



# Pathophysiology of Endocrine System

# Principles of hormone's action

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## ■ **Types of effects:**

- **Endocrine effect (target cells are far from endocrine gland)**
- **Paracrine effect (target cells in the same organ)**
- **Autocrine effect (affection on the same cell type)**

## ■ **Interaction with receptors:**

- **Receptors inside cells (influence on gene expression).**
- **Receptors on the cell surface (influence on enzyme activity or ion channels).**

# Symptoms of endocrine disorders

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- **Common symptoms:**
  - fatigue/weakness
  - metabolism disorders
  - alterations in height, weight, BMI
  - mental disturbances
- **Principles of diagnostics:**
  - physical examination
  - blood plasma level
  - CT, MRI

# Endocrine Gland Hypofunction

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# Endocrine Gland Hypofunction

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## **Problems outside the endocrine gland:**

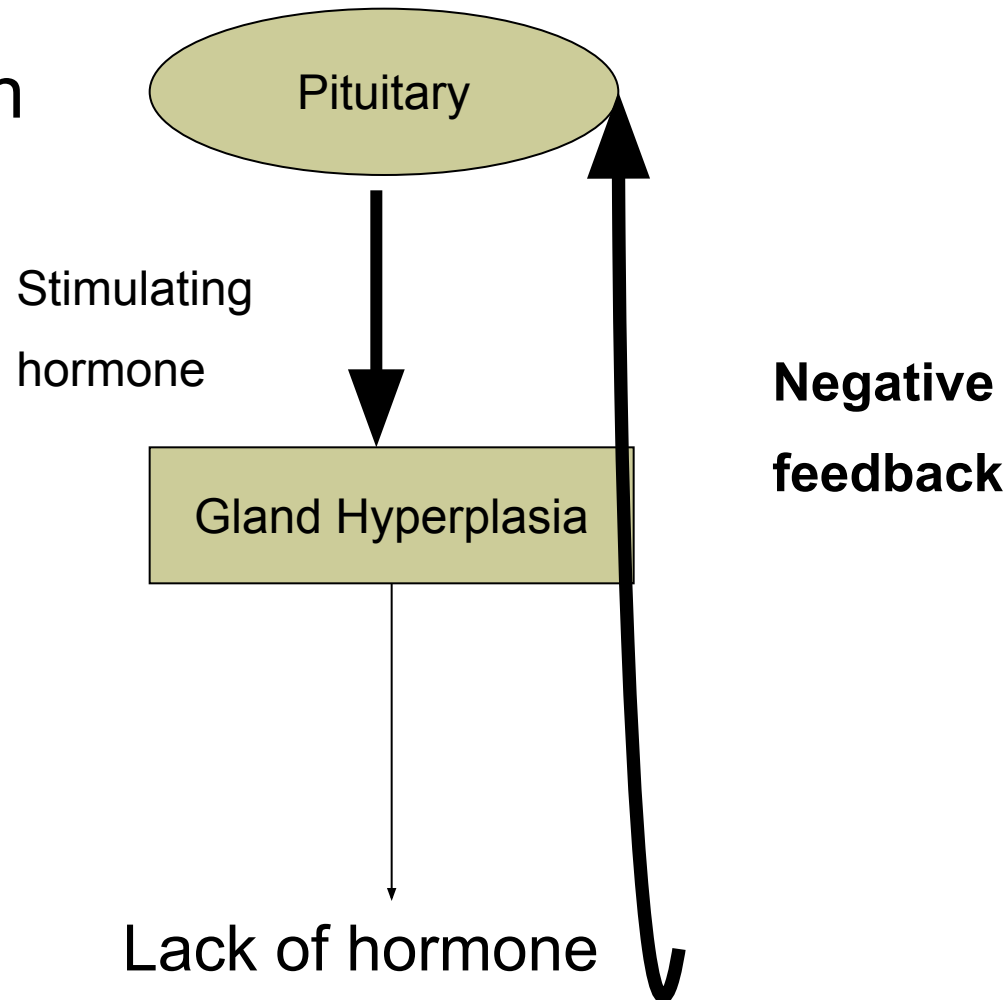
- understimulation by the pituitary
- lack of substances needed for hormone synthesis
- depression of hormones secretion by drugs or food
- circulating antibodies against hormone

## **Receptor defects:**

- absence of receptor
- defective receptor
- antibodies to receptor
- impaired cellular responsiveness to the hormone.

