



ENDOCRINE BLOCK

LECTURE 11

The Adrenal Gland 'Glucocorticoids'



DONE BY:

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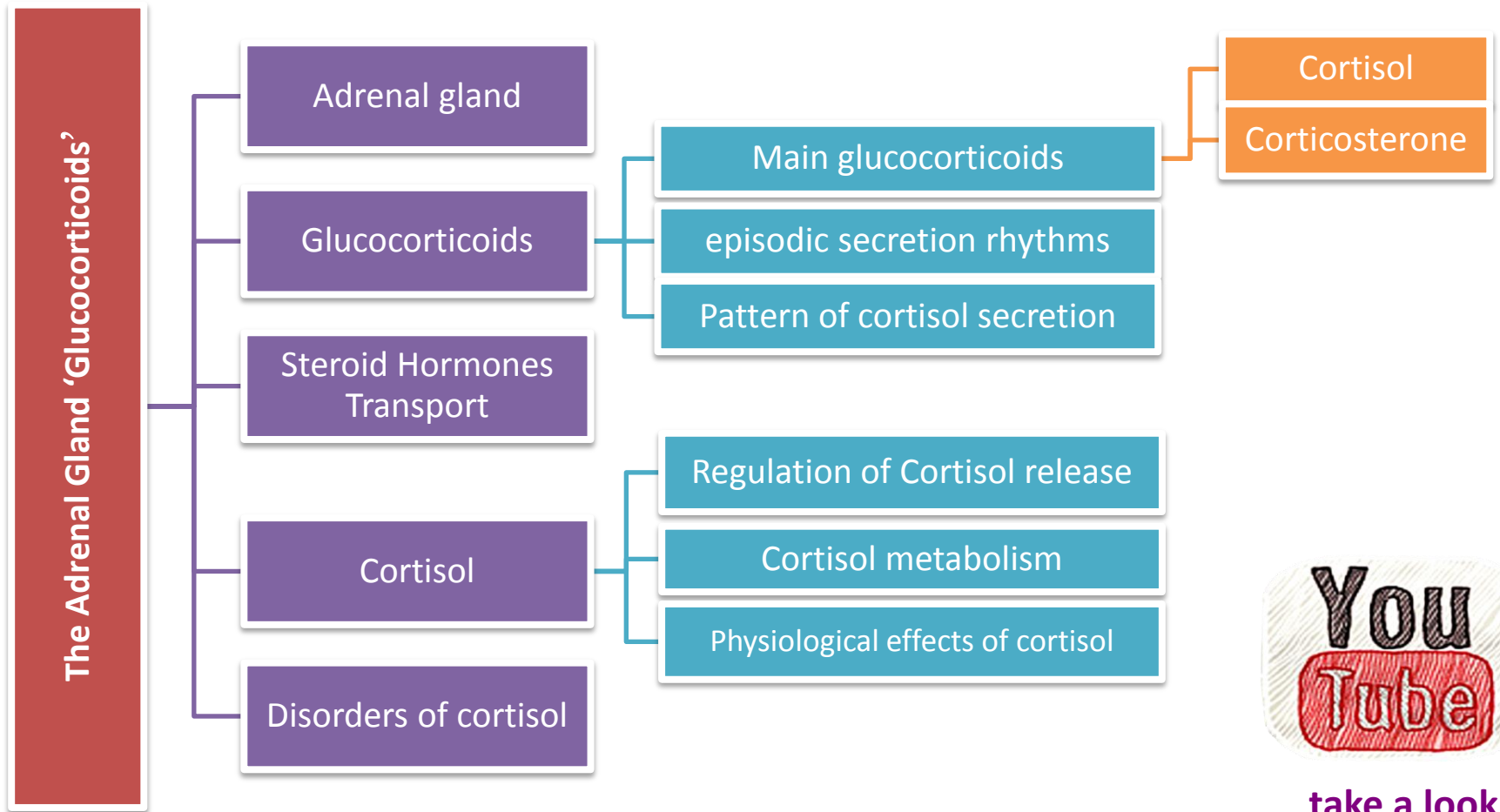
REVISED BY:

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OBJECTIVES

Not Given :|



[take a look !](#)



Small, triangular glands loosely attached to the kidneys.

