

Laboratory assesment of thyroid gland function

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Thyroid diseases

- 90 % endocrinopathies
- 5-7 % population of CR
 - Women 4-6 x more frequently
- Hypothyroidism, hyperthyroidism
 - Primary (periferal)
 - Secondary (central)

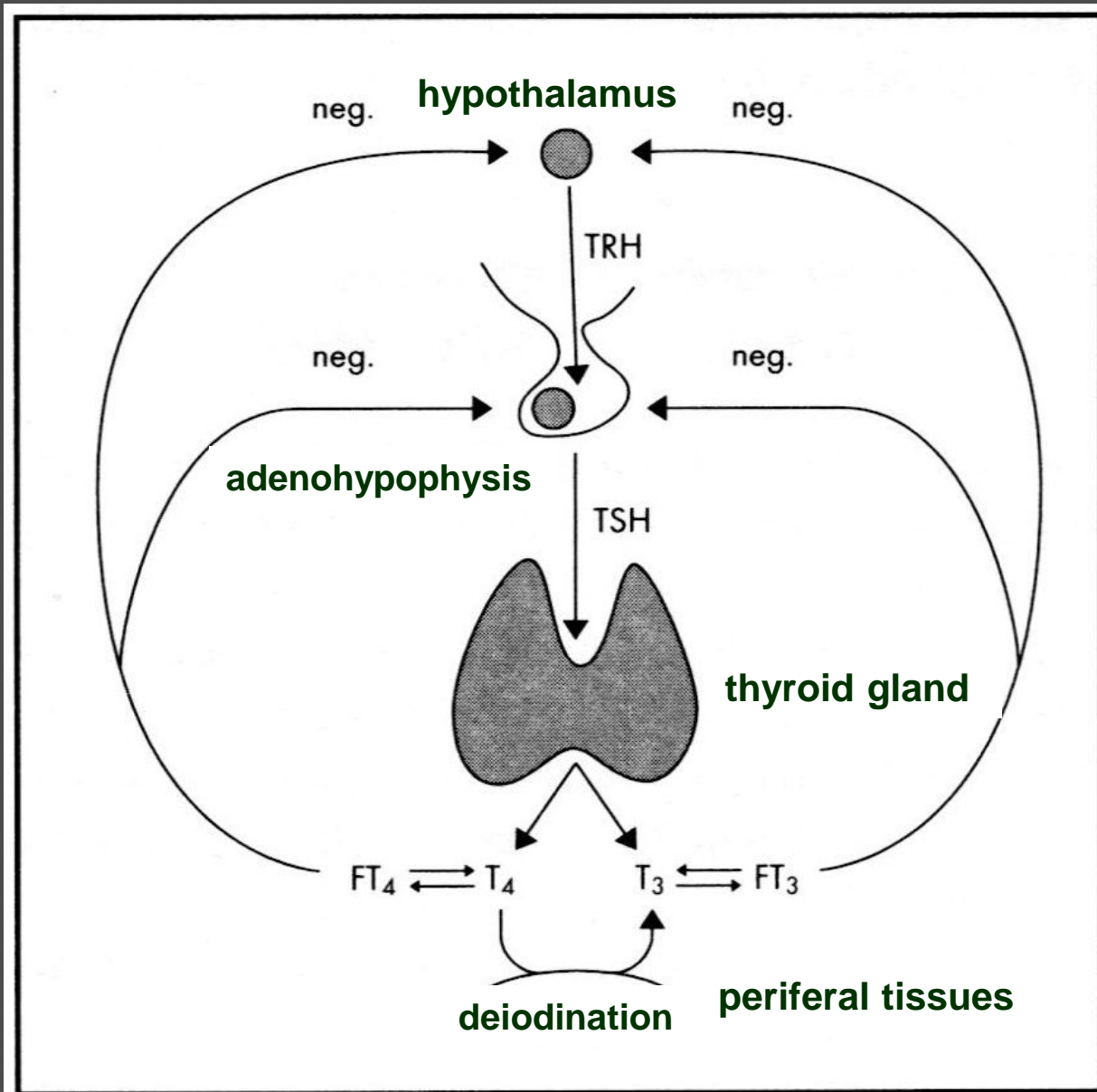
T4 - thyroxine

- Prohormone (ineffective)
 - Deiodination to T3 in tissues
- Bound to proteins - 99,95 %
 - Thyroxin binding globulin, albumin, prealbumine
- Total T4 - no clinical relevant
 - Depends on protein concentration
 - tT4 - not measured
- fT4 - free thyroxin - biologically active

