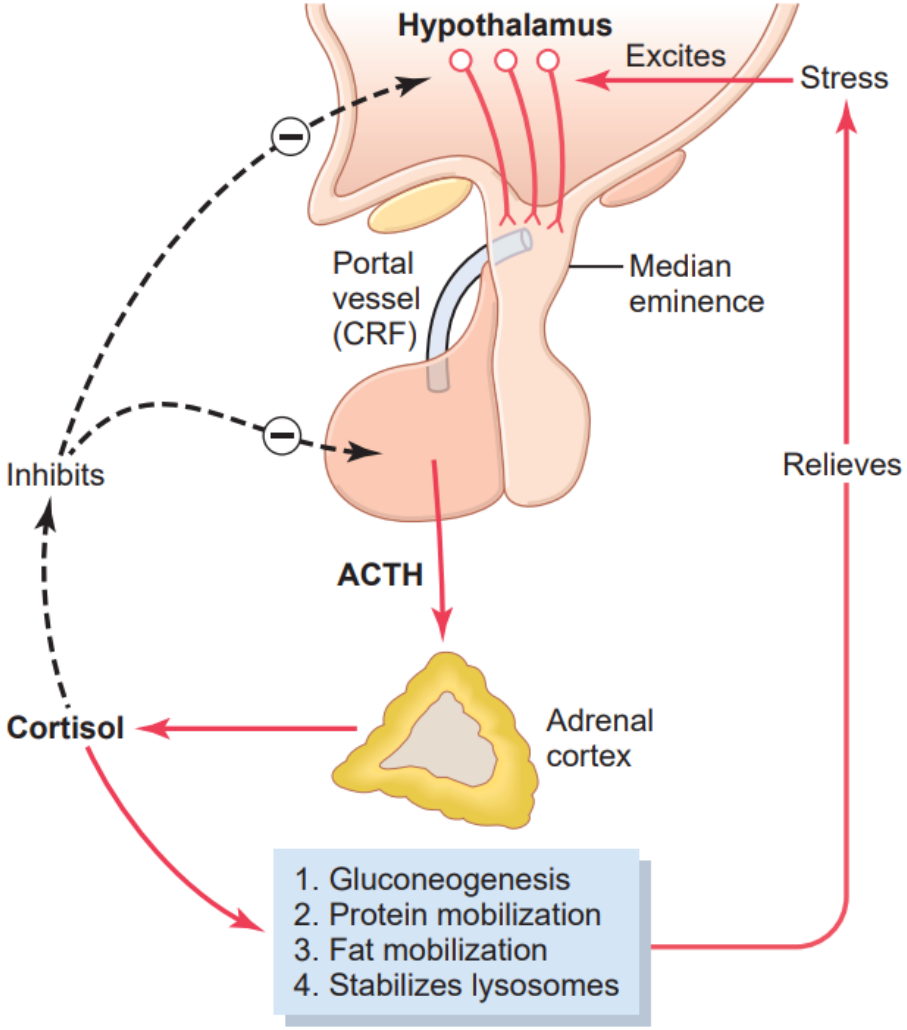
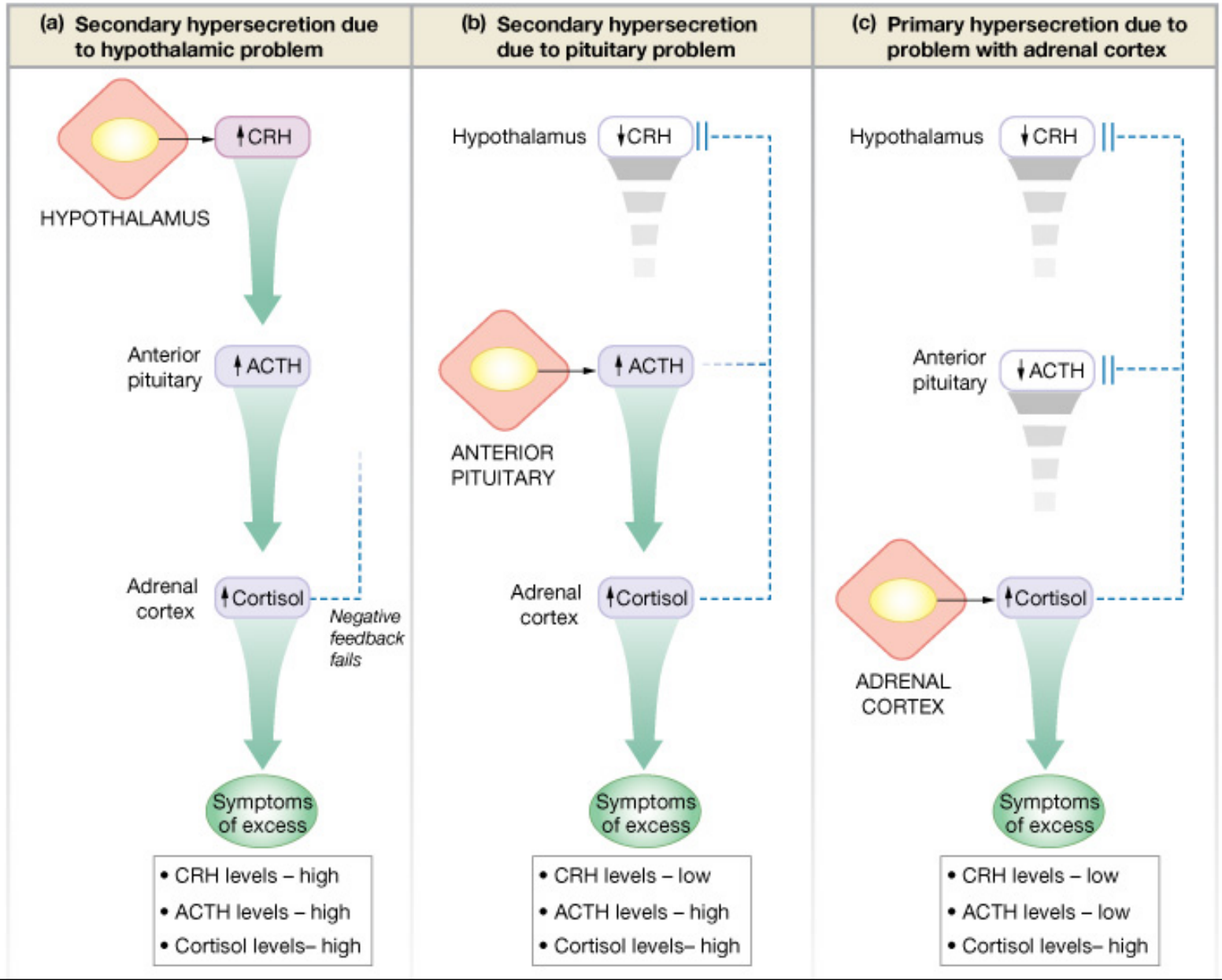
