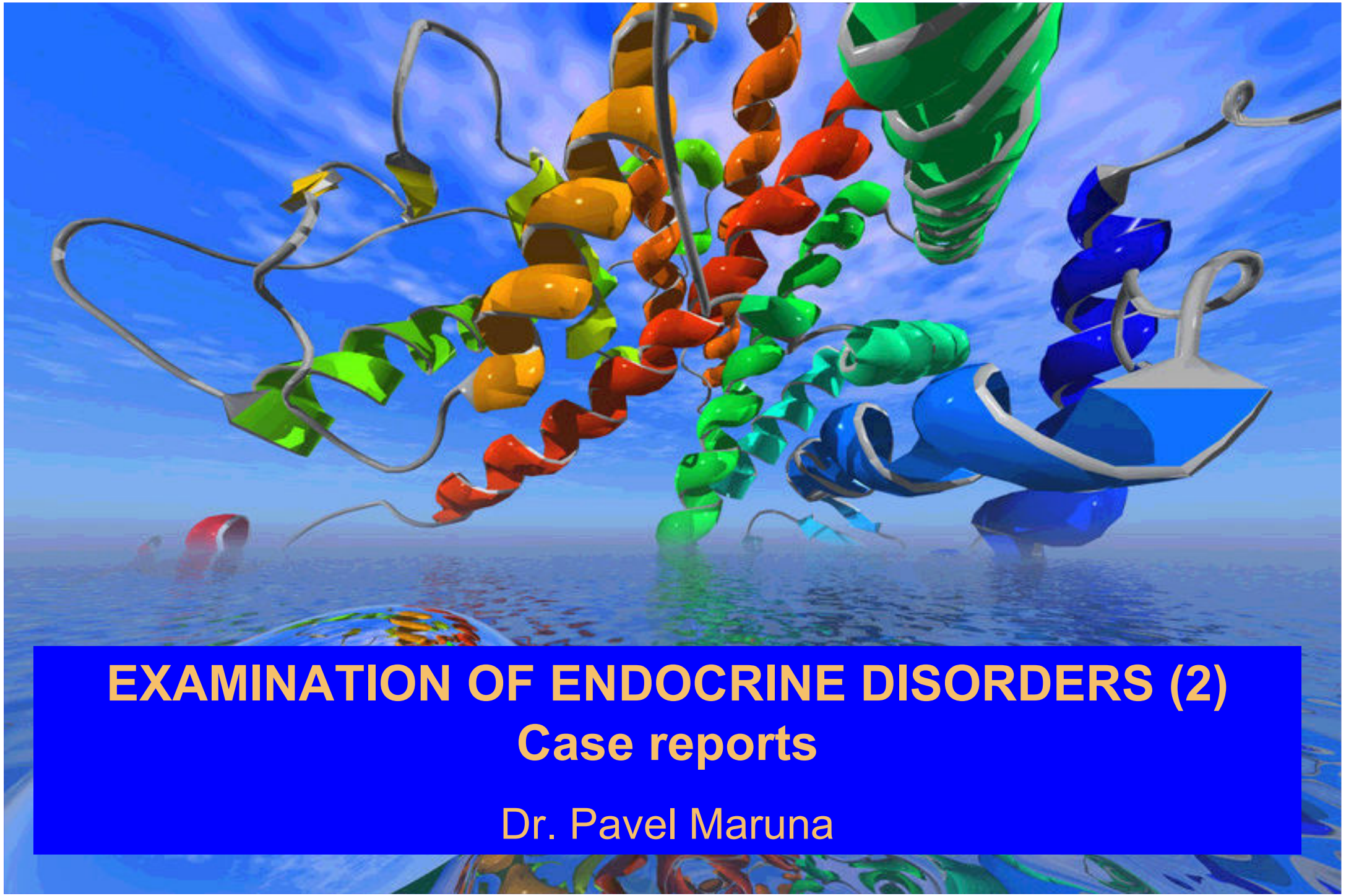
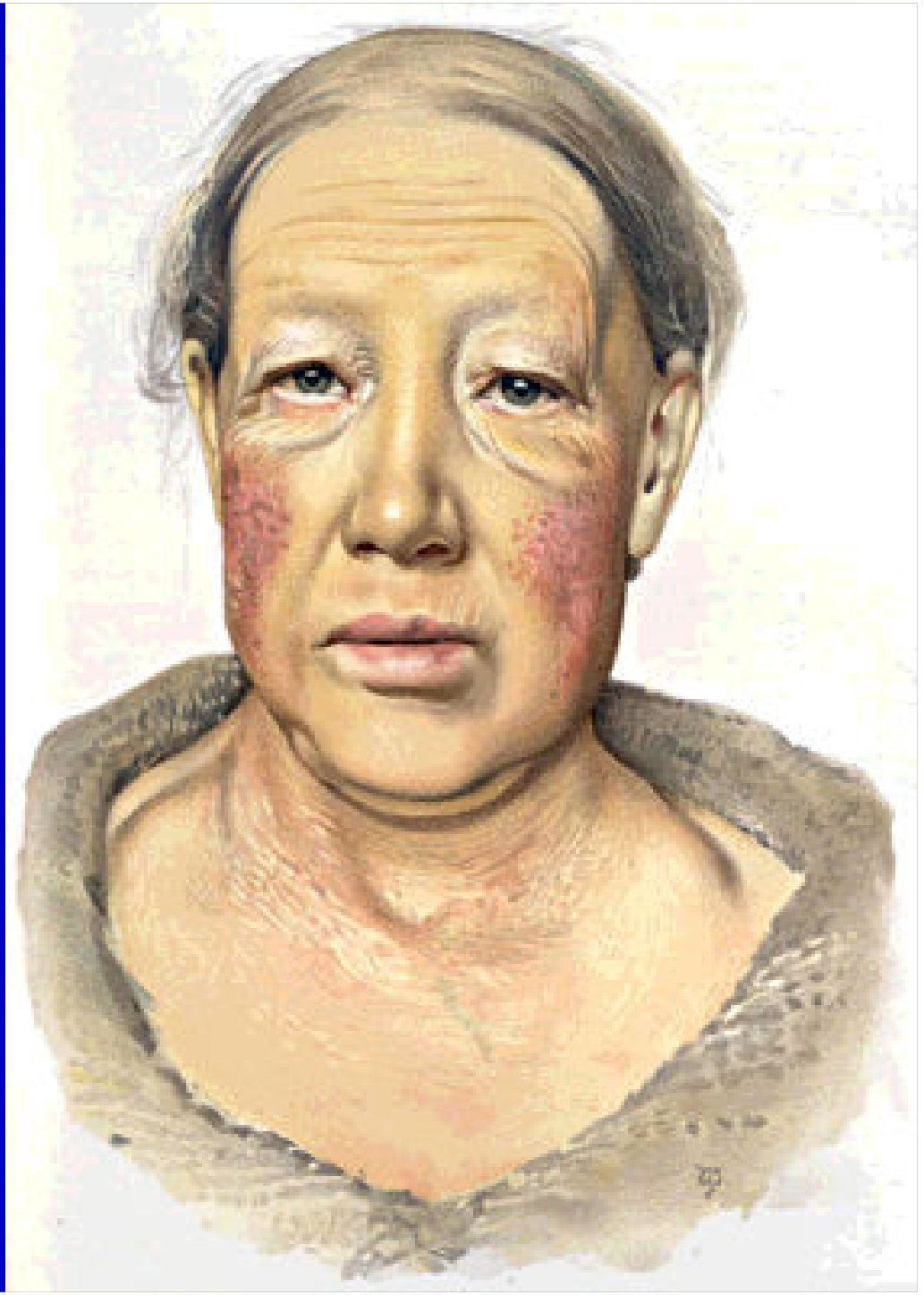


EXAMINATION OF ENDOCRINE DISORDERS (2)
Case reports

Dr. Pavel Maruna

Case report No. 1

Hypothyroidism



Female, 46 yr.

