The Adrenal Gland, Stress

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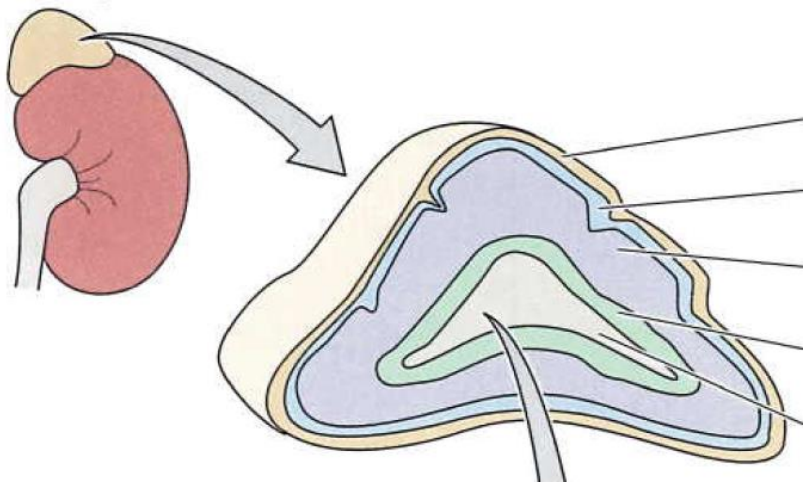
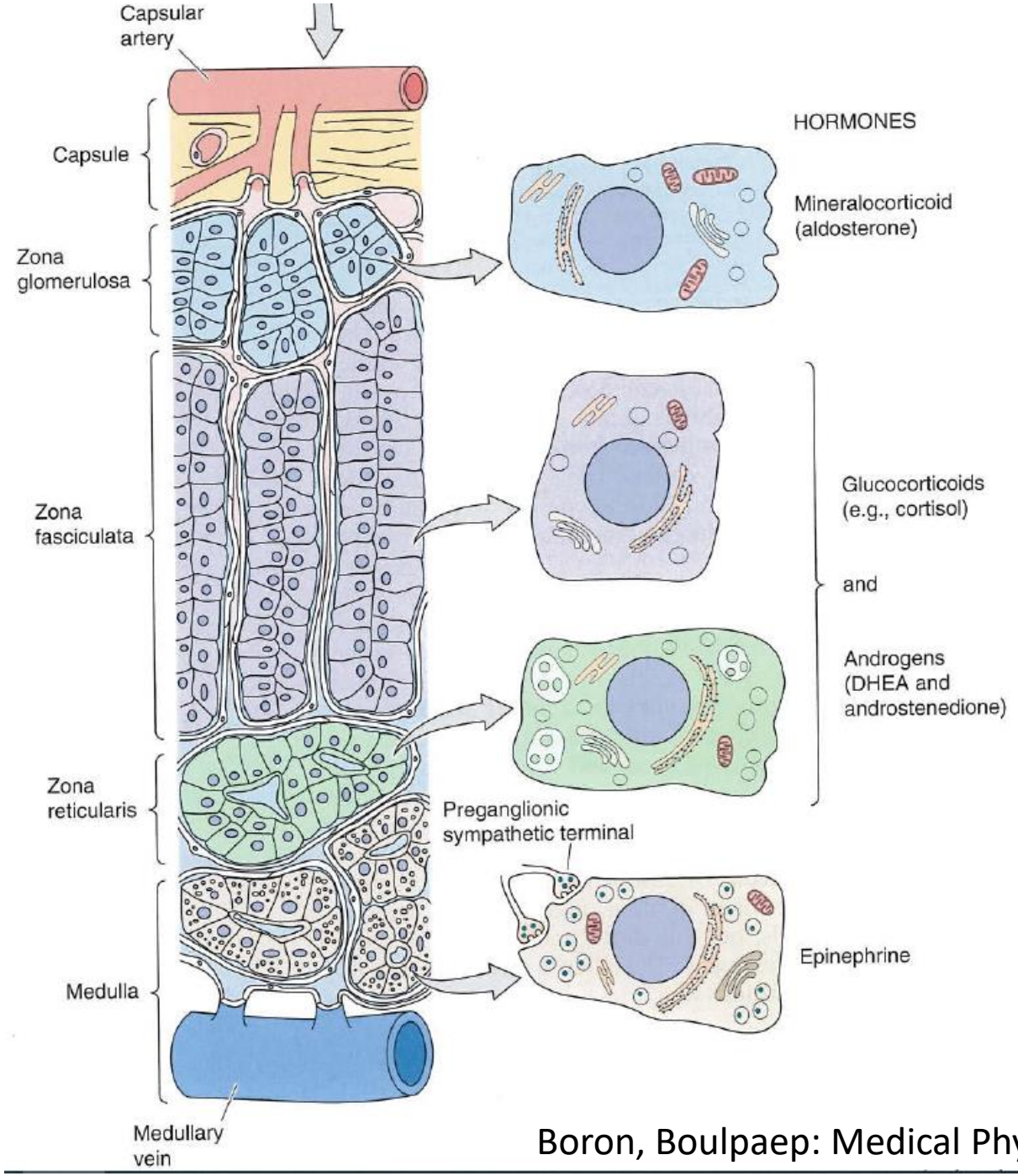
2022

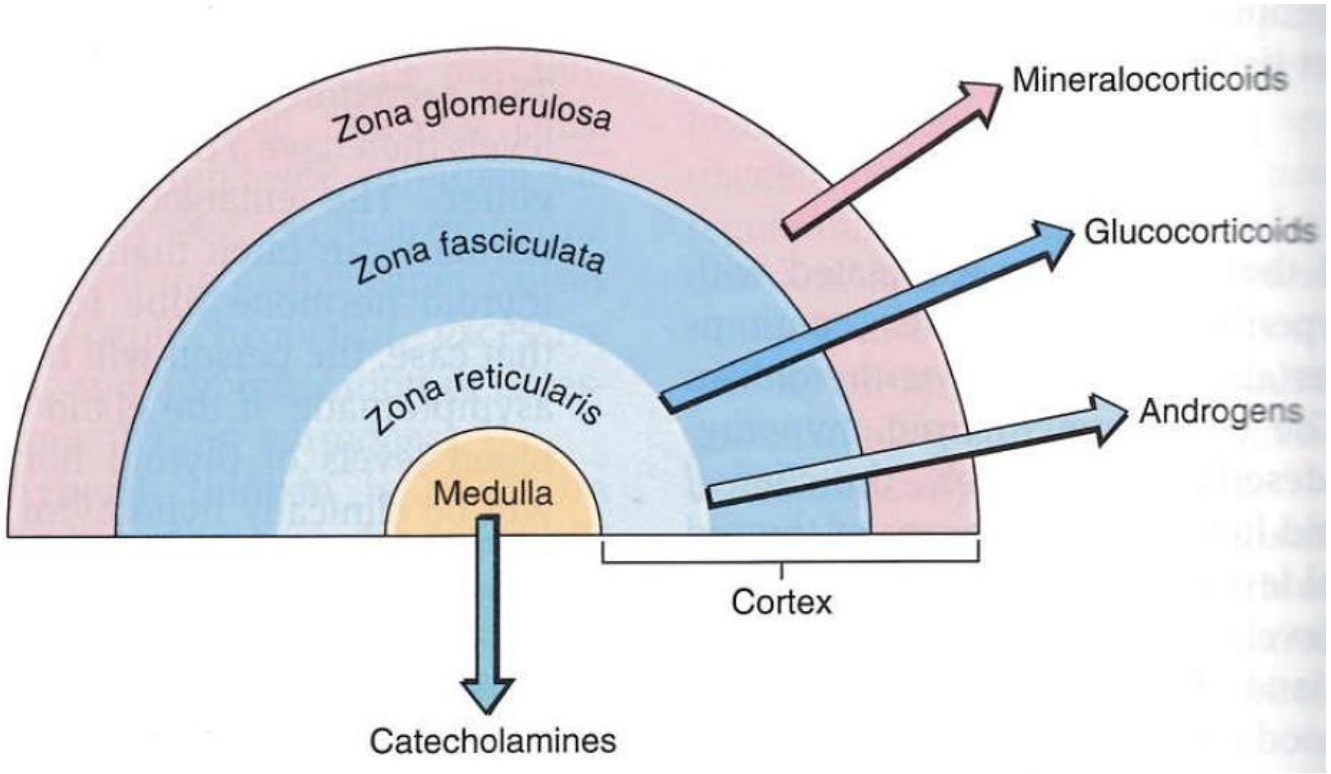


Anatomy of the adrenal gland



Boron, Boulpaep: Medical Physiology, 2003

Secretions of the adrenal medulla and adrenal cortex



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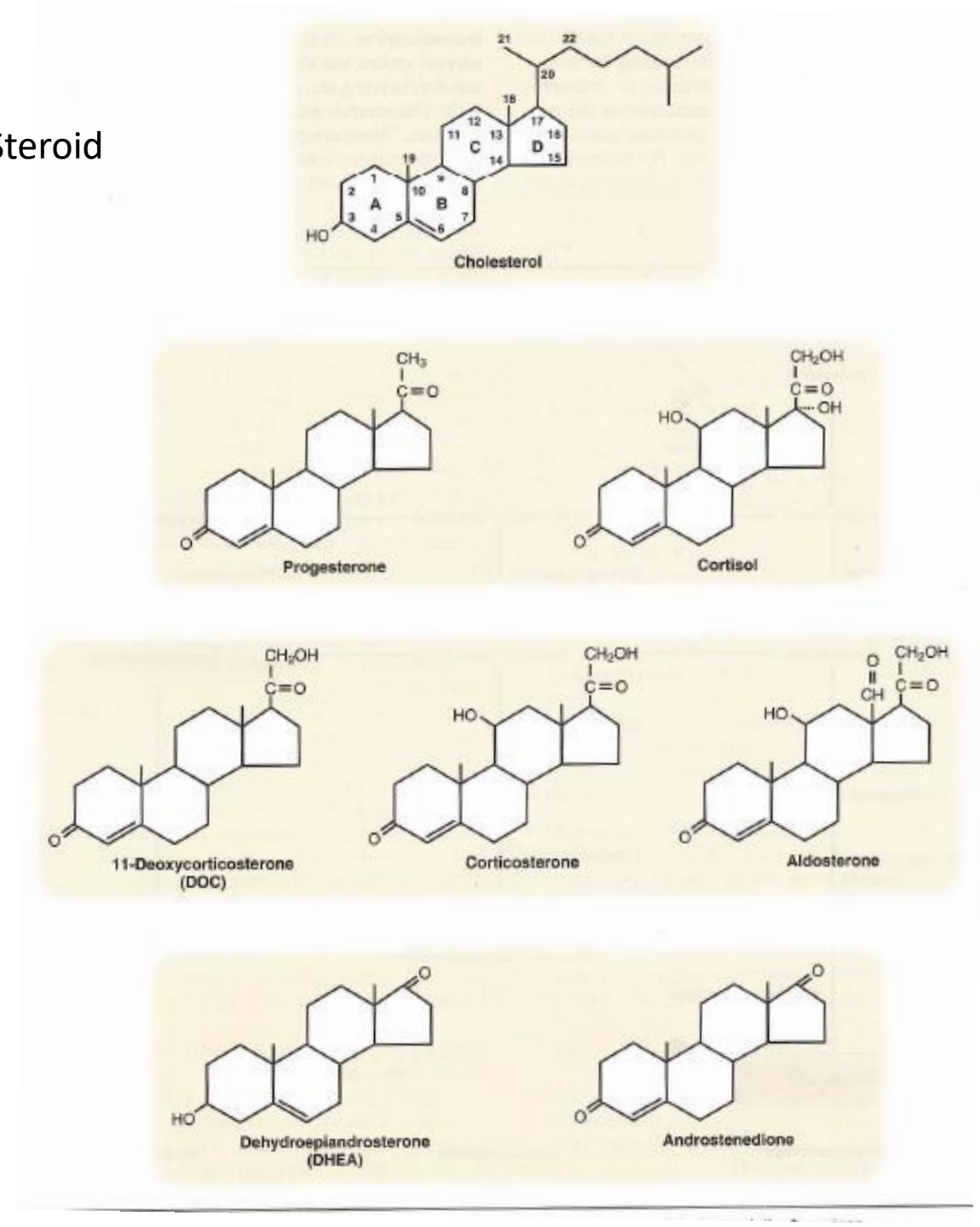
Structures of Adrenocortical Steroid Hormones