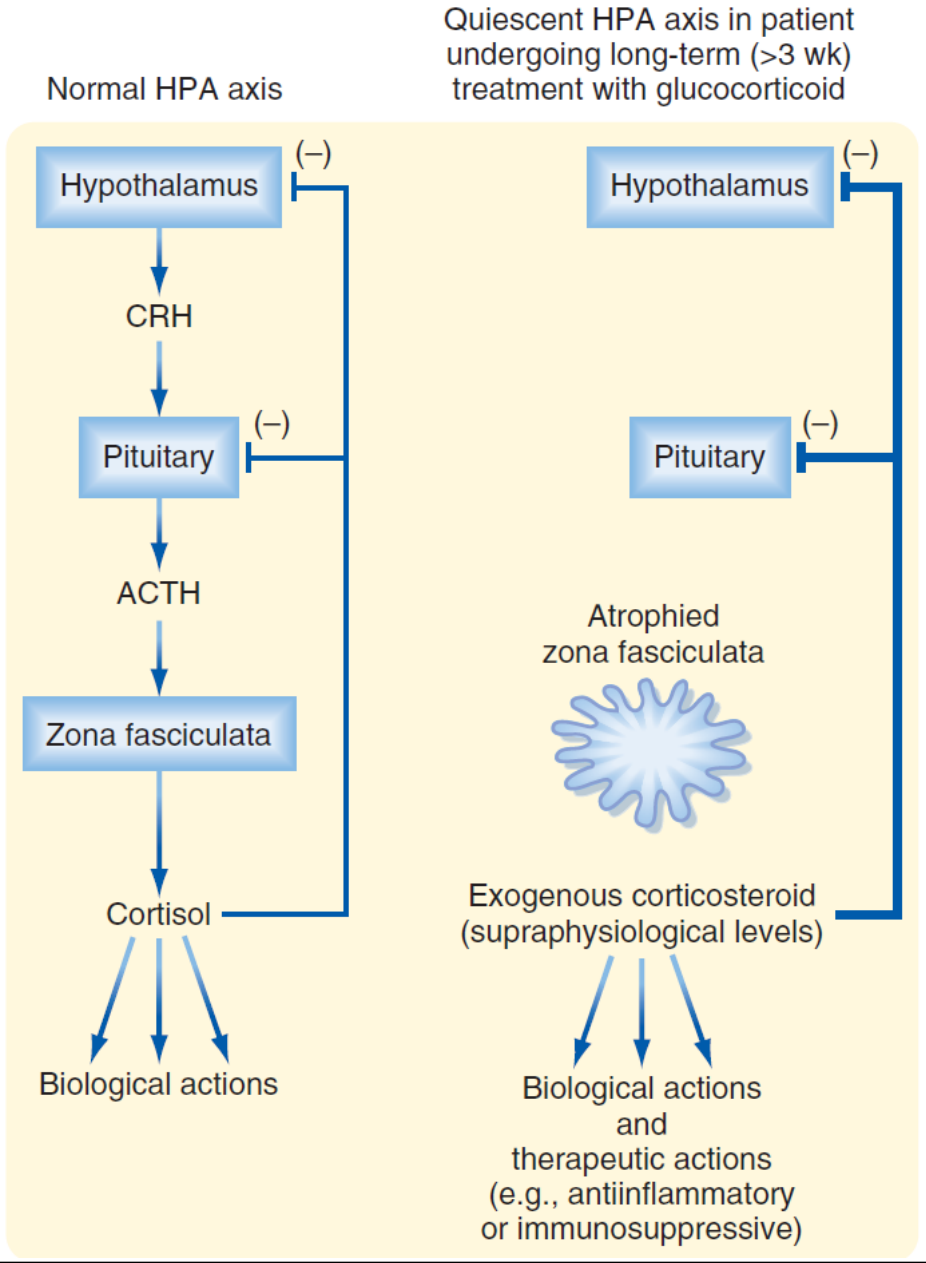


