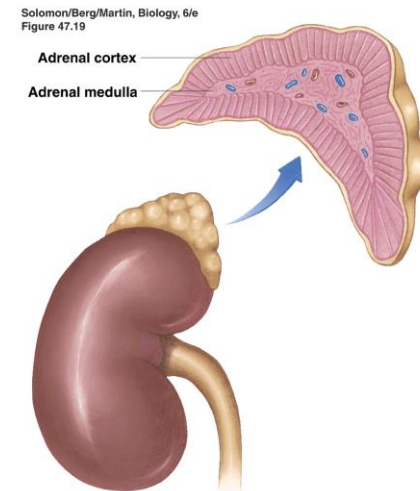


# Endocrine Physiology

## The Adrenal Gland 2

*Dr. Khalid Alregaiey*



# Glucocorticoids

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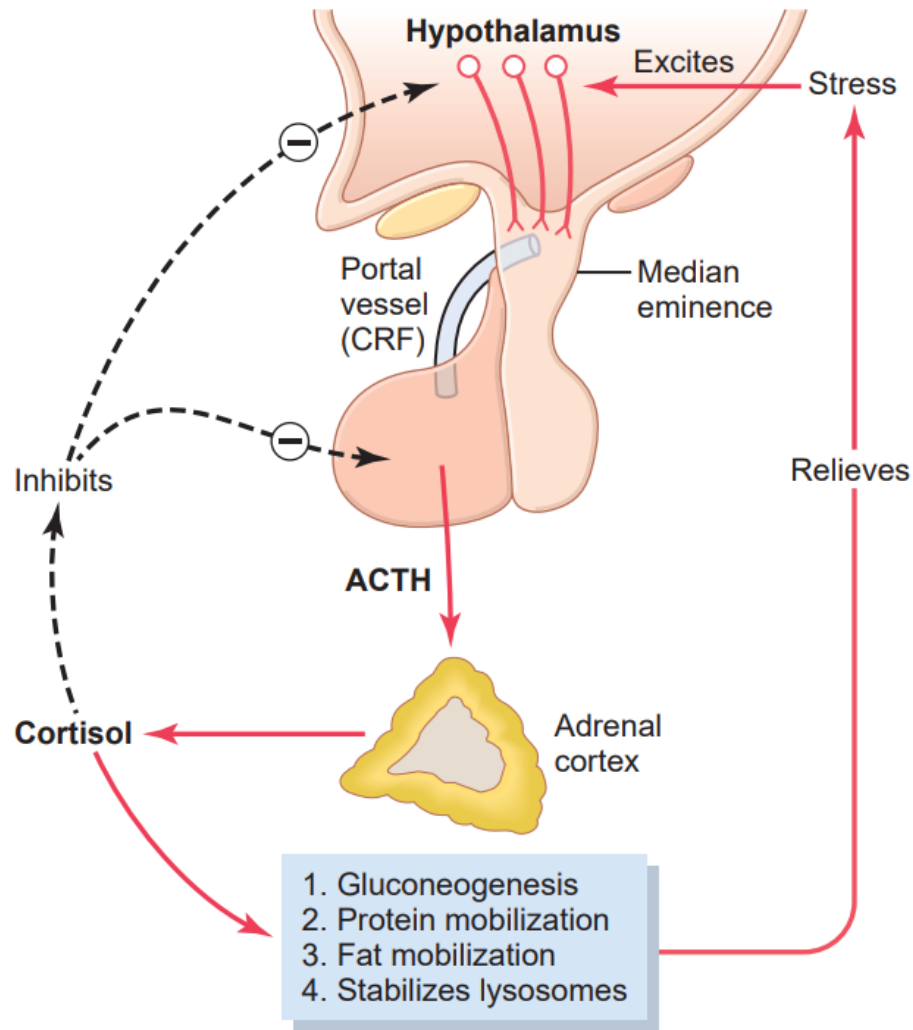
- Produced by the **fasciculata** and reticularis layers of the adrenal cortex
- Glucocorticoids (cortisol): recognized early to increase plasma glucose levels:
  - Mobilization of amino acids from proteins
  - Enhance liver gluconeogenesis
- Target tissues: most body tissues