Divided into two morphologically and distinct regions:

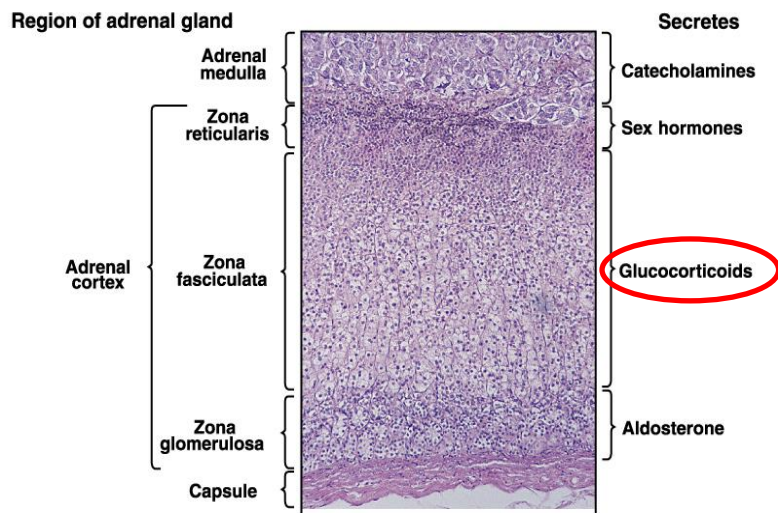
• **Adrenal cortex: (Secretes steroid hormones)**

- **Glucocorticoids.**
- Mineralocorticoids.
- Androgens.

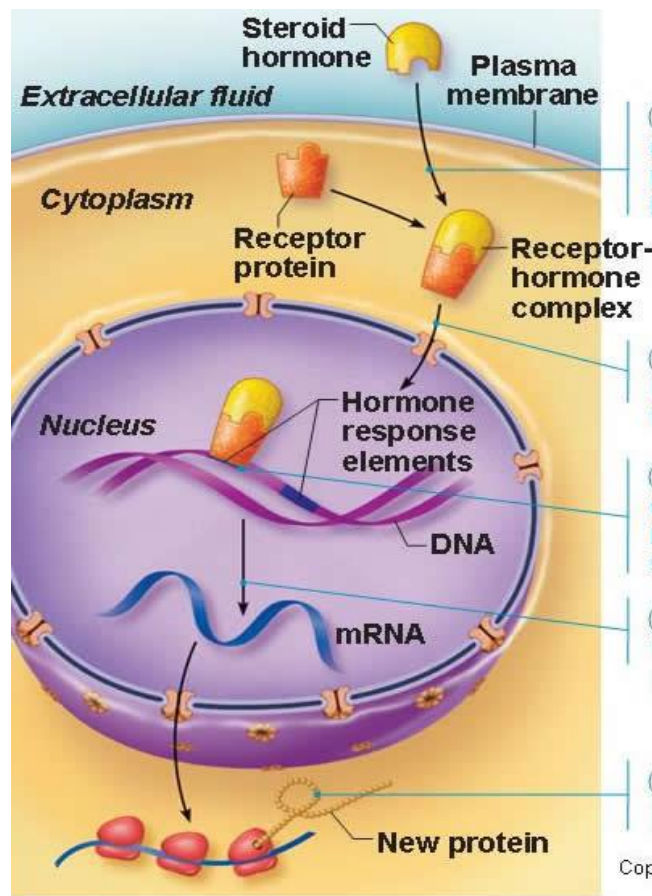
• **Adrenal medulla: (Amino acid secretions)**

Catecholamines

- Called glucocorticoid, because first action recognized is ↑ levels of glucose.



Mechanism of action of steroid hormones



① The steroid hormone diffuses through the plasma membrane and binds an intracellular receptor.

② The receptor-hormone complex enters the nucleus.

③ The receptor-hormone complex binds a hormone response element (a specific DNA sequence).

④ Binding initiates transcription of the gene to mRNA.

