Hypothalamus- pituitary - adrenal glands

Magdalena Gibas MD, PhD
Dept. of Physiology
University of Medical Sciences
Poznań, Poland
The hypothalamus is the general director of the hormone system. At every moment, the hypothalamus analyses messages coming from: the brain and different regions of the body.

Afterwards, it performs a number of functions, such as maintaining a stable body temperature, controlling blood pressure, ensuring a fluid balance, and even proper sleep patterns.
Cell bodies of neurons that produce releasing/inhibiting hormones

Hypothalamus

Primary capillaries in median eminence

Arterial flow

Releasing hormones

Anterior pituitary hormone

ANTERIOR PITUITARY

Secretory cells that produce anterior pituitary hormones

Anterior pituitary hormones

Venous outflow

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Hypothalamus releases hormones at median eminence and sends to anterior pituitary via portal vein.
Control of pituitary hormone secretion by hypothalamus

• Secretion by the anterior pituitary is controlled by hormones called hypothalamic releasing hormones and inhibitory hormones secreted within the hypothalamus itself and then conducted to the anterior pituitary through hypothalamic-hypophysial portal vessels.

• Posterior pituitary secretes two hormones, which are synthesized within cell bodies of supraoptic and paraventricular nuclei of the hypothalamus and transmitted through axons of these neurons.
Function of the releasing and inhibitory hypothalamic hormones

- **Thyrotropin-releasing hormone (TRH)**
  - causes release of thyroid-stimulating hormone (TSH)

- **Corticotropin-releasing hormone (CRH)**
  - causes release of ACTH

- **Growth hormone releasing hormone (GHRH)**
  - causes release of growth hormone, and

- **Growth hormone inhibitory hormone (GHIH)**, which is the same as the hormone somatostatin and which inhibits the release of growth hormone.
Function of the releasing and inhibitory hypothalamic hormones

• Gonadotropin - releasing hormone (GnRH)
  - causes release of the two gonadotropic hormones, LH and FSH

• Prolactin inhibitory hormone (PIH),
  - believed to be dopamine - causes inhibition of prolactin release.

• PRL- releasing factor (PRF).
  - believed to be TRH - increases prolactin release
The location of pituitary (hypophysis) relative to brain and hypothalamus
The pituitary is controlled largely by the hypothalamus and regulates numerous processes.

**Anterior** = endocrine, 6 hormones

**Intermediate** = minor, 1

**Posterior** = neuroendocrine, 2
Six very important hormones are secreted by anterior pituitary:

- Secreted by lactotropes prolactin (PRL)
- Secreted by thyrotropes thyroid stimulating hormone (TSH)
- Secreted by gonadotropes follicle-stimulating hormone (FSH), and luteinizing hormone (LH)
- Secreted by corticotropes adrenocorticotropic hormone (ACTH)
- Secreted by somatotropes growth hormone (GH; somatotropin)
Hypopituitarism

- deficiency of one or more anterior pituitary hormones, which results in insufficient stimulation and therefore insufficient hormonal output of the respective target glands
- Tumors
- Pituitary irradiation
- Pituitary apoplexy
- Postpartum pituitary necrosis (Sheehan’s syndrome due to postpartum hemorrhage and hypovolemia)
How can pituitary tumors cause hypopituitarism?

e.g. what is the effect of prolactinoma on fertility in both sexes?
Posterior pituitary receives axons from the supraoptic (→ADH) and paraventricular nuclei (→oxytocin).
Two hormones are secreted by posterior pituitary:

- **Antidiuretic hormone** (ADH; vasopressin)
- **Oxytocin**

Intermediate lobe cells secrete:

- **POMC** (proopiomelanocortin), which is precursor of alpha-MSH (melanotropin)
Growth hormone

(somatotropin)
- GHRH, somatostatin (GHIH) and ghrelin control GH release

- pancreatic somatostatin has other functions (inhibits hormone secretion by α and β cells)
Stimuli that increase secretion of GH:

- GHRH; Ghrelin (brain-gut peptide)

- Deficiency of energy substrate:
  - Hypoglycemia
  - Exercise
  - Fasting

- Increase in circulating levels of certain amino acids

- Glucagon

- Stressful stimuli

- NREM stage of sleep
GH is released in pulses, with a major peak during deep sleep before REM.
Ghrelin