# Glucocorticoids (cont.)

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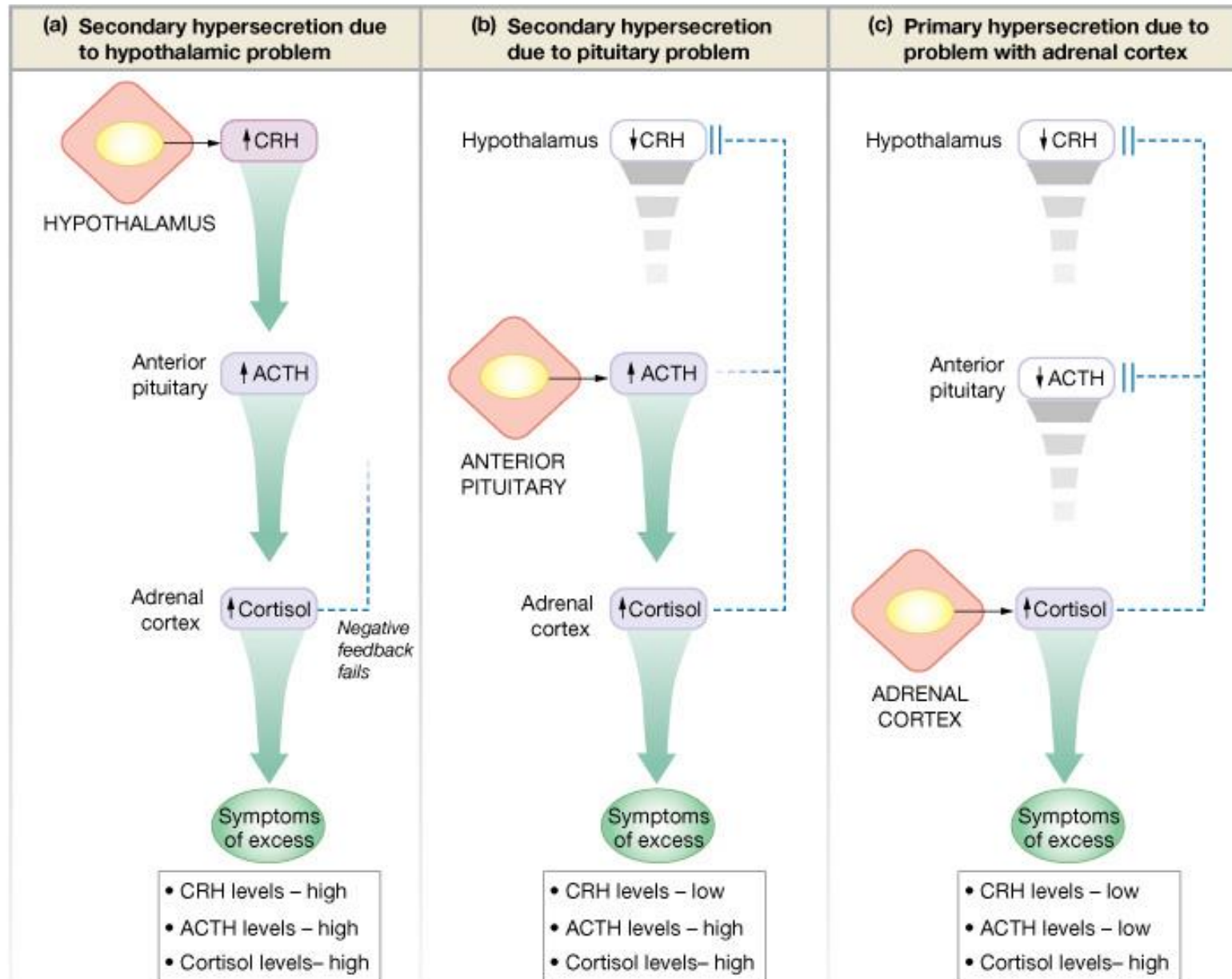
- CRH from hypothalamus is the major regulator of ACTH secretion
- ADH is also secretagogue for ACTH
- ACTH from anterior pituitary stimulates cortisol synthesis and secretion
- CRH (and ACTH) are secreted in pulses
- The greatest ACTH secretory activity occurs in the early morning hours and diminish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