⑤ The mRNA directs protein synthesis.

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Main glucocorticoids in humans:

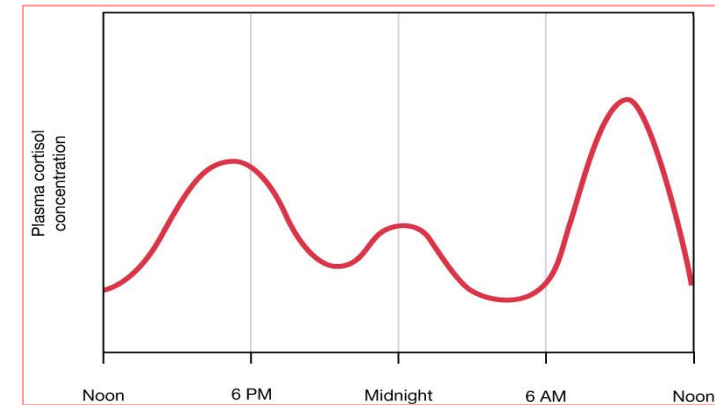
- Cortisol
- Corticosterone
- Cortisol:corticosterone produced in humans in a ratio of 10:1
- **90-95% bound to plasma protein.**
- **Under control primarily by ACTH**

Natural episodic secretion rhythms:

- controlled by hypothalamus CRH. Also ACTH exhibits the same diurnal pattern.
- in fact the pattern of ACTH secretion that drives the diurnal pattern of steroid hormone secretion.
- After ACTH has been produced, cortisol will be evident 15 to 30 minutes later.
- There are usually 7-15 episodes per day.
- There is a major burst in the early morning before awakening and diminish late in the afternoon.
- ADH is also a potent ACTH secretagogue (The purpose of ADH is to retain water in the body. It does it through two ways: through acting on the kidneys and through stimulating the release of ACTH. ACTH causes the adrenal cortex to release aldosterone. Aldosterone also acts on the kidney to reabsorb sodium and water back into the body.)

Pattern of cortisol secretion

- increased release with **coffee** consumption.
- increases with increased **exercise** time & intensity.



Note that the increase in **ACTH** levels precedes the rise in **cortisol**.



Steroid hormones when released from adrenal cortex into blood stream they bind to protein carriers:

- **Cortisol binding globulin (CBG)** (transcortin).
- **Albumin.**
- Only unbound steroid hormones are biologically active (~2%).
- To cross the target tissue membrane, the hormone must dissociate from its carrier protein.

Importance: Binding to plasma proteins act as a reservoirs and ensure a uniform distribution to all tissues.

Cortisol is anti stressful hormone that also cause stress . It helps in the consequence of the stress .e.g. in exams , exercise , fasting or starvation ,cortisol will be high.

Glucocorticoid help in withstand stressful condition by

- maintain blood pressure.
- maintain blood Glucose level.

In some patients with long term stress they may develop hypertension and diabetes by the action of Glucocorticoid, catecholamines ,...etc.

Aldosterone has a lower half life than cortisol?

Because 90-95% of glucocorticoids bound to plasma protein. Act as a reservoirs and ensure a uniform distribution to all tissues.