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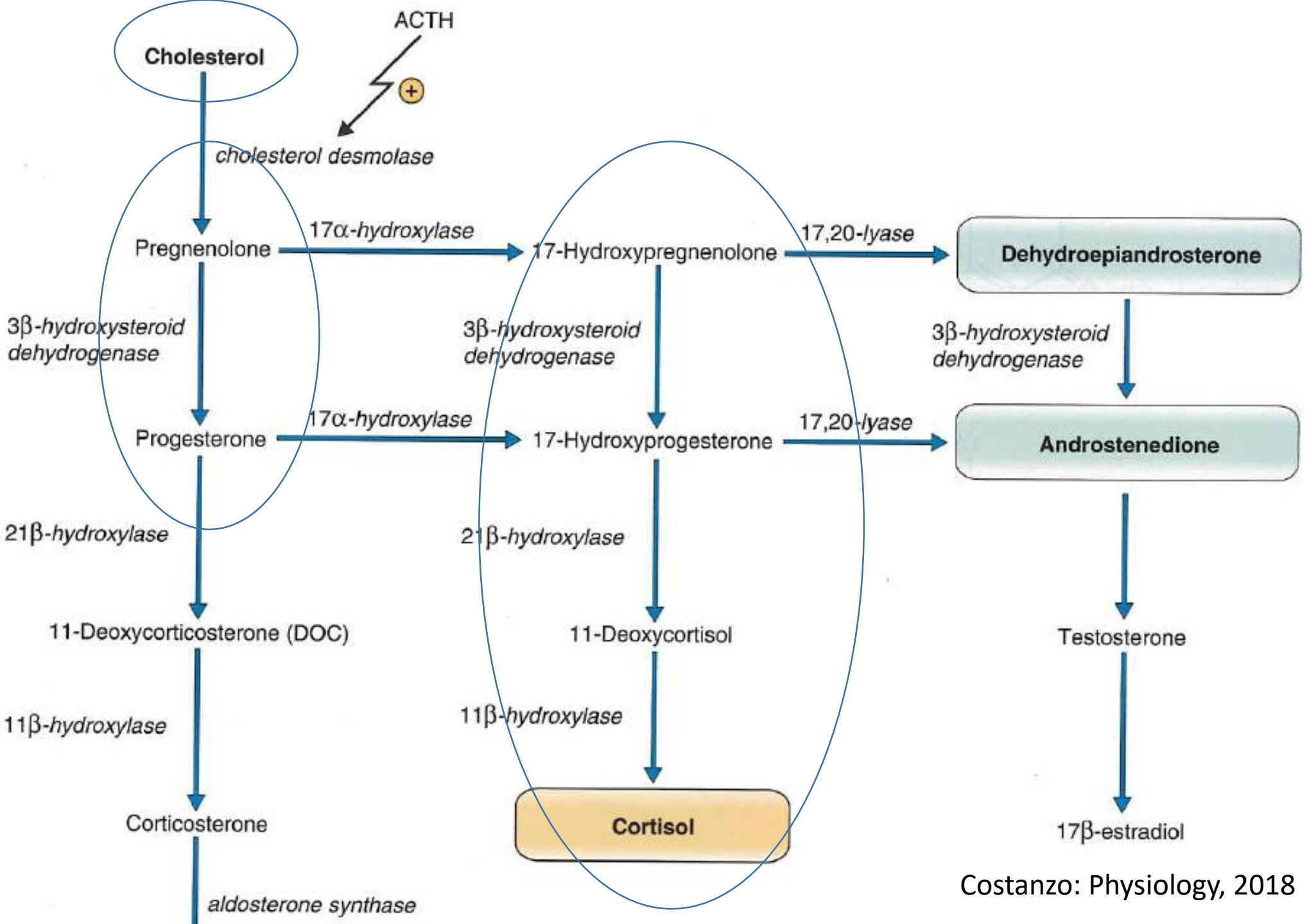
Biosynthesis of glucocorticoid



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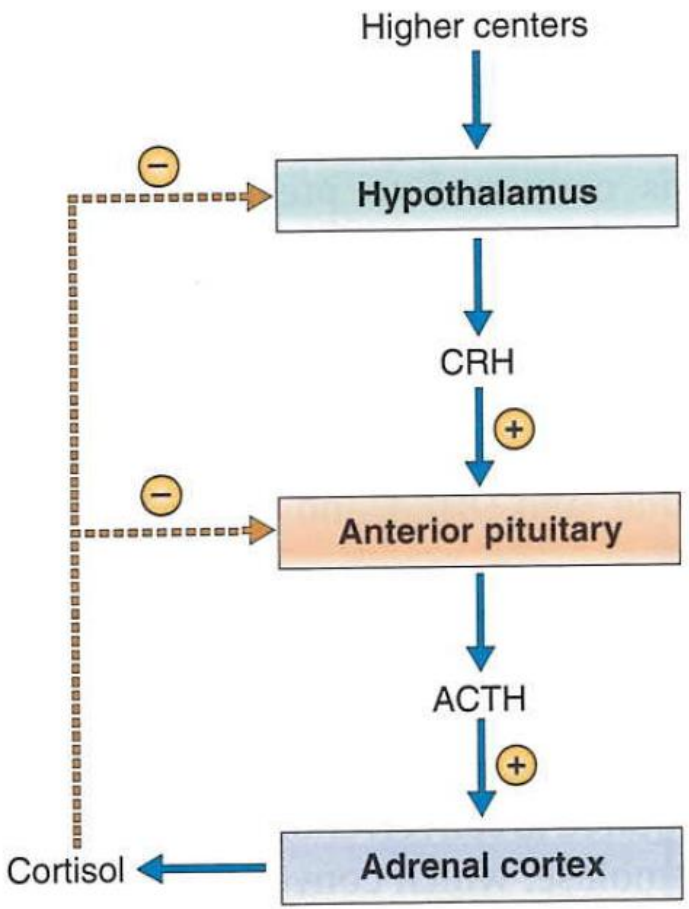
Glucocorticoids - regulation
The hypothalamic-pituitary-adrenocortical axis



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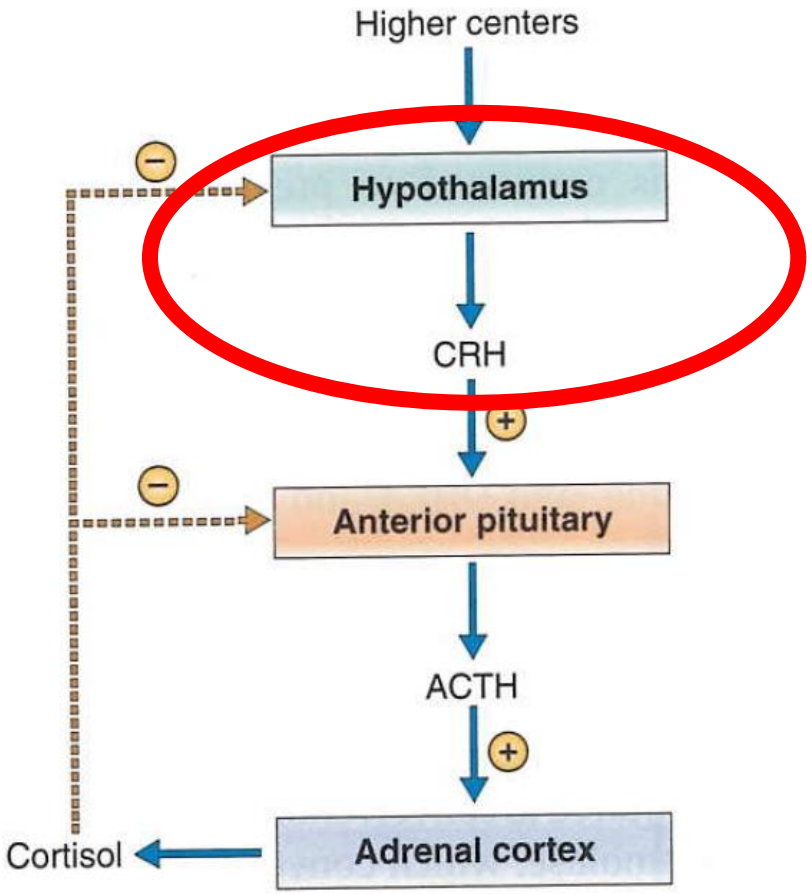