Patient treated with arterial hypertension 3 years;

Palpitations for many years, established diagnosis of neuro-circulatory asthenia, higher frequency of palpitations in last months, reported as paroxysmal heart pulsation, accompanied with a pant, independently on her physical activity;

Impaired glucose tolerance, last 3 yr. on a diet;

As a new problem, paresthesis in fingers, swelling of hands developed several weeks ago.

Allergy: negative
Chronic medication: ramipril (angiotensin-converting enzyme inhibitor) as an anti-hypertensive treatment
Abuse: alcohol and smoking - negative

Gynecological history: menses from 12 to 44 yr. (e.g., menopause 2 yr. ago), 2 deliveries, 1 abortion.

Social situation: married, 2 kids, working as a shop assistant.

Family history: twin sister treated with thyroid dysfunction; without other serious diseases in her family.

Actual problems:

Progressive difficulties in a last year:
Patient is a slow, non effective, sleepy.
Tiredness, worsening memory.
Poorer pronunciation, rhonchus (=low pitch wheezing).
Constipation.
Weight increase about 5 kg for last 12 months.

Physical examination:

BP 130 / 85 mmHg, heart rate 50 / min., regular, temperature 36,0 °C

Height 165 cm, weight 74 kg, BMI 27,2

Differences from a normal status:

- Moderated/ slowed down psycho-motor tempo,
- limited mimics in face,
- rhonchus,
- dry skin with a yellow tone,
- spare hair,
- symmetrically edematous (upper) eyelids,
- symmetric soft painless goiter,
- hand and finger swelling,
- peri-maleolar edemas.

Laboratory findings

Na	138 mmol/l	(137 - 146)
K	4,1 mmol/l	(3,8 - 5,0)
Cl	101 mmol/l	(97 - 108)
glycemia	5,5 mmol/l	(3,9 - 5,6)
urea	6,9 mmol/l	(2,8 - 8,0)
creatinin	112 µmol/l	(44 - 110)
cholesterol	7,8 mmol/l	(3,8 - 5,8)
triacyl-glycerols	1,1 mmol/l	(0,68 - 1,69)
total bilirubin	17 mmol/l	(2,0 - 17,0)
ALT	0,46 ukat/l	(0,10 - 0,78)
AST	0,72 ukat/l	(0,10 - 0,72)

Blood count

Leukocytes	8,6 x 10^3/mm^3	(4,1 - 10,2)
Erythrocytes	3,12 x 10^6/mm^3	(4,19 - 5,75)
Hemoglobin	101 g/l	(135 - 174)
HCT	32,8	(0,39 - 0,51)
MCV	105 fl	(82 - 98)
MCH	0,32 pg	(28,0 - 34,6)
Platelets	295 x 10^3/mm^3	(142 - 327)

Thyroid examinations

free T4	4,2 pmol/l	(11,0 - 21,0)
free T3	0,7 nmol/l	(1,5 - 3,0)
TSH	33,3 mIU/l	(0,5 - 5,0)
anti-TSHR Ab	negative	
anti-TPO Ab	+++	
anti-thyroglobulin Ab	++	

USG imaging

Volume of thyroid gland 25 ml (normal limits to 20 ml), lobes are symmetric, bilaterally numerous foci with low echo-genity. Thyroid gland delimited (without invasion to surrounding structures). Lymph nods of a normal shape.

Achilles tendon reflex: markedly protracted

ECG

Sinus rhythm, ventricular activity 50 / min., horizontal axis, PR segment 220 ms, QRS duration 90 ms, QT-c interval 420 ms, low voltage of QRS complex, ST segment in iso-electric line, normal shape of T wave.

Recommendation:

To start a treatment with levothyroxine (Euthyrox tbl.) in a dose 25 ug per day (1 tbl. in the morning).
After 4 weeks, Euthyrox may be increased to 50 ug per day.
After 2 months, laboratory control of TSH, free T3 and free T4 levels.

Question No. 1

Diagnosis of hypothyroidism in this patient can be established with a knowledge of history and physical examination, still before laboratory examination.

Nevertheless, which laboratory parameters confirm hypothyroidism in this patient? What is their relation to thyroid dysfunction ?

Question No. 2

Mild anemia was found in this patients.
Based on morphological classification, which type of anemia is it?

What is a pathogenesis of anemia in hypothyroidism ?

Question No. 3

Discuss following findings and their possible links to hypothyroidism:

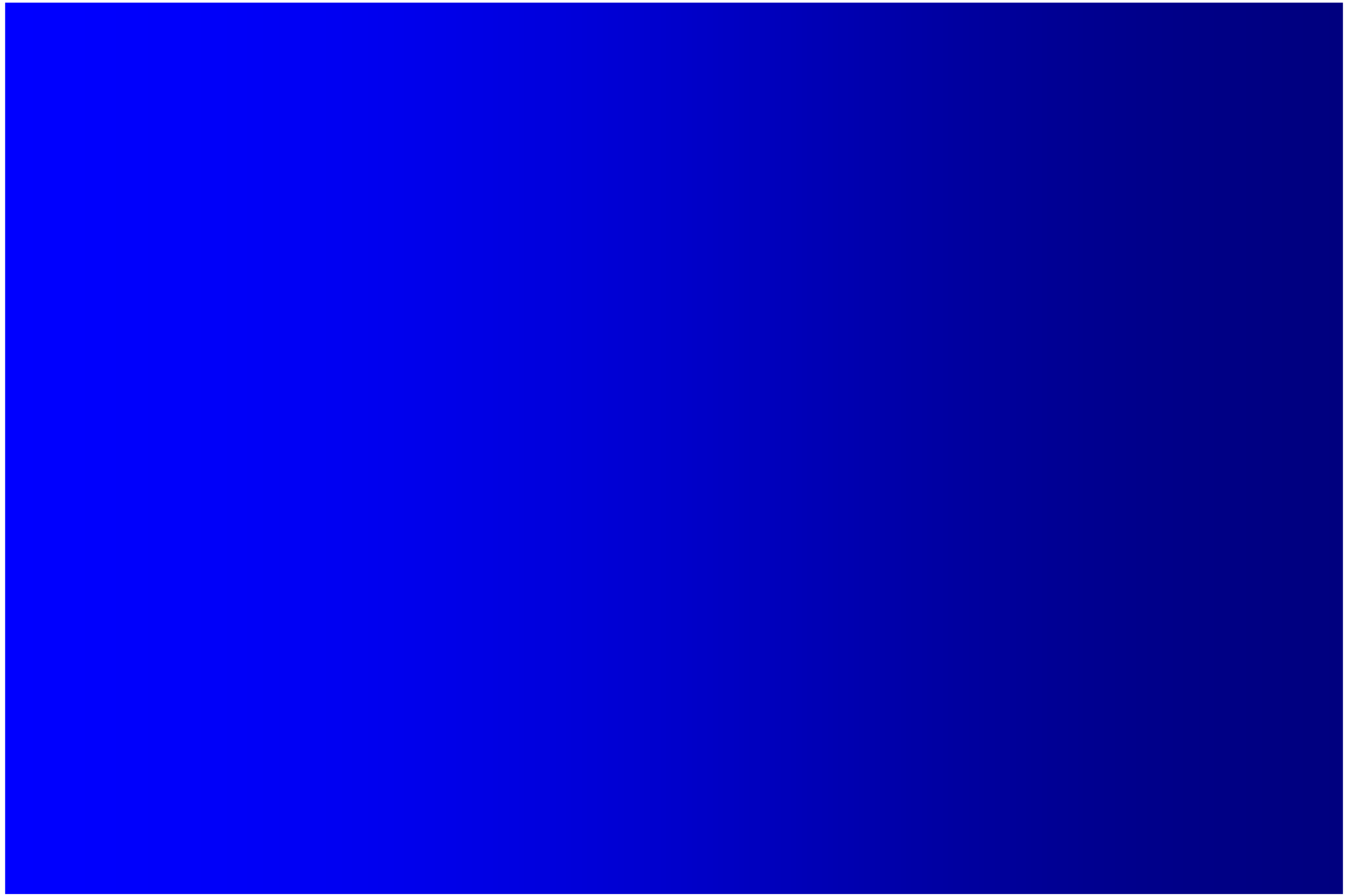
- hypercholesterolemia
- ECG curve changes

Question No. 4

The diagnosis of thyroid disorder is based on knowledge of:

1. Thyroid function (hypothyrodism, hyperthyroidism, euthyroid status);
2. Local signs (goiter, local expansion - trachea, esophagus, vessels);
3. Etiological classification.

What is a cause (etiology) of hypothyroidism in this patient?



Case report No. 2

Osteomalacia

History

Recorded in 2008

Female, 60 yr. old

Past history: without severe diseases in anamnesis

Chronic treatment: irregularly analgetic drugs for dorsalgia (back pain)
Allergy: negative
Abuse: negative

Family history: without important diseases in parents and siblings

Gyn. history: delivery 1, abortion 0.

Social status: solitary, old-age pension

History

Patient was admitted to internal department of regional hospital in Moravia for progressive dyspnoe stage II.-III. (according to NYHA classification)

In physical examination
- cachexia,
- heavy kyfo-scoliosis,
- short stature (136 cm),
- pectus excavatum
- tachypnoe, dyspnoe in minimal activities (walking).

In laboratory – markedly elevated D- dimers (>6000), high activity of ALP (16 μkat / l).

History

The examination in hospital excluded following diseases:

- acute coronary syndrome,
- pulmonary embolism,
- dissection of aortal aneurysma,
- pneumotorax
- …

X-ray imaging

Chest native X-ray: Heavy kyfoscoliosis of thoracic backbone.

Backbone skiagram: Diffuse osteoporosis with de-differentiation and destruction of vertebrae.

Skull skiagram: Without destructive changes of bones.

With these findings, the patient was send to hospitalization to Osteological department of the 3rd Internal clinic, 1st Faculty of Medicine in Prague

...to examine bone metabolism and to start a therapy.

With these findings, the patient was send to hospitalization to Osteological department of the 3rd Internal clinic, 1st Faculty of Medicine in Prague

...to examine bone metabolism and to start a therapy.

Newly patient reports a progressive lowering in body height in last 2 years.

As a main problem, patient complains about dorsal pain.

Physical examination

Height 136 cm, weight 29 kg, BMI 16.1

BP 130/90 mmHg, heart rate 115/min.,

O_2 saturation 95%

Kyfo-scoliosis, pectus excavatum.

Physical examination

Height 136 cm, weight 29 kg, BMI 16.1

BP 130/90 mmHg, heart rate 115/min.,

O_2 saturation 95%

Kyphoscoliosis, pectus excavatum.

ECG

Sinus tachycardia 105 / min., AV blockade of the 1st degree

Laboratory examination

Na	141 mmol/l	(137 - 146)
K	5,0 mmol/l	(3,8 - 5,0)
Cl	107 mmol/l	(7 - 108)
Ca	2,66 mmol/l	(2,00 - 2,65)
Ca^{2+}	1,45 mmol/l	(1,0 - 1,4)
PO4	0,93 mmol/l	(0,6 - 1,6)
Mg	0,79 mmol/l	(0,66 - 1,08)
LDH	2,63 ukat/l	(2,20 - 3,75)
Urea	6,0 mmol/l	(2,8 - 8,0)
Creatinine	61,0 µmol/l	(44,0 - 110,0)
Uric acid	411 mmol/l	(220 - 420)

Laboratory examination

ALT	0,26 µkat/l	(0,10 - 0,78)
AST	0,28 µkat/l	(0,10 - 0,72)
GGT	0,66 µkat/l	(0,14 - 0,84)
Bilirubin	8 mmol/l	(2,0 - 17,0)
ALP	13,53 µkat/l	(0,6 - 2,2)
Cholesterol	5,4 mmol/l	(3,8 - 5,8)
Triacylglycerols	1,8 mmol/l	(0,68 - 1,69)
Total protein	78 g/l	(65,0 - 85,0)
Albumin	40 g/l	(35,0 - 53,0)
TSH	6,821 mIU/l	(0,5 - 5,0)
Free T4	15.2 pmol/l	(11,0 - 21,0)
PTH	257,2 pmol/l	(1,6 - 6,9)

USG of thyroid and parathyroid glands

Enlargement of a parathyroid body bellow left lobe of thyroid gland.

Thyroid gland of a normal size and shape.

