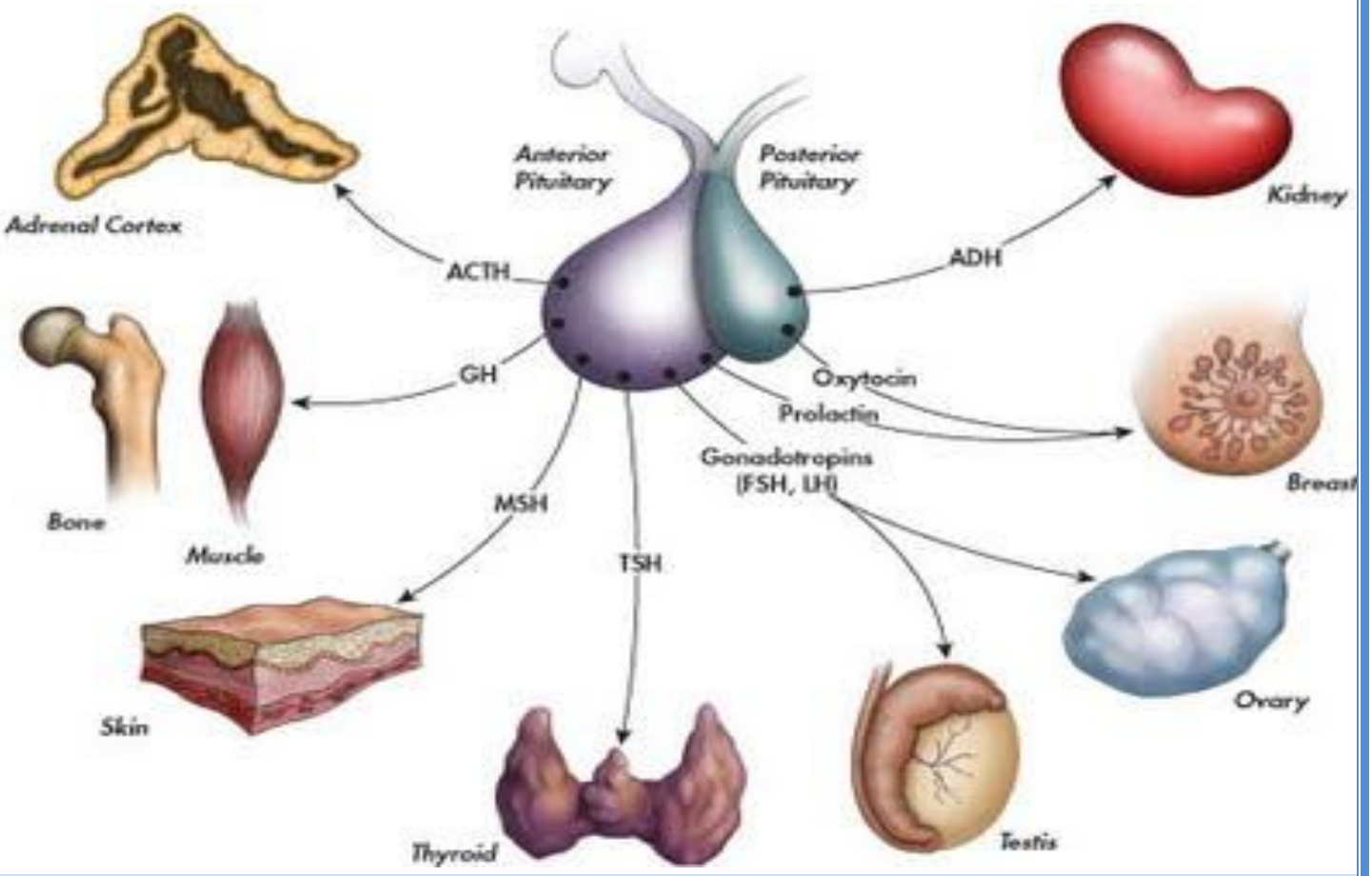
Endocrine Block

11th & 12th Lecture

Adrenal Hormones



PHYSIOLOGY TEAM – 430

Physiology Team Leaders:

Al-Waleed Al-Johar Layan Akkielah

This Lecture is done by:

Al-Waleed Al-Johar Hadeel Al-Sajjan

Ali Al-Qahtani Hanan Al-Shalaan

Organized by: Al-Waleed Al-Johar

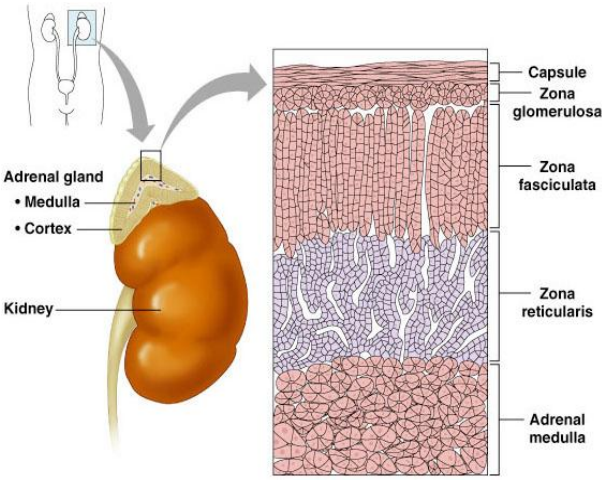
Adrenal Hormones

☒ Adrenal (Suprarenal) Glands

- Adrenal glands – paired, retroperitoneal, pyramid-shaped organs atop the kidneys
- Weigh 4-8 g.
- Structurally and functionally, they are two glands in one
- Adrenal cortex (80-90%) – glandular tissue derived from embryonic mesoderm
- Adrenal medulla (10-20%) – Functionally related to the sympathetic nervous system. (Neuroectodermal)

☒ Adrenal Cortex

- Synthesizes and releases steroid hormones (corticosteroids)
- Different corticosteroids are produced in each of the three layers:

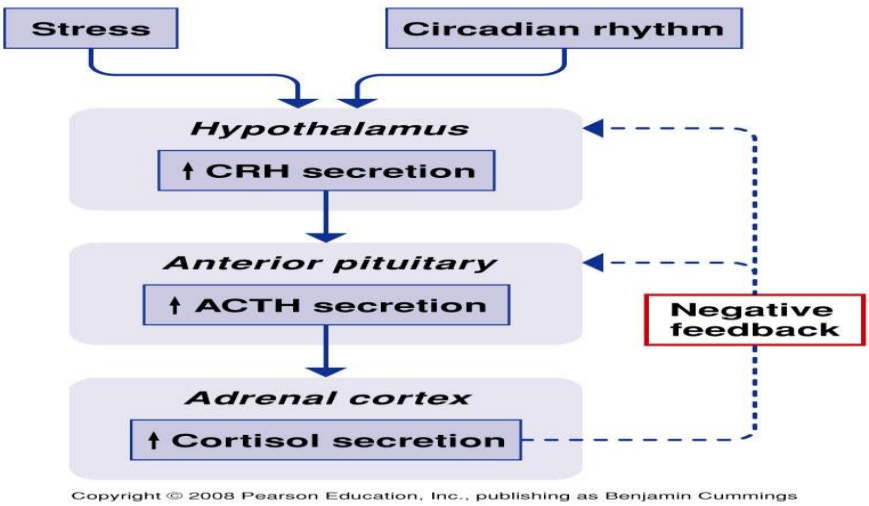


✓ **Zona glomerulosa (15% of the cortex):** mineralocorticoids (aldosterone)