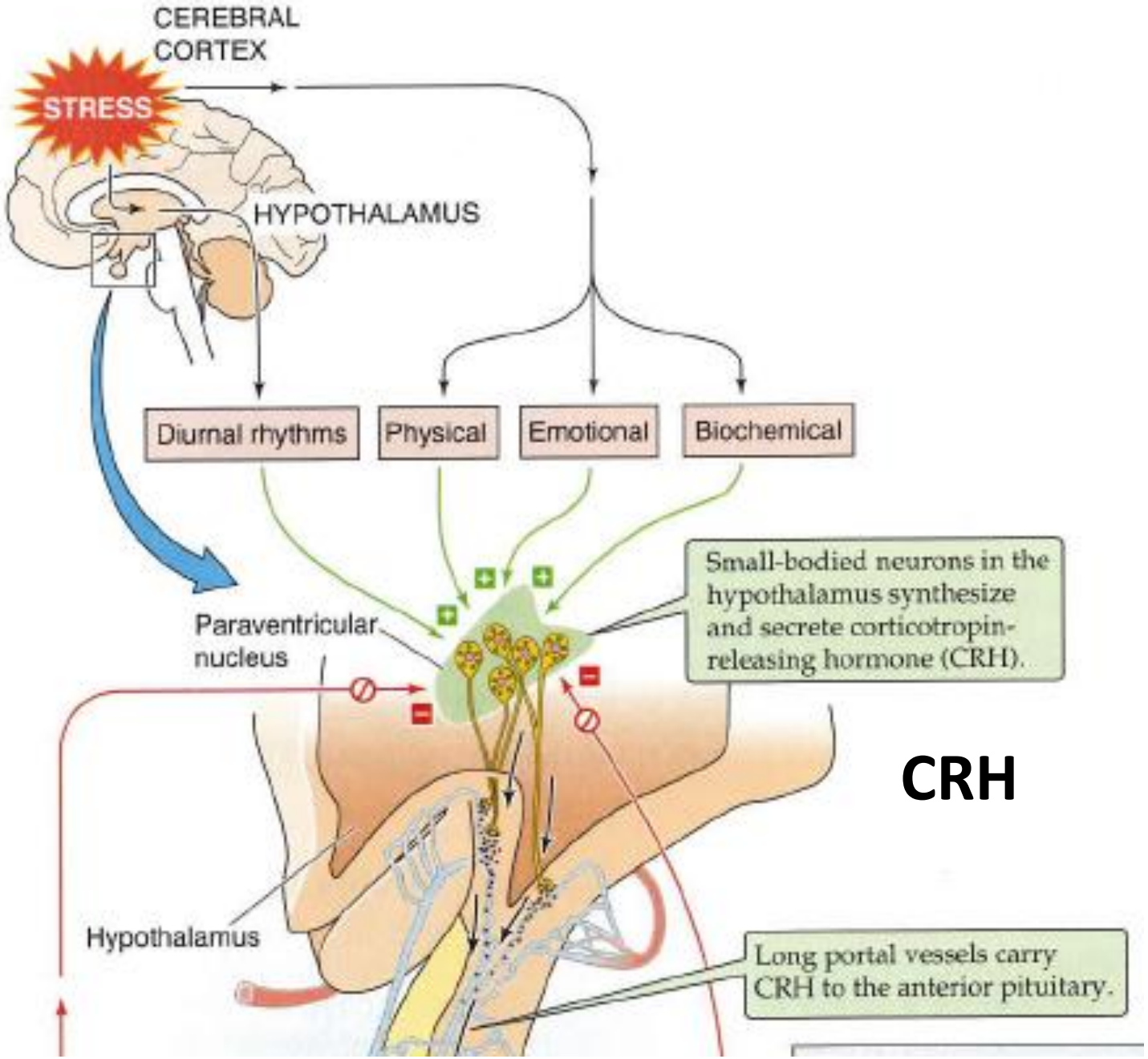

CRH

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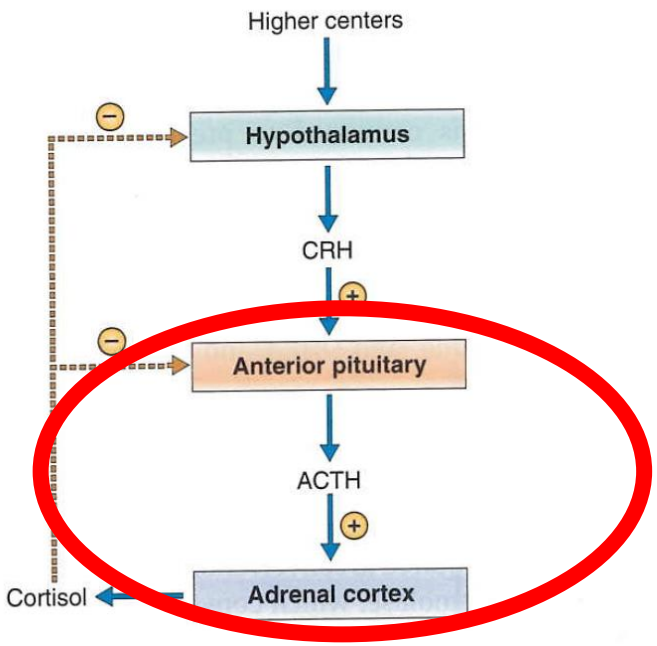
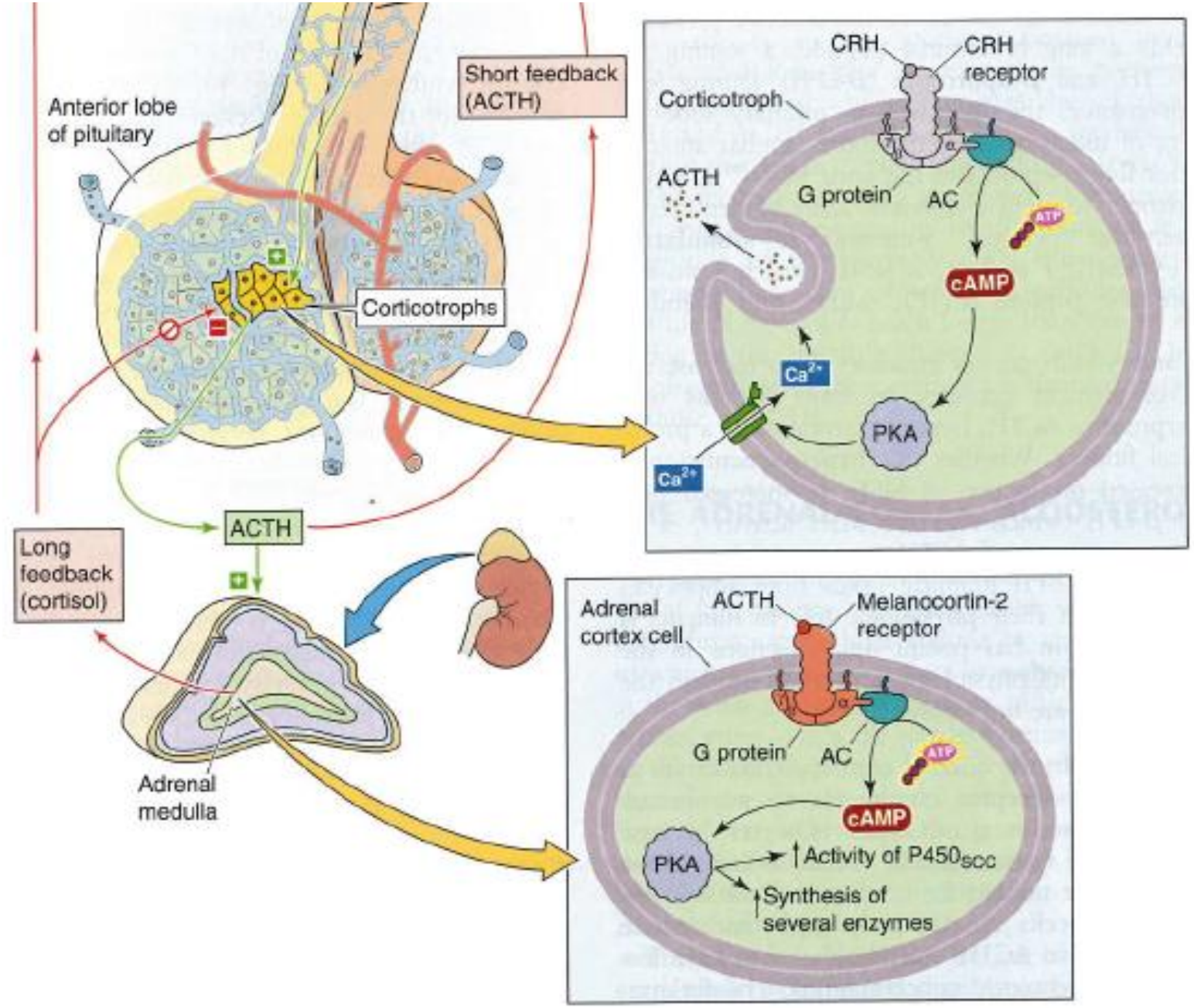
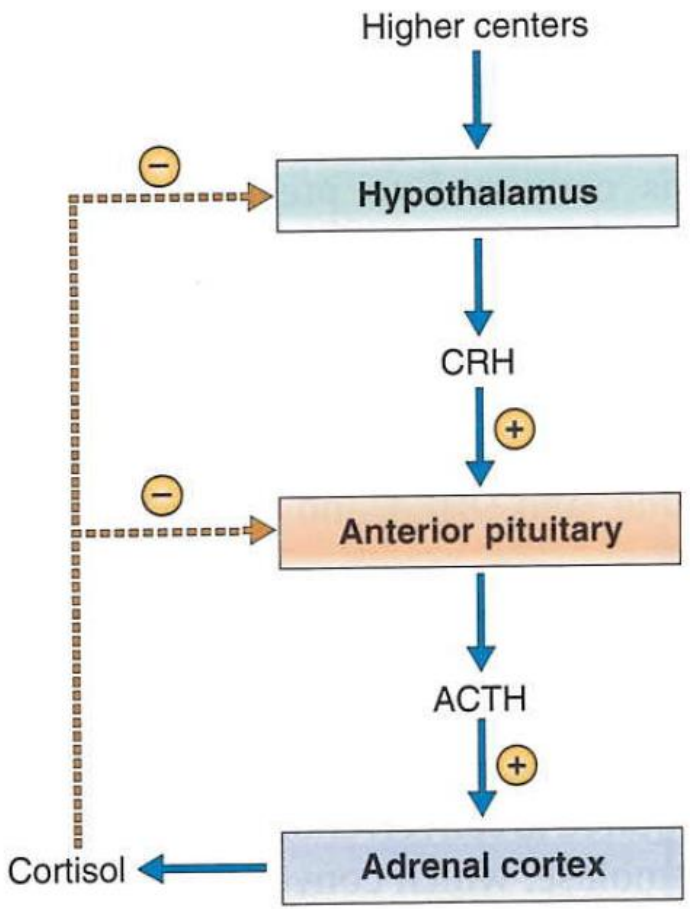
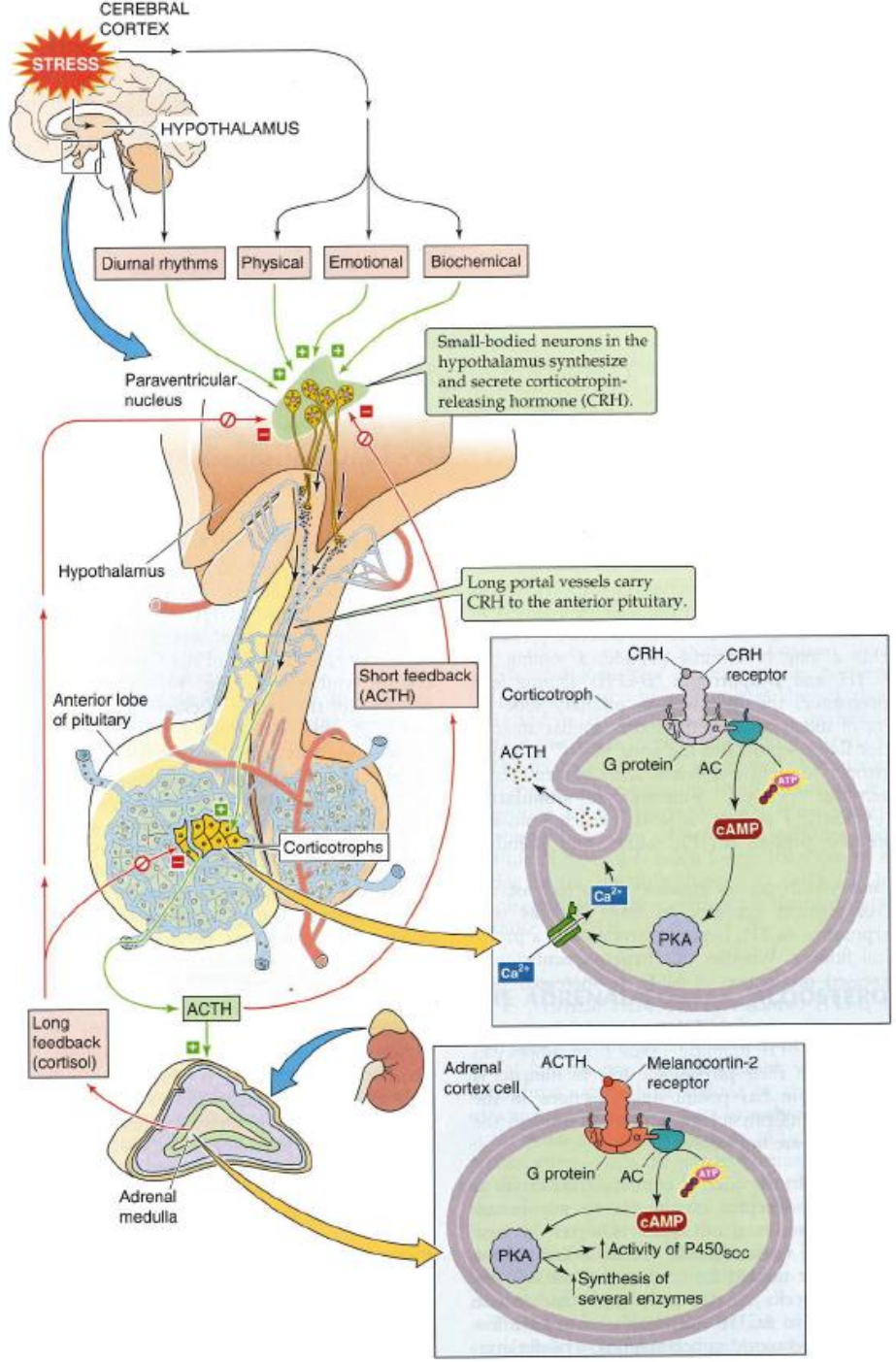
The hypothalamic-pituitary-adrenocortical axis



