Signs and symptoms of endocrine disorders

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1.General overview

2. Endocrine glands

a- physiology

b- diseases

Endocrine glands

Coordinate systems to control homeostasis acccording to demands of organism and in reaction to environment

Mediators – hormones in circulation - endocrine

tissue hormones – effect from one cell to adjacent cells
- paracrine

Hormone

Chemical mediator of information produced in a specialised endocrine cell

- ✓ Collections of specific cells in strictly anatomically defined structures - glands
- ✓ Parts of organs (beta cells in Langerhans islets in pancreas)
- ✓ Cells dispersed in mucose (enteroendocrine cells- in stomach, small bowel, colon)
- ✓ Adipose tissue – adipocytes, macrophages

Hormones

Chemically

- Proteins, glycoproteins, peptides
- Steroids (cortisol, sex hormones - basis cholesterol)
- Derivatives of amino acids (thyroid hormones, catecholamins – AA tyrosine)
- Others

Hormones

Eutopic x ectopic hormone production

Endocrine diseases

Hormone overproduction- increased number of hormone producing cells, abnormal regulation of hormone synthesis or release

Hormone underproduction-destruction of hormone producing cells by
autoimunity
surgical removal

Altered tissue responses – resistance to hormone (insulin resistance, Laron dwarfism - GH)

Tumours of endocrine glands – with overproduction, non functioning (pituitary tumours)

Hyperfunctional endocrine syndroms

1. Adenoma or carcinoma of a gland

2. Hyperfunction of adenohypophysis→ increase in tropin → glandular hyperplasia

3. Ectopic hypersecretion

4. Iatrogenic, hormone application

Hypofunctional endocrine syndroms

1. Primary (peripheral) disorder of gland

2. Secondary – disorder of stimulatory function of adenohypophysis

3. Tertiary – disorder of hypothalamus

Hormones produced by:

Hypothalamo-hypophyseal region

Thyroid gland

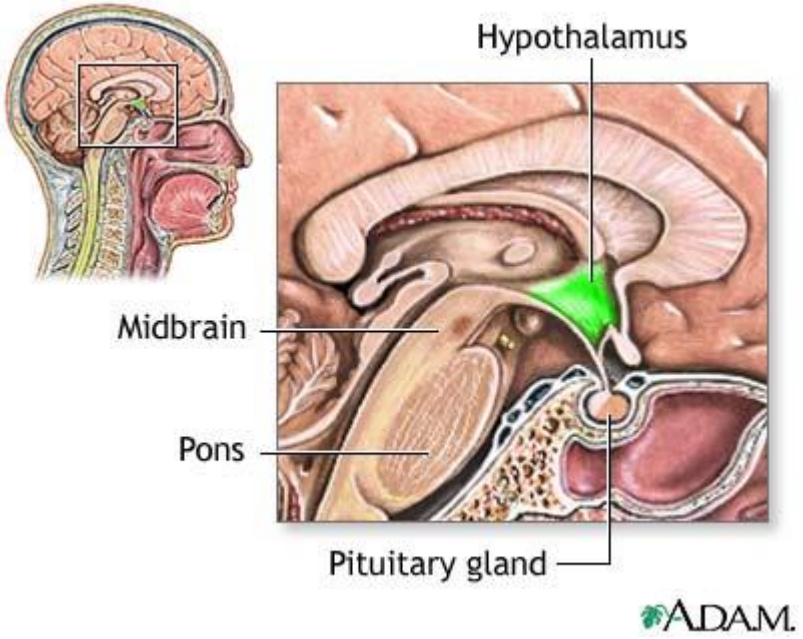
Parathyroid glands

Adrenal glands

Langerhans islets of pancreas, juxtaglomerular apparatus of kidneys

Other tissues- GIT, adipose tissue

Hypothalamus and pituitary



Hypothalamus and pituitary

Hypothalamus-

3 types of neurosecretory cells

- magnocellular neuron – vasopressin (ADH), oxytocin

  neurohypophysis target kidney, uterus, mammary gland

- parvicellular. hypophyseotrophic neuron- TRH, CRH, GHRH, GnRH-**liberins**, somatostatin, dopamin (prolactin inhibiting factor,PIF) **statins**

  target anterior pituitary gland

- hypothalamic neuron -MCH (melanin-concentrating hormone), orexins, POMC (pro-opiomelanocortin), CART (cocaine-amphetamine regulated transcript)