• Produced mainly by stomach (released into blood)
• Other sources: intestines; hypothalamus
• Receptors located in pituitary (↑GH), hypothalamus (↑food intake), heart, blood vessels (↓BP)
Ghrelin causes:

- ↑ GH release
- ↑ food intake (appetite-stimulatory peptide) via NPY neurones in hypothalamus
- ↓ fat utilization (GH-independent mechanism)
- ↑ glucose utilization
Stimuli that decrease secretion of GH:

- REM sleep
- High blood glucose concentration (↓ of ghrelin release)
- Cortisol
- FFA (↓ of ghrelin release)
- Growth hormone
- Somatomedins
Physiology of growth
GH stimulates cartilage and bone growth by:

- increased deposition of protein by the chondrocytic and osteogenic cells that cause bone growth
- increased rate of reproduction of these cells
- the specific effect of converting chondrocytes into osteogenic cells, thus causing specific deposition of new bone.
Direct and indirect effects of GH

- Direct effects are the result of growth hormone binding its receptor on target cells.
- Indirect effects are mediated primarily by an insulin-like growth factor-1 and 2 (IGF-1; IGF-2), hormones that are secreted from the liver and other tissues in response to GH.
Somatomedins - the polypeptide growth factors secreted by the liver (IGF-I, IGF-II)

- **IGF-I** (insulin-like growth factor) stimulates skeletal growth by increasing collagen and protein synthesis in chondrocytes. IGF-I may be also produced locally.

- **IGF-II** stimulates tissue growth and increases organ size especially during fetal development (by increasing the rate of: protein synthesis, RNA synthesis, DNA synthesis).
Distinguish between:

- Somatotropin - GH
- Somatostatin - GHIH
- Somatomedin - polypeptide growth factor
Physiology of growth

Growth is affected by:

- thyroid hormones
- androgens
- estrogens
- glucocorticoids
- insulin
- genetic factors
- adequate nutrition
Physiology of growth – growth periods:

- In humans, there are 2 periods of rapid growth, the first in infancy and the second in late puberty just before growth stops.

- The first period is a continuation of the fetal growth period.

- The second growth spurt is due to an interaction between sex steroids, GH, and IGF-1.

  - Sex hormones $\rightarrow$ Amplitude of the spikes of GH secretion $\rightarrow$ IGF-1 $\rightarrow$ Growth
Although androgens and estrogens initially stimulate growth, they finally terminate growth by causing the epiphyses to fuse to the long bones.
1. Why pituitary dwarfs treated with testosterone first grow few inches and then stop?

2. Why people who were castrated before puberty tend to be tall?
Physiology of growth - role of thyroid hormones:

- Thyroid hormones have a permissive action to GH, possibly via potentiation of the actions of somatomedins. They also appear to be necessary for a completely normal rate of GH secretion.

- Thyroid hormones have a widespread effects on the ossification of cartilage, the growth of teeth, the contorous of the face, and the proportions of the body.
Long bones continue to grow and elongate (lengthen) through adolescence.

This process is called ossification.
While still in the embryonic stage, a baby's heart develops under the supervision of the growth hormone.

Developing heart that appears as a red nodule.

Adult heart.
Metabolic effects of GH
GH plays role in promoting protein deposition

• GH directly enhances transport of most amino acids through the cell membranes to the cytoplasm

• GH stimulates the transcription of DNA in the nucleus, causing formation of increased quantities of RNA. This in turn promotes more protein to be synthesized

• GH also increases rate of RNA translation, causing protein to be synthesized

• GH decreases protein and amino acids catabolism, thus acting as a “protein sparer”
**GH increases fat utilization for energy:**

- It causes release of fatty acids from adipose tissue (increases the concentration of FFA in the body fluids)

- It also causes increased conversion of FFA to acetylcoenzyme A (acetyl-CoA) with subsequent utilization of this for energy (ATP)

- Excessive amounts of GH may produce excessive mobilization of fat from the adipose tissue, causing ketosis
GH has 4 major effects on carbohydrate metabolism:

- It decreases use of glucose for energy
- It stimulates gluconeogenesis
- It produces decreased uptake of glucose by the cells and increased blood glucose concentration
- The increase of blood glucose concentration caused by GH stimulates the beta cells of the pancreas to secrete extra insulin
**Insulin-like GH effects:** \( \uparrow \) liver and muscle protein synthesis;

**Anti-insulin:** \( \downarrow \) glucose uptake, \( \uparrow \) lipolysis
**IGF-I** stimulates bone growth by stimulating chondrocytes, which make cartilage.
IGF-II stimulates tissue growth and repair by stimulating RNA and protein synthesis.
GH - summary

**Exercise**

Sleep

Stress

Hypothalamus

GHRH

Somatostatin

Pituitary

GH

Muscle

Bone
(chondrocyte differentiation from fibroblasts)

Liver

IGF-1

Adipose tissue

Direct effects:
- (antagonizes insulin, synergizes with cortisol; also causes local production of IGF-1)

Indirect effects:
- (antagonized by cortisol; insulin-like)

Growth promotion (clonal expansion, e.g. chondrocytes)
- (bones, soft tissue, gonads, viscera)
Abnormalities of GH secretion

- Panhypopituitarism
- Dwarfism (in 30% - isolated ↓GH)
- Laron dwarfism
- Gigantism
- Acromegaly
GIGANTISM

- excessive production of GH before adolescence
ACROMEGALY - excessive production of GH after adolescence.

Intradental separation and prognathism in a patient with acromegaly.
Acromegaly
The somatopause is directly related to the decline of growth hormone produced by the body during aging.

- **Clinical Signs of the Somatopause:**
  - Weight gain
  - Energy Loss
  - Skin wrinkling
  - Decreasing muscle mass
  - Loss of bone density
  - Increasing body fat (especially around the waist)
Age-related lowering of GH (somatopause):

- decrease in muscle mass and muscle strength
- impairment of psychical efficiency (GH contribute to the function of the hippocampus, a brain structure important for the learning and memory)
- osteoporosis
- cardiac failure
- altered immune function (GH slows atrophy of thymus and controls differentiation and activity of some cells in the immune system eg. neutrophils) and many others.
- increased rate of oxidative stress
- increased risk of cardiac mortality (cholesterol, free radicals etc.)
GH - youth hormone?

- GH may reverse biological effects of aging
- GH is not recommended for common use in adults
- GH supplementation:
  - GHD
  - AIDS wasting syndrome
  - short bowel syndrome
Other hormones of anterior pituitary:

**ACTH, TSH, FSH, LH, PRL**
**ACTH - adrenocorticotropic hormone**

- It strongly stimulates cortisol production of adrenal cortex
- It also stimulates the production of other adrenocortical hormones
- ACTH also exhibits some extraadrenal effects - it has a pigmenting action (MSH activity)
- CRH, ACTH and cortisol secretion exhibit circadian rhythm (high in the early morning, low in the late evening)
TSH stimulates the thyroid gland follicles:

- it increases the rate of thyroglobulin synthesis
- it increases the uptake of iodide ions from the blood by thyroid cells
- it activates all of the chemical processes that cause T4 production and release by the thyroid gland
- the rate of TSH secretion by anterior pituitary is controlled mainly by the negative feedback effect of T4
With the sounding of the alarm, the hypothalamus secretes the special GnRH hormone. This hormone sends a command to the pituitary gland to secrete two hormones, the Follicle Stimulating Hormone (FSH) and the Luteinizing Hormone (LH).

Because of the "hidden" clock, the brain's hypothalamus area "understands" when a person's adolescence has started.
FSH functions:

- **FSH** stimulates early growth of the ovarian follicle

- **FSH** stimulates spermatogenesis
LH functions:

- **LH** stimulates ovulation and luteinization

- **LH** stimulates testosterone secretion
Prolactin
Prolactin \(\rightarrow\) \(\uparrow\) milk synthesis and secretion into alveoli

Birth \(\rightarrow\)
\(\downarrow\) Prolactin,
\(\uparrow\) neural control (breast mechanorec.)