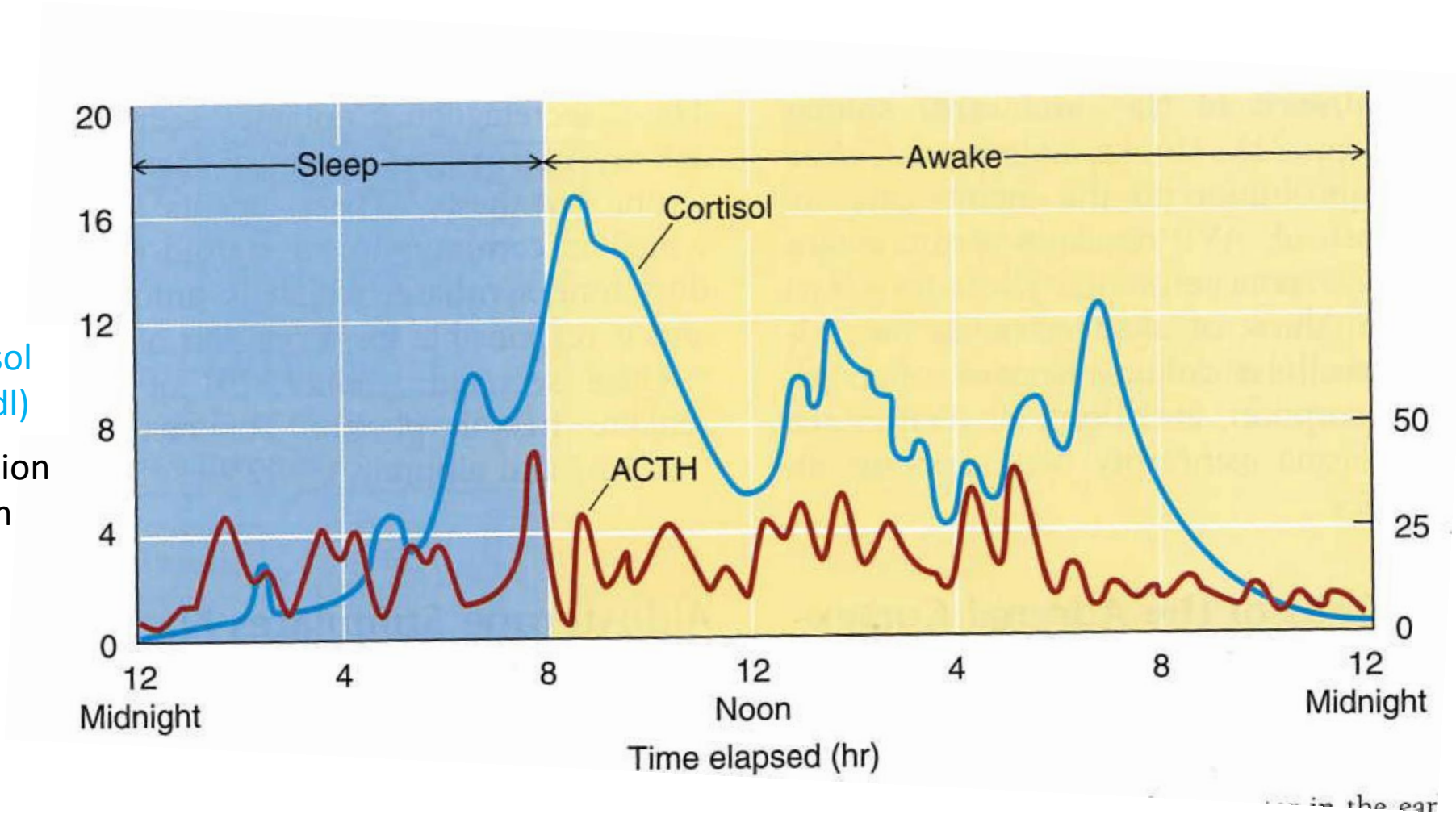


Negative feedback of cortisol
on hypothalamic-pituitary (CRH-ACTH) axis





Diurnal secretion of
ACTH and cortisol



Cortisol
(mg/dl)

Pulsatile secretion
Diurnal pattern

ACTH
(pg/ml)

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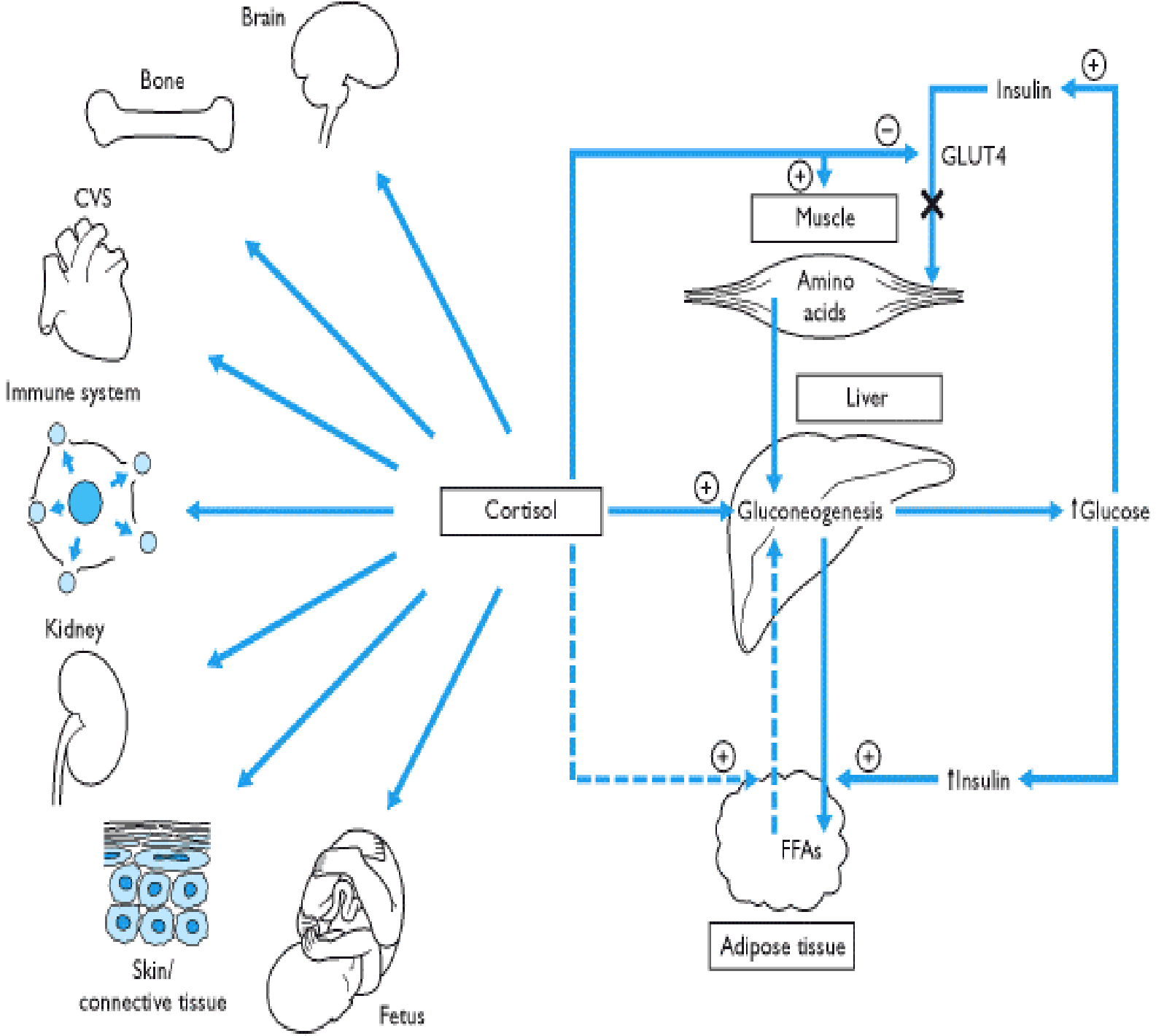
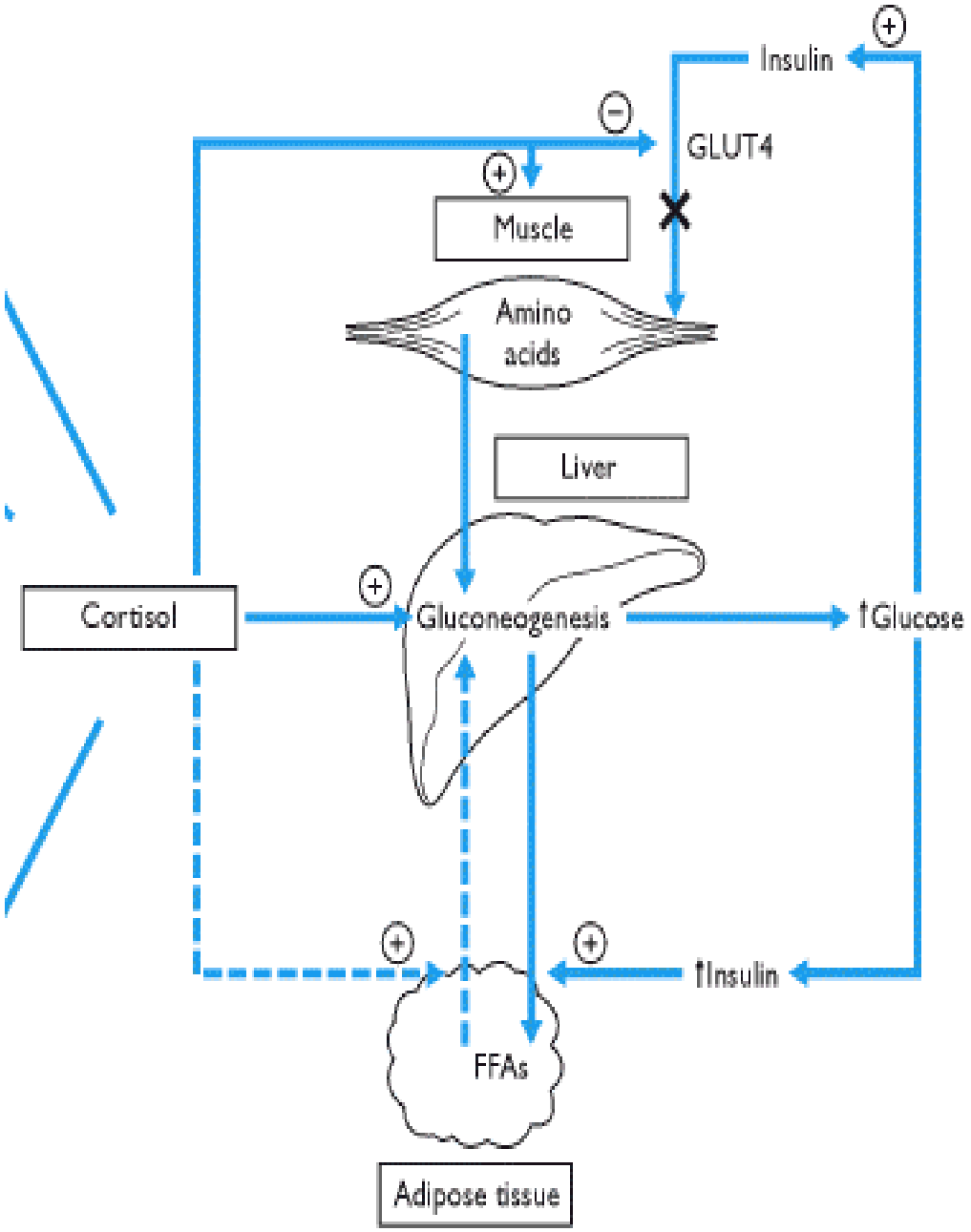
The Many Actions of Glucocorticoids





The Many Actions of Glucocorticoids

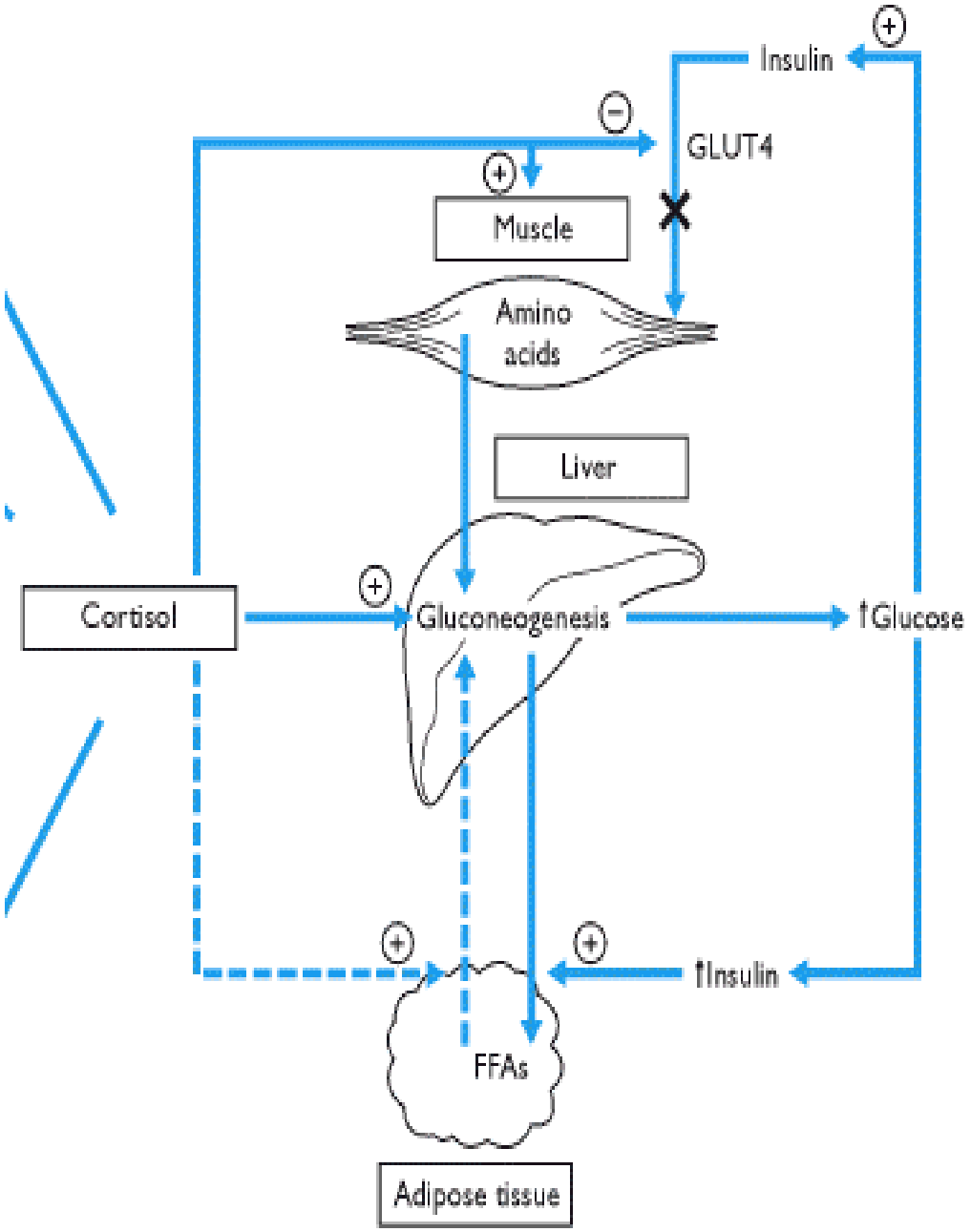
- **Overall effect is to increase blood glucose concentrations.**
- **Muscle – proteocatabolism - AA**
- **Adipose tissue – lipolysis – glycerol (FFA)**
- **Liver – gluconeogenesis**