# Endocrine Gland Hypofunction

A decrease in hormone can lead to peripheral endocrine gland hyperplasia



# Endocrine Gland Hyperfunction

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- Causes of increased hormone level:
  - overstimulation by the pituitary
  - hyperplasia or neoplasia of the gland
  - stimulation of gland by antibodies
  - rapid destruction of a gland
  - ectopic tumor
  - excess exogenous hormone administration.

# General principles of therapy

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## Hypofunction:

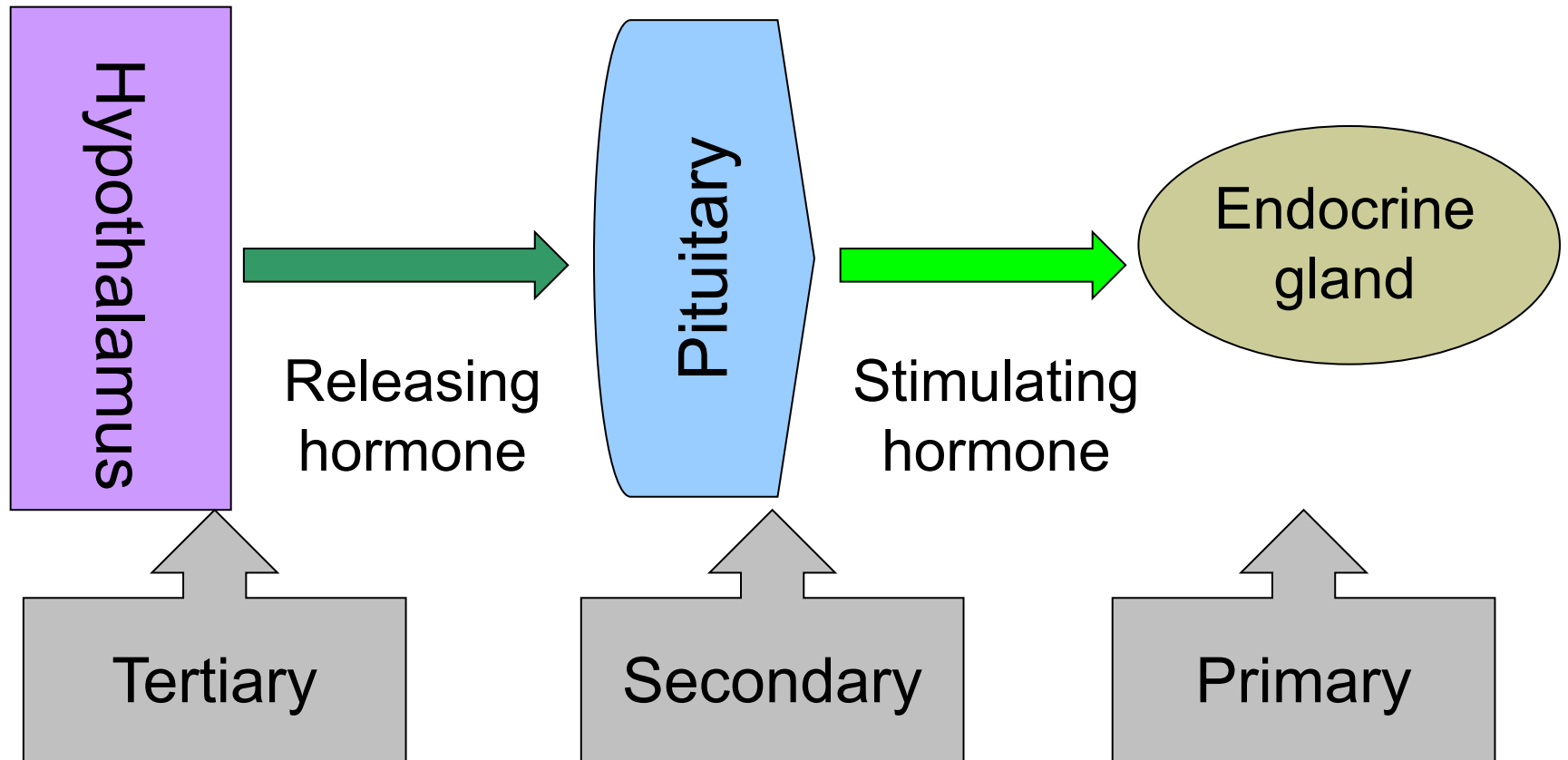
- replacement of the hormone
- hormone resistance.

