Adrenal gland

Hormones of the adrenal cortex

- the paired adrenal glands (4-5 g each) are located at the upper pole of the kidneys embedded in adipose tissue
- medulla: adrenalin (80%) and noradrenalin (20%)
- cortex:
  - zona glomerulosa, outmost layer (5%): mineralocorticoids
  - zona fasciculata: mostly glucocorticoids, but also androgens
  - zona reticularis: mostly androgens, but also glucocorticoids
- androgen (dehydroepiandrosterone, DHEA) secretion starts at the age of 5 (adrenarche), decrease after 40-50
- transformed to testosterone and dihydrotestosterone at the periphery; main source of androgens in females
- overproduction of POMC increases androgen secretion

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Glucocorticoids

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- diverse effects: adjustments to fasting, effects on nervous system, inflammation, healing of wounds, growth
- in humans cortisol, in rats corticosterone is the most important
- cortisol has 21 C atoms similarly to aldosterone, but the latter has an additional aldehyde group
- they bind to intracellular plasma receptors:
  - type I receptor (kidney distal tubule, colon, secretory duct in salivary glands: similar affinity for mineralo-, and glucocorticoids, but the latter hormones are degraded quickly by the cells
  - type II receptor (liver cell, muscle cell, lymphocyte): much stronger affinity for glucocorticoids
- synthetic steroids: tissue-dependent effect is possible – medicines!

Glucocorticoid effects I.

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- glucocorticoids are transported in the blood coupled to transport proteins – transcortin (corticosteroid-binding globulin), but might be coupled to albumin as well (aldosterone is transported mostly by albumin)
- adjustment to fasting – permissive: enables appropriate level of enzymes activated by hormones produced during fasting (glucagon, adrenalin)
- but: cortisol level does not increase during fasting
  - gluconeogenesis
    - protein synthesis decreases in muscles – more amino acids are available
    - level of enzymes needed for gluconeogenesis increases in the liver, cAMP (increased by glucagon, adrenalin) activates these – cAMP itself is ineffective
  - decreased glucose uptake in muscle and adipose cells
  - lipolysis – glucocorticoids are needed for the effect of hormones increasing lipolysis, decrease of glucose uptake itself has also lipolytic effect

Glucocorticoid effects II.

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- CNS effects
  - differential receptor distribution in the brain –high level in hippocampus
  - malfunctioning might be caused by both too low and too high levels: depression, disturbances of sleep-wake cycle, etc.
  - drastic lowering of cholesterol level – depression
- anti-inflammatory effect
  - occurring at high doses, physiological effect?
  - various noxious effects cause inflammation with classic symptoms: rubor, calor, dolor, tumor
  - release and accumulation of paracrine inflammatory mediators, positive feedback: kinins (e.g. bradykinin), cytokines (e.g. interleukins, interferon), eicosanoids (produced from arachidonic acid – e.g. prostaglandins, leukotrienes), histamine – cortisol inhibits their production in several ways
  - lymphocytes disintegrate in rats, leave the vessels in humans – cortisol inhibits proliferation

Regulation of secretion

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- CRH-ACTH-adrenal gland axis
- ACTH is needed for the survival of z. fasciculata and reticularis
- cortisol synthesis and secretion follows faithfully ACTH pulses, but with a delay of a few minutes
- synthesis starts from cholesterol esters stored in intracellular lipid droplets, from LDL taken up from blood, end from cholesterol synthesized de novo
- ACTH stimulates cortisol production through cAMP
- fast effect: cleavage of cholesterol ester, facilitation of LDL uptake, speeding up cleavage of cholesterol side-chain, transport into mitochondria
- slower effect: increased synthesis of these enzymes, receptors, transporters at the level of transcription