Suckling \(\rightarrow\)
Hypothal. \(\rightarrow\)
\(\uparrow\)Prolactin 1 hr \(\rightarrow\)
\(\uparrow\)Milk production

Effect weakens over months
ADH and oxytocin
- posterior pituitary hormones
Hormones of the posterior pituitary gland

• **Oxytocic hormone:**
  - it causes contraction especially of the uterus and to a lesser degree other smooth muscles of the body
  - it stimulates myoepitelial cells in the breast causing milk ejection
  - it also participates in the process of sperm ejection
Suckling, baby sounds → hypothal → ↑ oxytocin (paraventricular nucleus) → ↑ myoepithel. contract → milk let-down
Regulation of oxytocin secretion (paraventricular nucleus):

- suckling via stimulation of touch receptors in breast
- distension of female genital tract (during labour)
- pain
- psychological stimuli (baby’s cry, orgasm)
Hormones of the posterior pituitary gland

• **Antidiuretic hormone (ADH; vasopressin):**
  - increases the permeability of the kidney collecting ducts and tubules to water
  - it allows the water to be reabsorbed, thereby conserving water in the body
  - it has also vasoconstrictor and pressor effects (higher concentrations of ADH cause an increase in arterial blood pressure by vasoconstriction)
There are special sensors in the hypothalamus area of the brain called osmoreceptors. These sensors measure the amount of fluid in your blood at every moment you are alive. If they determine that the amount of fluid in the blood has fallen, they immediately react and stimulate supraoptic nucleus.
Regulation of ADH production:

**Osmotic regulation**

- when the ECF becomes too concentrated, fluid is pulled by osmosis out of the osmoreceptors, decreasing their size and initiating signals in the hypothalamus to cause additional ADH secretion
Regulation of ADH production:

• **Hemodynamic regulation**: changes in blood volume and blood pressure affect vasopressin secretion via baroreceptors. However, stimulation of ADH release requires more than 10% blood volume decrease.

• **Other stimulators** for ADH secretion include: angiotensin II, nicotine, pain, increased temperature, and some emotions

• **Alcohol strongly inhibits** ADH release
Regulation of ADH secretion
Adrenal glands
Location of **adrenal glands**

- the outer **cortex** (80%) releases **steroids**;
- the inner **medulla** (20%) releases **catecholamines**

![Adrenal gland diagram](image)
The adrenal cortex - three zones

- Zona glomerulosa
- Zona fasciculata
- Zona reticularis

(a) Histological section of the adrenal gland showing the three zones.

(b) Medullary section of the adrenal gland.

- Capsule
- Venous sinuses
- Zona glomerulosa (secretes mineralocorticoids)
- Zona fasciculata (secretes glucocorticoids)
- Zona reticularis (secretes androgens)
Adrenal gland secretion

• **Adrenal cortex secrets:**
  - corticosterone (all 3 cortical zones)
  - cortisol (→ z. fasciculata)
  - aldosterone (→ z. glomerulosa)
  - sex hormones (→ z. reticularis)

• **Adrenal medulla secrets:**
  - catecholamines (epinephrine, norepinephrine, dopamine)
Control of the Secretion of Glucocorticoids by the Adrenal Cortex and of Catecholamines by the Adrenal Medulla

Hypothalamus
Corticotropin-releasing hormone (CRH)
ACTH (adrenocorticotropic hormone)
Glucocorticoids
Adrenal cortex (z. fasciculata)
Adrenal medulla
Epinephrine and norepinephrine

Anterior pituitary gland
Neuron of sympathetic nervous system
The anatomical analogy between cells of adrenal medulla and sympathetic postganglionic neurons

- Postganglionic fiber has effects on one specific effector organ, such as the heart.
- The cells of adrenal medulla may influence the activity of various organs in the body (they secrete hormones to the circulation).
Adrenal catecholamines

The release of AK is carried out by direct connection of nerve fibers from hypothalamus to intermediolateral cells (IML), and then to adrenal medulla.
Chromaffin cells secrete epinephrine into the blood, instead of NE at a synapse.