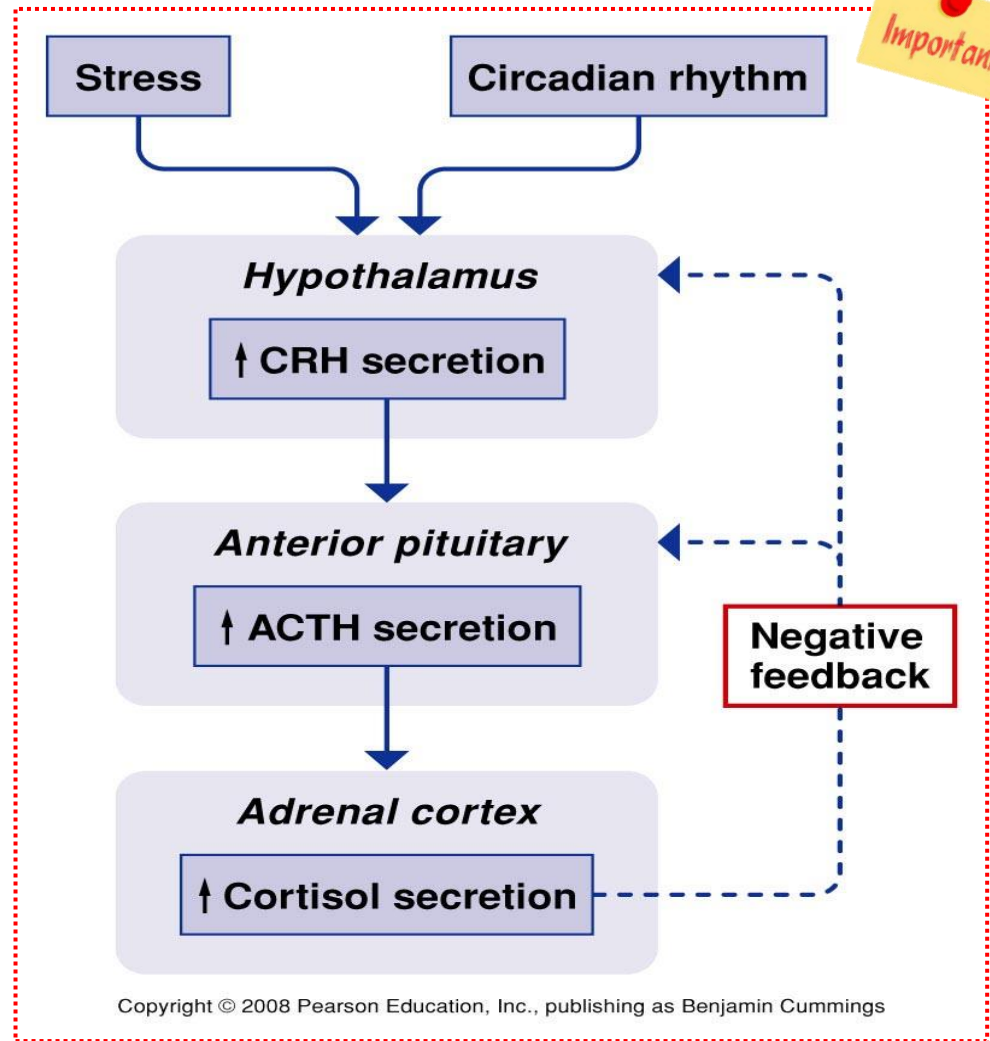
Regulation of Cortisol release

Stimuli releasing cortisol:

- physical trauma.
- infection.
- extreme heat and cold.
- exercise to the point of exhaustion.
- extreme mental anxiety.

Cortisol metabolism

- Metabolized in liver by **reductases** & conjugated to **glucuronides** and excreted via kidney.
- **Free** cortisol is excreted into urine.

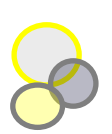




Physiological effects of cortisol

Important

Carbohydrate Metabolism	Protein Metabolism	Fat Metabolism
<p>Increases blood glucose levels by:</p> <ul style="list-style-type: none"> (+) gluconeogenesis in the liver. Decreasing utilization of glucose by cells via direct inhibition of glucose transport into cells. 	<ul style="list-style-type: none"> Reduces protein formation in all tissues Except liver. for Gluconeogenesis . 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 gluconeogenesis and protein synthesis in liver. 	<ul style="list-style-type: none"> Lipolytic. Mobilizes fatty acids & glycerol from adipose tissue lead to ↑ their blood concentrations makes more glycerol available for gluconeogenesis. 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 Increases appetite.
Anti-inflammatory		Blood Cells and Immunity
<ul style="list-style-type: none"> Stabilizes lysosomal membrane. To prevent increasing in lysosomal permeability that cause tissue digestion. Reduces degree of vasodilatation. To decrease the edematous reddish area after insect pit that produce foreign antigen in the body causing inflammation . Decreases permeability of capillaries. same as above to decrease the edema. Decreases migration of white blood cells. Suppresses immune system. Used in autoimmune diseases and organs transplantation . 		<ul style="list-style-type: none"> Decrease production of eosinophils and lymphocytes. Suppresses lymphoid tissue systemically therefore decrease in T cell and antibody production → decreasing immunity Hodgkin lymphoma treatment. Decrease immunity could be fatal in diseases such as tuberculosis. Decrease immunity effect of cortisol is useful during transplant operations in reducing organ rejection.