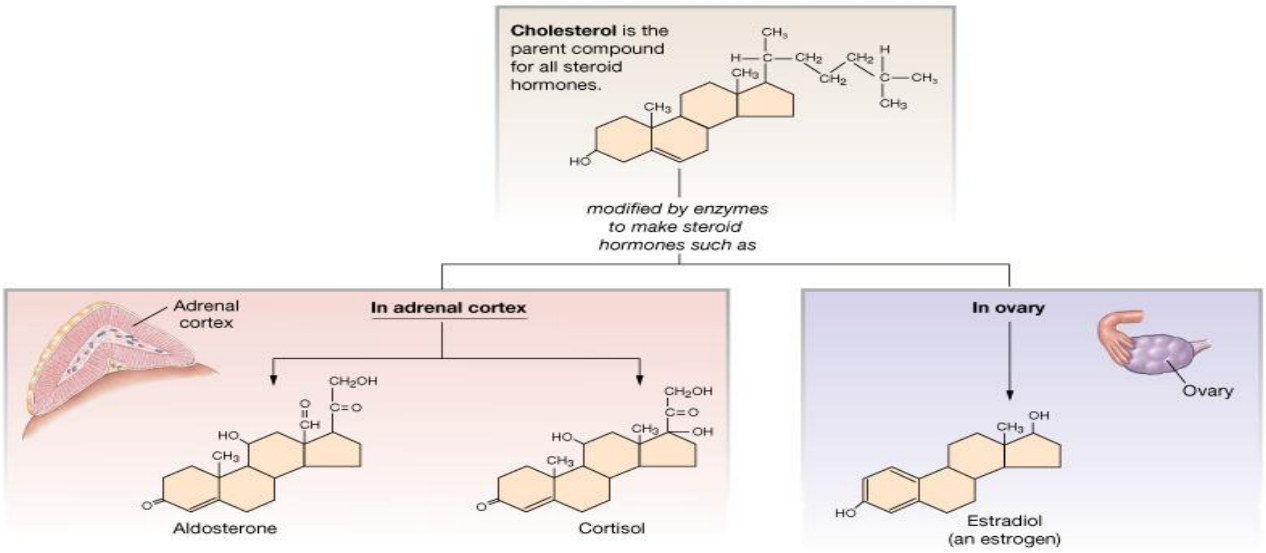
✓ **Zona fasciculata (75%):** glucocorticoids (mainly cortisol and corticosterone) + small amounts of Androgens, estrogens.

✓ **Zona reticularis:** gonadocorticoids (DHEA, androstenedione) + few amounts of glucocorticoids