  targets neurons

Hypothalamus and pituitary

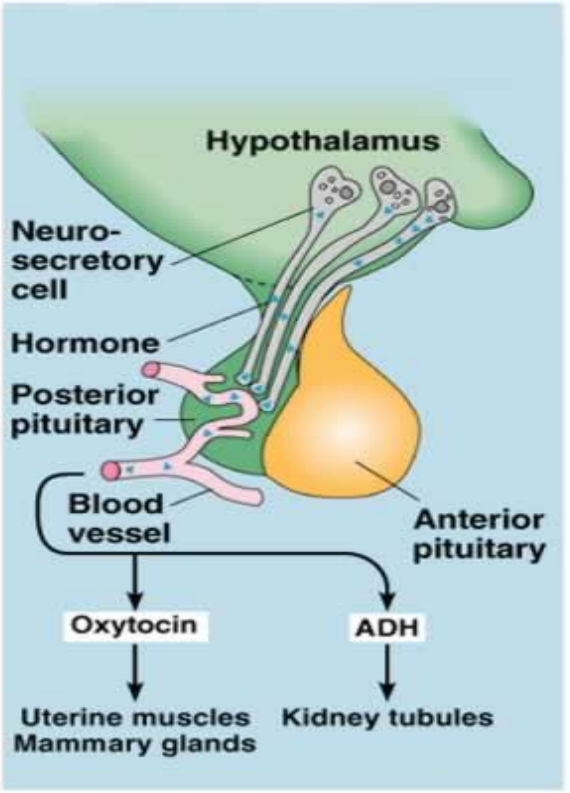
Pituitary

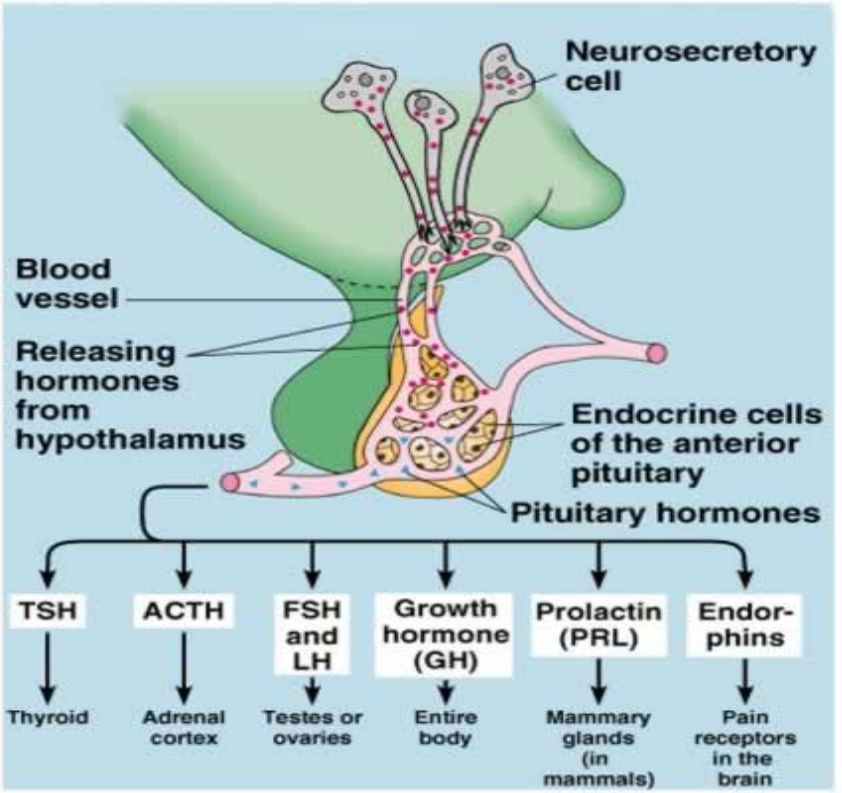
adenohypophysis -glandotropic hormones- tropins

GH growth hormone (GH), prolactin, thyrotrophic hormone(TSH),
gonadotropins – LH (luteinizing), FSH (follicle stimulating h.)
from proopiomelanocortine (POMC) - ACTH, alpha MSH,
beta-endorphin, beta-lipotropin

neurohypophysis – vasopressin (ADH antidiuretic hormone), oxytocin

Hypothalamus and pituitary





Hypothalamo-pituitary disorders

Hypopituitarism

Hypopituitarism in adults

Cause: chromofobe adenoma, their complications (bleeding into tumor) and treatment (surgery, irradition), other tumours, autoimmune, craniocerebral trauma

acute after delivery (Sheehan´s syndrome, bleeding),

Symptoms from the most frequent: gonadotropic – thyrotropic – adrenocorticotropic functions – growth hormone – diabetes insipidus

Therapy: substitution- sex steroids, thyroid hormones, Hydrocortisone tabl., GH, desmopresin

Hypothalamo-pituitary disorders

Hypopituitarism

Hypopituitarism in childhood – hypophyseal nanism

cause: idiopathic- hypothalamic process with lower GH-RH, hereditary pituitary deficiency, Laron syndrome – autosomal recessive resistence on GH, resulting in absence of IGF-I, craniopharyngioma, other tumours, trauma

symptoms: growth, gonadotropic function

Therapy: hormone replacement- GH (Laron IGF-I?)

Hypothalamo-pituitary disorders

Pituitary tumours

Chromophobe adenoma a craniopharyngioma

compression of surrounding healthy tissue (optic chiasma), decreased or normal pituitary function

symptoms: headache, impotence in men, secondary amenorrhoe in women, bitemporal visual loss (hemianopia)

Therapy: surgery -transsphenoidal approach, radiotherapy -x-ray irradiation, radiosurgery (stereotactic conformal therapy, gamma knife)

Hypothalamo-pituitary disorders

Pituitary tumours with hyperfunction and syndromes of pituitary hypefunction

Adenomas

Acromegaly, gigantism

Cushing disease, Nelson syndrome

Prolactinoma

Hypothalamo-pituitary disorders

Acromegaly, gigantism

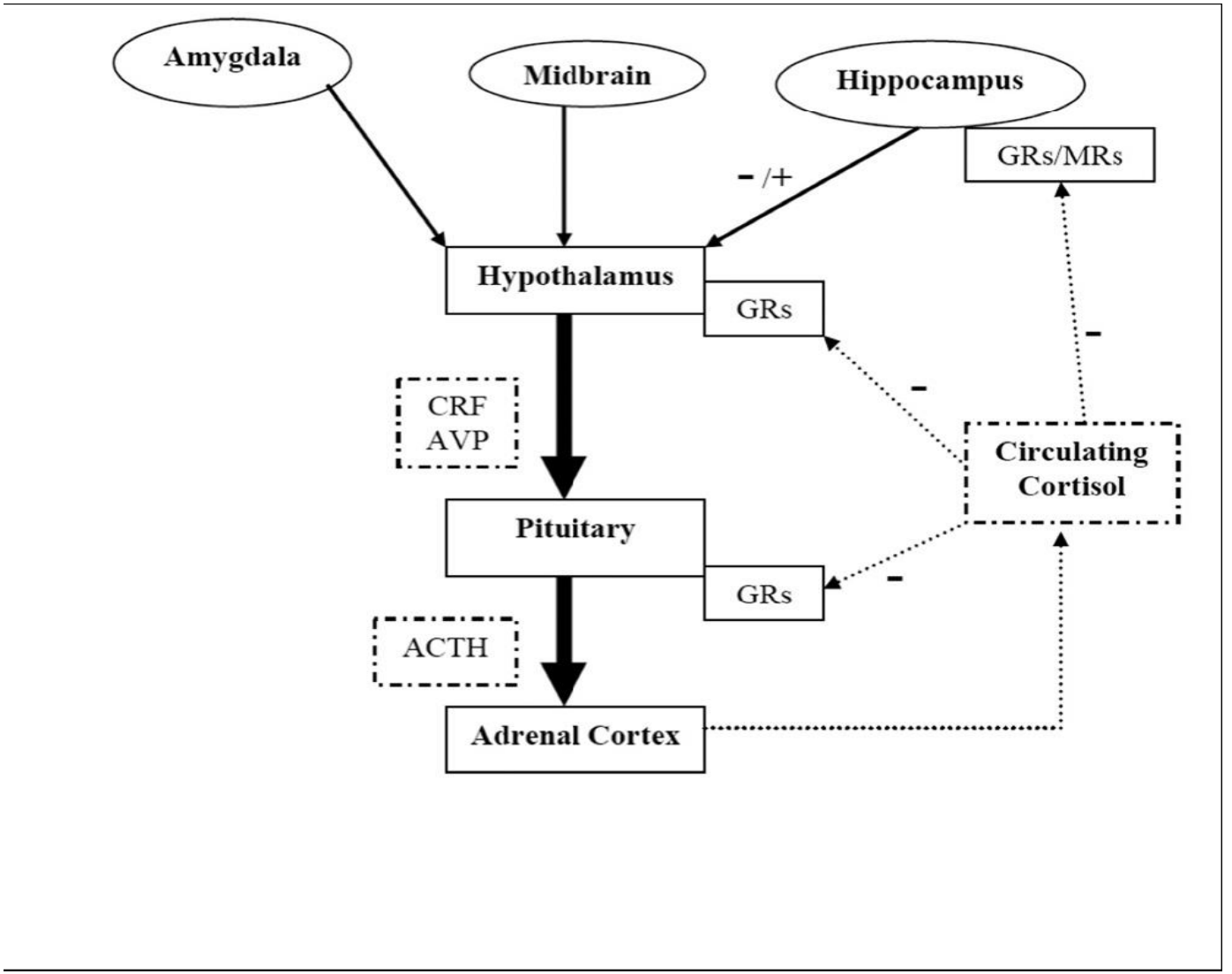
GH cell adenoma , hyperplasia

high GH, in oGTT – fails decrease of GH, NMR

symptoms: acral and soft tissue growth, headache, hirsutism, arthropathy, DM, cardiac