Carbohydrate Metabolism

- enzymes required to convert amino acids into glucose are increased .
- increase in glycogen storage in liver cells .

Protein Metabolism

Proteoanabolic effect in the liver :

- enhanced liver proteins.
- increased plasma proteins.

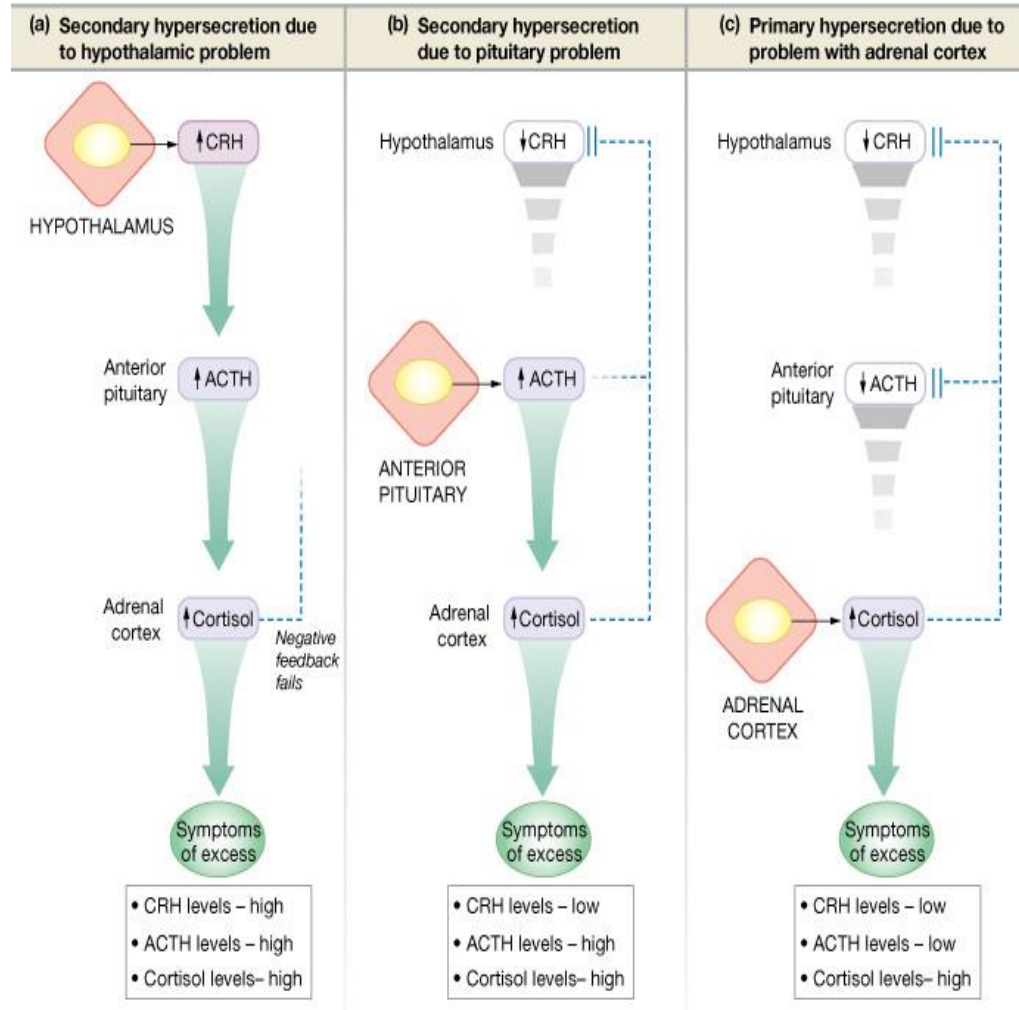
Fat Metabolism

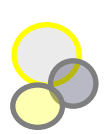
- Mobilization of stored fat (activation of HSL*) and its use in β -oxidation and the production of ketone bodies .
 - Glucocorticoid use fat is energy not glucose.
- * HSL = Hormone Sensitive Lipase