- **Cortisol - Decreases insulin sensitivity**

SURVIVAL DURING FASTING

HYPOCORTISOLISM (Addison disease) –

HYPER (Cushing syndrome) -



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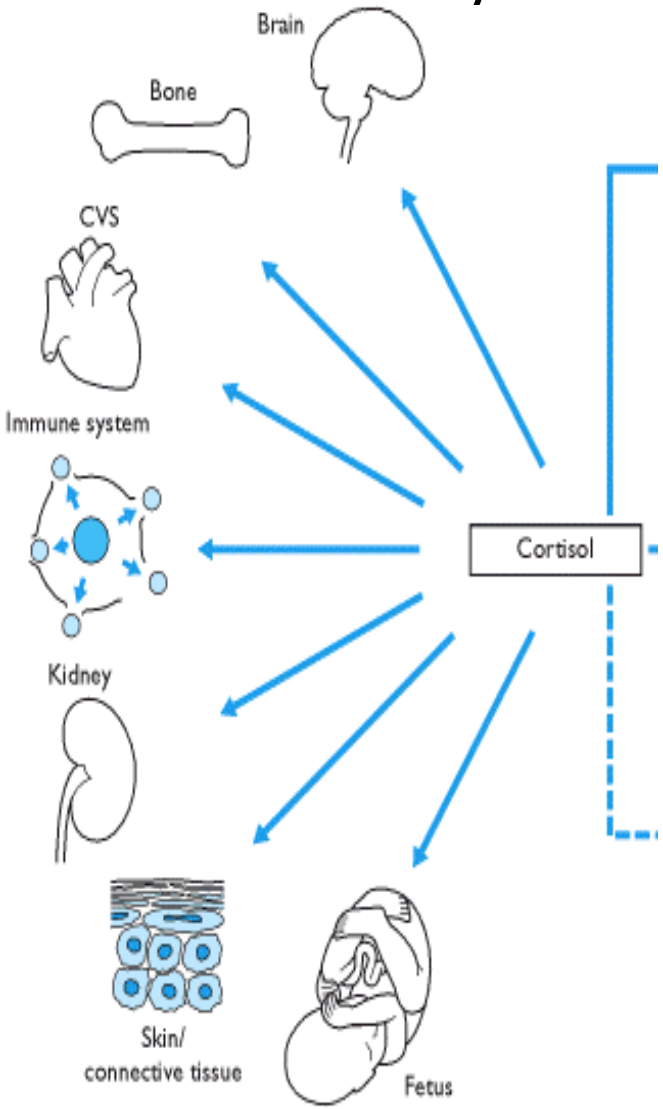
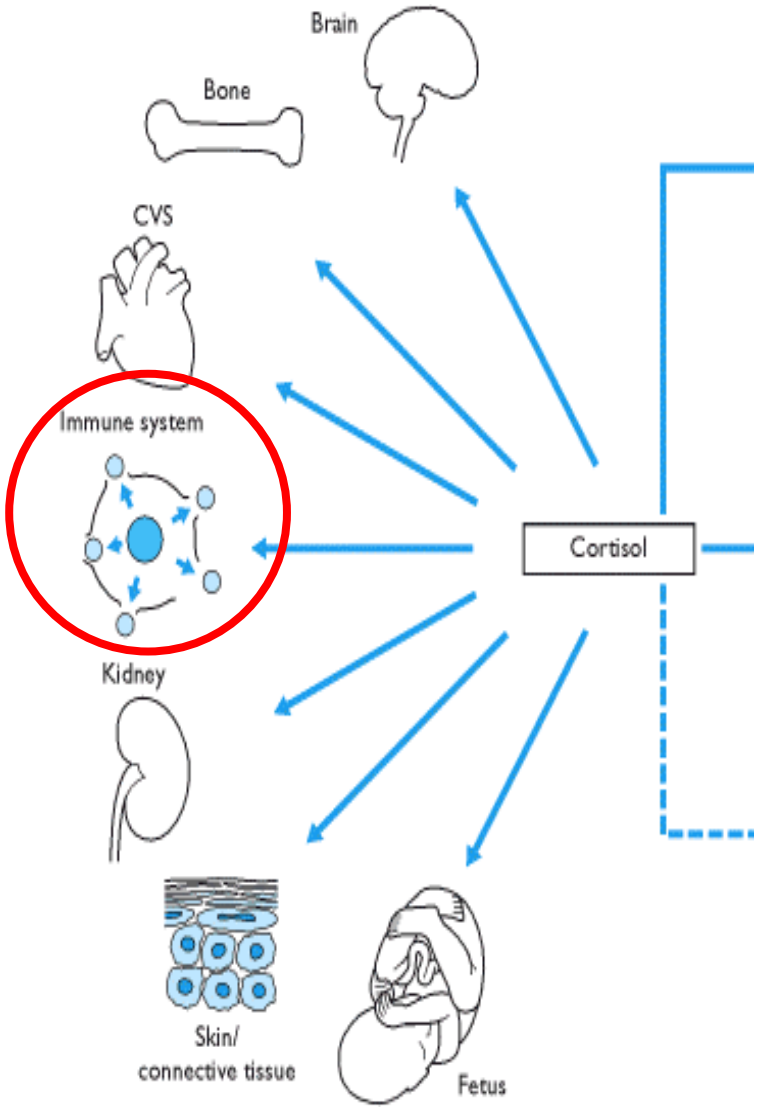
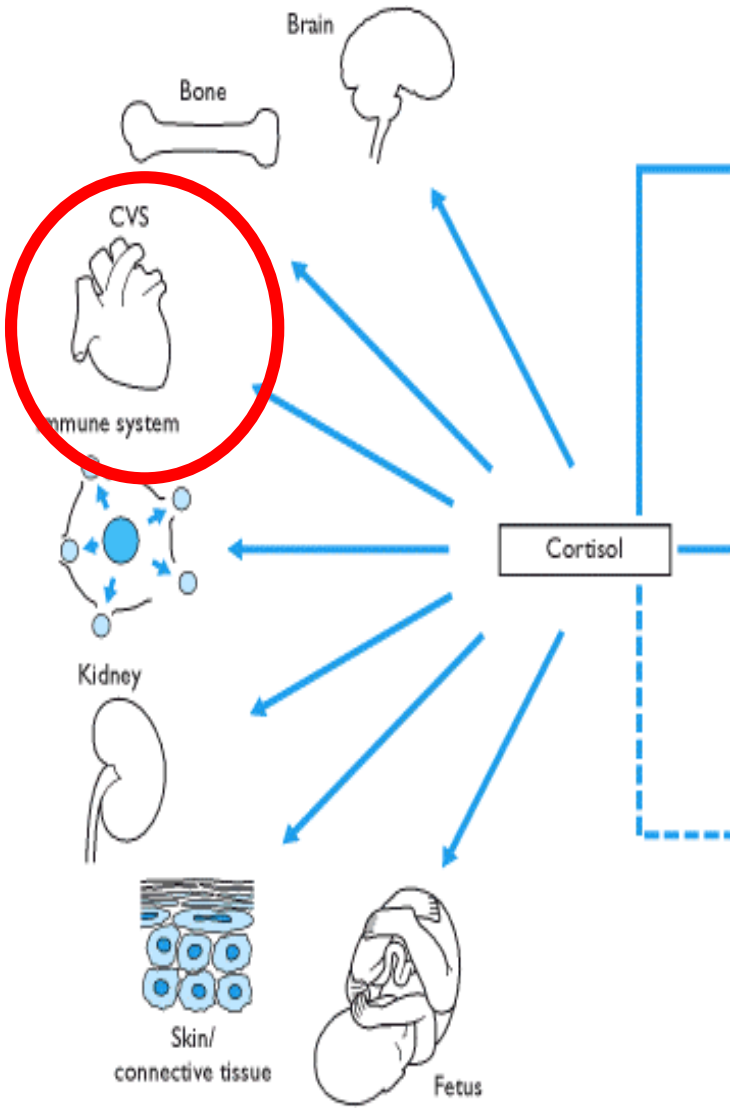


- **Anti-inflamatory effects**
- 1. Cortisol induces the synthesis of LIPOCORTIN – inhibit synthesis of prostaglandins and leukotriens
- 2. Cortisol inhibits the production of IL-2.
- 3. Cortisol inhibits the release of histamin and serotonin from mast cells and

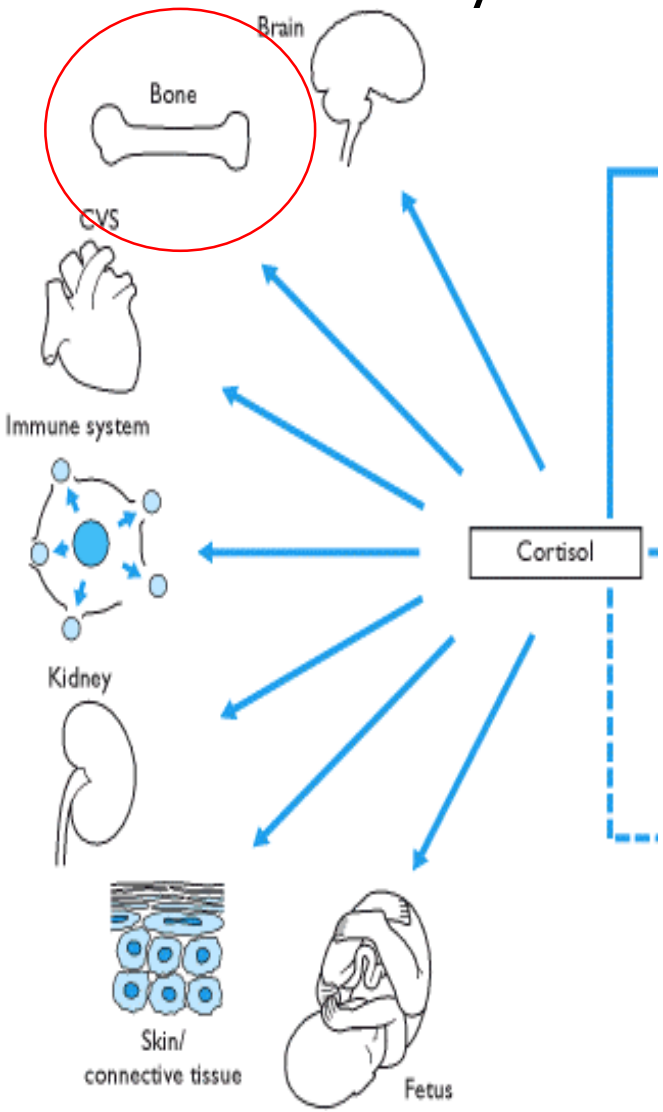


- **Cortisol supress immune responses.**
- glucorticocoids reduce the number of circulating thymus derived lymphocytes (T- cells) and as a result the recruitment of B lymphocytes.
- They also affect the numbers and functions of circulating neutrophils, eosinophils and fibroblasts
- The net result is to reduce both cellular and humoral immunity.