# Regulation of Glucocorticoid Secretion

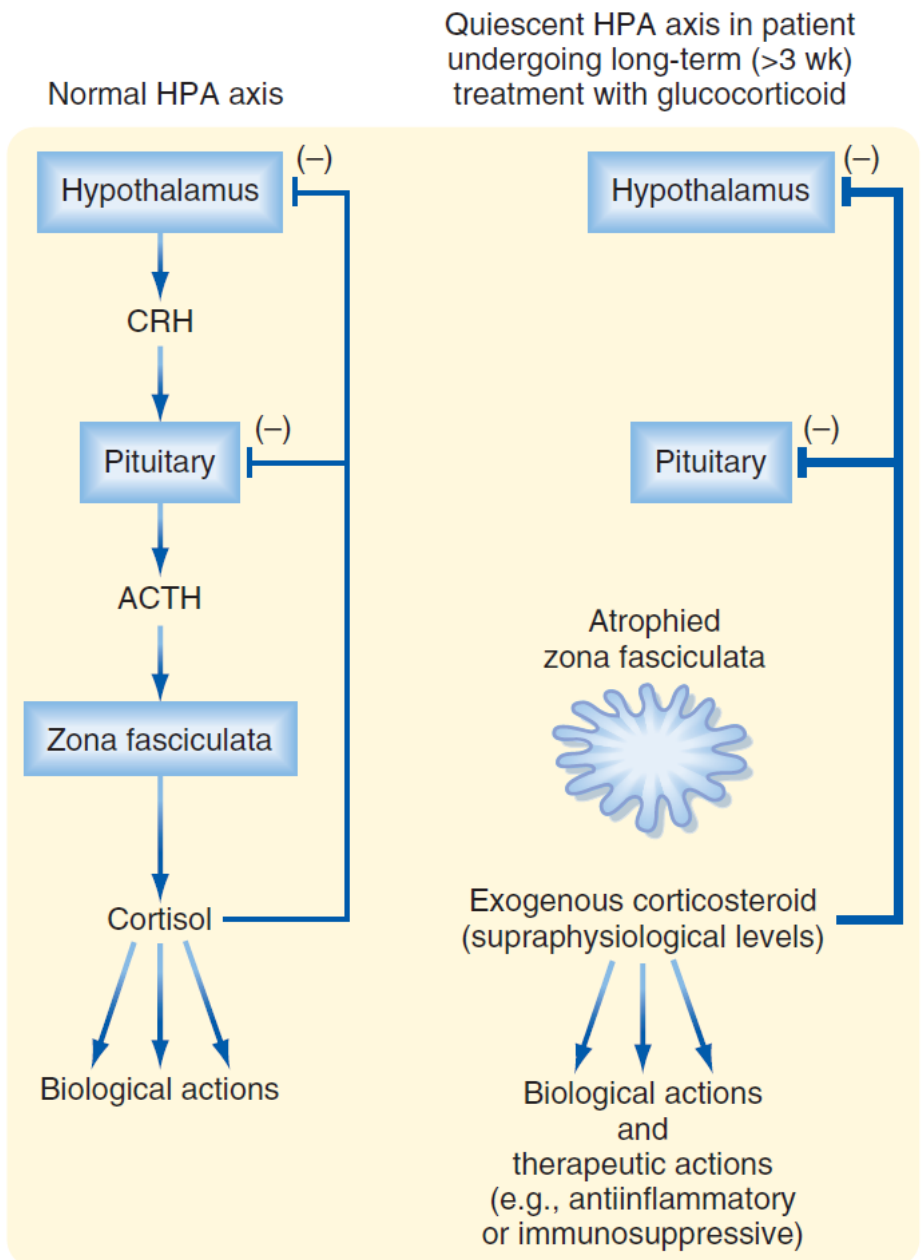


**Figure 78-7.** Mechanism for regulation of glucocorticoid