Figure 78-7. Mechanism for regulation of glucocorticoid secretion. ACTH, adrenocorticotropic hormone; CRF, corticotropin-releasing factor.

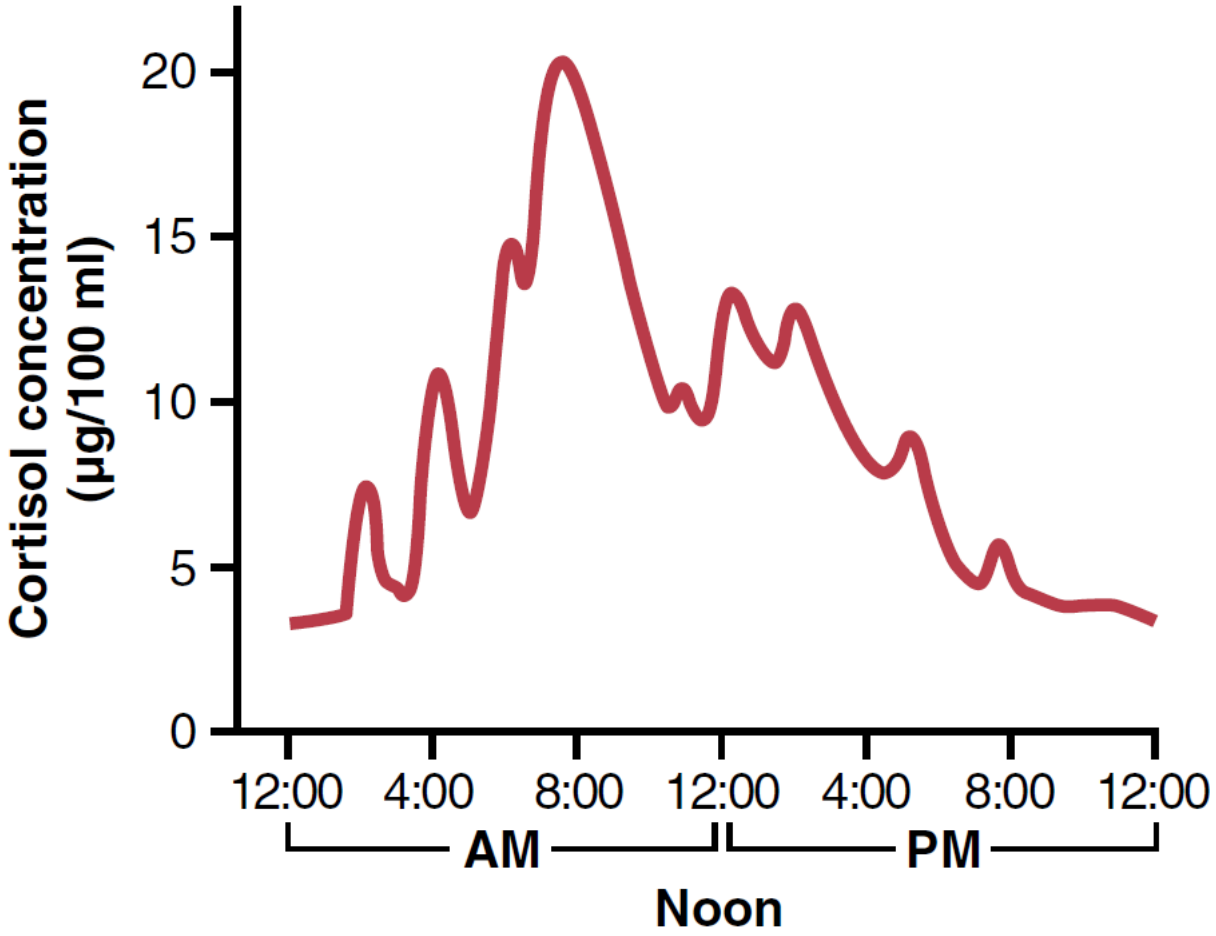
Primary and secondary hypersecretion of cortisol