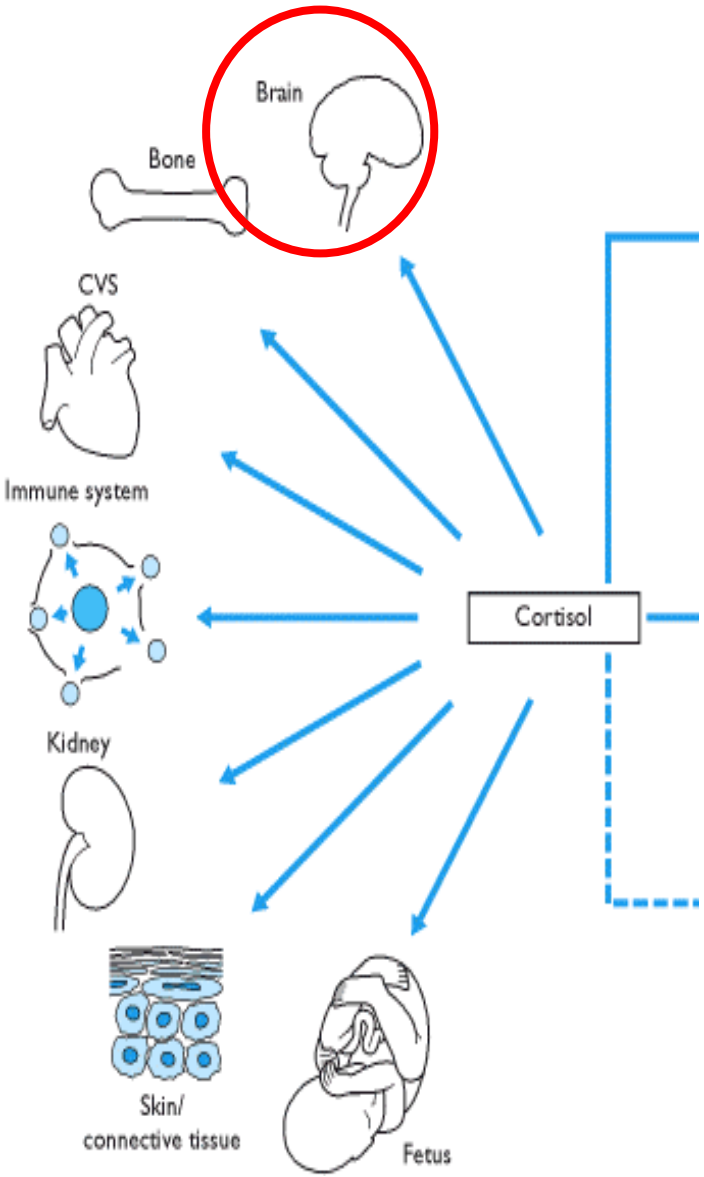


- **In the cardiovascular system**, it is required for sustaining normal blood pressure by maintaining normal myocardial function and the responsiveness of arterioles to catecholamines and angiotensin II.

The Many Actions of Glucocorticoids

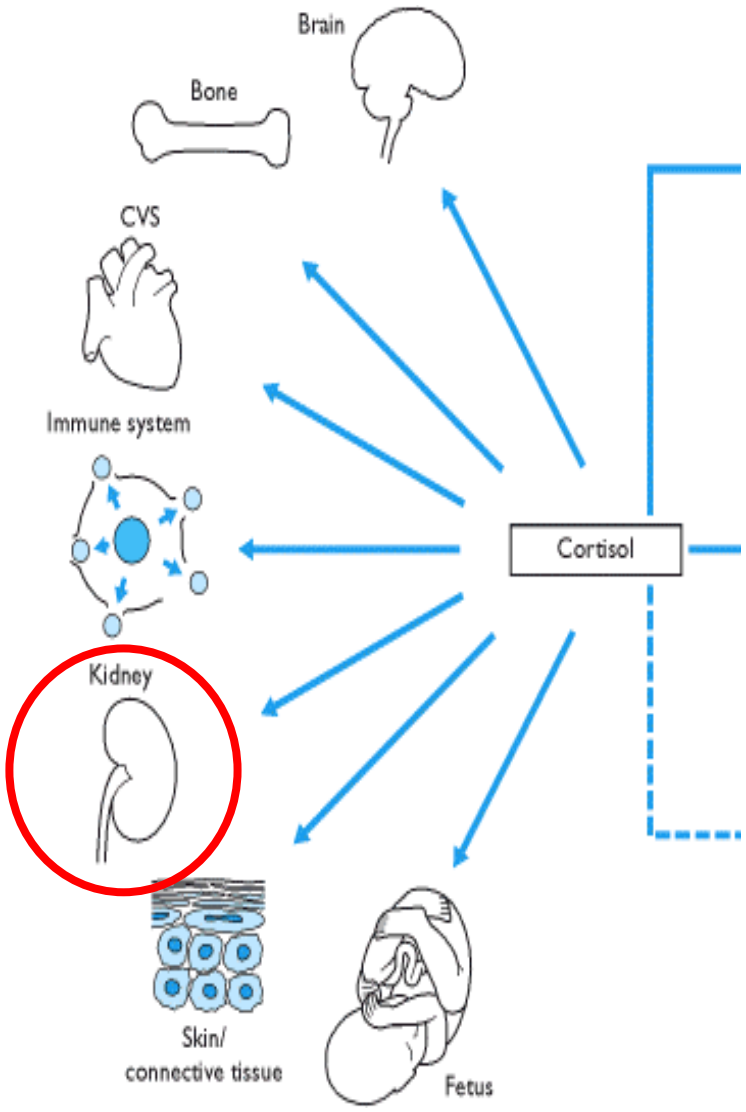


- **Inhibition of bone formation**
- Cortisol decreases osteoblast function and decreases new bone formation; decrease synthesis of type I collagen.
- Furthermore, glucocorticoids decrease gut calcium absorption thus adversely affecting calcium balance.



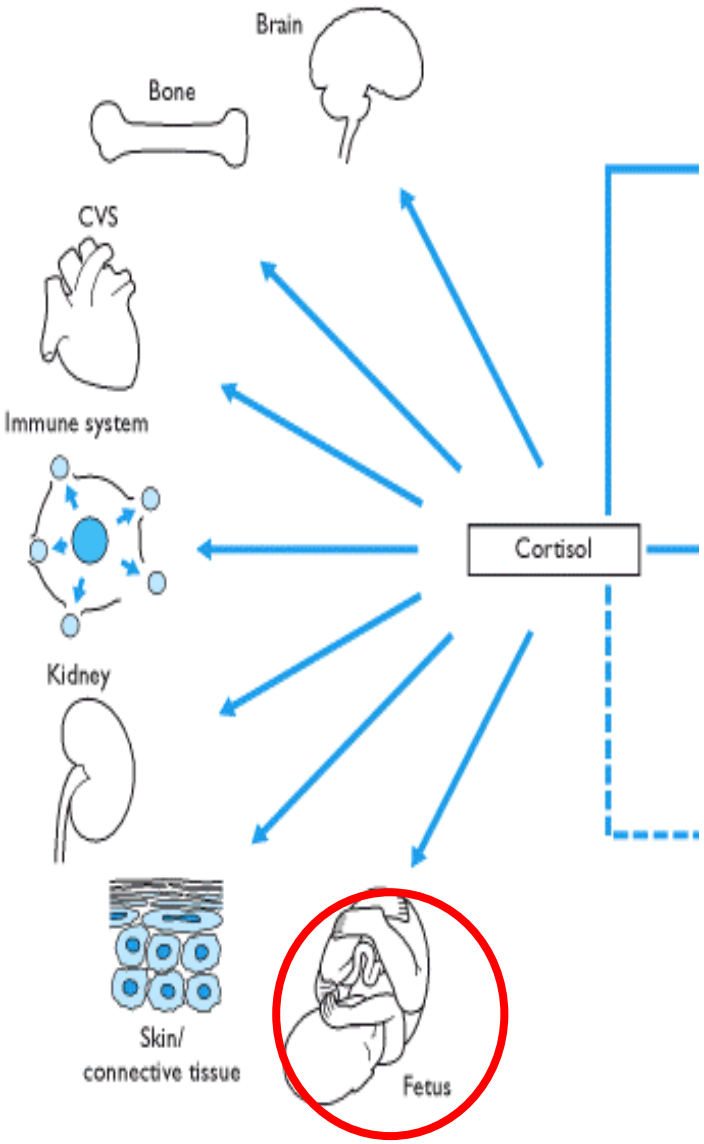
- In the **CNS**, cortisol can alter the excitability of neurons, induce neuronal death (particularly in the hippocampus) and can affect the mood and behavior of individuals.

- Depression may be a feature of glucocorticoid therapy.



- **In the kidney**, cortisol increases glomerular filtration rate by increasing glomerular blood flow and increases phosphate excretion by decreasing its reabsorption in the proximal tubules.

- In excess, cortisol has aldosterone-like effects in the kidney causing salt and water retention.



- Cortisol also facilitates **fetal maturation** of the central nervous system, retina, skin, gastrointestinal tract and lungs.

- It is particularly important in the synthesis of alveolar surfactant which occurs during the last weeks of gestation.

Actions of Adrenocortical Steroids

Require transcription of DNA, synthesis of specific mRNA, and induction of new protein synthesis

Essencial for life

Essencial for life

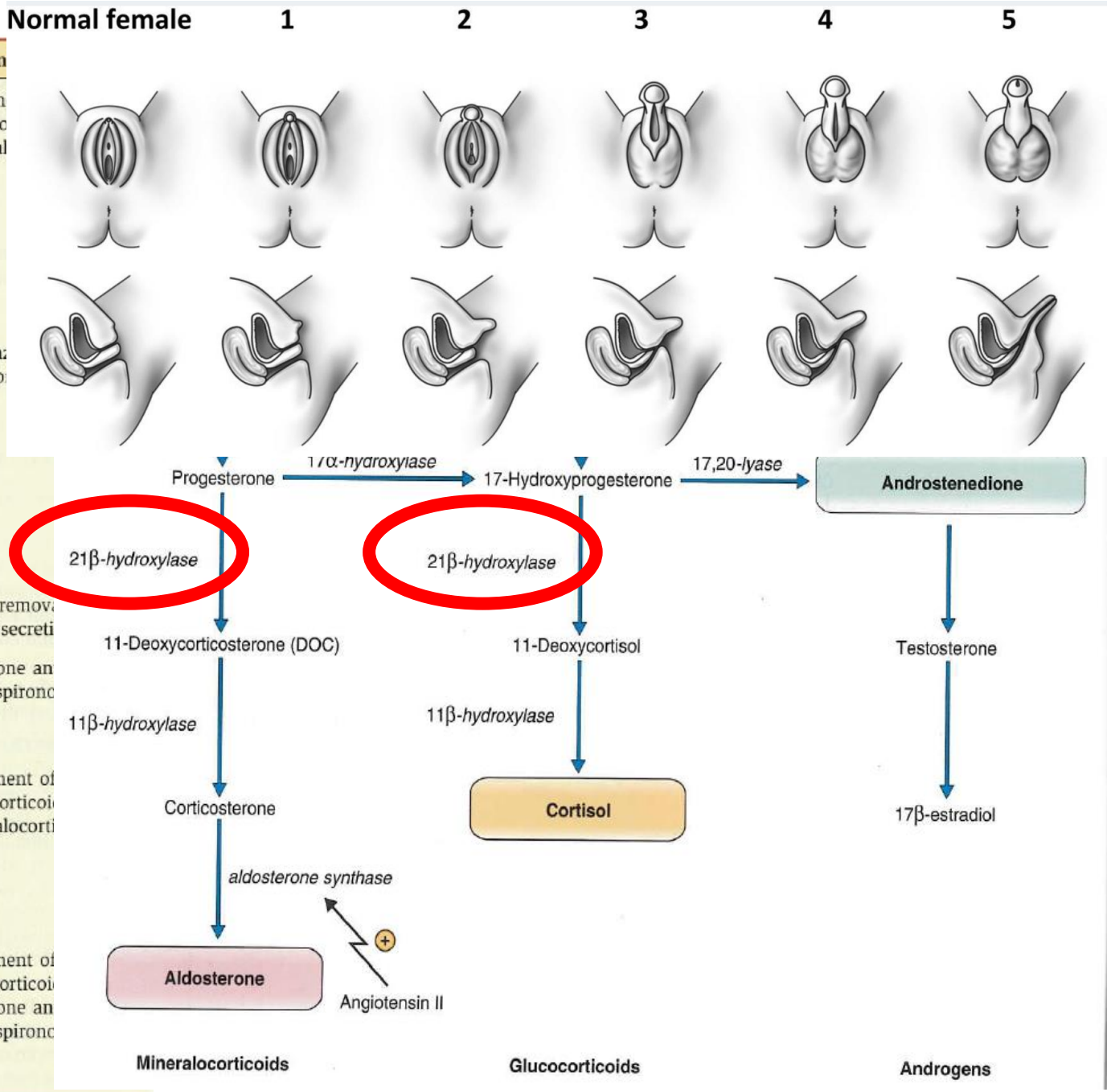
Actions of Glucocorticoids	Actions of Mineralocorticoids	Actions of Adrenal Androgens
Increase gluconeogenesis	Increase Na^+ reabsorption	Females: stimulate growth of pubic and axillary hair; stimulate libido
Increase proteolysis (catabolic)	Increase K^+ secretion	Males: same as testosterone
Increase lipolysis	Increase H^+ secretion	
Decrease glucose utilization		
Decrease insulin sensitivity		
Inhibit inflammatory response		
Suppress immune response		
Enhance vascular responsiveness to catecholamines		
Inhibit bone formation		
Increase GFR		
Decrease REM sleep		

GFR, Glomerular filtration rate; *REM*, rapid eye movement.