Therapy: surgery, irradiation, gamma knife, dopamin agonists (cabergolin), somatostatine analogs (octreotid, lanreotid), recombinant analogue of GH- binding on GH receptors (pegvisomant) and combination of methods

Hypothalamo-pituitary-adrenal axis



Hypothalamo-pituitary disorders

Cushing´s disease

adenoma of corticotroph cells, more often microadenomas

dg-increase of ACTH, cortisol, dynamic tests (dexamethasone)

Symptoms: plethora of face, central fat distribution, hypertension, type 2 DM, violet striae, osteoporosis, hypogonadism, psychic disorders

Therapy: transsphenoidal surgery, x ray irradiation, metyrapon, bilateral adrenalectomy

Ectopic secretion of ACTH: parvicellular ca of lung, carcinoid

Nelson syndrome after total adrenalectomy for Cushing´s disease (increase of ACTH, pigmentation)

Hypothalamo-pituitary disorders

Prolactinoma, hyperprolactinaemia

prolactinoma, other pituitary tumour inhibiting dopamin, idiopatic hyperprolactinaemia, macroprolactinaemia* , hypothyroidism (increased TRH stimulates PRL production), drugs (neuroleptics, antagonists of dopamin receptors, metoclopramide, cimetidin, verapamil etc)

PRL level, NMR

symptoms: galactorrhoea, amenorrhoe, infertility, sexual dysfunction

Therapy: dopamin agonists (cabergoline), surgery, irradiation

*makroprolactin-lower clinical effect

Hypothalamo-pituitary disorders

Diabetes insipidus

Decreased secretion of vasopressin (ADH)

tumour of hypothalamus, inflammation, trauma, after hypophysectomy, idiopathic, hereditary

concentration test – diuresis 5-20 l, low urine osmolality,CT, NMR of brain

symptoms: polyuria, polydipsia

x psychogenic polydipsia, nephrogenic

Therapy: desmopresin sublingual tbl., Adiuretin drops intranasally, according to the cause

Thyroid gland

Thyroxine (T4), triiodothyronine (T3),

T4 a T3 – parts of thyroglobuline in colloid of thyroid

regulation TRH (thyrotropin releasing hormone, thyroliberin)-TSH (thyroid stimulating hormone, thyrotropin)

in circulation bound by TBG (thyroxin binding globulin)

TBG production is influenced by estrogen level (increase), androgen level (decrease)

T4 in peripheral tissues – de-iodination resulting in T3 or inactive rT3 (reverse T3)

Calcitonin

produced by nonfollicular thyroid C cells, regulation of Ca metabolism

Thyroid gland

Laboratory tests

fT4, fT3, TSH
(TSH in capillary blood- hypothyroidism screening in newborns)

autoantibodies against thyroid peroxidase, against thyreoglobulin
autoantibodies against TSH receptor (TRAK)
thyreoglobulin-monitoring after therapy for thyroid carcinoma

Immunoreactive calcitonin (medullary ca)

Thyroid

Examination

US

morphological characteristics – nodular or diffuse goiter, cystic areas

Doppler- measurement of blood flow – enhanced in GB thyrotoxicosis

goiter: from 18 ml in women, from 22 ml in men

Substernal or intrathoracic goiter is not depicted

CT or NMR

Fine needle aspiration biopsy (FNAB), cytological exam

nodule > 1 cm, fast growing goiter, fast growing nodule

Sciagrammatic (xray) exam of upper mediastinum- compression of trachea, deviation of esophagus- signs of compression

Thyroid

Examination

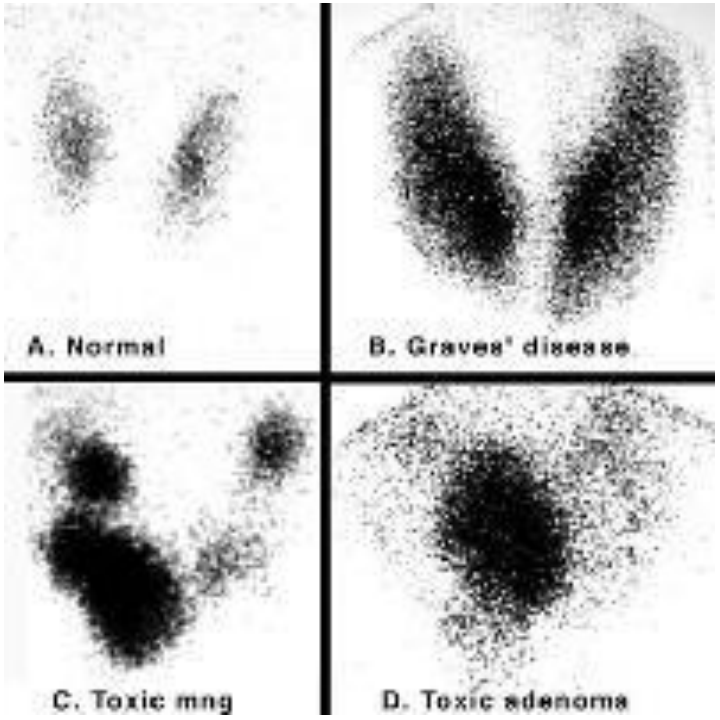
scintigraphy- functional activity

- Sodium pertechnetate (technecistan)^{99m}Tc

cold, hot nodules, diffused decreased accumulation

- Iodine (^{131}I and ^{123}I)

dg and treatment of thyroid carcinoma



Disorders of thyroid

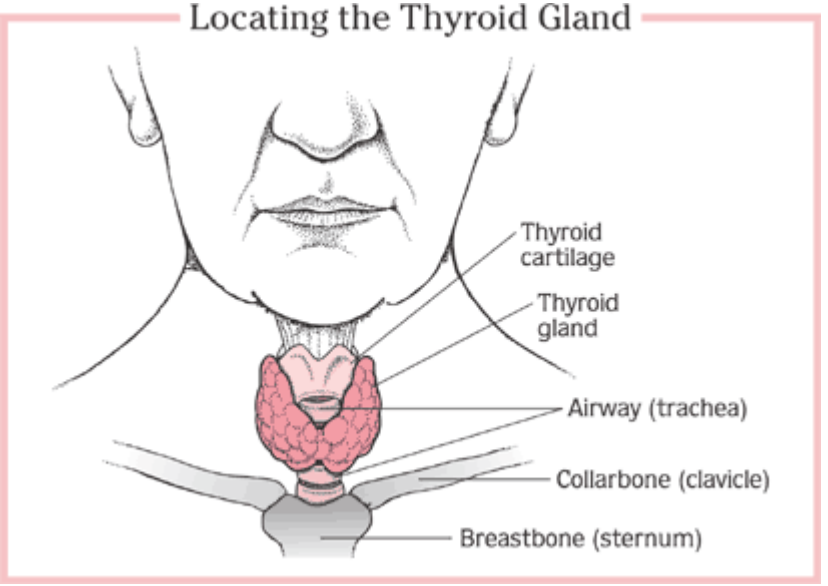
Euthyroid

simple (nontoxic) goiter

often insufficient amount of I in food, initial phase of autoimmune process, strumigens in food, genetic susceptibility(familiar)

diffuse, multinodular

Therapy: sufficient intake of I
(100ug/day, gravidity 200ug/day)