☒ HPA Axis



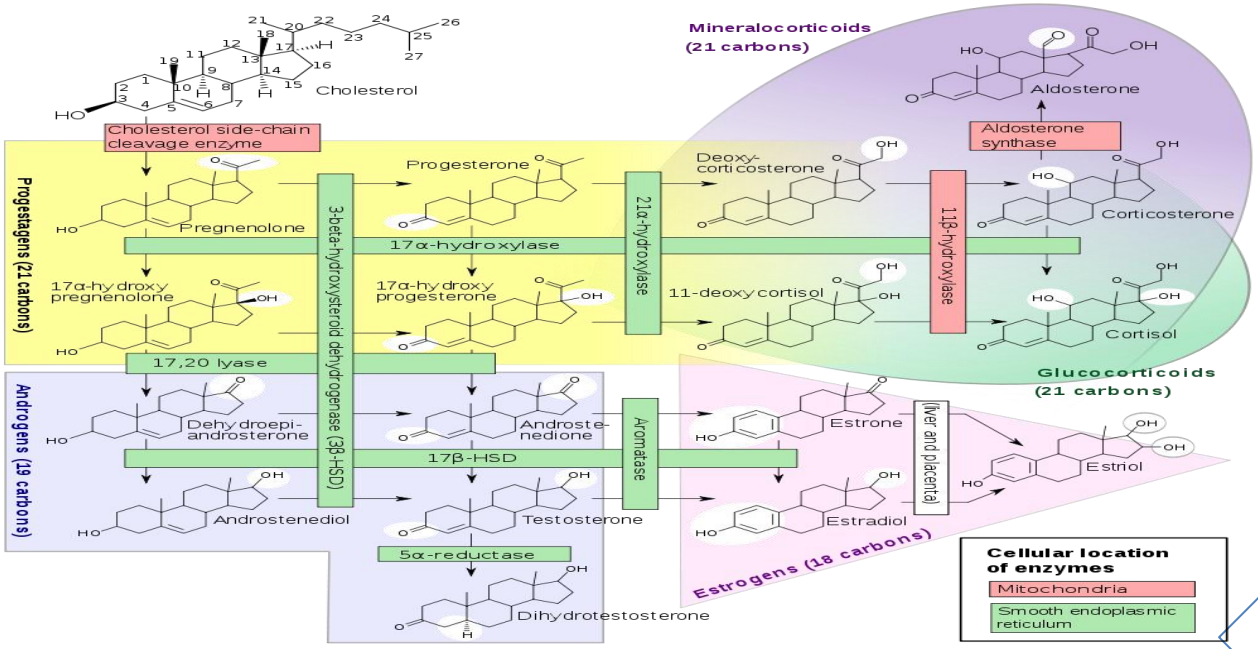
☒ Steroid Hormones: Structure



☒ Steroid Hormones Synthesis

- Steroids are derivatives of cholesterol
- Cholesterol is from the lipid droplets in cortical cells (cholesterol esters in LDL)
- Removed cholesterol is replenished by cholesterol in LDL in blood or synthesized from acetate
- Steroid hormones are synthesized and secreted on demand (not stored)
- The first and rate-limiting step in the synthesis of all steroid hormones is conversion of cholesterol to pregnenolone by the enzyme cholesterol dismolase (aka cholesterol side chain cleavage (SCC) enzyme
- Newly synthesized steroid hormones are rapidly secreted from the cell
- Following secretion, all steroids bind to some extent to plasma proteins: CBG (transcortin) and albumin

☒ Steroidogenesis



☒ Genetic Defects in Adrenal Steroidogenesis :

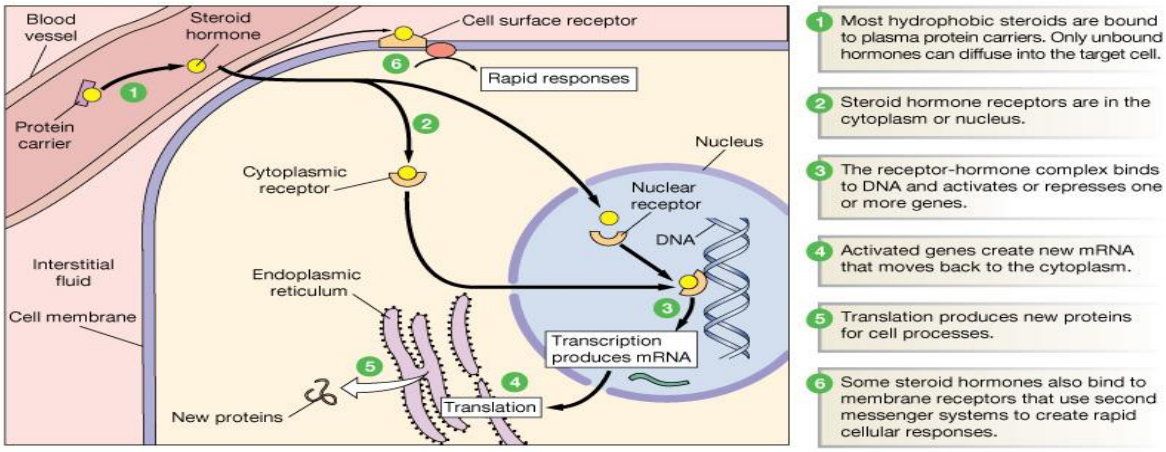
- Congenital adrenal hyperplasia also known as Adrenogenital syndrome :
- Refers to a group of inherited disorders of the adrenal gland that affects both boys and girls.
- People with CAH lack of an enzyme (21-hydroxylase - P450c21) which is needed by the adrenal gland to make the major steroid hormones of the adrenal cortex: cortisol, corticosterone and aldosterone.
- Without these hormones , there is an abnormal 'feedback' and steroids are 'diverted' to becoming androgens (a form of male sex hormones) and this will cause :

A) In pre-pubertal males it causes the rapid develop of secondary sexual character

B) In females causes beard growth, deeper voice, masculine distribution of body hair, and growth of the clitoris to resemble a penis.