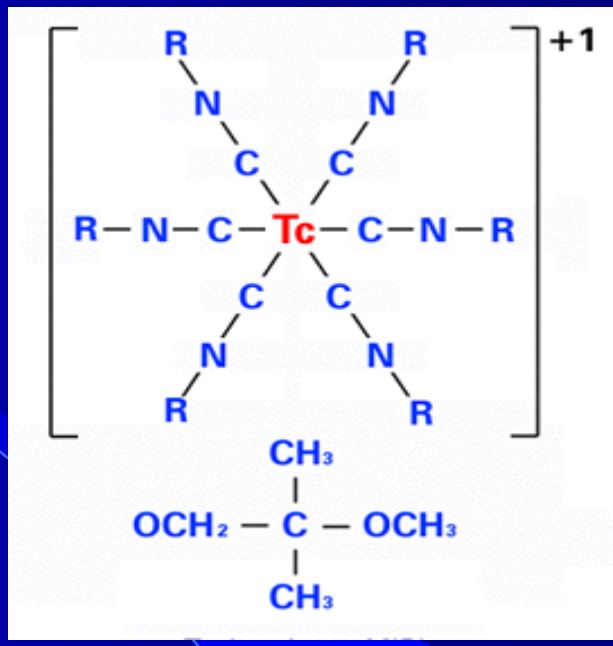
^{99m}Tc-MIBI

Higher accumulation of ^{99m}Tc-MIBI near a lower edge of a left thyroid lobe

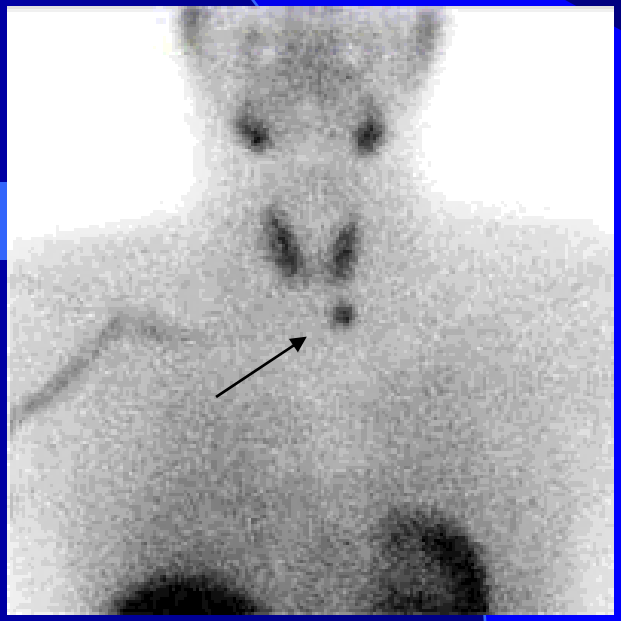
^{99m}Tc-MIBI

= methoxy isobuthyl isonitril

The molecule passes cells membranes passively, once intracellular it further accumulates in the mitrochondrias.
Detection of ^{99m}Tc gamma emission



Adenoma of a parathyroid gland



Abdominal USG imaging

Without pathological changes.

Echocardiography

Normal ventricular function, normal valvular morphology and function.

Spirometry

Severe restrictive respiratory failure.

Severe reduction of a vital lung capacity to 25% of normal values.

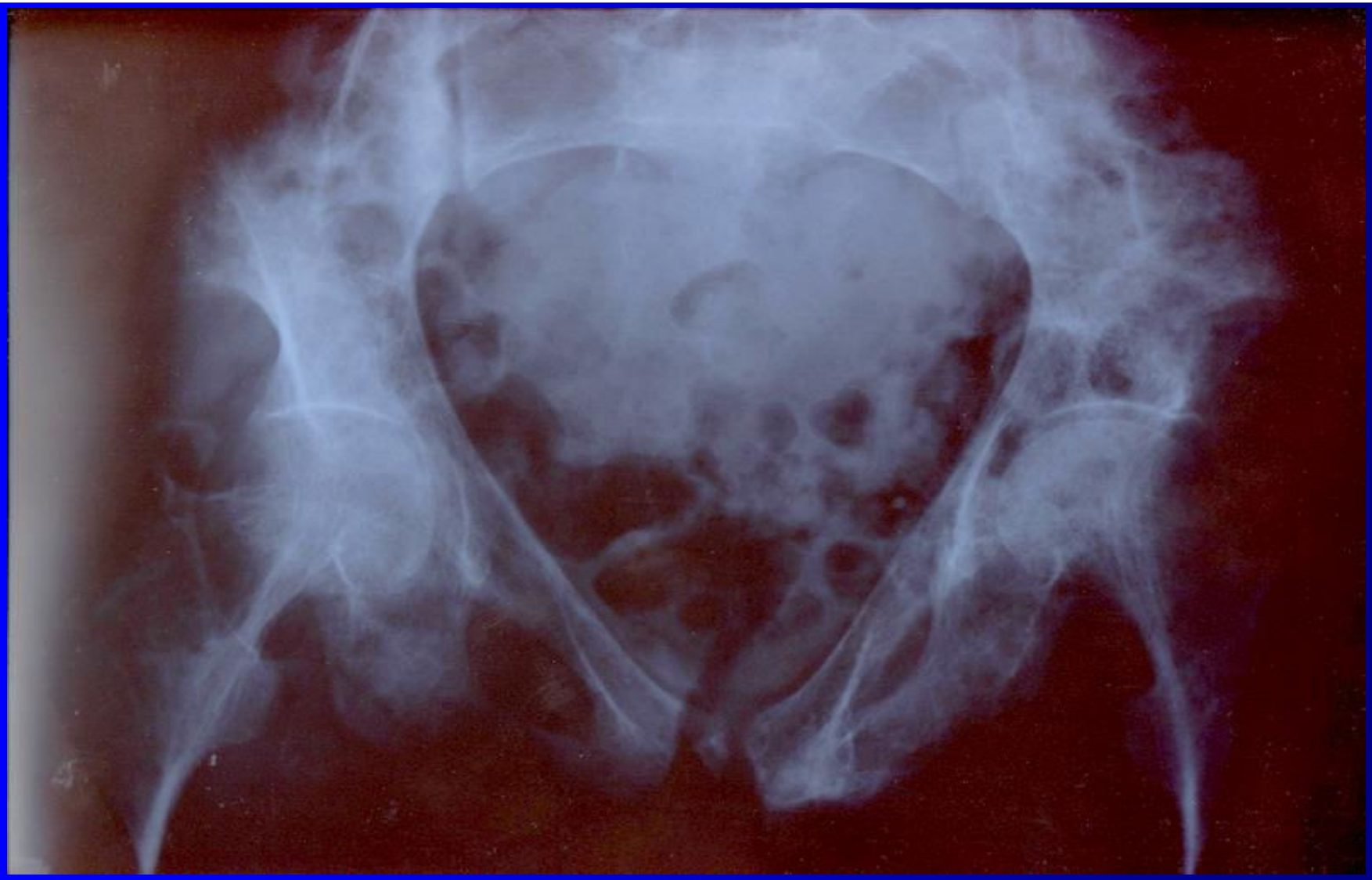
Diagnostic consideration (1)

Findings of ↑ PTH, ↑ Ca, and PO_4 near a lower limit support a diagnosis of primary hyperparathyroidism. A severe bone syndrome in a clinical and laboratory examination.

Suspicious adenoma of a left lower parathyroid gland.

There is an indication to surgical removal of parathyroid adenoma.

...And following surgical treatment of deforming kyphoscoliosis with markedly decreased lung capacity.