Disorders of thyroid

Hypothyroidism

primary autoimmune thyroiditis (Hashimoto), TTE (total thyroidectomy), irradiation, enzymatic defects

myxedema, pre or perinatal - cretenism

low fT3, fT4, high TSH, autoantibodies

symptomatology: fatigue, sleepiness, cold intolerance, constipation, dry skin, oligomenorrhoea (increase in TRH causes increase in PRL), hoarse voice

secondary in panhypopituitarism

Therapy: thyr.hormones

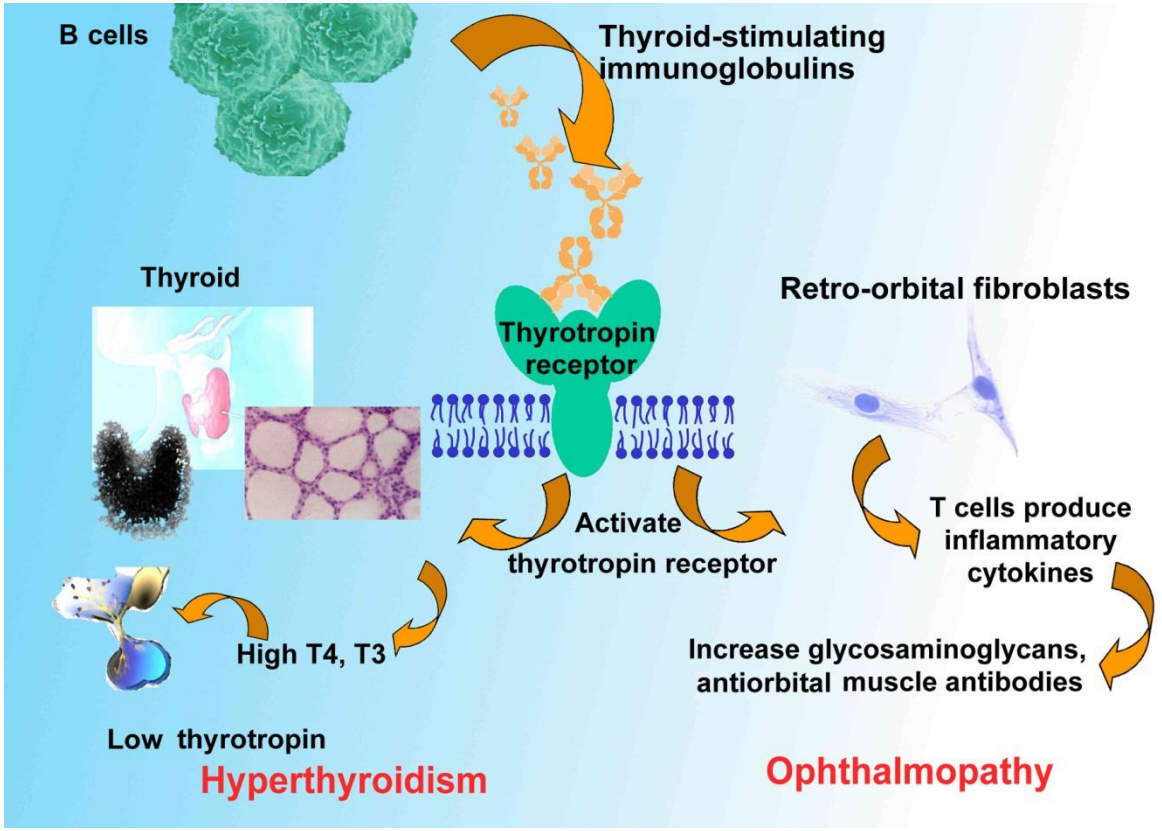
Disorders of thyroid

Hypothyroidism – oral manifestations

1. Delayed eruption
2. Enamel hypoplasia in both dentitions
3. Anterior open bite
4. Macroglossia
5. Micrognathia
6. Thick lips
7. Dysgeusia
8. Mouth breathing

Disorders of thyroid

Graves Basedow disease



Disorders of thyroid

Hyperthyroidism

Graves Basedow disease

autoimmune diasease, familiar appearance

Increase in fT4, fT3, supression of TSH, autoantibodies against thyrotropin receptors -TRAK, Achille tendon reflex duration

hyperfunction, hyperplasia of thyroid, orbitopathy, dermopathy, thyrotoxic crisis (thyroid storm)

tachycardia, warm, fine, sweating skin, dyspnoea, muscle weakness, weight loss, psychiatric symptomatology, tremors, impaired glucose tolerance

sthenic form (without weight loss, weakness, often only arrythmia)

Therapy:thyrostatic drugs -propythiouracil, thiamasol-thyrosol, beta-blockers, anxiolytics, TTE, radiojodine

Disorders of thyroid

Hyperthyroidism

Graves Basedow disease

orbitopathy

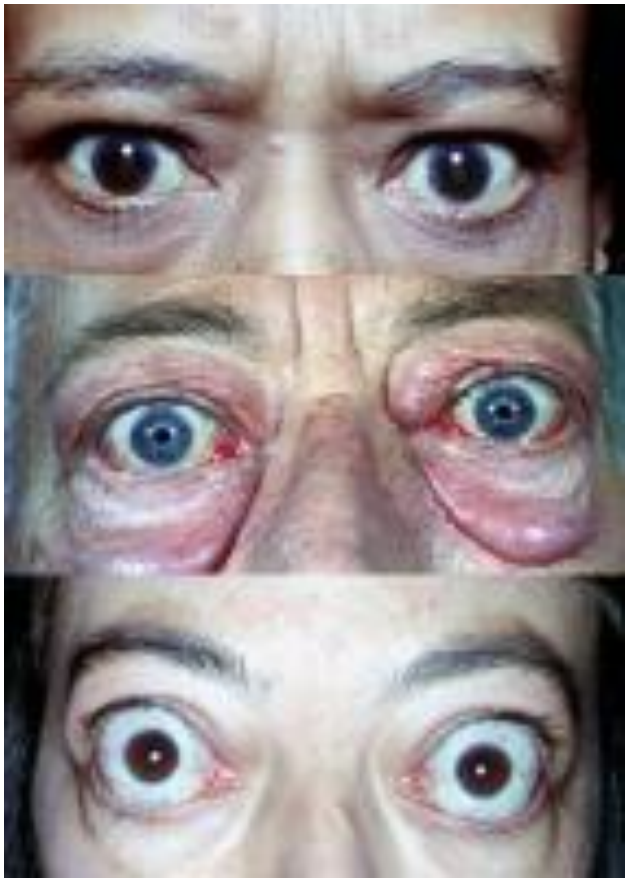
Proptosis of eye bulbs, Hertel, Graefe sign, tearing, eyelid retraction