secretion. ACTH, adrenocorticotropin hormone; CRF, corticotropin-releasing factor.

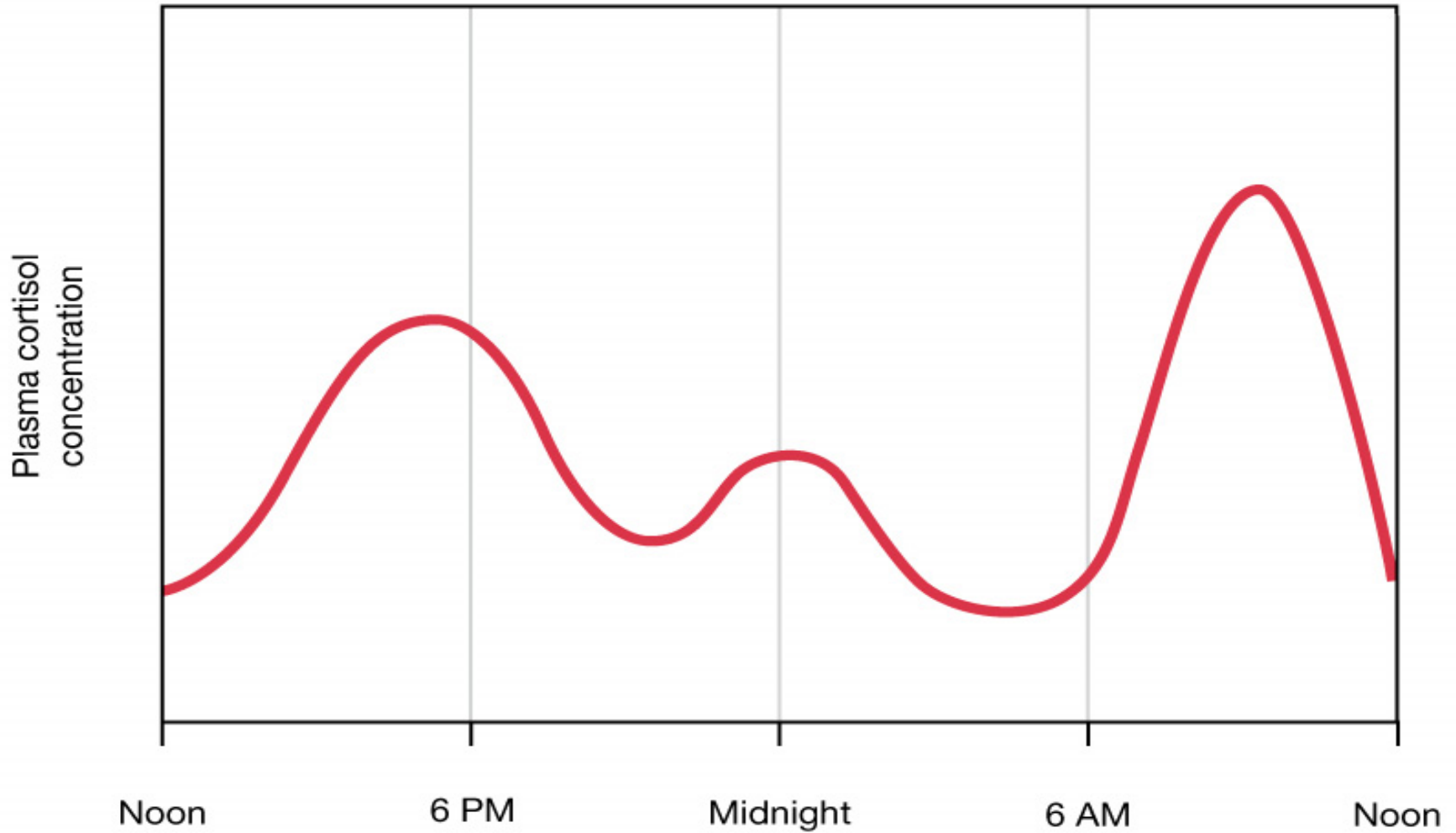
# Primary and secondary hypersecretion of cortisol