T3

- Active hormon
 - ▶ 80 % of T3 rise by deiodination from T4 in periferal tissues
 - ▶ 20 % - thyroid gland
 - ▶ 99,8 % is bound to proteins (TBG, albumin, PA)
- tT3 (total T3) - may be measured ?
- fT3 (free T3) - biologically active
 - ▶ Better predictive value than tT3

Regulation of thyroid hormones secretion



TSH

- Relationship between the level of fT4 and secretion of TSH
 - Logarithmic-linear
- \downarrow f T4 by 50 % \rightarrow \uparrow TSH 160x !!
- **TSH = the most sensitive test for detection thyroid gland dysfunction!**
- **TSH is primary laboratory test for detection of thyreopathy**

Laboratory analysis


- TSH
- ~~tT4 - total T4~~
- fT4 - free T4
- (tT3 - total T3)
- fT3 - free T3
- TBG
 - Thyroxin bind globulin
- Ioduria
- Anti TPO
- Anti TG
- TRAb;
- Thyreoglobulin
- Calcitonin

free T4 measurement - indication

- If an \uparrow or \downarrow of TSH
 - To confirm hyper- or hypothyroidism
- Monitoring the effect of treatment

Free T3 measurement - indication

- Diagnosis of T3 thyreotoxicosis
- Dg. of subclinical primary hyperthyroidism
- Unsuitable for
 - ▶ Dg. hypothyroidism
 - ★ Delayed reaction
 - ★ Mild ↓
 - Up to quarter of population !
 - Other diseases (non-thyroidal) - syndrome of low T3
 - ▶ Monitoring of treatment

- TG (thyreoglobuline)
 - Ca. of thyroid gland
 - Calcitonin
 - Medullary ca. of t.g.
- 
- Tumor markers
- Ioduria - supply of iodine in the body
 - ↓ = marked iodopenia

Antibodies

- Anti TPO

- ▶ Thyroperoxidase antibodies
- ▶ Antimicrosomal antibodies

Hashimoto's
thyroiditis

- TRAb

- ★ TSH-receptors stimulating antibodies
- ▶ TGI - thyroid growth IG

Graves'-
Basedow
thyrotoxicosis

Anti TG

- ▶ Thyroglobulin antibodies

Functional testing of t. g.

- TRH stimulating test
 - ▶ 200 μg TRH i.v.
 - ▶ TSH determination after 20 min. (2 - 25 mU/l)
- Indication
 - ▶ Subclinical hyperthyroidism
 - ★ Insufficient increase of TSH

Changes of TSH non-thyroid

- ↑ TSH
 - Convalescence
- ↓ TSH
 - Acute diseases
 - ★ Fever, MI, trauma, surgery,
 - Chronic diseases
 - ★ Tu, DM, CHF, nephrotic sy, malnutrition
 - Mental illness
 - ★ Akute, chronic
- Usually normal level fT4

Reference ranges

- TSH (0,3 - 4,2 mU/l)
- fT4 (9 - 25 pmol/l)
- fT3 (3 - 6 pmol/l)
 - ▶ tT3 (1,3 - 3,1 nmol/l)

- TBG (12-30 mg/l)
- Ioduria (> 100 ug/l)

- TG (0 - 55 ug/l)
- Calcitonin (do 150 ng/l)

↑ TSH

TSH normal

↓ TSH

↓ fT4

**Primary
hypothyroidism**

**Secondary
hypothyroidism**

fT4 normal

**Subclinical
primary
hypothyroidism**

**Normal thyroid
function**

**Subclinical
primary
hyperthyroidism
(T3-thyreotoxikóza)**

↑ fT4

**Secondary
hyperthyroidism**

**Primary
hyperthyroidism
(doplnit fT3)**

	↑ TSH	TSH normal	↓ TSH
↓ fT4	Primary hypothyroidism		Secondary hypothyroidism
fT4 normal	Subclinical primary hypothyroidism	Normal thyroid function	Subclinical primary hyperthyroidism (T3-thyreotoxikóza)
↑ fT4	Secondary hyperthyroidism		Primary hyperthyroidism (doplnit fT3)

Laboratory testing of the adrenal cortex gland function

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Adrenal cortex - structure and function

