Thyroid gland

Thyroid hormones

- thyroid gland consists of two lobes weighing 20 g
- thyroid cells surround follicles filled with a colloid (thyroglobulin – glycoprotein): storage
- thyroid gland produces two active hormones: triiodothyronine (T₃) and tetraiodothyronine (T₄ or thyroxine)
- I⁻ is taken up by Na-K-pump dependent active transport – details are not known
- thyroglobulin consists of two subunits; following synthesis they unite, carbohydrates are added; moves toward the follicles in small vesicles
- upon entry the follicle, tyrosine side-chains are iodinated by a peroxidase enzyme that also helps coupling of two tyrosine side-chains through an O-bridge to form either T₃ or T₄ still within the protein chain
- if needed, colloid is taken up by endocytosis, lysosomes digest the protein, T₃ and T₄ are released, iodine is cleaved from other tyrosines
Regulation of $T_3/T_4$ level

- $T_3$ is much more effective, then $T_4$ (thyroxine)
- thyroxine is de-iodinated in the thyroid cells and other cells to $T_3$
- inactivation is achieved through de-iodination or deamination
- thyroid hormones are transported in the blood attached to proteins (thyroxine-binding globulin 85%, thyroxine-binding prealbumin 15%, albumin 5%)
- level of free hormones is very low - this is the active form - blood level is relatively constant
- pulses in every two hours, maximum at early dawn, minimum in the afternoon - amplitude small
- secretion is regulated by TSH, it also controls hypertrophy/atrophy of the gland
- TSH in turn is regulated by TRH (tripeptide)
- negative feedback dominates, but open-loop regulation is also present: fasting, stress decrease, cold (in newborns and animals) increase
TSH effects

- TSH receptor: glycoprotein with two subunits
- TSH acts through different ways, most importantly by increasing cAMP level
- cAMP facilitates uptake of iodine, synthesis of thyroglobulin and its iodination, formation of the thyronine structure, and colloid endocytosis
- TSH causes hypertrophy of the thyroid cells
- lack of thyroid hormones (e.g. caused by lack of iodine) leads to increased TSH production (no negative feedback) and goiter
- the primary cause of goiter is the low iodine level in food and drinking water (rapid streams in the mountains)
- in Africa the extensively cultivated manioc (mainly the bitter version) is rich in thiocyanites competing with iodid to enter thyroid cells
- not proper preparation might lead to goiter
- 200 million people live with goiter world-wide, 1 billion are close to insufficient I- supply

Effects of T₃/T₄ I.

- hydrophobic hormones, regulate expression of genes entering the cells
- cytoplasmic receptor has strong affinity for T₃, direct role of T₄ is debated
- receptor-hormone complex binds to TRE (thyroid response element) domains of the regulated genes, the process depends on a further nuclear protein (see cAMP, CRE, CREB)
- thyroid hormones have profound effects on development and morphogenesis
- postnatal development of the nervous system (myelination, dendritic arborization, formation of synapses) depends on the thyroid hormones
- these hormones are also indispensable for the functioning of the mature nervous system
- direct effect on cartilage and bone; hGH expression also depends on these hormones
**Effects of T₃/T₄ II.**

- morphogenetic role in tadpoles: thyroid lesion - giant tadpole; pulverized thyroid gland into the water - dwarf frogs
- the hormones influence the turnover of glycoproteins in the subcutis; lack of hormones - protein accumulation, increased osmotic pressure, myxedema
- strong effect on basal metabolic rate - calorigenic (except: brain, gonads, spleen)
- thermogenesis increases, mechanism unknown
- circulation increases (stroke volume and pulse rate, thus output of the heart)
- hyperthyroidism is most commonly caused by autoimmune stimulation of TSH-receptors by antibodies formed against the receptors - usually no goiter, only Basedow-syndrome
- increased food intake, but weight loss, increased O₂ consumption and respiration, faster circulation, hand tremor, agitation, emotional lability

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**Hypothyroidism**

- food contains iodide in different concentrations: high in seafood, low in rapid streams in the mountains
- 90% of the total iodide content is located in the thyroid gland
- iodide supply can be assessed by the amount of iodide in the urine
- endemic goiter and cretinism occur in remote geographical locations (mountain villages) because of iodide deficiency - there are 3 million cretins (hypothyroidism during development) world-wide
- longitudinal growth is retarded, development of bones and teeth disturbed, wide, flat nose, protruding tongue, hoarse skin, enlarged belly (low muscle tone), lack of puberty, mental retardation
- hypothyroidism in adults: decrease of basal metabolic rate, myxedema, enlarged tongue, hoarse skin, impaired intellectual and sexual functions, goiter, high cholesterol level
- iodinated salt and oil
Anatomy of the thyroid gland

Thyroid hormones

Berne and Levy. Mosby Year Book Inc, 1993, Fig. 49-1
Fonyó: Orvosi Élettan, Medicina, Budapest, 1997, Fig. 30-2,4.
Goiter