Quiescent HPA axis: Long-term GC treatment



Circadian rhythm of cortisol secretion



Actions of Glucocorticoids

- Cortisol acts primarily through the **glucocorticoid receptor.**
- which regulates gene transcription
- Metabolic response to fasting:
  - Gluconeogenesis from amino acids (increased expression of the enzymes) **(PEPCK).**
  - Cortisol also decreases GLUT4-mediated glucose uptake in skeletal muscle and adipose tissue.
  - Mobilization of stored fat (activation of HSL) and its use in β-oxidation and the production of ketone bodies

Effect of glucocorticoids: on carbohydrate metabolism

- Increases the enzymes required to convert amino acids into glucose in liver cells (gluconeogenesis)
- Mobilization of amino acids from extrahepatal tissues (muscles) for gluconeogenesis
- Antagonizes insulin's effects to inhibit gluconeogenesis in the liver.
- Increase glycogen storage in liver cells
- Decreased glucose utilization by the cells
- Promote glucose sparing by potentiating the effects of catecholamines on lipolysis, thereby making FFAs available as energy sources.
- Adrenal diabetes

Effect of glucocorticoids: on protein metabolism

- mobilization of amino acids from non-hepatic tissues
- proteocatabolic effect in all body cells except of the liver
- decreased protein synthesis
- decreased amino acids transport into extrahepatic tissues (muscles, lymphatic tissues)
- Proteoanabolic effect in the liver
  - enhanced liver proteins
  - increased plasma proteins

Effect of glucocorticoids: on fat metabolism

- Mobilization of Fatty Acids which increases the concentration of free fatty acids in the plasma.
- Excess cortisol causes obesity

Anti-inflammatory Effects of GC

- Glucocorticoids are used to alleviate inflammation
  - stabilize lysosomal membranes (reduce their rupture and release of proteolytic enzymes).
  - Inhibit production of prostaglandins, leukotrienes, and thromboxane (mediate inflammation). This occurs via inhibiting phospholipase A2.
  - decrease permeability of capillary membranes, reducing swelling
  - They also reduce the effects of histamine
  - Attenuates fever mainly because cortisol reduces the release of interleukin-1 from white blood cells.