# 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 GLUT<sub>4</sub>-mediated glucose uptake in skeletal muscle and adipose tissue.
  - Mobilization of stored fat (activation of HSL) and its use in  $\beta$ -oxidation and the production of ketone bodies



# Effect of glucocorticoids: on carbohydrate metabolism

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- 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.
- Mobilization of amino acids from extrahepatal tissues (muscles) for gluconeogenesis

# 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

# 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 A<sub>2</sub>.
  - 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 eosinophils and 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

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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

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- 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:

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- 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

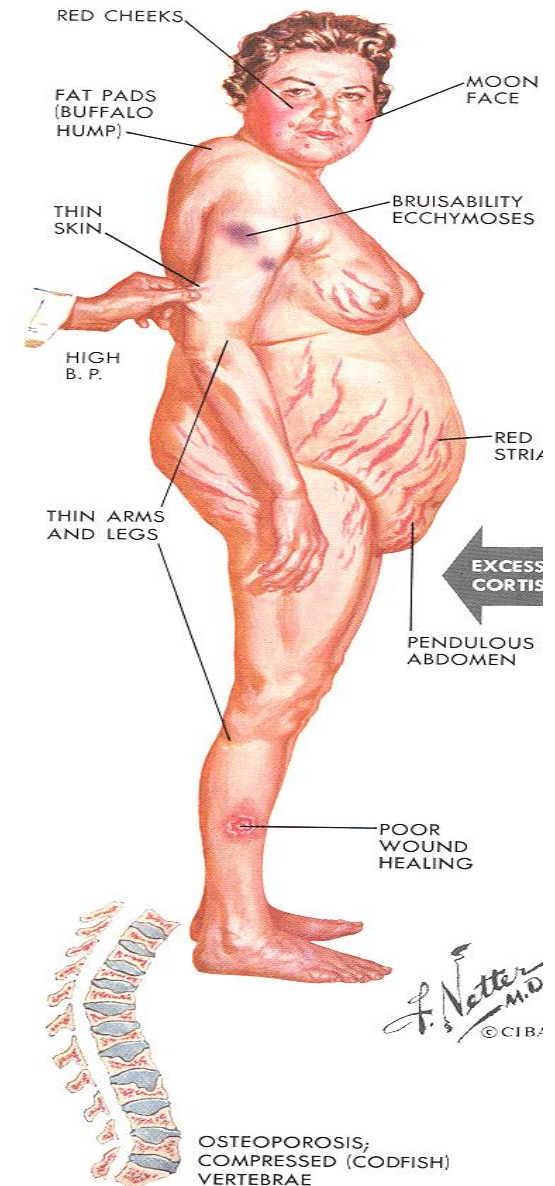
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- Cushing's syndrome results from continued high glucocorticoid levels
- 3rd - 6th decade, 4 to 1 females
- Causes:
  - pharmacologic
  - pituitary adenoma
  - adrenal adenoma, carcinoma
  - ectopic ACTH