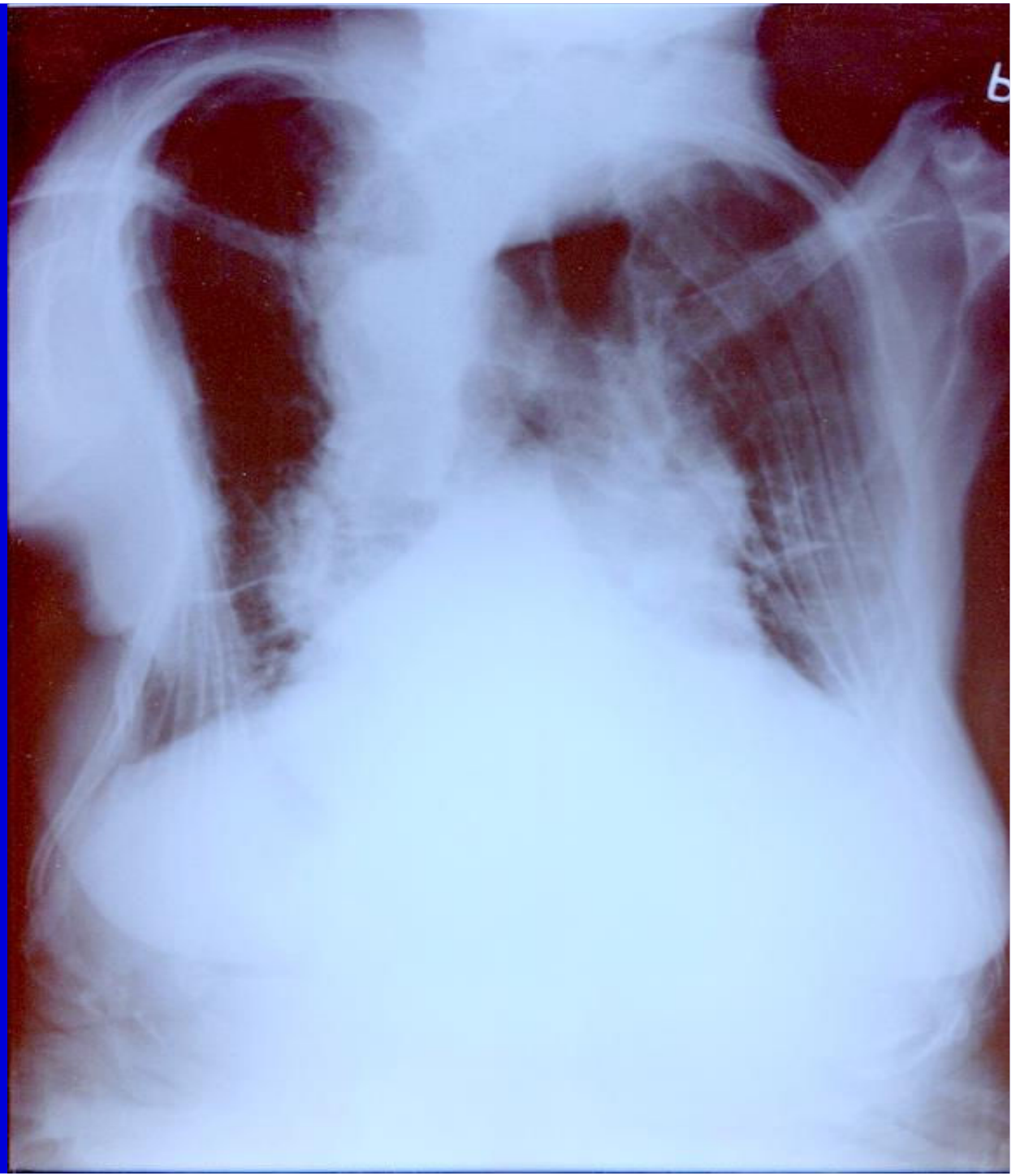
X-ray examination of pelvis and femoral bones

Marked deformation of pelvic skeleton, „heart-shaped“ pelvis, deflection of both femoral bones, low density of all displayed bones

Chest X-ray image

Bell-shaped chest with gibbus,

Total resorption of humerus head on the left side.