Suppression of Immune System

- Decrease the production of eoisinophils and T lymphocytes
- Administration of large doses of cortisol causes significant atrophy of lymphoid tissue throughout the body
- Decrease immunity could be fatal in diseases such as tuberculosis
- Decrease immunity effect of cortisol is useful during transplant operations in reducing organ rejection.
- Cortisol increases the production of red blood cells

Functions - circulation

- Maintains body fluid volumes & vascular integrity
- Cortisol levels vary with water intake
- Cortisol has mineralcorticoid effect, Not as potent as aldosterone.
- BP regulation & cardiovascular function:

  Sensitizes arterioles to action of norepinephrine (Permissive effect).
- Decreased capillary permeability
- Cortisol stimulates **erythropoietin** synthesis and hence increases red blood cell production.

Functions - continued

CNS responses:

- Negative feedback control on release of ACTH
- Modulates perception & emotion

Mineral metabolism:

Anti-vitamin D effect, reduces osteoblast differentiation, reduces calcium absorption.

GIT:

Increases HCl secretion

Functions - developmental

- Permissive regulation of fetal organ maturation, required for the development of CNS, retina, skin, GI tract, and lungs.
- Surfactant synthesis (phospholipid that maintains alveolar surface tension).
- Inhibition of linear growth in children due to direct effects on bone & connective tissue

Glucocorticoids and Stress:

- Without GCs, the body cannot cope with even mild stressors
- Fat & glucose metabolism
- Maintenance of the vascular response to norepinephrine
- Effects on CNS

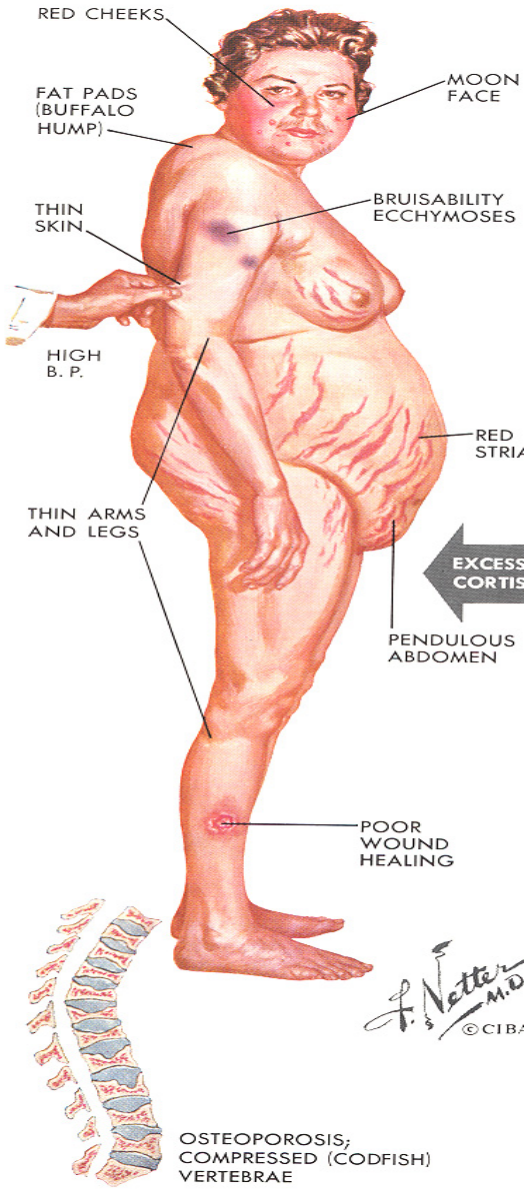
Cushing's Syndrome

- Cushing's syndrome results from continued high glucocorticoid levels
- 3rd - 6th decade, 4 to1 females
- Causes:
  - pharmocologic
  - pituitary adenoma
  - adrenal adenoma, carcinoma
  - ectopic ACTH