Anti-inflammatory

- Inhibit production of prostaglandins and leukotrienes
- This occurs via inhibiting phospholipase A2, which is needed for PG synthesis
- They also reduce the effects of histamine

Primary and secondary hyper-secretion of cortisol





Physiological effects of cortisol



Circulation	CNS responses	Mineral metabolism
<ul style="list-style-type: none"> • Maintains body fluid volumes & vascular integrity • Cortisol has mineralocorticoid effect, Not as potent as aldosterone. so it will reabsorb Na and secret K. • BP regulation & cardiovascular function: Sensitizes arterioles to action of noradrenaline (Permissive effect). (maintenance of vascular responsiveness to catecholamines by up regulating α_1 adrenergic receptors). • Decreased capillary permeability. • Maintiens normal renal function. 	<ul style="list-style-type: none"> • Negative feedback control on release of ACTH. • Modulates perception & emotion . <p>glucocorticoid receptors are found in the brain, particularly in the limbic system causing emotional disturbance if there excessive amount of the hormone.</p>	<ul style="list-style-type: none"> • Anti-vitamin D effect. <p>(only in case of excessive amount, leading to osteoporosis)</p>

GIT	Developmental Functions
<p>Increases HCl secretion</p> <p>(also will cause ulcer only in excessive amount)</p>	<ul style="list-style-type: none"> • Permissive regulation of fetal organ maturation. • Surfactant synthesis (phospholipid that maintains alveolar surface tension). (mothers who are about to deliver prematurely can be given glucocorticoids. This speeds the production of surfactant, and babies won't get respiratory distress syndrome). • Inhibition of linear growth in children due to direct effects on bone & connective tissue. ((1) by decreasing the synthesis of type 1 collagen "the major component of bone matrix". (2) by decreasing osteoblast production. (3) by decreasing intestinal Ca absorption) (not in physiological level, only in abnormal amount of the hormone) , (\uparrowcortisol cause dwarfism)



Cortisol excess: (exogenous & endogenous)

1- Exogenous:

Most cortisol excess is induced by steroid therapy (prednisone) to manage diseases as:

- asthma
- rheumatoid arthritis
- lupus
- other inflammatory diseases
- immunosuppression after transplantation

2- Endogenous:

Due to excessive production of cortisol:

- **ACTH- independent:**
 - Primary adrenal defect (adenoma)
- **ACTH-dependent:**
 - Overproduction of ACTH by pituitary
 - Overproduction of ACTH by ectopic ACTH-producing tumor

Cushing's disease:

over production of ACTH by pituitary

Cushing's syndrome:

over production of cortisol by adrenal cortex.

- Both exogenous & endogenous hyperfunction show manifestations of **Cushing's**

Cushing's (excess amount of cortisol)

Carbohydrate metabolism		Protein metabolism	Bone matrix & mass losses; bone formation
<ul style="list-style-type: none"> • ↑ blood glucose levels • ↓ sensitivity to insulin 		<ul style="list-style-type: none"> • ↑ protein loss • muscle atrophy • thin skin 	<ul style="list-style-type: none"> • ↓ less Ca²⁺ absorbed & more excreted in urine • osteoporosis
Fat metabolism	Effects on CNS	Circulation	inflammation & immunity
redistribution of body fat: ↑ trunk & face fat deposition ↓ extremities fat deposition	Initially euphoria but replaced with depression.	<ul style="list-style-type: none"> • Hypertension (due to Na retention & K excretion) • Hypervolemia (due to water reabsorption secondary to Na reabsorption) • Hyponatremia (due to increased Na absorption) • Hypokalemia (due to increased K excretion.) 	<ul style="list-style-type: none"> • Decreases inflammatory response • Increased infection susceptibility • Ab synthesis suppressed & normal immune responses to infecting pathogens suppressed • Decrease in fibrous tissue formation