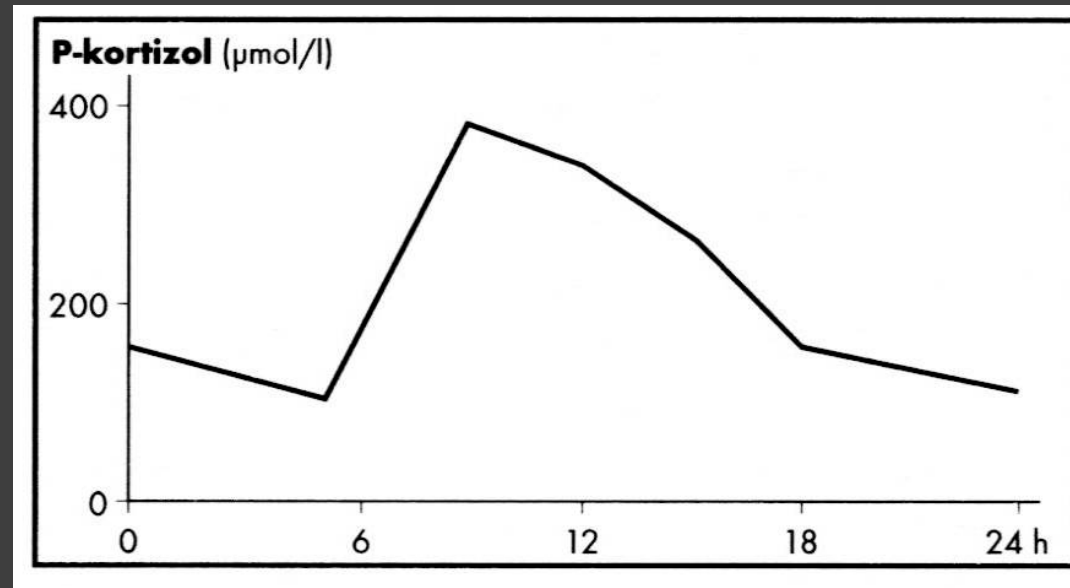
- 3 zones (glomerulosa, fasciculata, reticularis)
- 2 functional units
 - ★ Independently controlled, express different enzymes
 - ▶ Zona glomerulosa
 - ★ Aldosteron
 - ★ Controlled by - renin, angiotensin system
 - ▶ Zona fasciculata, zona reticularis
 - ★ Glucocorticoids
 - ★ Androgens (testosteron), a little amount of oestrogens
 - ★ Controlled by ACTH

Cortisol (hydrocortisone)

- Synthesis control
 - ▶ Negative feedback
 - ★ \downarrow cortisol = \uparrow CRH, \uparrow ACTH
 - ★ \uparrow cortisol = \downarrow CRH, \downarrow ACTH
 - ▶ Stress
 - ▶ Hypoglycaemia
 - ▶ Circadian rhythm
- Metabolism
 - ▶ Binding to prot. (90 %)
 - ★ Transcortin
 - ▶ Urinary excretion
 - ★ Cortisol
 - ★ 17-OH-steroids

Circadian rhythm of cortisol

- Basal value - 8 h. morning
 - ▶ M: 250-650 nmol/L; F: 140-740 nmol/L
- Afternoon - 5 h. p.m.
 - ▶ If cortisol at 5 p.m. < 410 nmol/L = impaired circadian rhythm
- Free cortisol in urine
 - ▶ 50 - 250 nmol/day



Testing of thyroideal x glucocorticoid function

- Thyroid function - TSH
- Glucocorticoid function - ACTH ???

- Glucocorticoids and ACTH
 - ▶ Circadian rhythm
 - ▶ Stress, physical activity,
 - ▶ Ectopic syntesis
 - ▶ ACTH - secretion of androgens

Hypercorticism (Cushingův sy.)

- Types

- ▶ Peripheral (20 %) - suprarenal gland
- ▶ Central (70 %) - hypophysis
- ▶ Paraneoplastic (ectopic production of ACTH)

- Laboratory tests

- ▶ Free cortisol - urine
- ▶ Rhythm of plasma cortisol (impaired)
 - ★ Serum cortisol: 8 h. and 17 h.
 - ★ Impaired circadian rhythm = early sign of Cushing sy
- ▶ ACTH
 - ★ Diff. dg. primary x secondary hypercorticism

Hypercorticism - lab. tests (functional tests)

- Dexamethasone suppression test
 - ▶ Function of negative feedback
 - ▶ ↓ secretion CRH, ACTH, → ↓ cortisol (< 50 %)
 - ▶ Adenoma SR gland - without ↓ cortisol (no response)
- CRH stimulating test
 - ▶ ↑ACTH, → ↑cortisol (> 50 %)
 - ▶ Cushing - exaggerated reaction
 - ▶ Ectopic secretion of ACTH - no response