Therapy: cortikoids pulse ther., sometimes in combination with radiotherapy of orbits and immunosupressives (cyclofosfamide), surgery transnasal orbital decompression, later TTE

thyreotoxic crisis (thyroid storm)-hyperthermia, agitation, adynamy, anxiosity, coma

Therapy: thyreostatics iv., glukocorticoids

Disorders of thyroid orbitopathy



Disorders of thyroid

Hyperthyroidism

Toxic adenoma

Similar symptomatology

Without orbitopathy

Autoantibodies not present (only in case of current autoimmune thyroiditis)

Multi-nodular toxic goiter

Therapy: first phase thyrostatics, second phase TTE

Thyrotoxicosis facticia –misuse of thyroid hormones

Disorders of thyroid

Hyperthyroidism – oral manifestations

1. Accelerated dental eruption in children
2. Maxillary or mandibular osteoporosis
3. Enlargement of extraglandular thyroid tissue (mainly in lateral posterior tongue)
4. Increased susceptibility to caries
5. Periodontal disease
6. Burning mouth syndrome
7. Development of connective-tissue diseases
8. Mouth breathing

Treatment
restrict the use of epinephrine or other pressor amines
in local anesthetics, limit stress,
In case of inflammation – blood count (leucopenia after thyreostatics)

Disorders of thyroid

Neoplasia

Thyroid carcinoma

Papillary-70-80%

Follicular-15%, higher tendency to distant metastases (lung, bone)

therapy: surgery TTE+Iodine (^{131}I)

Anaplastic, undifferentiated, very aggresive

actinotherapy+chemotherapy

surgery only radical or from vital indication

Microcarcinoma – < 2 cm, adjacent normal thyroid tissue, low biological activity, very good prognosis, preventive TTE

Disorders of thyroid

Neoplasia

Medullary thyroid carcinoma – from parafollicular cells
in 20% autosomal dominant inheritance

Th: TTE, block dissection of neck lymphnodes (nodular metastases)

As a part of a **multiple endocrine neoplasia**
mutations in the *RET* proto-oncogene

MEN2A +pheochromocytoma, hyperparathyroidism
MEN2B + pheochromocytoma, mucous ganglioneurosis, gastrointestinal, skeletal and dermatological abnormalities.

Parathyroid gland

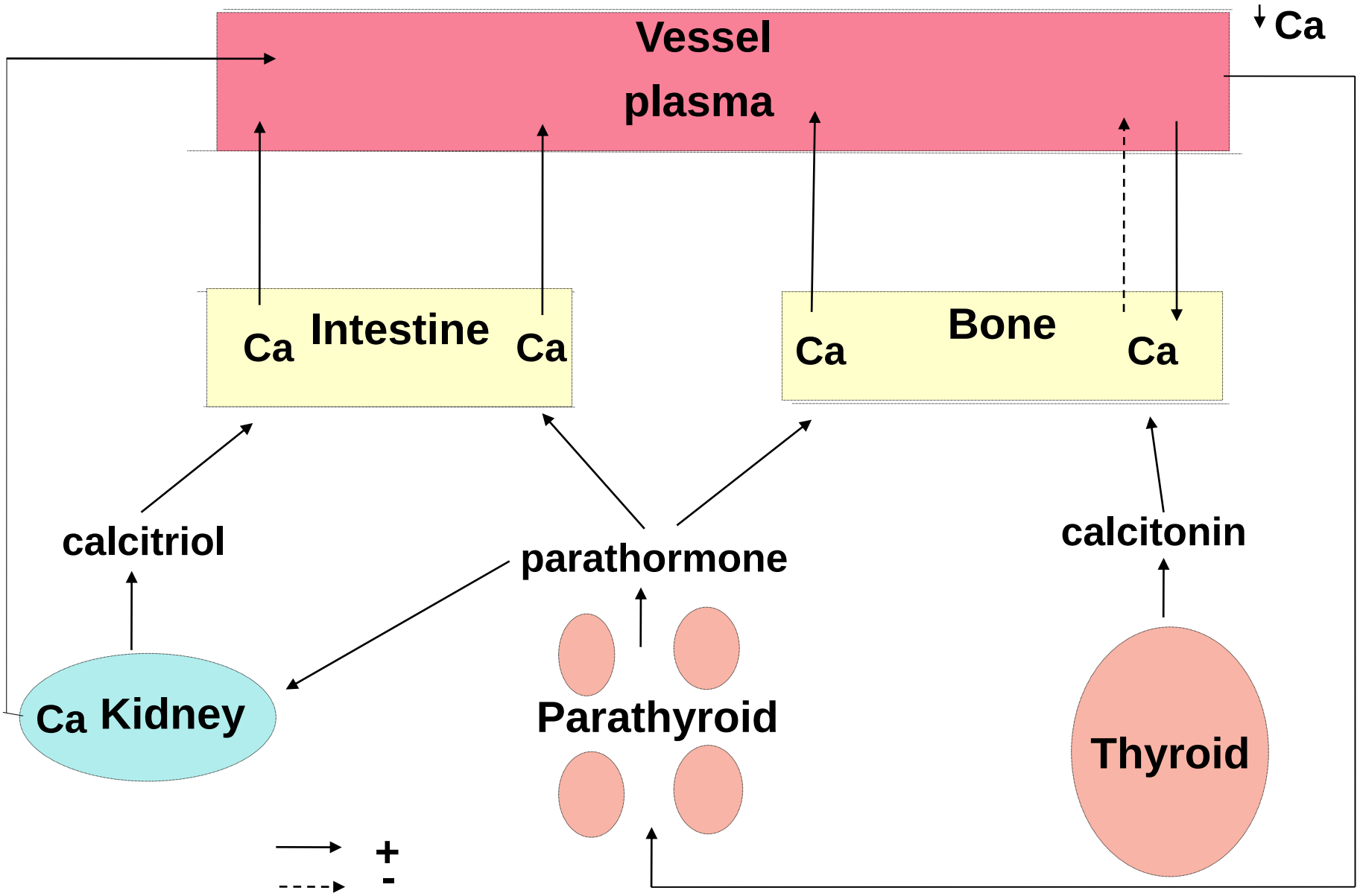
Parathormone

Secretion regulated by serum calcium

Examination

Serum PTH level

Homeostasis of Ca



Parathyroid gland

Hyperparathyroidism

Primary: adenoma of one or more parathyroid glands, or hyperplasia of all PT glands, part of MEN2A, carcinoma of PT

2nd most often endocrinopathy

Secondary: result of hypocalcemia

Tertiary: adenoma as a result of secondary hyperPT

Pseudohyperparathyroidism: source of PTH is ectopic tissue (tumour - bronchogenic carcinoma)

Parathyroid gland

Hyperparathyroidism

Hypercalcaemia- elevated ionized calcium
PTH

US thyroid –localization of the adenoma
CT, NMR
scintigraphy-^{99m}Tc-MIBI

X-ray of hands – subperiostal usurations

Parathyroid gland

Hyperparathyroidism

Skeletal – osteodystrophy, decreased bone density, subperiostal resorption - usurations- hands, skull, osteolytic (brown tumours)