Effects on Carbohydrate Metabolism

“Adrenal diabetes”

- Hypersecretion of cortisol results in increase blood glucose levels, up to 2 x normal (200mg/dl)
- Prolonged oversecretion of insulin “burns out” the beta cells of the pancreas resulting in life long diabetes mellitus

Effects on Protein Metabolism

- Decrease protein content in most parts of the body resulting in muscle weakness
- In lymphoid tissue – decrease protein synthesis results in suppression of the immune system
- Lack of protein deposition in bones can result in osteoporosis
- Collagen fibers in subcutaneous tissue tear forming striae





Buffalo torso

- Redistribution of fat from lower parts of the body to the thoracic and upper abdominal areas.

Moon Face

- Edematous appearance of face.
- **Acne & hirsutism** (excess growth of facial hair).



weight gain

- Hypersecretion of glucocorticoids by the adrenal cortex characterized by **weight gain** in the trunk of the body but not arms and legs.

Other features of Cushing's:

- Proximal muscle wasting & weakness.
- Osteoporosis.
- Glucose intolerance.
- HTN, hypokalemia.
- Thromboembolism.
- Depression, Psyc
- Infection
- Glaucoma

Treatment

- **Removal of adrenal tumor** if this is the cause.
- **Microsurgical removal** of hypertrophied pituitary elements to reduce ACTH secretion.
- **Partial or total adrenalectomy** followed by administration of adrenal steroids to compensate insufficiencies that develop.