↓ Cortisol → ↑ ACTH → adrenal hyperpalsia
ACTH ↓ → Adrenal hypertrophy and high amounts of androgen

☒ Steroid Hormones: Action



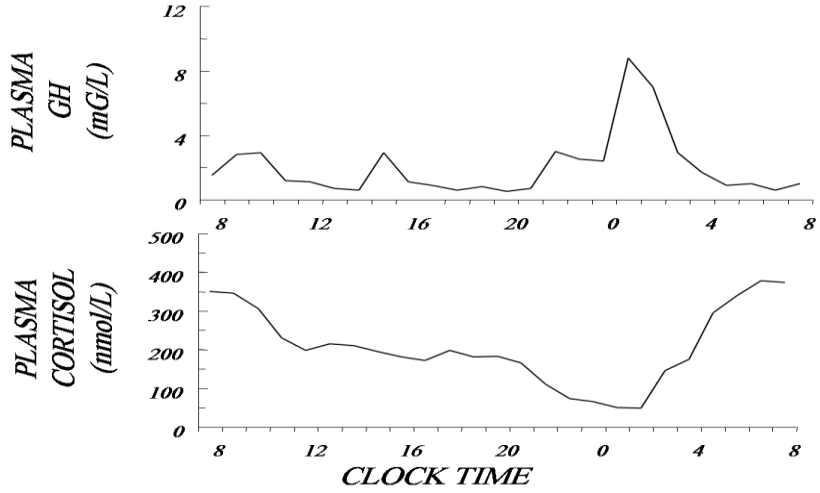
☒ Glucocorticoids

- Produced by the fasciculata and reticularis layers of the adrenal cortex (Mainly from the zona fasciculata)
- Glucocorticoids (cortisol): recognized early to increase plasma glucose levels:

✓ Mobilization of amino acids from proteins
✓ Enhance liver gluconeogenesis

- Target tissues: most body tissues
- CRH from hypothalamus is the major regulator of ACTH secretion
- ADH is also a potent ACTH secretagogue
- 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 (lowest level around midnight)

☒ Hormone Secretion Profiles



☒ Corticosteroids & Their Relative Glucocorticoid & Mineralocorticoid Activities Compared to Cortisol

Steroids	Average Plasma Concentration (free and bound, µg/100 ml)	Average Amount Secreted (mg/24 hr)	Glucocorticoid Activity	Mineralocorticoid Activity
Adrenal Steroids				
Cortisol	12	15	1	1
Corticosterone	0.4	3	0.3	15.0
Aldosterone	0.006	0.15	0.3	3000
Deoxycorticosterone	0.006	0.2	0.2	100
Dehydropiandrosterone	175	20	—	—
Synthetic Steroids				
Cortisone	—	—	0.7	1.0
Prednisolone	—	—	4	0.8
Methylprednisone	—	—	5	—
Dexamethasone	—	—	30	—
9α-fluorocortisol	—	—	10	125

Table 77-1, Guyton & Hall

☒ Regulation of Cortisol Release

Enhanced release can be caused by:

- Physical trauma
- Infection
- Extreme heat and cold
- Exercise to the point of exhaustion
- Extreme mental anxiety

☒ Physiological effects of cortisol

Cortisol is
- Hyperglycemic
- Lipolytic
- Catabolic on Proteins

✓ Carbohydrate metabolism

Increases blood glucose levels by:

- Increasing glucogenesis in the liver via stimulating the enzymes involved in glucogenesis
- Decreasing utilization of glucose by cells via direct inhibition of glucose transport into cells

✓ Protein metabolism

- Reduces protein formation
- Occurs everywhere EXCEPT liver
- Extrahepatic protein stores reduced (catabolic)
- Amino acids not transported into muscle cells ↓ protein synthesis & ↑ amino acid blood levels
- These high blood amino acid levels are transported more rapidly to hepatic cells for glucogenesis and protein synthesis in liver