Cushing's Syndrome

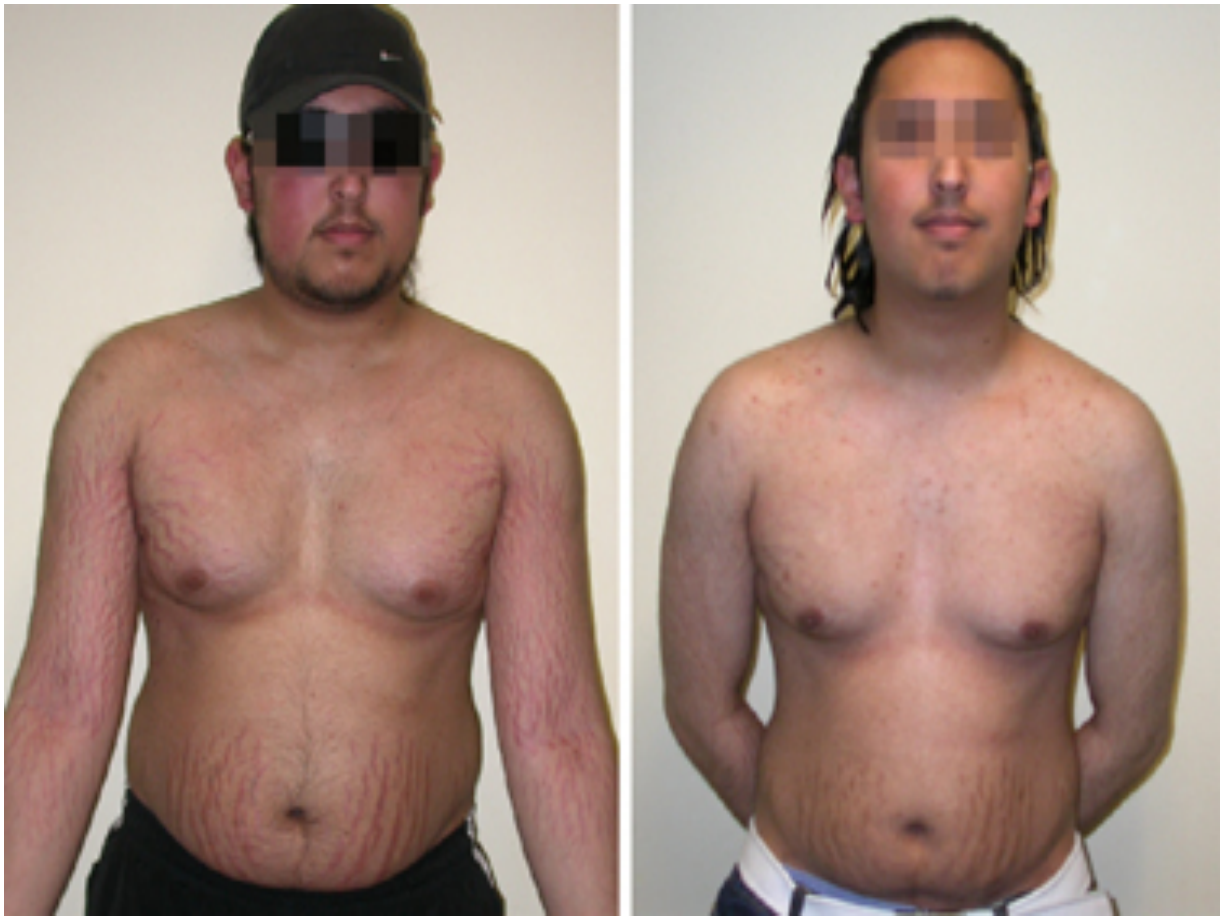
Signs:

- Fat is deposited in the body trunk (central obesity)
- Buffalo hump
- Moon facies (subcutaneus fat in cheeks and submandibular)
- Purple striae
- Blood-glucose levels rises chronically, causing adrenal diabetes
- May cause beta cells to die
- memory and attention dysfunctions, depression
- Susceptibility to infections