Hypercorticism - other lab. tests

- Glycaemia
 - ▶ Prediabetes, diabetes
- Ions
 - ▶ Hypokalaemia, MAL

Diff. dg. - Cushing syndrom

	Hypophysis (Cushing dis.)	Ektopic production ACTH	Tumour of the cortex suprarenal gl.
Cortisol - urine/24 h.	↑	↑ ↑ ↑	↑
Cortisol - serum	Inhibition of circandian rhythm only	↑ ↑ ↑	Inhibition of circandian rhythm only
ACTH - serum	↑	↑ ↑ ↑	↓ ↓
Dexamethazon supress. test	without response	without response	without response

Hypocortisolizmus

- Primary - Addison´s disease
 - ▶ Autoimmune, infection,
- Secondary - due to deficit of ACTH
 - ▶ Pituitary diseases
- Lab. tests
 - ▶ Serum cortisol
 - ▶ Plasma ACTH
 - ★ Diff. dg. central x periferal form
 - ▶ Stimulating tests

Stimulating test (suspicion of central hypocorticalism)

- ACTH test (synacthen test)
 - ▶ Synthetic ACTH → ↑ cortisol
 - ★ ↑ cortisol > 700 nmo/l → adrenocortical insuff. is excluded

Testing of glucocorticoid secretion

- Hypocorticalism
 - ▶ Cortisol in serum
 - ▶ ACTH in serum
 - ▶ Stimulation tests (Synacten - ACTH, Metyrapon)
- Hypercorticalism
 - ▶ Cortison in urine
 - ▶ Cortisol in serum - circadian rhythm
 - ▶ ACTH in serum
 - ▶ Supression test (dexamethazon)
 - ▶ Stimulation test (CRH)

Lab tests - mineralocorticoids

- ▶ Na^+ , K^+ : serum, urine output/d.,
 - ★ Fractional excretion
- ▶ PRA (plasma renin activity)
 - ★ Blood collection - morning in bed rest
 - Positional changes or stress readily increase the PRA
- ▶ Plasma aldosterone
 - ★ Blood collection - morning in bed rest
- ▶ Captopril test
 - ★ Renovascular x essential hypertension
 - ★ Captopril = inhibitor ACE (angiotensin converting enz.)
 - ★ Distinct \uparrow of PRA = renovascular h.

- Congenital adrenal hyperplasia (CAH)
Adrenogenital syndromes (AGS)
- Neonatal screening: 17α -OH-progesterone

Stimulating tests (suspicion of central hypocorticalism)

- ACTH test (synacthen test)
 - ▶ Synthetic ACTH → ↑ cortisol
 - ★ ↑ cortisol > 700 nmol/l → adrenocortical insuff. is excluded
- Insulin stimulating test
 - ▶ Hypoglycaemia (< 2,2 mmol/L) → ↑ CRH, ACTH, cortisol
 - ★ Diff. dg. Cushing sy. x overproduction of corticoides due to stress
- Metyrapone blocking test
 - ▶ Metopirone inhibits 11 β -hydroxylase (cortisol synthesis)
 - ▶ ↓ cortisol → ↑ ACTH → ↑ stimulation of SR gland →
↑ 11-deoxycortisol synthesis
 - ▶ Measuring of serum cortisol and urine 17-OH-steroids
 - ★ Week response - ectopic ACTH secretion
 - ★ High response - Cushing's disease

Adrenal medulla

- Adrenaline, Noradrenaline, Dopamine
- Hyperfunction - pheochromocytoma

Pheochromocytoma - lab. tests

- Adrenaline, NA
- Metabolites
 - ▶ Metanefrine, normetanefrine
- Serum, urine

- Clonidine test
 - ▶ Inhibition of NA releas from sympatic n. system
 - ▶ No inhibition NA from pheochromocytoma
- Glukagone test
 - ▶ Glukagone i.v.
 - ▶ Pheochromocytoma - 3x ↑ adrenaline, NA
 - ▶ Risk of hypertension crisis

Adrenogenital syndromes (AGS) - lab. tests

- **17 α -hydroxyprogesterone**

- ▶ Deficiency of 21-hydroxylase

- ★ Simple virilizing, salt-wasting form

- ★ 17 α -OH-progesterone: norm.- mírně ↑

- ★ Synacthen test: ↑ > 30 nmol/L za 60 min (fysiol. < 18 nmol/L).

- **11-deoxycortisol**

- ▶ Deficit 11 β -hydroxylázy

- ★ ↑ > 350 pmol/L (spolu s 11-desoxykortikosteronem)

- ★ ↑↑ po Synacthenu u homozygotů

- **S-DHEA-sulfát bez androgenní aktivity**

- ▶ Skrece nadledv.(nepatrně gonádami)

- ▶ Sérum 800 – 7 000 nmol/L

- ★ ↑ u nádorů, hyperplazie nadledvin, u hirsutismu