TABLE 9.12 Pathophysiology of the Adrenal Cortex

Disease	Clinical Features	ACTH Levels	Treatmen
Addison Disease (Primary Adrenocortical Insufficiency)	Hypoglycemia Anorexia, weight loss, nausea, vomiting Weakness Hypotension Hyperkalemia Metabolic acidosis Decreased pubic and axillary hair in females Hyperpigmentation	Increased (negative feedback effect of decreased cortisol)	Replacem glucocc mineral
Cushing Syndrome (e.g., Primary Adrenal Hyperplasia)	Hyperglycemia Muscle wasting Central obesity Round face, supraclavicular fat, buffalo hump Osteoporosis Striae Virilization and menstrual disorders in females Hypertension	Decreased (negative feedback effect of increased cortisol)	Ketoconaz Metyrapo
Cushing Disease (Excess ACTH)	Same as Cushing syndrome (see earlier)	Increased	Surgical remov ACTH-secreti
Conn Syndrome (Aldosterone-Secreting Tumor)	Hypertension Hypokalemia Metabolic alkalosis Decreased renin levels	—	Aldosterone an (e.g., spironc Surgery
21β-Hydroxylase Deficiency	Virilization in females Early acceleration of linear growth Early appearance of pubic and axillary hair Symptoms of deficiency of glucocorticoids and mineralocorticoids	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoi mineralocorti
17α-Hydroxylase Deficiency	Lack of pubic and axillary hair in females Symptoms of deficiency of glucocorticoids Symptoms of excess mineralocorticoids	Increased (negative feedback effect of decreased cortisol)	Replacement of glucocorticoi Aldosterone an (e.g., spironc

ACTH, Adrenocorticotropic hormone.



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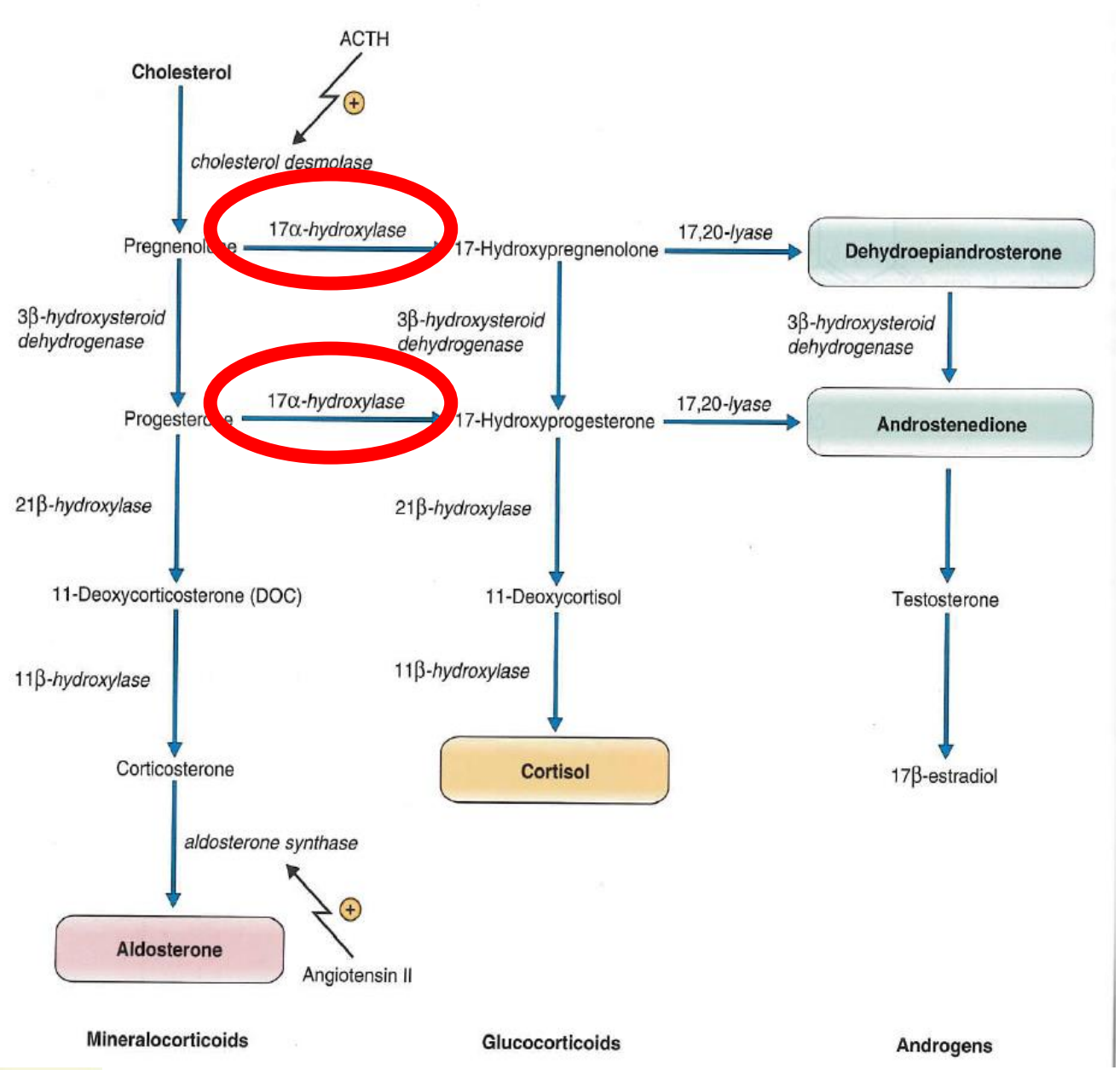


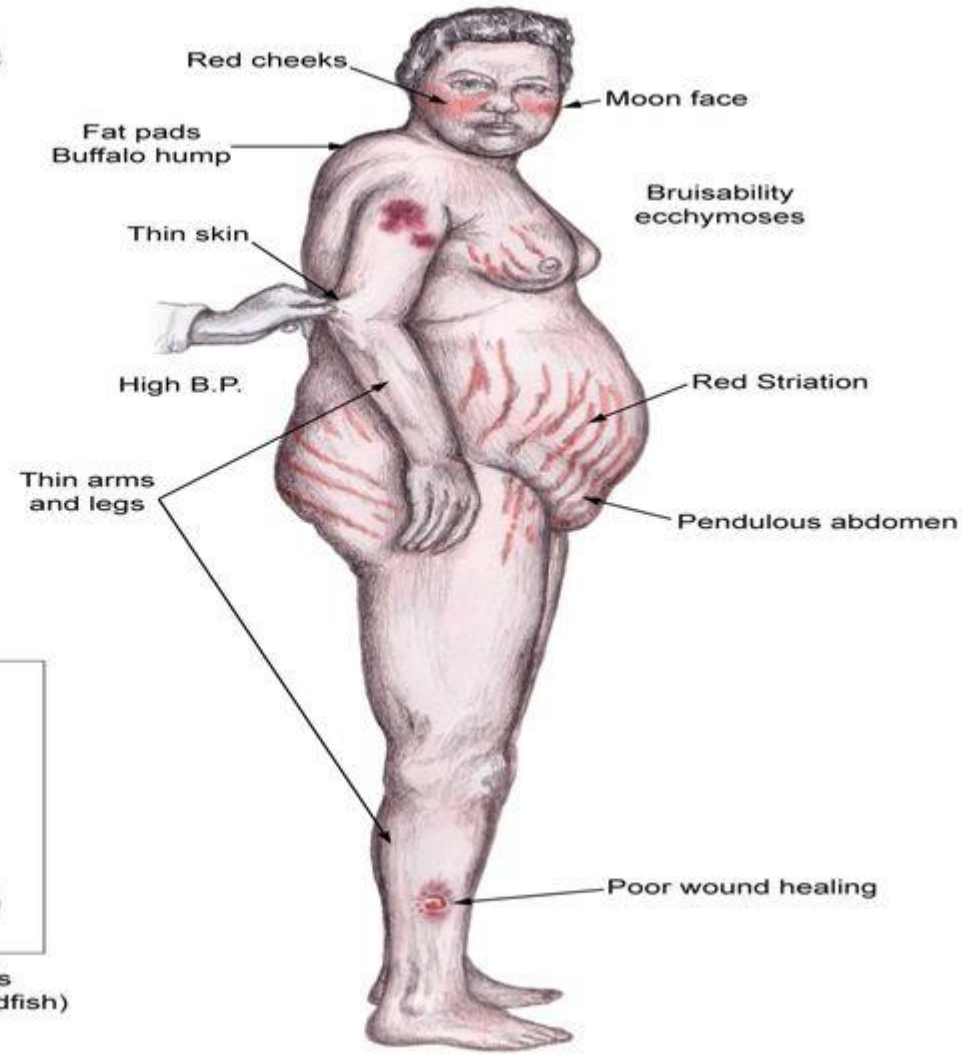
Therapy with Glucocorticoids

CUSHING Syndrome

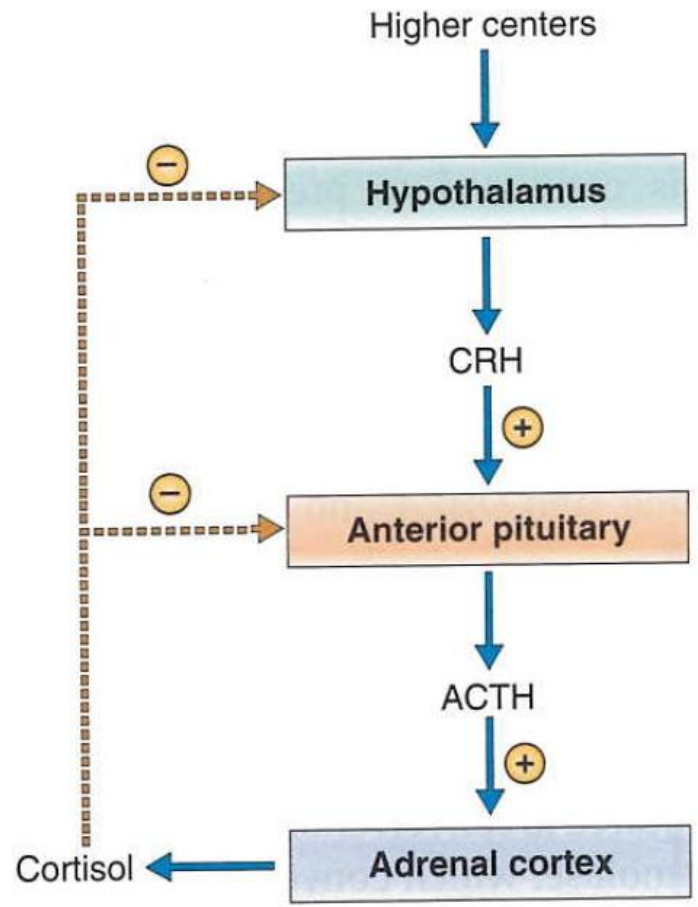
Background

Cushing syndrome is caused by prolonged exposure to elevated levels of either endogenous glucocorticoids or exogenous glucocorticoids

Osteoporosis compressed (codfish) vertebrae

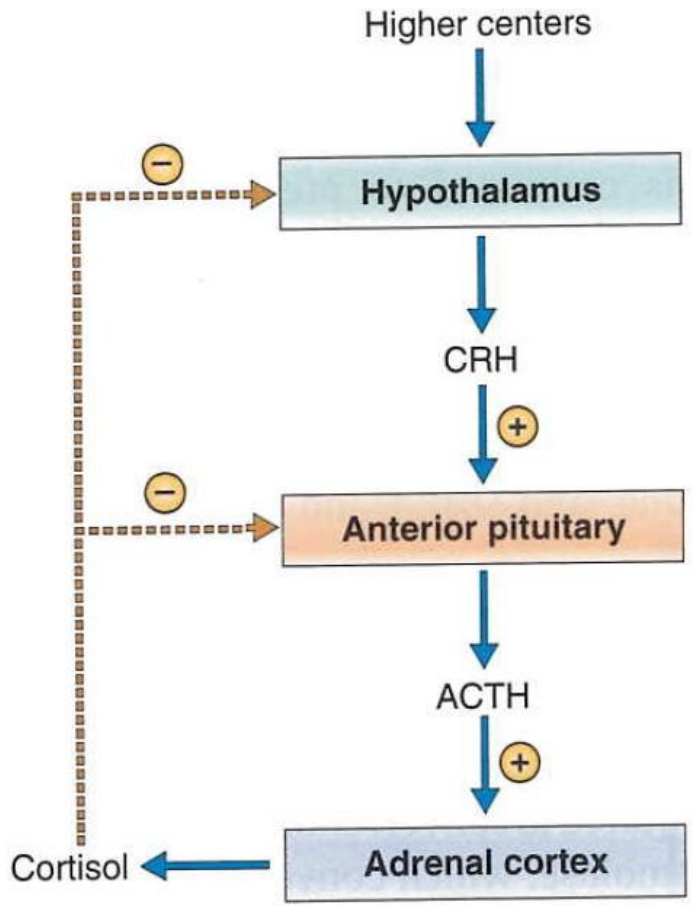


Why the glucocorticoid therapy must not be suddenly interrupted?