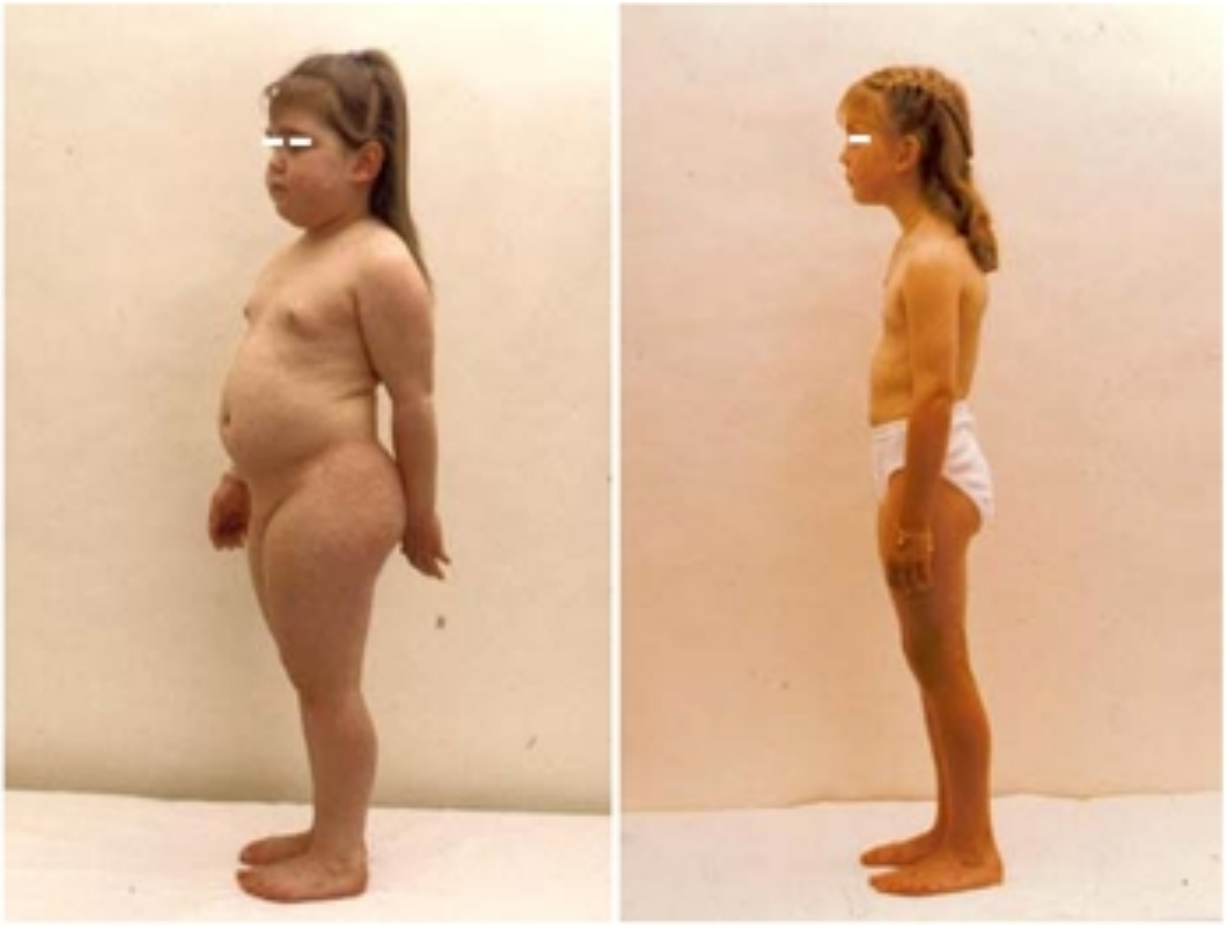
Cushing's Syndrome

- Purple striae



Cushing's Syndrome

- treatment based on cause



Adrenocortical insufficiency

- primary causes, ie. **Addison's disease**
  - autoimmune disease, tumors, infection, bleeding, impaired steroidogenesis, adrenal dysgenesis
- secondary causes
  - hypopituitarism, suppression by exogenous steroids

Adrenocortical insufficiency

- symptoms, signs
  - fatigability, weakness, anorexia, nausea, weight loss, hyperpigmentation, hypotension, women loss of axillary and pubic hair
  - can lead to severe volume depletion and shock
  - Reduced cortisol results in poor blood glucose regulation
  - Patient cannot cope with stress
  - Adrenal crisis: asthenia, severe pains in the abdomen, hypoglycemia, hyponatremia hyperkalemia, hypercalcemia, vascular collapse.

Adrenocortical insufficiency

- treatment
  - glucocorticoid replacement, mineralocorticoid replacement