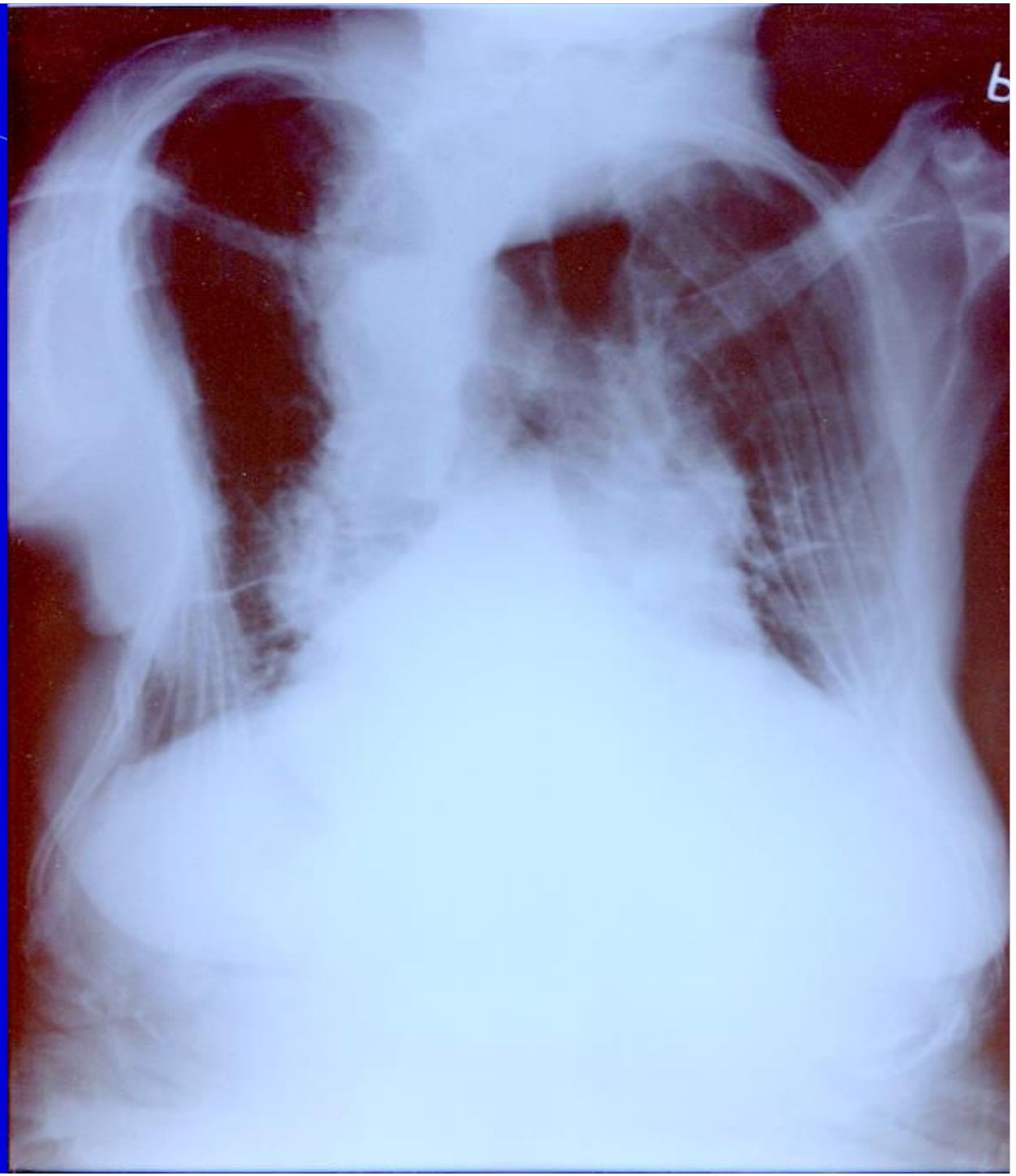
Chest X-ray image

Bell-shaped chest with gibbus,

Total resorption of humerus head on the left side.

Conclusion

Skeletal deformities are typical for **osteomalacia**



„Bone“ laboratory parameters

Osteocalcin	201,8 µg/l	(15 - 46)
25(OH)-D_3 vitamin	5 ng/ml	(15 - 42)
1,25(OH)-D_3 vitamin	48,4 ng/l	(19 - 67)
U - Ca	2,5 mmol/24 h	(3,5 - 6,5)
U - PO_4	19,1 mmol/24 h	(13 - 42)

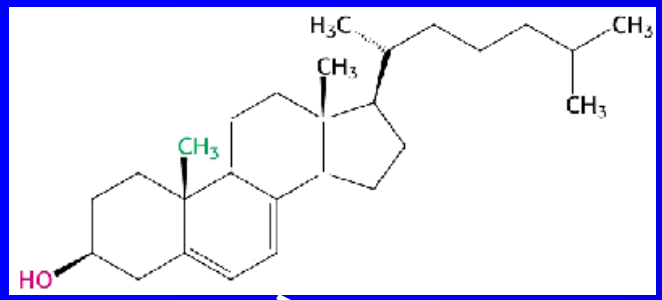
Diagnostic consideration (2)

Skeletal deformities are characteristic for **osteomalacia**, not for primary hyperparathyroidism.

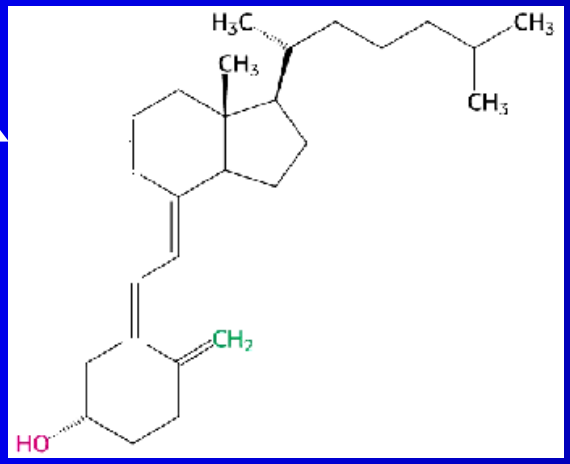
Extremely low levels of **kalcidiol** (25-OH-D_3 vitamin), as a marker of vitamin D storage in organism.

Vitamin D_3 metabolism

7-Dehydrocholesterol (liver)



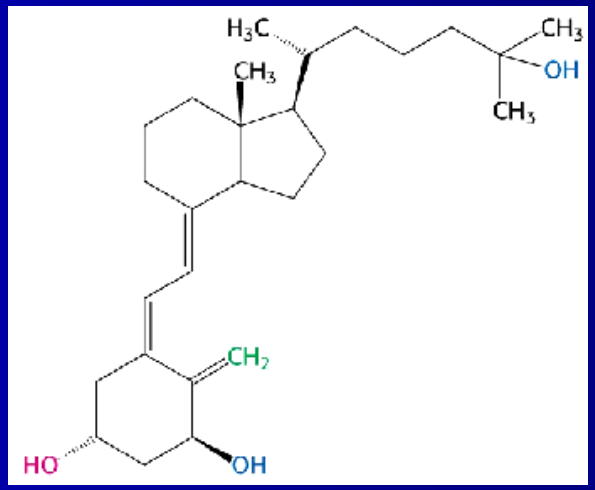
Photoreaction
(skin)



Calciol
(cholekalciferol, D_3)

25-hydroxylation (liver)
1α-hydroxylation (kidneys)

Calcitriol
(1α,25-dihydroxycalciol)



Diagnostic consideration (2)

Skeletal deformities are characteristic for **osteomalacia**, not for primary hyperparathyroidism.

Extremely low levels of **kalcidiol** (25-OH-D_3 vitamin), as a marker of vitamin D storage in organism.

Marked skeletal decalcification – low **calciuria, high ALP** (marker of increased osteoblastic activity).

Diagnostic consideration (2)

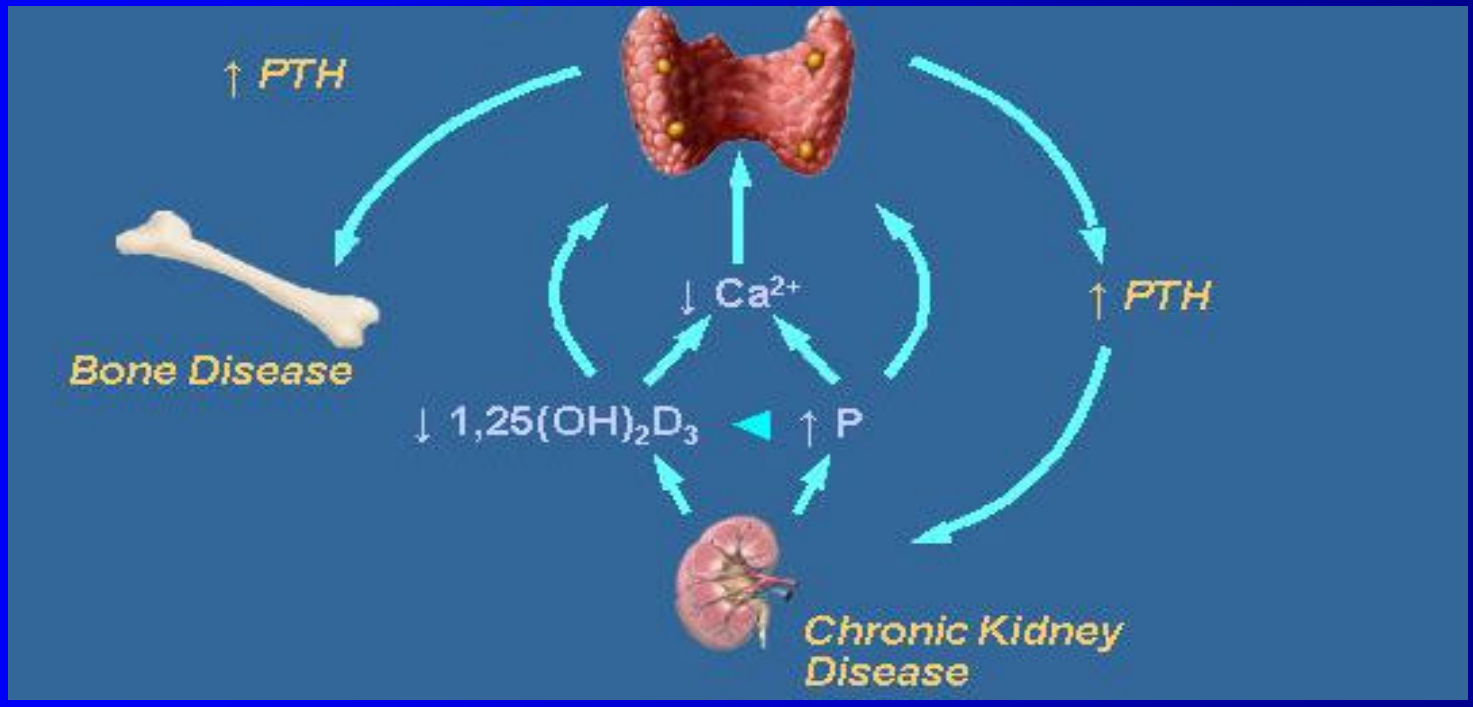
Findings give evidence against primary hyperparathyroidism