Why the glucocorticoid therapy must not be suddenly interrupted?

Glucocorticoid drugs (similarly as cortisol itself) inhibit hypothalamic CRH and pituitary ACTH.
Tapering must be done carefully to avoid possible cortisol deficiency resulting from hypothalamic-pituitary-adrenal axis (HPA) suppression during the period of steroid therapy.



Function of the Adrenal Medullae

Stimulation of the sympathetic nerves to adrenal medullae – epinephrine and noreponephrine released into circulating blood
epinephrine 80% and noreponephrine 20%

Circulating epinephrine and noreponephrine - almost the same effect as direct sympathetic stimulation, except that the effect is longer (2 – 4 minutes)

Noreponephrine
- constriction of essentially all the blood vessels of the body
- increased aktivity of the heart
- inhibition of GIT
- dilation of the pupils of the eyes …

Epinephrine differs in following respects
1. Greater effect in stimulating the beta receptor – greater effect on cardiac stimulation
2. Only weak constriction of the blood vessels in the muscles
3. Greater metabolic effect on tissues

Value of the Adrenal Medullae to the Function of the Sympathetic Nervous System

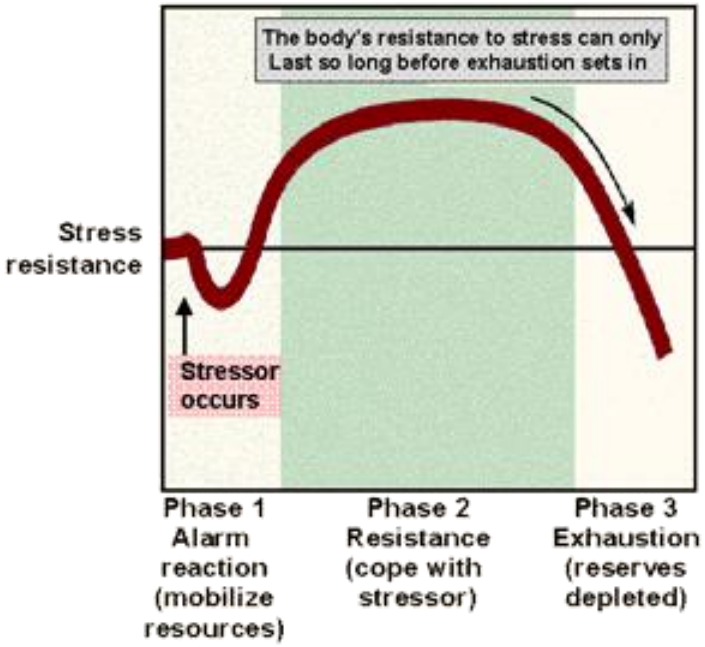
1. Organs are stimulated in two ways: directly by symp nerves
indirectly by the adrenal medullary hormones

One system can substitute for the other
destruction of symp pathway – E, NE in blood indirectly cause stimulation
loss of the two adrenal medullae has little effect (symp pathways still perform necessary duties)

Dual mechanism of sympathetic stimulation provides a safety factor

2. Capability of hormones E, NE to stimulate structures that are not innervated by symp fibers
metabolic rate of every cell of the body is increased by hormones (epinephrin) even though it is not innervated

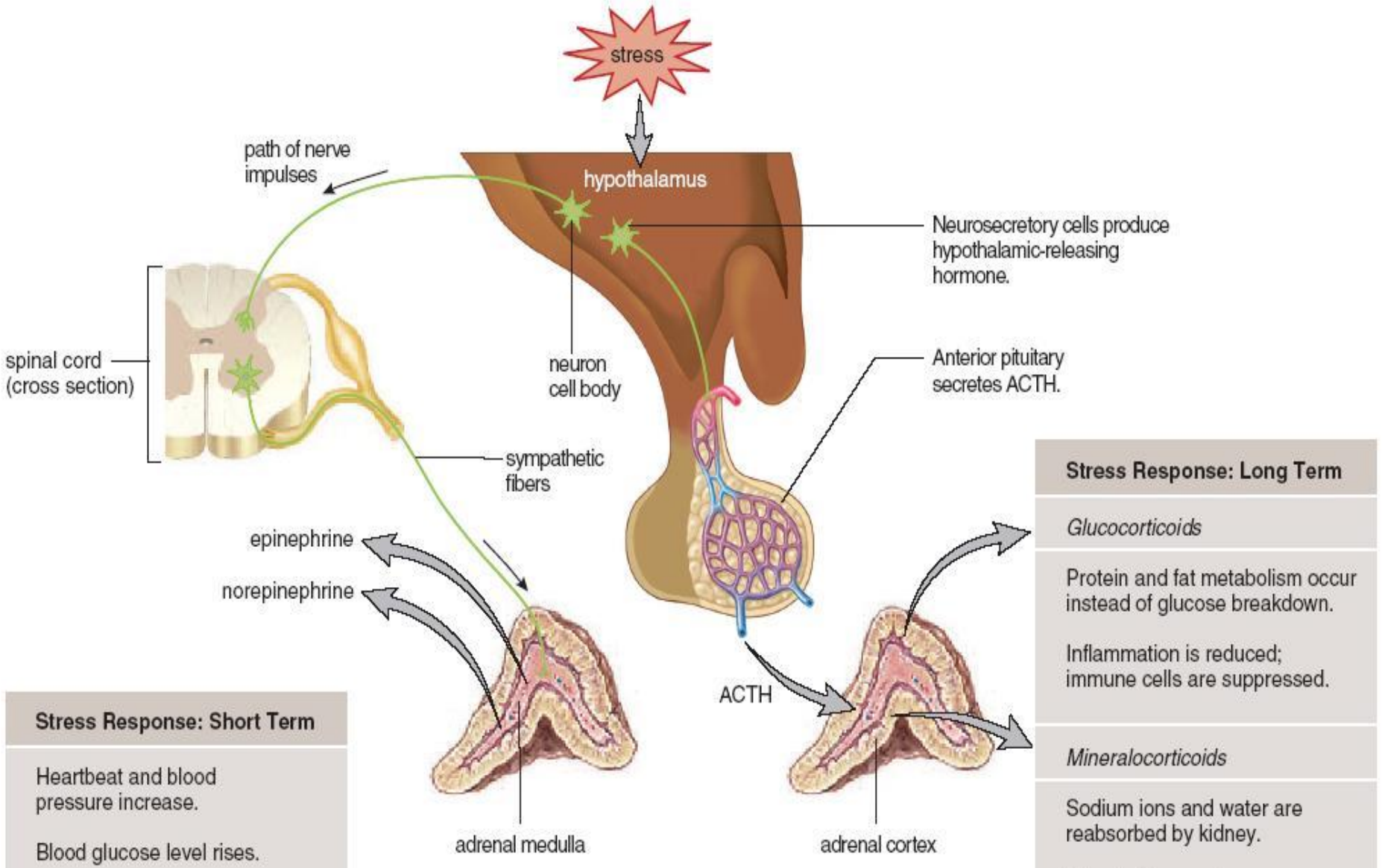
Stress...
External factors (stimuli) perceived by the individual as a threat to homeostasis of the organism.
Stress stimuli may be physical, psychological, anatomical...

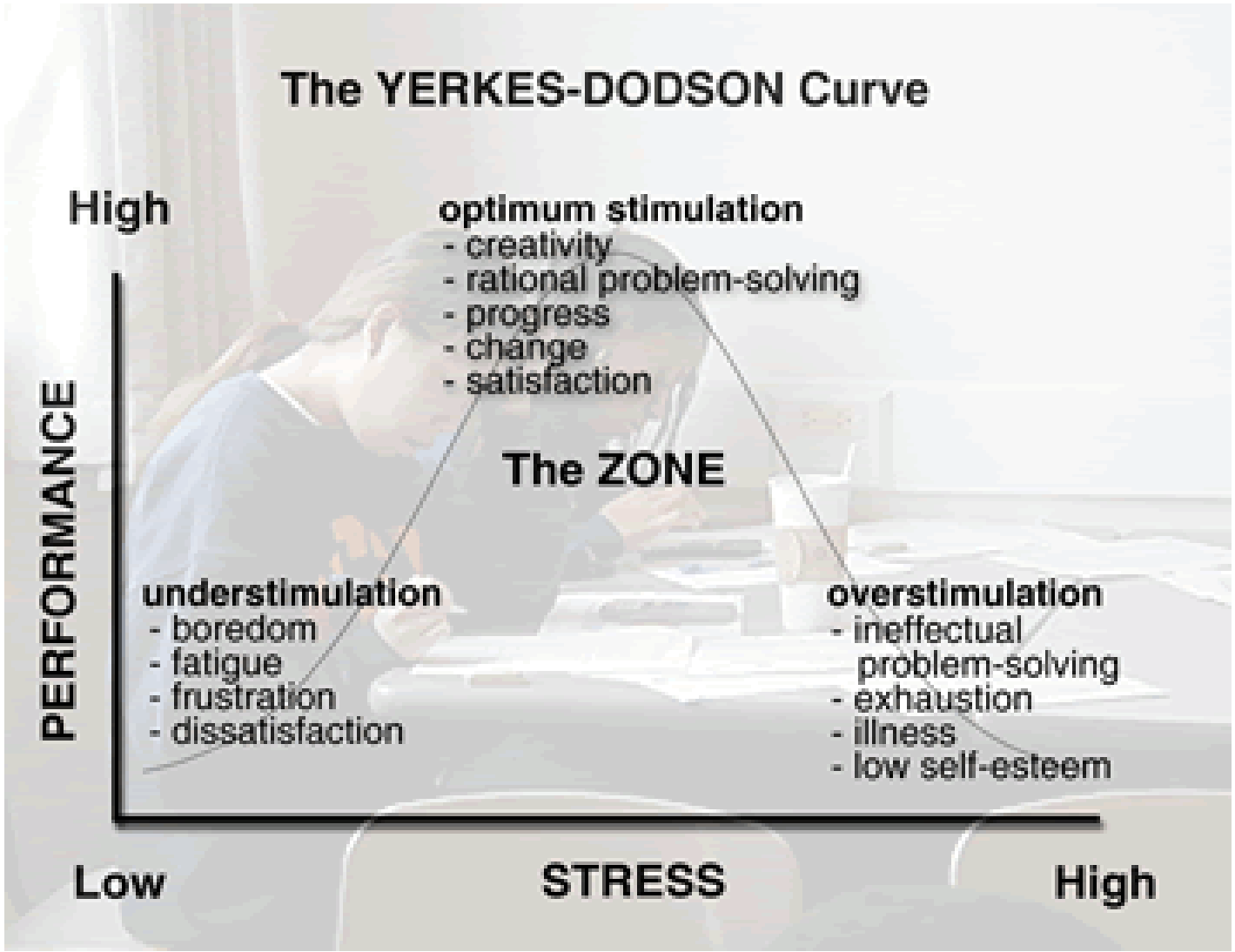


The Stress Response graph developed by Dr. Hans Selye

Stress reaction:
Coordinated sum of endocrine, Visceromotor (effect on breathing, increase cardiac output) and Somatomotor (change muscle tone, fight-or-flight) responses to a stress event.
→ Function:maintain homeostasis!!

Upon a stress stimuli...





Adequate stress