✓ Fat metabolism

- Lipolytic
- Mobilizes fatty acids & glycerol from adipose tissue lead to↑ their blood concentrations makes more glycerol available for gluconeonesis
- Fat broken down & less formed due to less glucose transported into fat cells
- Redistribution of body fat:
  ↑ Formation of fat in trunk areas & face
  ↓ fat (& muscle) from extremities

☒ Anti-inflammatory Effects of GC

- Glucocorticoids are used to alleviate inflammation
- Inhibit production of prostaglandins and leukotrines (mediate inflammation)
- This occurs via stimulation of an inhibitor of phospholipase A2, which is needed for PG synthesis
- Decrease the inflammation reaction by decreasing permeability of capillary membranes, reducing swilling
- They also reduce the effects of histamine

☒ Suppression of Immune System

- When administered in high doses, GC can:
- Suppress antibody formation
- Kill immature T and B lymphocytes

☒ 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 the action of norepinephrine (Permissive effect)
- Decreased capillary permeability
- Maintains normal renal function

☒ Functions - 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

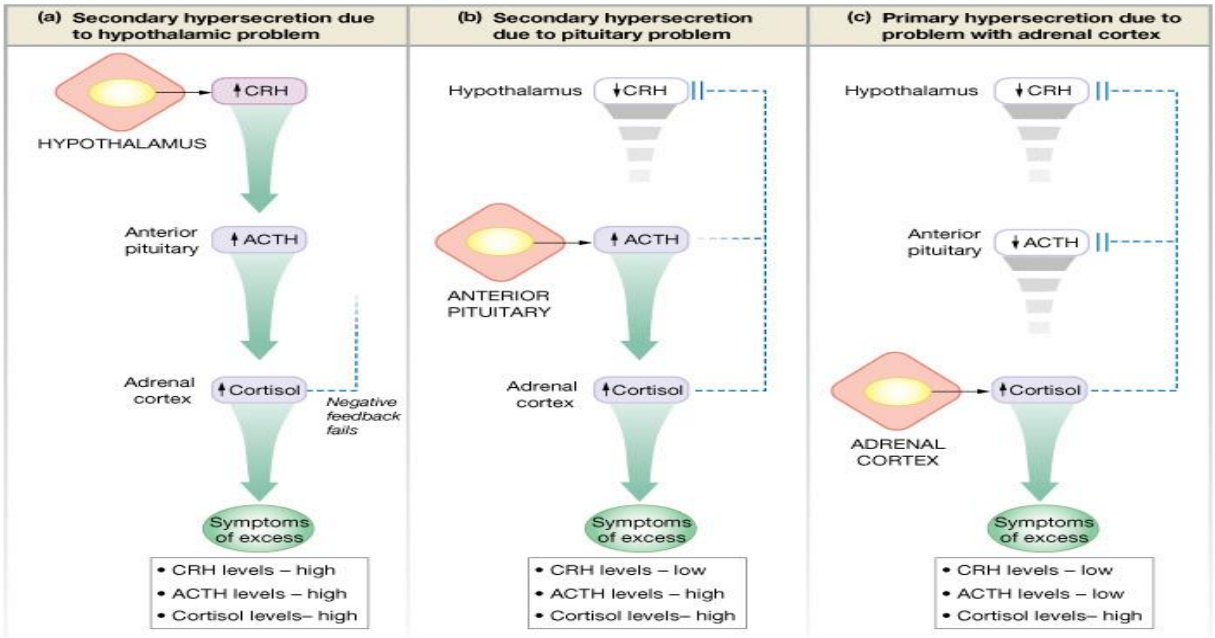
☒ Glucocorticoids and Stress:

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

- Mood negative or positive, memory.
- Initially euphoria followed by depression.
- Seizure threshold lowered.