Regulation of cortisol release

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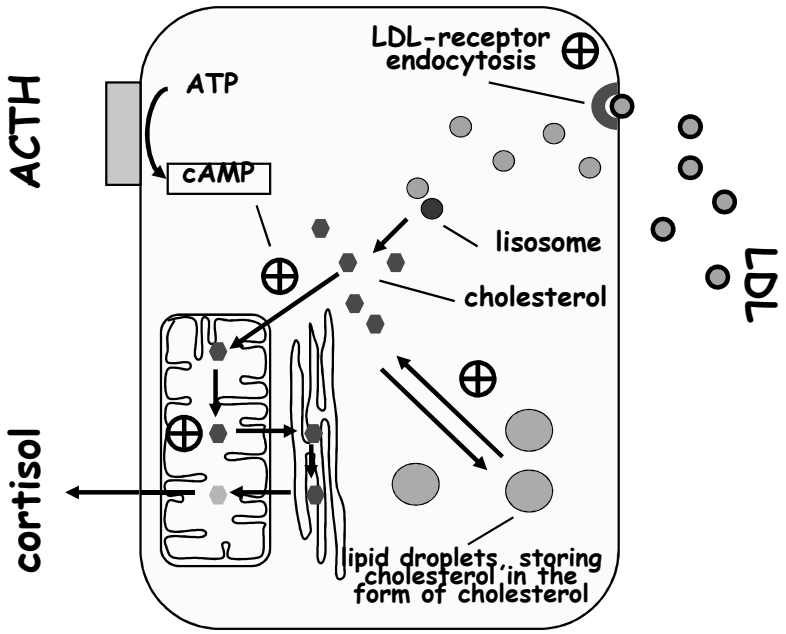

Stress

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- Selye described in rats in the 30's the „alarm reaction" induced by harmful stimuli
- common symptoms: enlargement of adrenal cortex, shrinkage of lymphoid glands (thymus) – the latter does not occur in humans
- stress – stressor
- process started by the nervous system – CRH – ACTH – glucocorticoids
- if this chain is broken, or glucocorticoid receptors are missing, weak stress (e.g. bleeding) can be lethal
- mechanism is unknown, limitation of cytokinin release is a possibility
- in stress there is a considerable increase in the arginnin-vasopressin release from small neurosecretory neurons – it increases ACTH release in synergy with CRH, but is less sensitive to feedback from glucocorticoids

Malfunctioning of adrenal cortex

- lesion of the adrenal cortex (over 90%) – Addison's disease – usually autoimmun reaction
  - hypoglycaemia, low resistance against stress, hypodynamia – due to lack of cortisol
  - sodium loss, potassium retention – due to lack of aldosteron – hypopolarization of heart muscle, decrease of blood volume
  - overproduction of POMC – melanocyte stimulating effect – darkening of the skin (tanning)
  - in females loss of body hair and libido due to lack of androgen hormons
- overproduction of glucocorticoids – Cushing's disease
- CRH, ACTH or cortisol overproduction, sometimes for iatrogen causes
  - shrinkage of muscles, lypolysis on extremities and in subcutis, fat deposition on the head, neck and trunck region (causes?)
  - sometimes androgen overproduction - virilism

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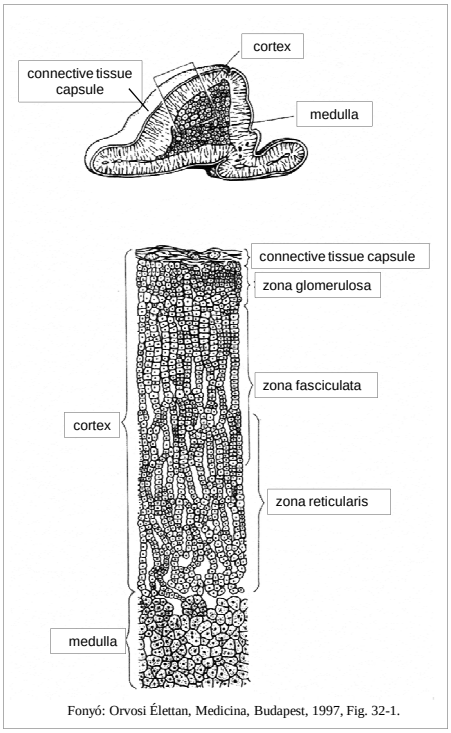
Anatomy of the adrenal cortex



Fonyó: Orvosi Élettan, Medicina, Budapest, 1997, Fig. 32-1.