Hypercalcemia– to 3mmol/L clinically asymptomatic

over 4mmol/L dehydration, enhanced T, oliguria, circulatory collapse

Kidney – nephrolithiasis, rarely nephrocalcinosis

GI – peptic ulcer, pancreatitis, constipation

Psychologic symptoms- affective lability, depression

Arterial hypertension

Ophtalmological- corneal calcifications

Therapy: surgical removal of adenoma

Parathyroid gland

Hyperparathyroidism

Therapy of hypercalcemic crisis
rehydration
Diuretics -furosemid
Calcitonine
Glucocrticoids
(ionexchange resonium)

Parathyroid gland

Hyperparathyroidism

In the oral cavity
brown tumor, loss of bone density, weak teeth, malocclusions, soft tissue calcifications and dental abnormalities such as development defects,alterations in dental eruption and widened pulp chambers

Stomatological treatment:
a higher risk of bone fracture, so we must take precaution in surgical treatments.
On the other hand, it is important to recognize the presence of a brown tumor

Parathyroid gland

Hypoparathyroidism

Most often - after TTE

autoimunne (idiopatic)

part of polyglandular insufficiency

after destruction of PT glands (tumour, inflammation)

agenesis (together with thyme aplasia and immunodeficit- sy DiGeorgi)

functional-in newborns (in case of mother hyperCa), after PT adenoma removal, gradual start of function

pseudohypoparathyroidism- resistence of peripheral tissue to PTH, molecular defects in the gene (*GNAS1*) encoding alpha subunit of the stimulatory G protein (Gsa)

Parathyroid gland

Hypoparathyroidism

acute

tetany – paresthesia, muscle cramps, bronchospasm, laryngospasm, generalized tonic-clonic cramps

diff. dg - hyperventilatory alkalosis (decrease of ionized Ca), febrile cramps in children

Therapy: Ca iv., Mg, breathing into a plastic bag

Parathyroid gland

Hypoparathyroidism

chronic

latent tetany- enhanced neuromuscular irritability

carpal spasm (Trousseau sign), Chvostek sign, non specific , elongation of QT interval

psychical changes- depressions

neurological symptoms. - cephalea, in children epileptic paroxysms type GM

cataract- subcapsullar type

dry skin

hypocalcemia, hypocalciuria, hyperphosphatemia, low PTH

Therapy: Ca, D vit., dihydrotachysterol (synthetic analogue of vit D), cholecalciferol (D3-Vigantol), calcitriol (Rocaltrol)

Parathyroid gland

Hypoparathyroidism

In oral cavity:

enamel hypoplasia in horizontal lines, poorly calcified dentin, widened pulp chambers, dental pulp calcifications, shortened roots , hypodontia and mandibular tori

Stomatological treatment:
more susceptibility to caries because of dental anomalies.
Dental management
prevention of caries with periodic reviews, advice regarding diet and oral hygiene instructions

Adrenal glands

Adrenal cortex

steroid hormones– cortisol, dexamethasone, aldosteron

↑ ↑

regulation CRH - ACTH renin - angiotensin

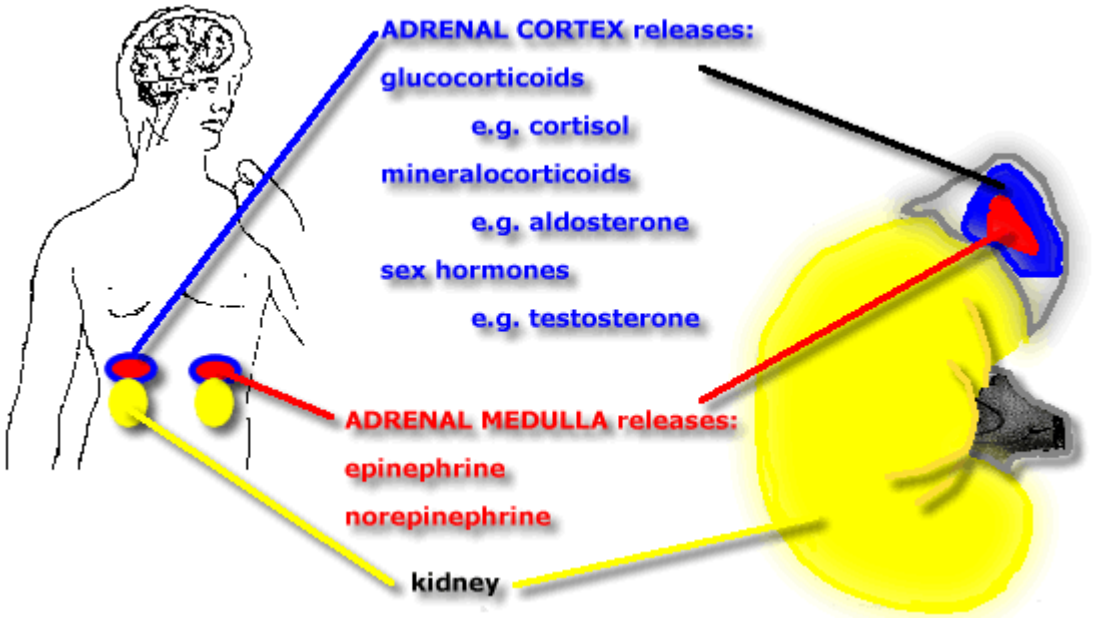
Adrenal medulla

catecholamines

↑

regulation- sympathetic nerves

Adrenal glands



Adrenal glands

Adrenal cortex

- glucocorticoids- cortisol – z.fasciculata
- mineralocorticoids - aldosterone -z. glomerulosa (under fascia)
- androgens- dihydroepiandrosterone, androstendion, testosterone- z.fasciculata, z.reticularis

Adrenal glands - cortisol

Hypocortisolism peripheral (primary) – Addison´s disease

central (secondary)

autoimmune, often familiar, only adrenal cortex

connected with autoimmune thyroiditis and type I DM -Schmidt syndrome

tbc (destruction of the whole gland incl. medulla), metastases, iatrogenic, inborn enzymatic defects of steroidogenesis

ACTH, cortisol in plasma, free urinary cortisol/24 hr.,salivary cortisol, ACTH test

When suspection on central etiology – stimulation of ACTH secretion (eg. hypoglycemic test)

Adrenal glands - cortisol

Hypocortisolism peripheral (primary) – m.Addison

fatigue, weakness, weight loss

skin hyperpigmentation, graphite maculations on mucosa of oral cavity, pigmentation of palmar creases

arterial hypotension, orthostatic hypotension, anorexia, nausea, hypoglycemia

lab. anemia, hyponatremia, hyperkalemia, hypochloremia, autoantibodies against adrenal cortex, cortisol basal, test with insulin.hypoglycaemia

Therapy: hydrocortisone, increase of the dosis during infections, stress, surgery

persisting signs of mineralocorticoid deficit (hypotension, hyponatremia, hyperkalemia)- fluorohydrocortison