# Cushing's Syndrome

## Signs:

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



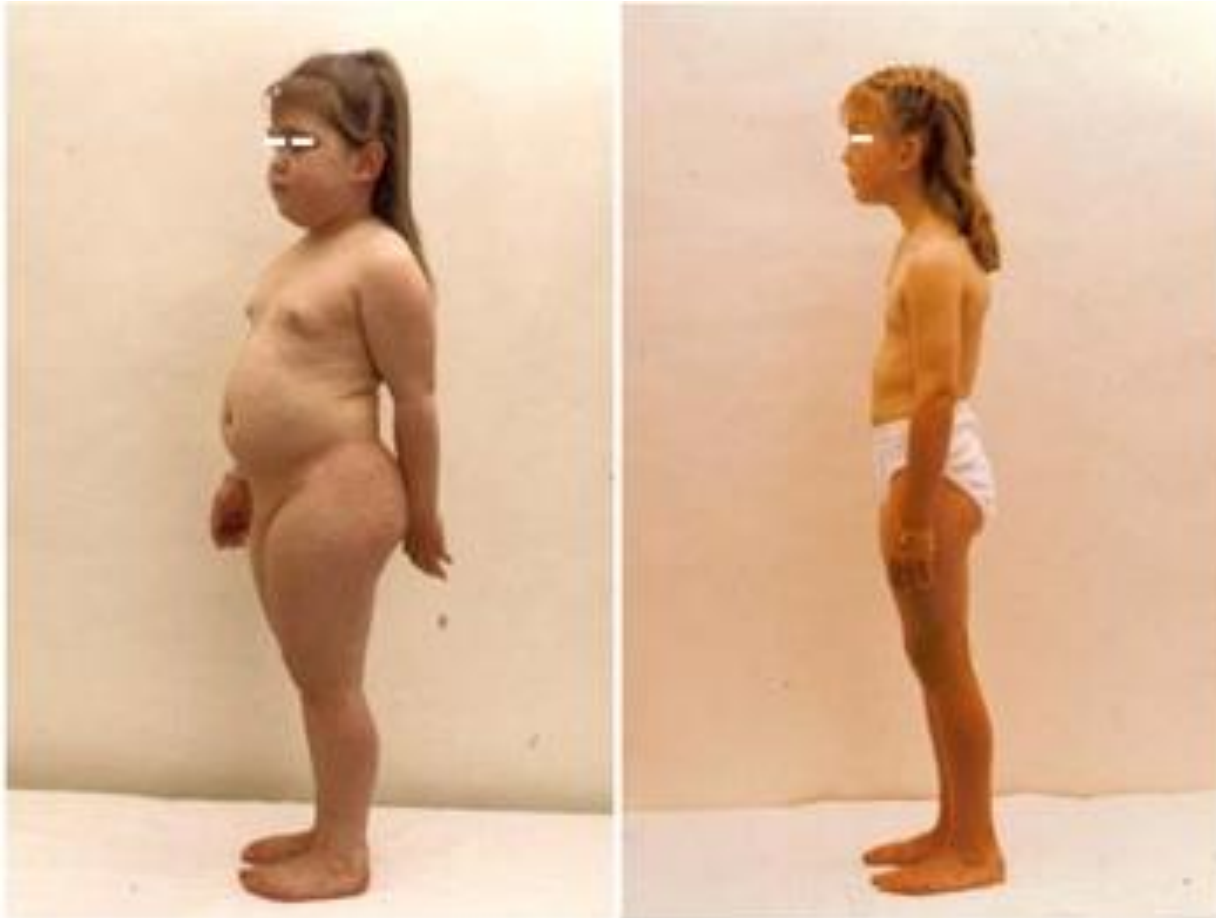
# Cushing's Syndrome

- Purple striae



# Cushing's Syndrome

- treatment based on cause



# Adrenocortical insufficiency

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- primary causes, ie. **Addison's disease**
  - autoimmune disease, tumors, infection, hemorrhage, metabolic failure, ketoconazole
- secondary causes
  - hypopituitarism, suppression by exogenous steroids

# Adrenocortical insufficiency

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- 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, vascular collapse....

# Adrenocortical insufficiency

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- treatment
  - glucocorticoid replacement, mineralocorticoid replacement