Long-term hypo-calcemia leads to hyperplasia of parathyroid glands with following autonomous over-function of one of them.

This course suggests for tertiary hyperparathyroidism.

Tertiary hyperparathyroidism

Due to prolonged hypocalcemia, one hyperplastic parathyroid body developed functionally autonomous adenoma. Hypocalcemia has changed to hypercalcemia.



Recommendation

- **Surgical revision of parathyroid glands**, displacement of autonomous body (v. s. adenoma) as well as other 3 (likely hyperplastic) parathyroid bodies, the maintenance of ½ of one of them - what is sufficient for normal PTH production.

- Post-surgery massive **re-calcification** due to expected „hungry bone“ syndrome.

Surgery

February 20 – 29, 2008, hospitalization at the 3rd Dept. of surgery, Faculty hospital in Motol.

February 22, 2008 – Extirpation of adenoma of the left lower parathyroid gland, currently total extirpation of upper and lower parathyroid body on the right side, subtotal ablation of the left upper body.

Post-surgical course:

Laboratory: Ca 1,71….1,75 mmol / l

Post-surgery creepiness of hands and face ... as expected manifestation of transitory hypocalcemia

2nd hospitalization

February 29 – March 02, 2008, 3rd Internal Department

Subjectively: Intermittently depressive.

Objectively: Rest scar above sternum, without other variations.

Laboratory: Ca 1,85 mmol/l (2,0 - 2,65)
PO_4 0,67 mmol/l (0,6 - 1,6)
ALP 25.45 ukat/l (0,6 - 2,2)
PTH 18,01 pmol/l (1,6 - 6,9).

Diagnostic consideration (3)

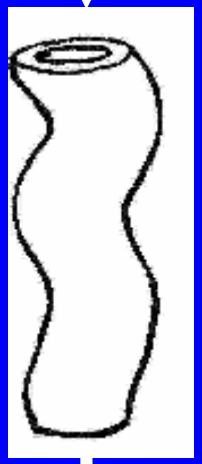
1. **Tertiary hyperparathyroidism** – extirpation of parathyroid adenoma which developed in long-term secondary hyperparathyroidism.

2. **Post-surgery „hungry bone“** bone syndrome with hypocalcemia.

3. **Osteomalacia** of an unclear origin as a primary disease

Ca balance in organism

Daily intake
approx. 25 - 30 mmol
(phosphates, oxalates...)



17 – 25 mmol /d

Absorption
upto 15 mmol / d

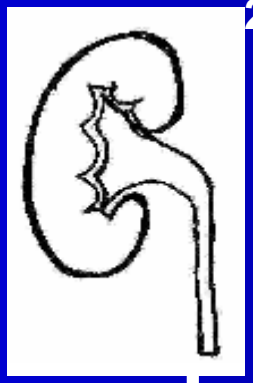
Secretion
to 7 mmol / d

ECT
2,5 mmol / l
totally only 35 mmol

ICT
signal function
0,1 µmol / l

Filtration
240 mmol/d

Tubular resorption
230 mmol / d

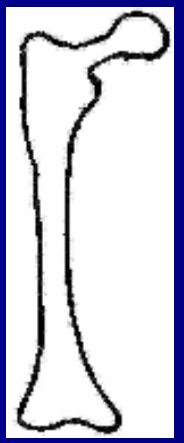


5 – 6 mmol /d

Mineral deposits
25 mol Ca
(rapidly replaceable
100 mmol)

Bone remodelation
7,5 mmol / d

Quick replacement
500 mmol / d



What now?

1. To establish etiology of osteomalacia – suspicion of malabsorption.

2. Repeated controls of calcemia during therapy:
   Calcium 1,5 g / den, Alpha-D3 1 ug/den.

(Alpha-D3 is vitamin D3 hydroxylated in position 1)