Tyrosine $\rightarrow$ DOPA $\rightarrow$ DA $\rightarrow$ **NE** (hydroxylation and decarboxylation of Tyrosine) $\rightarrow$ **PNMT** (cortisol elevates) $\rightarrow$ **EPI** (methylation of norepinephrine)
The effect of catecholamines on heart and circulation:

- **NOREPINEPHRINE**
  - via $\alpha$ receptors - vasoconstriction,
  - causes increase in systolic and diastolic blood pressure, reflex bradycardia and decrease in cardiac output per minute

- **EPINEPHRINE**
  - via $\alpha$ receptors - vasoconstriction,
  - via $\beta$ receptors - vasodilation
  - widening of the pulse pressure, and increase of HR and cardiac output per minute;
Circulatory effects of catecholamines

- Epi = Epinephrine
- Nor = Norepinephrine
The metabolic effects of catecholamines:

- increase in glycogenolysis
- increase in gluconeogenesis
- increase in secretion of glucagon
- inhibition of insulin secretion (via α receptors)
- increase in lipolysis
- increase in metabolic rate and calorigenic effect
The effects of catecholamines on smooth muscles and sphincters:

- **Epinephrine:**
  - causes dilation of the airway, gastrointestinal tract and urinary bladder
  - provokes constriction of gastric and urinary bladder sphincters
Function of dopamine:

- vasodilation in the mesentery and kidneys
- vasoconstriction (by releasing norepinephrine?) elsewhere
- positively inotropic effect on the heart (by β1 r-ors)
- increase in systolic pressure and no change in diastolic pressure
Regulation of adrenal medullary secretion

- The major stimulus for catecholamine release from adrenal medulla is sympathetic nervous system activation.
- Stress, change in posture, low blood sugar or sodium levels are the factors that activate the sympathetic nervous system.
  - Hemorrhage → epinephrine
  - Exercise → norepinephrine
The Fight or Flight System
Adrenergic responses of selected tissues

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<tr>
<th>Organ</th>
<th>Receptor</th>
<th>Effect</th>
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<tr>
<td>Heart</td>
<td>Beta-1</td>
<td>Increased inotropy</td>
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<tr>
<td></td>
<td></td>
<td>Increased chronotropy</td>
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<tr>
<td>Blood vessels</td>
<td>Alpha, Beta-2</td>
<td>Vasoconstriction</td>
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<td></td>
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<td>Vasodilation</td>
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<tr>
<td>Kidney</td>
<td>Beta</td>
<td>Increased renin release</td>
</tr>
<tr>
<td>Gut</td>
<td>Alpha, beta</td>
<td>Decreased motility</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Alpha</td>
<td>Increased sphincter tone</td>
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<tr>
<td></td>
<td>Beta</td>
<td>Decreased insulin release</td>
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<td></td>
<td></td>
<td>Increased glucagon release</td>
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<tr>
<td>Liver</td>
<td>Alpha, beta</td>
<td>Increased insulin and glucagon</td>
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<td></td>
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<td>release</td>
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<tr>
<td>Adipose tissue</td>
<td>Beta</td>
<td>Increased glycogenolysis</td>
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<tr>
<td>Skin</td>
<td>Alpha</td>
<td>Increased lipolysis</td>
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<tr>
<td>Bronchioles</td>
<td>Beta-2</td>
<td>Increased sweating</td>
</tr>
<tr>
<td>Uterus</td>
<td>Alpha, beta</td>
<td>Bronchodilation</td>
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<td></td>
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<td>Contraction, relaxation</td>
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</tbody>
</table>
EPI raises glycogenolysis in liver/muscle and lipolysis in adipose; elevates blood glucose.
Pheochromocytoma

- High blood pressure
- Other paroxysmal symptoms are usually nonexistent, unless the person experiences pressure from the tumor, emotional stress, changes in posture, or is taking beta-blocker drugs for a heart disorder
  - rapid pulse, palpitations
  - headache
  - nausea, vomiting
  - clammy skin; ↑sweating
Adrenal steroids
Adrenal hormones are derivatives of cholesterol

- Cholesterol
  - Pregnenolone
    - Progesterone
    - 17-OH-Pregnenolone
    - Dehydroepiandrosterone
    - 17-OH-Progesterone
      - Corticosterone
      - Aldosterone
      - Cortisol
      - Testosterone
      - Estradiol
Three steroids are the primary products of the adrenal cortex:

- Cortisol (glucocorticoid),
- Aldosterone (mineralocorticoid)
- DHEA (androgen, minor male)
• Cells take up and store cholesterol;
• Each cell makes steroids according to the enzymes it has.
Glucocorticoids

Cortisol
Circadian rhythms
Stress

Hypothalamic - pituitary adrenal axis

Corticotropes in hypothalamus → CRH → portal → pituitary → ACTH → adrenal cortex → cortisol
CRH, ACTH, cortisol show circadian sleep-wake rhythm, with peak at awakening.