Adrenal glands - cortisol

Hypocortisolism peripheral (primary) – m.Addison

Adrenal crisis

acute bilateral adrenal hemorrhage (eg. meninococcal sepsis - Waterhaus-Friedrichsen syndrome, during anticoagulant therapy), intercurrent severe disorder in patient with chronic adrenal insufficiency

symptoms: anorhexia, nausea, vomiting, diarrhoe, abdominal pain, hypotension, vascular collapse, hyperpyrexia, hypoglycemia

Therapy: Hydrocortisone 100 -200mg iv. , continuing infusion

Adrenal glands - cortisol

Hypocortisolism central (secondary)

most often after discontinuation of therapy with glucocorticoids

resulting in adrenal cortex atrophy

absent hyperpigmentation

Important to consider in case of hydrocortison treatment longer than 3 weeks in dosis 30 mg or corresponding dosis prednisolone 7.5 mg dexamethasone 0.75 mg/day

Adrenal glands - cortisol

Hypercortisolism

ACTH dependent -central (secondary) -Cushing disease

ACTH independent

peripheral (primary) – Cushing syndrome

ectopic – tumours (bronchogenic ca, medullar ca of thyroid, tumour of thyme, of pancreas)

most often- peripheral

hyperplasia of adrenal cortex, adenoma, carcinoma, administration of exogenous corticosteroids

free cortisol (urine, salivary), total cortisol, diurnal profile of cortisolemia, short, long dexamethasone test

US, CT, NMR, scintigraphy (marked derivatives of cholesterol)

Adrenal glands - cortisol

Hypercortisolism

obesity with central distribution of fat, plethora of face, moon face

muscle atrophy, adynamy

signs of skin thinning, purple stretch marks, worsened wound healing

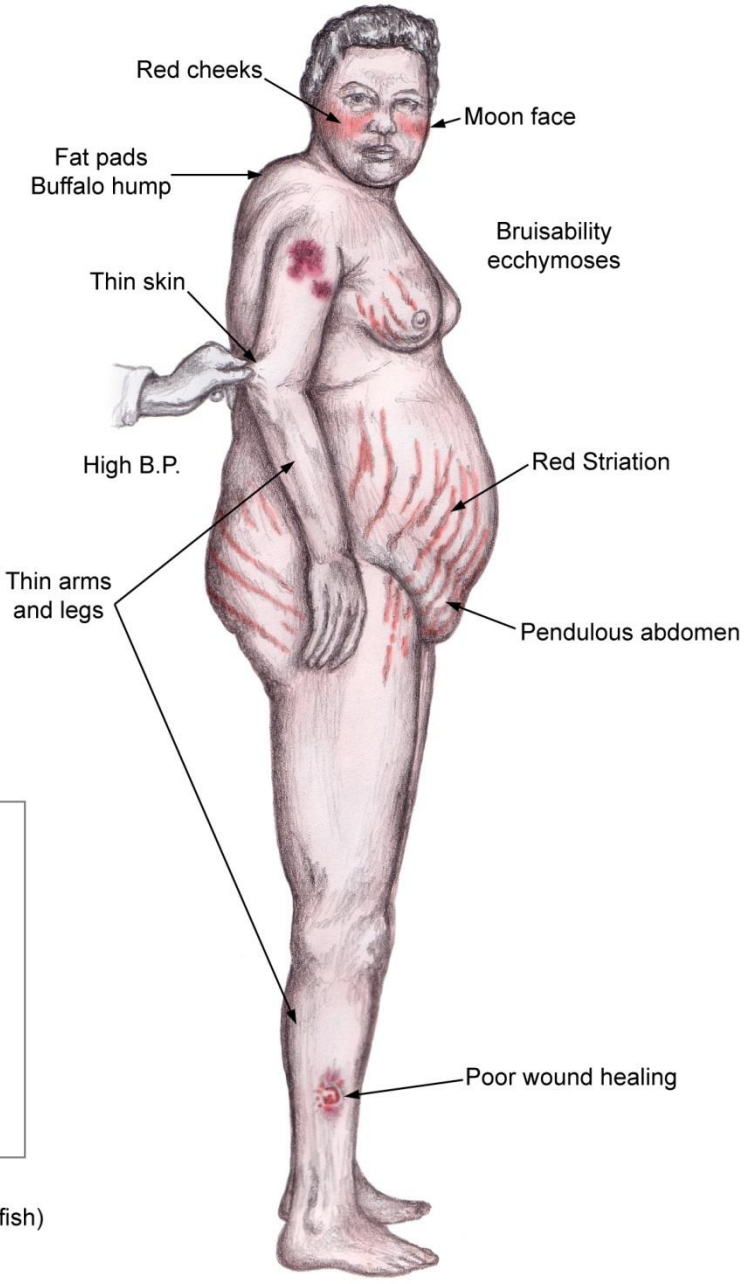
osteoporosis, type 2 DM

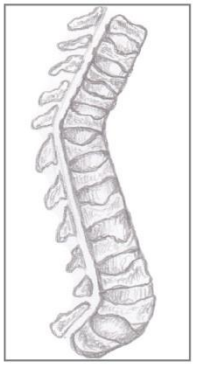
apathy, affective lability

hypertension, hypogonadism (supressive effect of cortisol on sex horm. production)

Therapy: surgery (adrenalectomia, bilateral adrenalectomia, transsphenoidal hypophysectomia), drug treatment-blockade of precursor synthesis - metyrapon

Hypercortisolism





Osteoporosis
compressed (codfish)
vertebrae

Adrenal glands - cortisol

Hypercortisolism

obesity with central distribution of fat, plethora of face, moon face

muscle atrophy, adynamy

signs of skin thinning, purple stretch marks, worsened wound healing

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Therapy: surgery (adrenalectomia, bilateral adrenalectomia, transsphenoidal hypophysectomia), drugs treatment-blockade of precursor synthesis - metyrapon

Adrenal glands - aldosterone

Hyperaldosteronism

primary

Conn syndrome

increased aldosterone secretion

supressed plasmatic renin activity

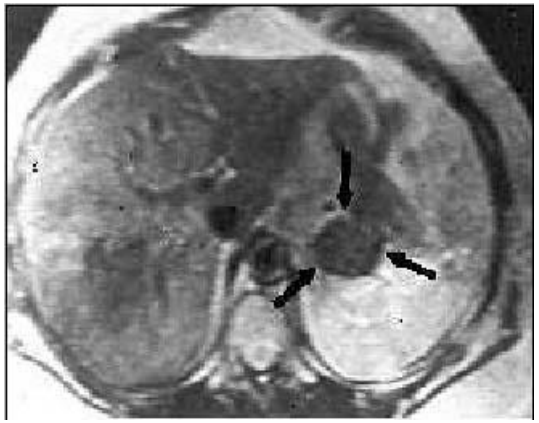
secondary

increased renin (cardiac insufficiency, hypovolemia, liver cirrhosis, chronic renal insufficiency),

with hypertension - primary hyperreninism, stenosis of renal artery, malignant hypertension