## Hyperfunction:

- radiation therapy
- surgery
- hormone production
- receptor antagonist



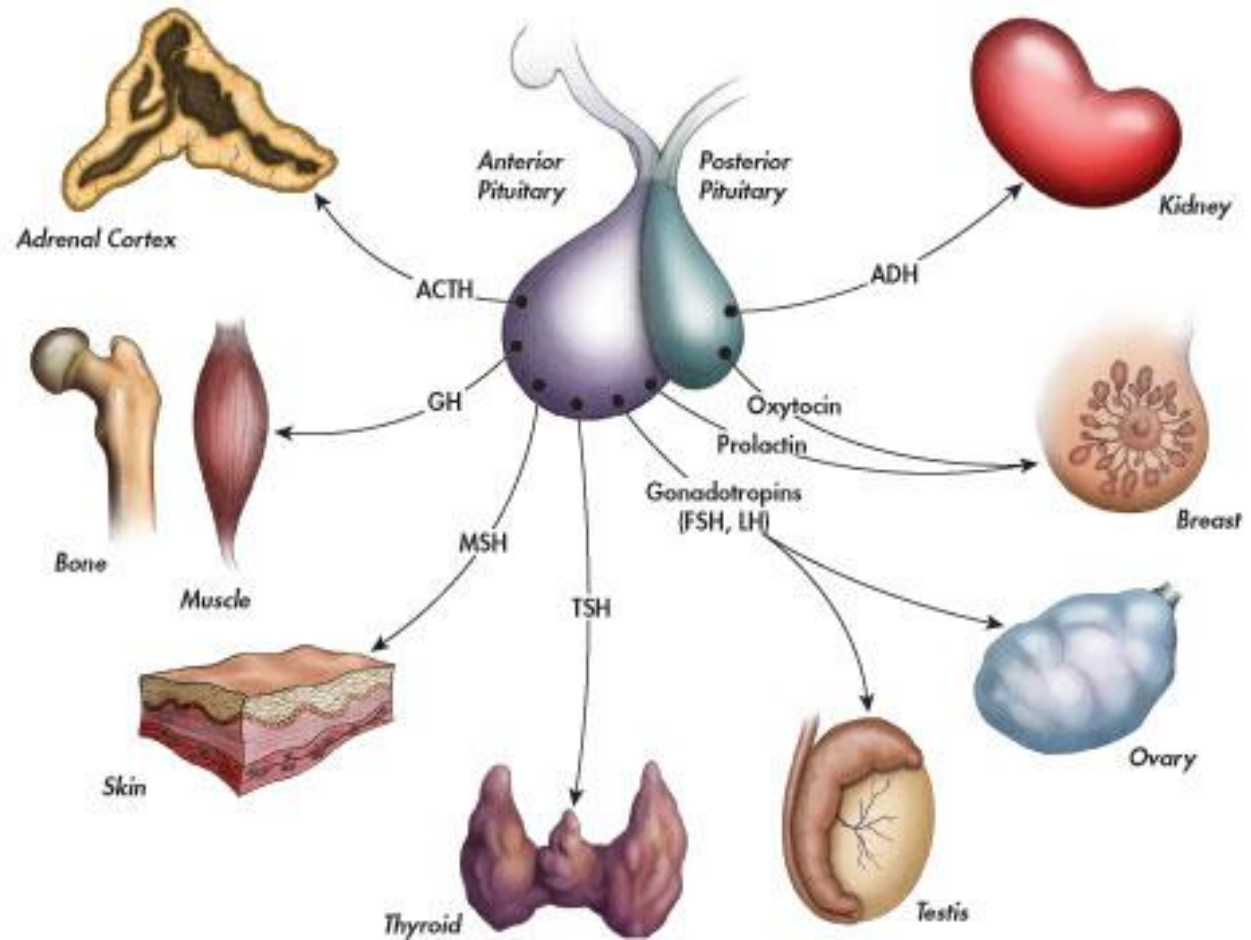
# The levels of disorders



# Pituitary disorders

Causes :

- tumor
- hemorrhage
- trauma
- irradiation



# Pituitary disorders

## Growth hormone deficiency

- children - short stature (**pituitary dwarfism**), normal intelligence, obesity
- adults - central obesity, reduced muscle mass and exercise capacity.