GCs have Anti-vitamin D effect plus they increase HCl production in GIT

☒ Primary and secondary hypersecretion of cortisol



☒ Cushing's Syndrome

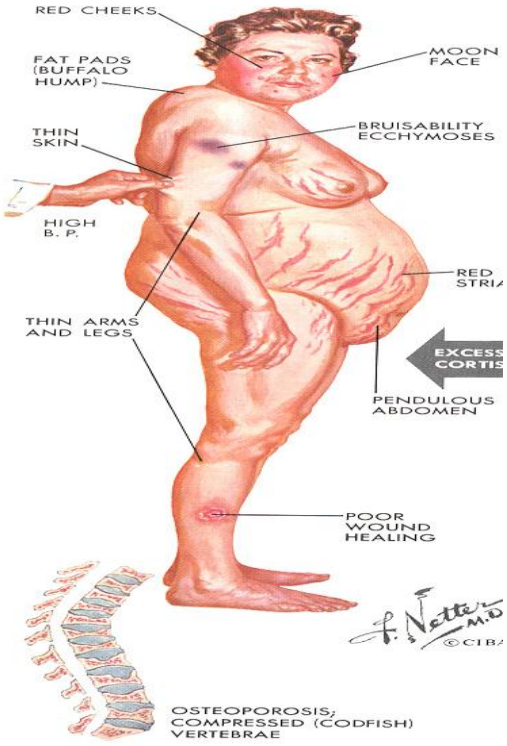
- Cushing's syndrome results from continued high glucocorticoid levels
- 3rd - 6th decade, 4 to1 females

✓ **Causes:**

- pharmocologic (Treatment with GC)
- pituitary adenoma 75-90%
- adrenal adenoma, carcinoma
- ectopic ACTH

✓ **Signs:**

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



Excessive cortisol could also cause:
Hypertension, Hypervolemia, Hypernatremia, Hypokalemia
↓ Immunity
Euphoria & depression
Seizures

☒ Adrenocortical insufficiency

✓ **Primary causes** → Addison's disease

- autoimmune disease, tumors, infection, hemorrhage, metabolic failure, ketoconazole
- Loss of all three types of steroids
- 90% of gland is destroyed

✓ **Secondary causes:**

- hypopituitarism, suppression by exogenous steroids

✓ **Adrenal crisis:** life-threatening, hypotension (resistant to catecholamines), can lead to adrenal failure

✓ **Symptoms & Signs:**

- fatigability, weakness, anorexia, nausea, weight loss, hyperpigmentation, hypotension, women loss of axillary and pubic hair, hypeglycemia, hyperkalemia, mild acidosis
- 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….

✓ **Treatment**

- glucocorticoid replacement, mineralocorticoid replacement

☒ Gonadocorticoids (Adrenal Androgens):

- Produced mainly by the inner reticularis layer of the adrenal cortex
- The adrenal cortex produces both androgens i.e. “male sex hormones” and estrogens or “female sex hormones.
- Androgens are the hormones that exert masculinizing effects. They promote protein anabolism and growth.
- Testosterone from the testis is the major active ,androgen. The adrenal androgens have less than 20% of its activity
- Most gonadocorticoids secreted are androgens mainly dehydroepiandrosterone (DHEA & DHEAS)
- DHEA(S) can be converted to androstenediol or androstenedione which can be also converted to testosterone or estrogen .
- Androstenediol can act like a classic estrogen while androstenedione is a main precursor of estrone, the major circulating estrogen in women.
- Androstenediones are converted metabolically to testosterone and to estrogens in the fat and other peripheral tissues. It is an important source of estrogen in men and postmenopausal women.
- Androstenedione were used as an athletic or body building supplement.
- The adrenal cortex in both sexes produces small amounts of sex hormone of the opposite sex. Additional small amounts of sex hormones come from nonadrenal sources.
- Some testosterone in males is converted into estrogen by the enzyme aromatase found in adipose tissues.
- In females, ovaries produce androgen as an intermediate step in estrogen production. Little of this androgen is released in the blood instead of being converted into estrogen

☒ Actions of Androgens

- Adrenal androgens secretion increases dramatically just before puberty
- Androgens contribute to:
- The onset of puberty
- The appearance of secondary sex characteristics
- Sex drive in females