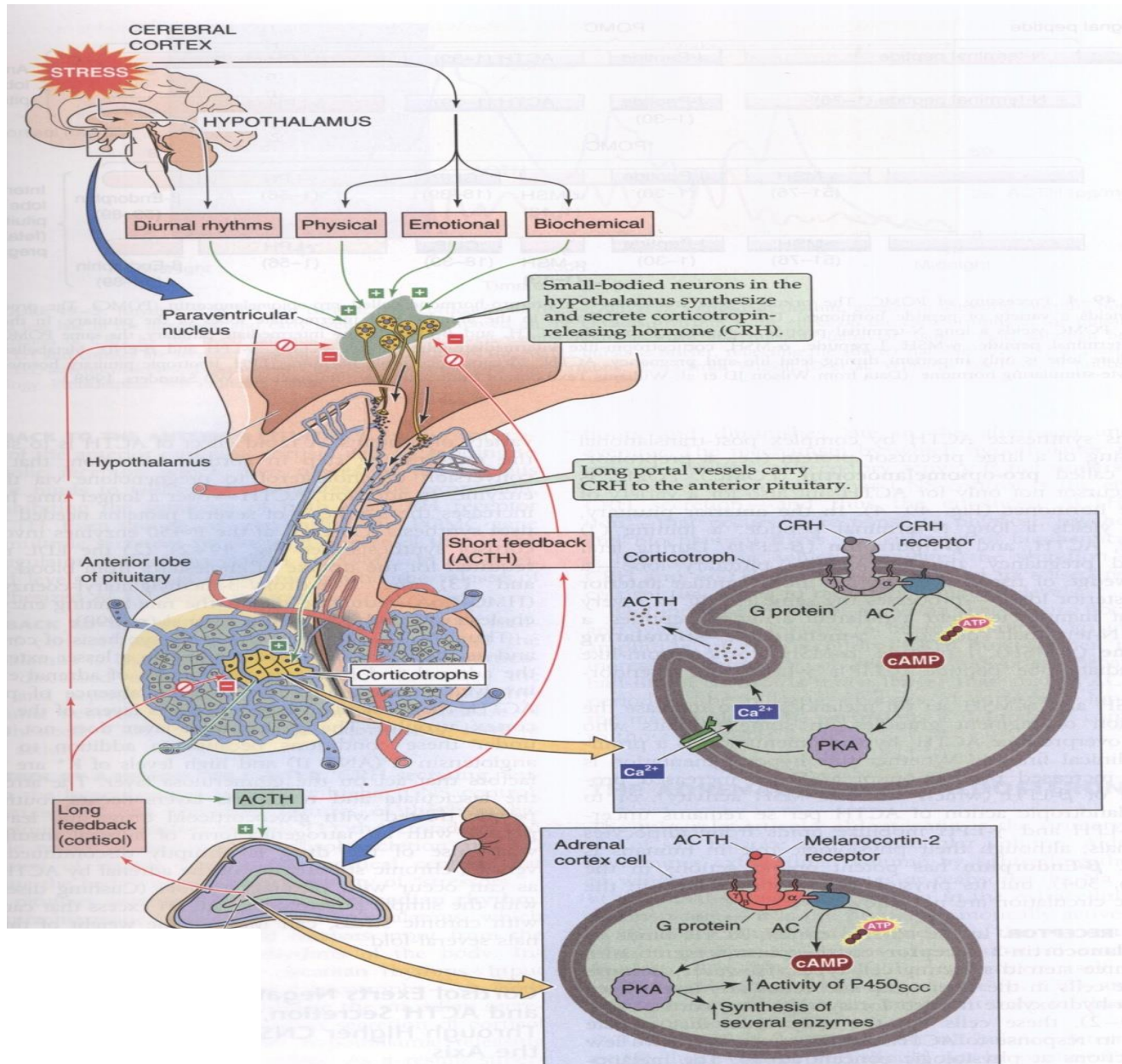
SUMMARY

- **GLUCOCORTICOIDS**
 - are hormones secreted from Adrenal cortex.
 - 90-95% **bound** to plasma protein.
 - **Main** glucocorticoids in humans: Cortisol and Corticosterone
- **CORTISOL**
 - Cortisol binding globulin (transcortin) and Albumin
 - There is a major burst for cortisol is in the early morning.
 - Cortisol is Metabolized in **liver** and excreted into **urine**.
 - Has a negative feedback on hypothalamus and anterior pituitary.
 - Physiological effect of cortisol (see slide 8 . 9)
- **EXCESS AMOUNT OF CORTISOL** either because of endogenous resources (from pituitary or adrenal cortex) or exogenous (Steroid therapy).
- **CUSHING'S (DISEASE OR SYNDROME)** affect carbohydrate metabolism by increasing glucose level, increasing protein catabolism, on bone leading to osteoporosis, redistribution of body fat in trunk and face, depression, and increase blood pressure.

Glucocorticoids	Mineralocorticoids
Secreted by cortical adrenal gland	
Receptor in the cytoplasm	
<ul style="list-style-type: none"> • Most of it is Cortisol 	<ul style="list-style-type: none"> • Most of it is Aldosterone.
<ul style="list-style-type: none"> • 90-95% bound to plasma protein 	<ul style="list-style-type: none"> • Less bound to plasma protein Than glucocorticoids.
<ul style="list-style-type: none"> • Under the control of ACTH 	<ul style="list-style-type: none"> • Under the control of ACTH, plasma potassium level, sodium and angiotensin II.



HPA axis (Male Slide)



1. Which one of the following is correct about Cushing

- A) Moon like face, hypoglycemia, osteoporosis
- B) Osteoporosis, Hypertension, Hyperglycemia
- C) Moon like face, Hypotension, Hyperglycemia
- D) Moon like face, Hypertension, Hypoglycemia

2. Which one of the following mechanisms of glucocorticoids increases the blood pressure:

- A) mineralocorticoid like action
- B) Sensitizes arterioles to action of noradrenaline
- C) Reabsorb Na and secret K
- D) All of the above

3. The major burst of cortisol secretion occurs in, and it decreases in.....:

- A) Early morning, Midnight
- B) Afternoon, Early morning
- C) Midnight, Afternoon

4. What is true about Cortisol:

- A) Vasodilator.
- B) Increase glucose level in the blood.
- C) Increase glycerol level in the blood.
- D) B and C

5. Protein formation reduced in all tissues except :

- A) Muscles
- B) Lymphatic Tissues
- C) Liver
- D) All of the above

1	B
2	D
3	A
4	D
5	C

THE END

If there are any Problems or Suggestions,
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THANK YOU



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