# Pituitary disorders

## Excess of GH in childhood

### Pituitary gigantism

- □ growth velocity
- proportional enlargement of skeleton and inner organs
- enlargement of the peripheral nerves
- delayed puberty and hypogonadism



# Pituitary disorders

## Excess of GH in adults

### Acromegaly

- reason –somatotrope adenoma
- hyperplasia and hypertrophy of soft tissues
  - □ size of hands, feet, nose, ears
  - cartilaginous proliferation of the larynx
  - coarsening of the facial features.
- enlarged tongue and increase of inner organs
- thick and dark skin.
- degenerative arthritis.



# Pituitary disorders

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## ■ GH excess – Metabolic disturbances

- □ GH and IGF-1.
- □ synthesis of lipids in adipocytes, □ lipolysis and free fatty acids level in blood plasma, □ of glycogen in hepatocytes
- □ tolerance to carbohydrates and diabetes mellitus
- hyperthyroidism
- CVS - hypertension, cardiomegaly, heart failure
- hyperphosphatemia (□ tubular reabsorption of phosphate)

# Pituitary disorders

Excess of ACTH - **Cushing's disease.**

High ACTH levels  bilateral adrenal hyperplasia.

Melanocyte stimulation by ACTH  
 hyperpigmentation of skin

## ■ Cushing's syndrome

- cortisol due to adrenocortical neoplasm
- Low ACTH



# Cushing disease/syndrome

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Clinical manifestation:

- "moon" face and "buffalo hump".
- muscle wasting and weakness - due to hypokalemia and □ glucose level in the muscles.
- atrophic skin, with poor wound healing and purple striae
  - activation of protein catabolism and □ of proteins synthesis in the skin.



# Cushing disease/syndrome

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- Hypertension – due to water and salt retention, □ vessels tone.
- Osteoporosis – □ catabolism in the bone □ high blood level of calcium.
- Hyperglycemia, and diabetes mellitus – due to contrainsular effect of cortizol.
- Secondary immune deficiency – □ of immune cells activity by cortizol
- Signs of virilism in the female – □ of androgens in addition to cortisol.

# Pituitary disorders

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Lack of ADH - **Diabetes insipidus** - polyuria, polydipsia, dehydration.

- **Central Diabetes insipidus** – lack of ADH (trauma, stroke, infection)
- **Nephrogenic Diabetes insipidus DI** - inability of the kidney to respond normally to ADH.

Excess of ADH - **Syndrome of Inappropriate ADH** (decreased excretion of free water).

- production of ectopic ADH or ADH-like substance by neoplasms.

# Thyroid disorders

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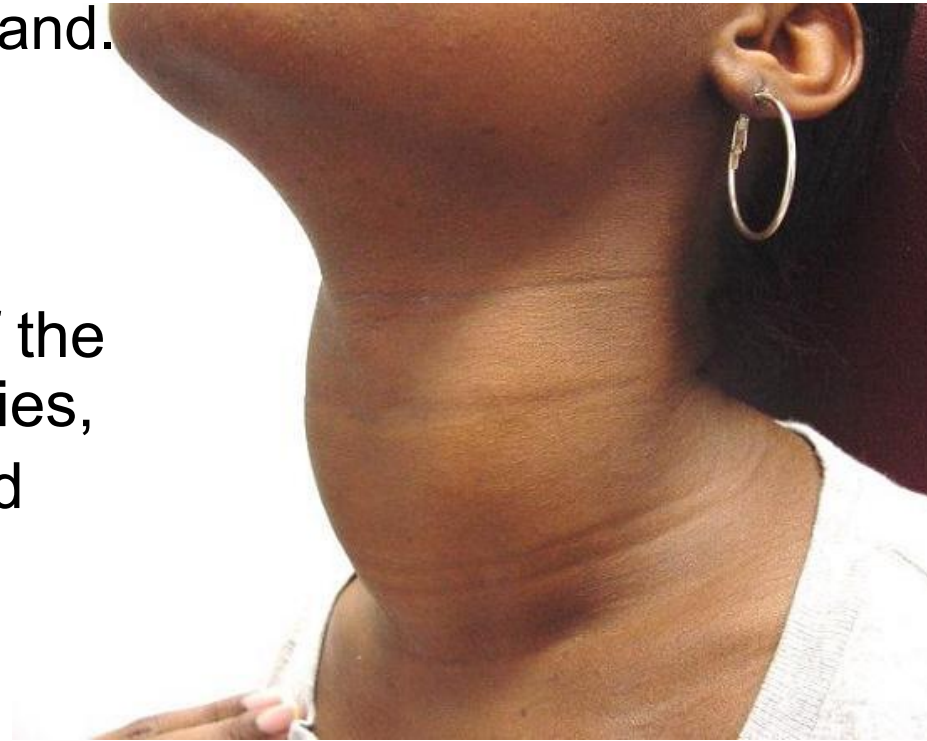
## Thyroid Hormone Action:

- adequate fetal growth
- development of neural and skeletal systems.
- regulation of BMR and O<sub>2</sub> consumption.
- heat production
- sympathetic effect on myocardium
- erythropoiesis.

# Thyroid disorders

**Goiter** - □ size of the thyroid gland.  
(not related of TH level)

- Complications of goiter:
  - difficulty in swallowing,
  - distention of the veins of the neck and upper extremities,
  - edema of the eyelids and conjunctiva,
  - syncope with coughing.



# Thyroid disorders

## Congenital hypothyroidism cretinism

### ■ Causes

- congenital absence of the thyroid gland
- abnormal biosynthesis of thyroid hormone
- deficient TSH secretion.

■ Clinics: mental retardation, impaired growth.



# Thyroid disorders

## Acquired hypothyroidism – myxedema

- accumulation of a mucopolysaccharide substance in the connective tissues.
- Causes
  - destruction or dysfunction of the thyroid gland,
  - impaired pituitary function
  - hypothalamic dysfunction.



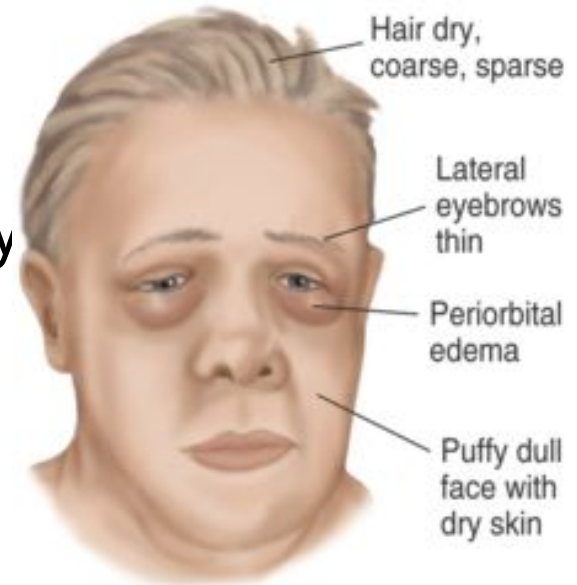
# Thyroid disorders

## hypometabolic state

- weakness and fatigue,
- tendency to gain weight,
- cold intolerance,
- decreased GIT motility,
- mental dullness, impaired memory

## myxedema

- enlarged tongue,
- hoarse and husky voice,
- pericardial or pleural effusion,
- bradycardia, cardiac dilatation



# Thyroid disorders

**Hyperthyroidism –  
clinically Thyrotoxicosis**

## **Graves' disease**

- hyperthyroidism
- goiter
- ophthalmopathy with exophthalmia

Graves' ophthalmopathy



Bulging,  
reddened  
eyes

thyroid-stimulating  
antibodies act through the  
normal TSH receptors and  
cause thyroid hyperfunction



# Thyroid disorders

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## Clinical manifestation:

- □ BMR and heat production, heat intolerance
- prevailing of sympathetic influences
- warm and moist skin, □ perspiration
- □ gases turnover in the lungs and dyspnea
- □ GIT motility and diarrhea.
- alterations in adrenal function

# Thyroid disorders

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## Clinical manifestation:

- tachycardia, □ of stroke volume
- hypertension, widening of the pulse pressure
- heart failure with minute blood volume.
- weight loss despite increased appetite.
- CNS - □ excitability, nervousness, insomnia
- tremor and weakness of the muscles

# Parathyroid disorders

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## **Hypoparathyroidism** reasons

- surgical removal of the gland
- autoimmune destruction
- Di George's syndrome

Low calcium, high phosphate

- increased neuromuscular excitability □ tetany
- paresthesia
- mental depression.
- ECG changes - prolonged Q-T S-T,.