Types of stress known to increase cortisol secretion:

**Physical stress**
- Hypoglycemia
- Trauma
- Heavy exercise

**Psychological stress**
- Acute anxiety (e.g. novel situations, exams, airplane flight)
- Chronic anxiety
In times of danger, the body goes into a state of alarm by means of a link between the brain and the adrenal glands.
Resistance to stress

• When the human is exposed to the stressor the secretion of \textit{ACTH} rises and consequently the level of glucocorticoids is elevated. This is essential for survival.

• The stressors also activate the \textit{sympathetic nervous system} and the permissive effect of glucocorticoids on vascular reactivity to catecholamines is observed.

• \textit{Glucocorticoids} are also necessary for the \textit{catecholamines} to facilitate their full FFA-mobilizing action (FFA are an important emergency energy supply).

• The high glucocorticoids levels caused by stress are life-saving only in the short term but over longer periods they are harmful.
Describe changes in human body that occur during stress
Effects of cortisol on carbohydrates:

1. Stimulation of gluconeogenesis

2. Decreased glucose utilization by the cells

3. Elevated blood glucose level and adrenal diabetes
The effects of cortisol on liver metabolism

Cortisol accelerates liver urea cycle and amino acid conversion to glucose.
Effect of cortisol on protein metabolism:

- reduction in cellular protein
- increase of liver and plasma protein level
- increase of blood aa transport into the liver
- decrease of blood aa transport into the extrahepatic cells
- gluconeogenesis (formation of carbohydrates from proteins)
The effects of cortisol on skeletal muscle

- Cortisol
- Amino acids
- Muscle protein
- Cortisol

Plasma
Effect of cortisol on fat metabolism:

- increased mobilization of fatty acids
- increased oxidation of FA in the cells
- ketogenic effect
- obesity - increased fat around neck ("buffalo-torso") and round face ("moon face")
Antiinflammatory effects of cortisol:

- stabilization of the lysosomal membranes
- decrease in permeability of the capillaries
- lowering of fever
- suppression of the immune system (T-lymphocytes)
- inhibition of mast cells releasing histamine
Cortisol lowers the temperature by inhibiting the production of IL-1, which activates the temperature center.
Effets of cortisol on blood cells:

- increases the number of circulating neutrophils, platelets and red blood cells
- decreases the number of other blood cells
Summary of effects of cortisol on metabolism:

**LIVER:**
- $\uparrow$ gluconeogenesis, and glycogen synthesis

**SKELETAL MUSCLE:**
- $\downarrow$ protein synthesis;
- $\uparrow$ protein degradation;
- $\downarrow$ glucose uptake;

**ADIPOSE TISSUE:**
- $\downarrow$ glucose uptake;
- $\uparrow$ lipid mobilization
What type of side effects may be related with glucocorticoid administration?
Cushing’s syndrome - long lasting increase in plasma corticoids
Cushing’s syndrome is the result of:

- Administration of exogenous hormones
- Adrenocortical tumors
- Hypersecretion of ACTH
- Ectopic secretion of ACTH
Cushing’s syndrome

- skin and subdermal tissues are thin, and muscles are poorly developed
- wounds heal poorly and minor trauma causes bruises and ecchymoses
- very severe osteoporosis
- facial hair and acne
- obesity with “buffalo torso” and “moon face”
- adrenal diabetes
- 80% of patients have hypertension
- mental symptoms and sleep disorders
- reduced sex drive and fertility in man
- irregular or stopped menstrual cycles in women
Explain following symptoms in Cushing’s syndrome:

• Lack of menses in women; infertility in men
• Excess body hair in women and acne
• Hypertension
Acne