Adrenal glands - aldosterone

Conn syndrome



solitary benign adenoma (in 90%)
usually left side,
multiple adenoma,
nodular hyperplasia of cortex (pseudoprimary hyperaldosteronism)

arterial hypertension
hypokalemia, low PRA, increased aldosteron
US, CT, NMR

Therapy: surgery, spironolactone

Adrenal glands - androgens

Adrenal hyperandrogenism

Primary (adrenal adenoma or carcinoma)

producing C19 steroids – DHEA

virilizing changes in women, hirsutism, hypertrichosis, hair loss, acne

isosexual changes in men in adulthood, isosexual pubertas praecox in boys

Steroid enzymopathies

inborn adrenal hyperplasia with virilization, most frequent blockade of 21 hydroxylase

Therapy: surgery, glucocorticoids, ev mineralocorticoids

Adrenal glands - medulla

Catecholamins

epinephrine, less norepinephrine, dopamine

catecholamins in urine, in serum, vanillylmandelic acid

CT, NMR, scintigraphy (^{123}I nebo ^{131}I MIBG, analogue of guanethidin and noradrenalin, OctreoScan – ^{111}In pentetreotide, analogue of somatostatine-pheochromocytoma contains somatostatine receptors), PET

Adrenal glands - medulla

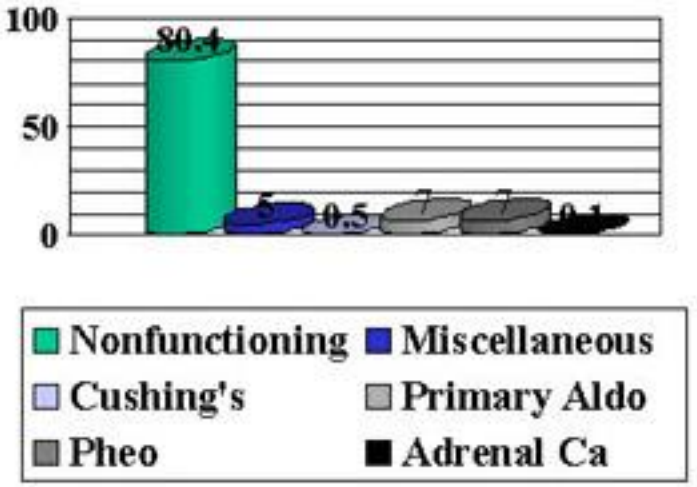
Pheochromocytoma

adenoma from chromafine cells (mostly unilateral)

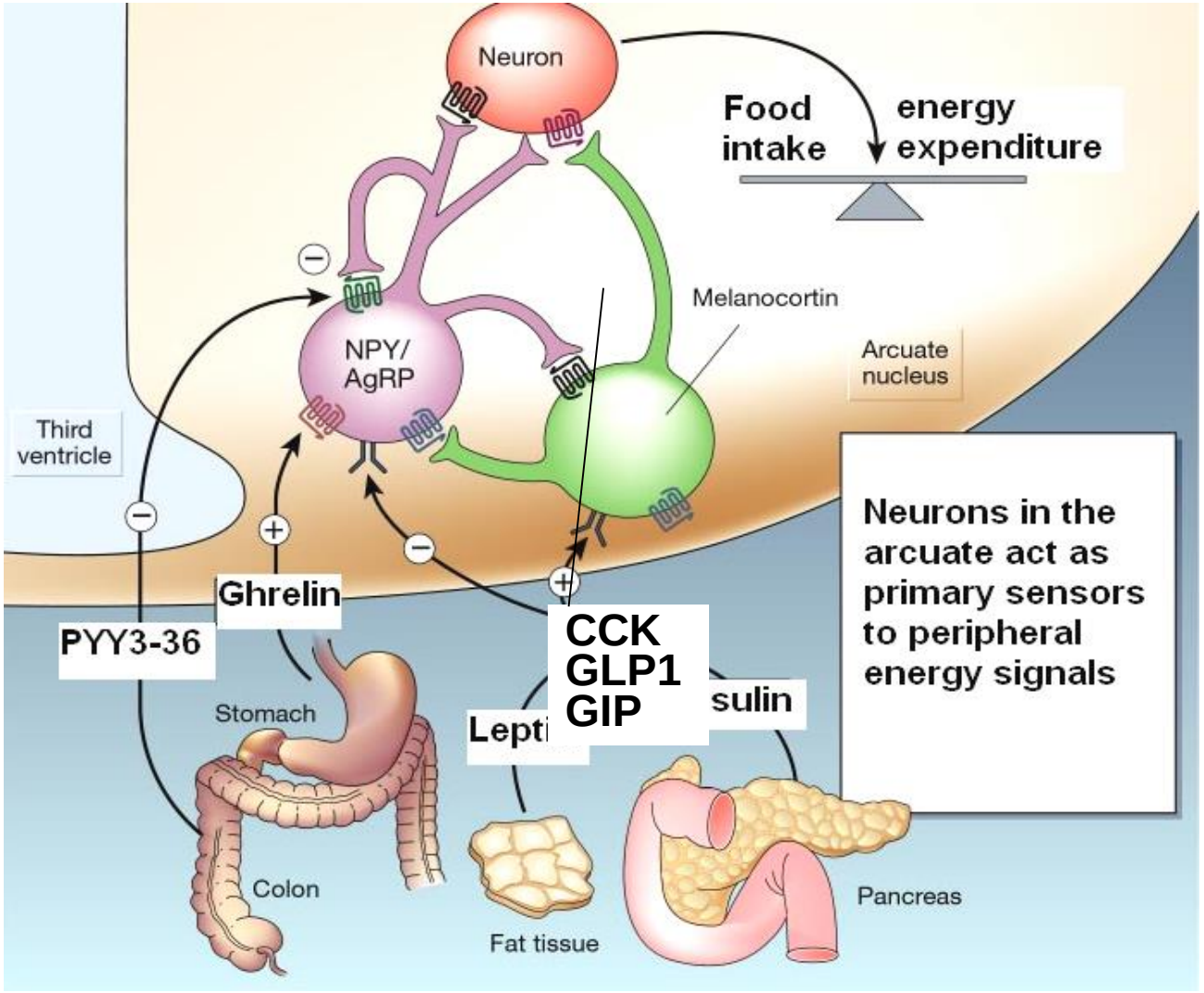
arterial hypertension – paroxysmal, more often permanent
headache, palpitations, paleness, tremor, epigastric pain, anxiety
disorder of glycoregulation

Therapy: surgery, alpha blockers (fenylefrin-Regitin)

Adrenal Incidentaloma by Disease type



Other tissues with endocrine acivity
GIT stomach, small bowel, colon,AT



Acute endocrinopathies in stomatological praxis

Tyreotoxicosis:

Risk of thyreotoxic crisis in untreated patient

Transport to the hospital

Hypoparathyroidism

Tetany - Ca iv

Hyperventilation tetany – breathing into a plastic bag

M. Addison

Increase Hydrocortison, in case of worsening Hydrocortison 100 mg iv