# Parathyroid disorders

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## Hyperparathyroidism

Causes :

- Primary (adenoma)
- Secondary
  - Chronic renal insufficiency
  - Vitamin D deficiency;
  - Intestinal malabsorption;

Hypercalcemia due to:

- bone resorption,
- Ca renal reabsorption
- intestinal calcium absorption

# Hyperparathyroidism

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## Clinical manifestations:

- osteodystrophy, osteomalacia
- disturbances of excitation in nervous system and muscles
- kidney stones
- metastatic calcification of soft tissues,
- hypertension, and heart palpitations,
- increase of gastric secretion

# Pathology of adrenal gland

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Hypofunction of adrenal cortex (cortisol, aldosterone, androgen).

## **Primary adrenal hypofunction - ADDISON'S DISEASE**

- Cause: atrophy of the adrenal cortex as a result of
  - autoimmune processes
  - tuberculosis
  - tumor or metastatic disease
  - surgical ablation
  - inflammatory necrosis

# Hypofunction of adrenal cortex

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## **Aldosterone deficiency**

- □ excretion of Na and □ excretion of K,
- low blood concentrations of Na and Cl and a high concentration of serum K.
- severe dehydration, plasma hypertonicity,
- decreased circulatory volume, hypotension.

## **Cortisol deficiency**

- disturbances in carbohydrate, fat, and protein metabolism
- low resistance to infection, trauma, and other stress
- hyperpigmentation of skin and mucous membranes

# Addison's disease clinical manifestation

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- Weakness, fatigue
- Increased pigmentation
- GIT: anorexia, nausea, vomiting, diarrhea
- Hypometabolism
- Heart activity disturbances
- Weight loss, dehydration, hypotension



# Acute adrenal failure – Adrenal crisis

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- Causes:
  - trauma,
  - hemorrhage (overdose of heparine, acute or fulminant sepsis)
- Clinical manifestation:
  - acute hypotension;
  - dehydration of the organism;
  - insufficiency of bloodflow on all the levels (results in patient's death).

# Hypofunction of adrenal cortex

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- Secondary hypofunction - due to a lack of ACTH.
- Causes:
  - destruction of the pituitary;
  - long term steroid administration.
- Clinical manifestation:
  - Patients are not hyperpigmented,
  - The disturbances of water and electrolyte levels are mild
  - In the case of panhypopituitarism – concomitant depressed thyroid and gonadal function

# Hyperfunction of adrenal cortex

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## ■ Causes

- congenital adrenal hyperplasia,
- acquired hyperplasia, adenomas, or adenocarcinomas.

ADRENAL VIRILISM (Adrenogenital Syndrome) -  
excess of androgens.

## ■ Clinical signs in women:

- hirsutism,
- baldness,
- deepening of the voice,
- amenorrhea, atrophy of the uterus,
- increased muscularity.

# Hyperaldosteronism

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## Primary Hyperaldosteronism - Conn's Syndrome

- Cause: tumor of the adrenal cortex or benign adrenal hyperplasia.

Clinical manifestations:

- Blood analysis: □ Na, □ Cl, □ K, hypervolemia.
- Hypokalemia
  - □ muscular weakness, paresthesias, transient paralysis, and tetany.
  - □ hypokalemic nephropathy with polyuria and polydipsia
- Hyponatremia and hypervolemia □ hypertension.
  - low or normal plasma rennin activity
- Hyperglycemia, glycosuria.

# Hyperaldosteronism

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Secondary hyperaldosteronism is caused by low blood circulating volume or low ABP

Causes:

- cardiac failure,
- cirrhosis with ascites,
- the nephrotic syndrome,
- reduced renal blood flow due to
  - obstructive renal artery disease (eg, atheroma, stenosis),
  - renal vasoconstriction (as occurs in accelerated hypertension).