Obesity with „buffalo torso“
Cushing syndrome
Mineralocorticoids

Aldosterone
(z. glomerulosa)

If the aldosterone of ten million people were pooled together, only one gram of the hormone would result.
Effects of mineralocorticoids:

• They cause $\text{Na}^+$ to be conserved in the ECF, while more $\text{K}^+$ and $\text{H}^+$ is excreted into the urine.
• They also increase the reabsorption of $\text{Na}^+$ and the secretion of $\text{K}^+$ by the ducts of salivary and sweat glands.
• Excessive amounts of aldosterone will cause: hypokalemia, muscle weakness and mild alkalosis.

Cells in the kidney channels (collecting tubule)

outside of cell

inside of cell

ATP

phosphate

phosphate released
Liver

Lung

Angiotensin-converting Enzyme (ACE)

Kidney ➔ Renin

Angiotensinogen

Angiotensin I

Angiotensin II

Zona glomerulosa cells

Aldosterone

Mineralocorticoids

- RAA system

Decreased kidney blood pressure (↓ ECF) ➔ renin ➔ converts angiotensinogen to angiotensin I. Lung ACE converts angiotensin I to II ➔ angiotensin II stimulates aldosterone release.

Aldosterone causes Na⁺ and H₂O retention, increase in ECF and finally inhibition of the primary stimuli.
Hyperaldosteronism
- Conn’s syndrome

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<thead>
<tr>
<th>Type</th>
<th>Cause</th>
<th>Source</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary (Conn’s syndrome)</td>
<td>Adrenal tumor or adrenal hyperplasia</td>
<td>Problem within adrenals</td>
<td>↑ECF, alkalosis, hypertension, K⁺ depletion</td>
</tr>
<tr>
<td>Secondary</td>
<td>Edematous states, CHF, ascites, nephrosis</td>
<td>Adrenals responding to low ECF</td>
<td>↑ECF, edema, alkalosis, hypertension, K⁺ depletion</td>
</tr>
</tbody>
</table>
Remember! Think about Conn’s syndrome if your patient has hypertension and very low K⁺ level.
Adrenal androgens
Effects of adrenal androgens and estrogens

- Androgens are the hormones responsible for masculinization, and they also promote protein anabolism and growth.

- They cause epiphyses to fuse in the long bones, thus eventually stopping growth.

- They slightly increase $\text{Na}^+$, $\text{K}^+$, $\text{H}_2\text{O}$, $\text{Ca}^{++}$, sulfate and phosphate retention and they increase the size of the kidneys.
The androgenital syndrome:

- **typical masculine characteristics:**
- much deeper voice
- occasionally baldness
- masculine distribution of hair on the body
- masculine features
- salt loosing form and hypertensive form
Deficiency of 21-beta hydroxylase (salt loosing form)

Deficiency of 11-beta hydroxylase - hypertensive form
The androgenital syndrome:

- Genitals of female baby masculinized by prenatal hypersecretion of adrenal androgens
Adrenal insufficiency

Loss of glucocorticoid and mineralocorticoid action - predict the typical findings
Addison's disease

- Low plasma Na\(^+\), high plasma K\(^+\)
- Inability to produce concentrated urine by the kidneys → excessive urination
- Vomiting, loss of appetite, anorexia, dehydration
- Low blood pressure
- Muscle weakness, fatigue
- Low blood sugar
- Excess pigmentation of skin in some patients
# The lack of all adrenocorticoids - Addison's disease

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<tr>
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<th>Effects</th>
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<tbody>
<tr>
<td>Primary</td>
<td>↓ Corticoids</td>
<td>Idiopathic, infection, surgery, cancer</td>
<td>Problem in adrenals</td>
<td>Weakness, fatigue, anorexia, hypotension, weight loss, hyperpigmentation (only in primary Addison’s), fasting hypoglycemia</td>
</tr>
<tr>
<td>Secondary</td>
<td>↑ ACTH</td>
<td>Hypothalamic-pituitary disease, Hypothalamic-pituitary inhibition (iatrogenic, ectopic steroids)</td>
<td>Problem in hypothalamic-pituitary axis</td>
<td></td>
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