Hospitalization on the 4th Internal Clinic, 1st Faculty of Medicine in Prague

Examinational hospitalization for suspicion of intestinal malabsorption syndrome

Auto-Ab, coeliakia

Auto-antibodies negative

Gastroscopy

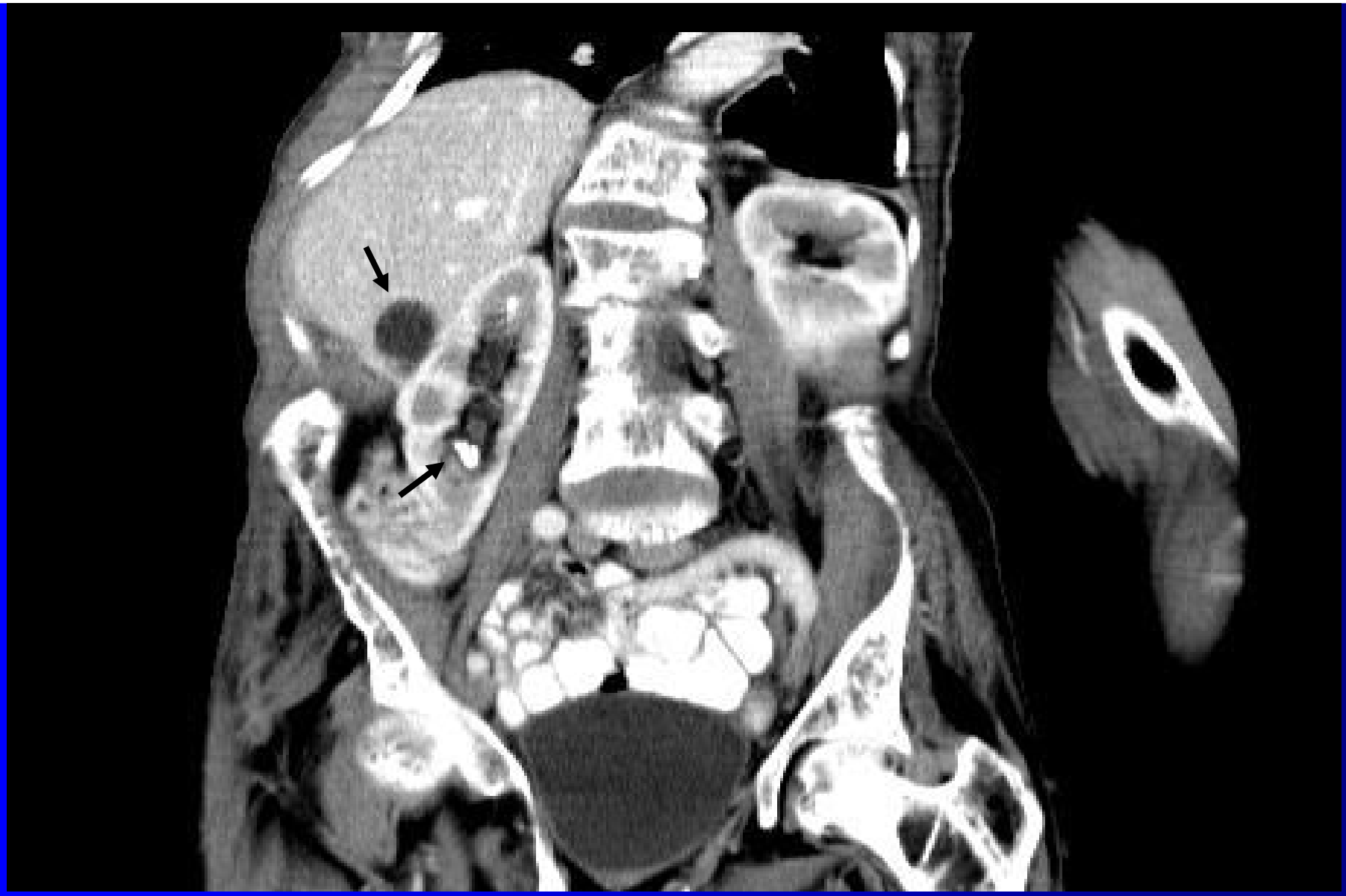
Normal macroscopic finding

Biopsy with normal histological image

Colonoscopy

Diverticolis of sigmoideum, other parts without pathological changes.

Histological examination from biopsies with normal findings.



Abdominal CT imaging

Without important changes. As an incidental finding, a cyst of right hepatic lobe and a renal stone of a right kidney (10x7 mm) were revealed.

Intestinal resorption of Ca^{2+}

Fc_{240} = 9 % (normal limits 20 - 22 %)

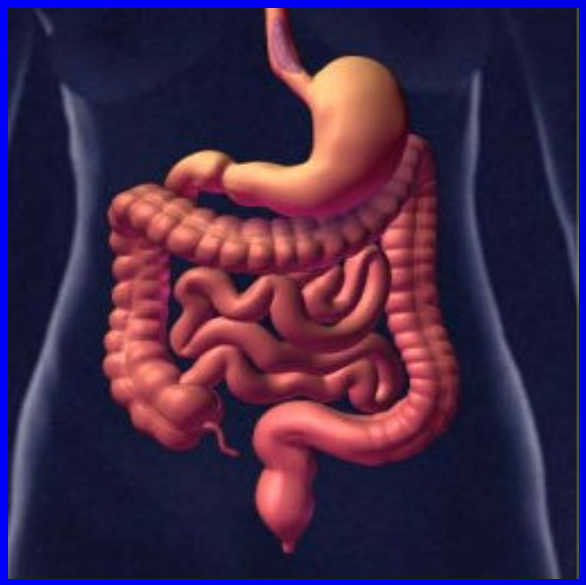
Intestinal resorption of Ca^{2+}

Fc_{240} = 9 % (normal limits 20 - 22 %)

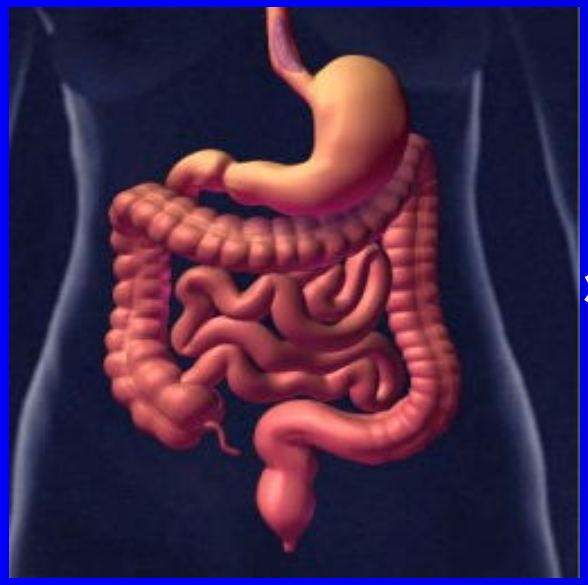
Principles of examination

Resorption of Ca^{2+} is derived from Sr^{2+} resorption.
After p.o. administration of 2,5 mmol $SrCl_2$, serum levels of Sr^{2+} are measured immediately (c_0) and after 240 min (c_{240}). Fc_{240} is calculated.

Causes of impaired gut resorption of Ca



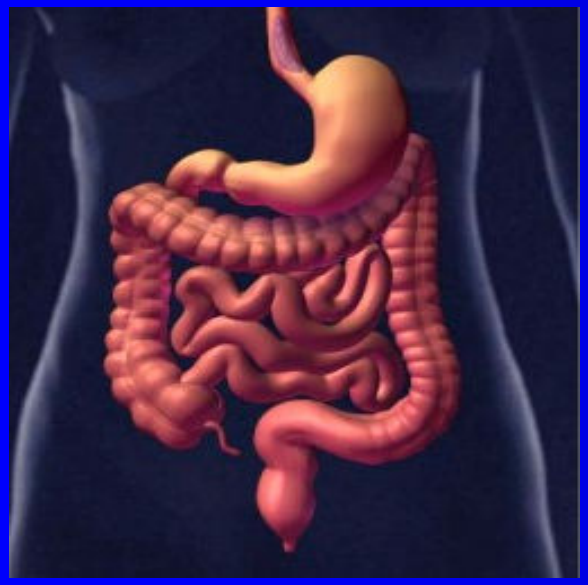
- Low intake of Ca in a food
- Low biol. availability of Ca in a food
- „Negative balance“ – secretion of Ca
- Impaired absorption of Ca



Physiology of Ca absorption

D-vitamin independent paracelullular absorption

D-vitamin dependent absorption



Ca resorption is independent on a specific transport protein

Calcitriol changes conformation of **calmodulin**. More effective linkage of Ca^{2+} to calmodulin facilitates a passing of Ca through intestinal wall

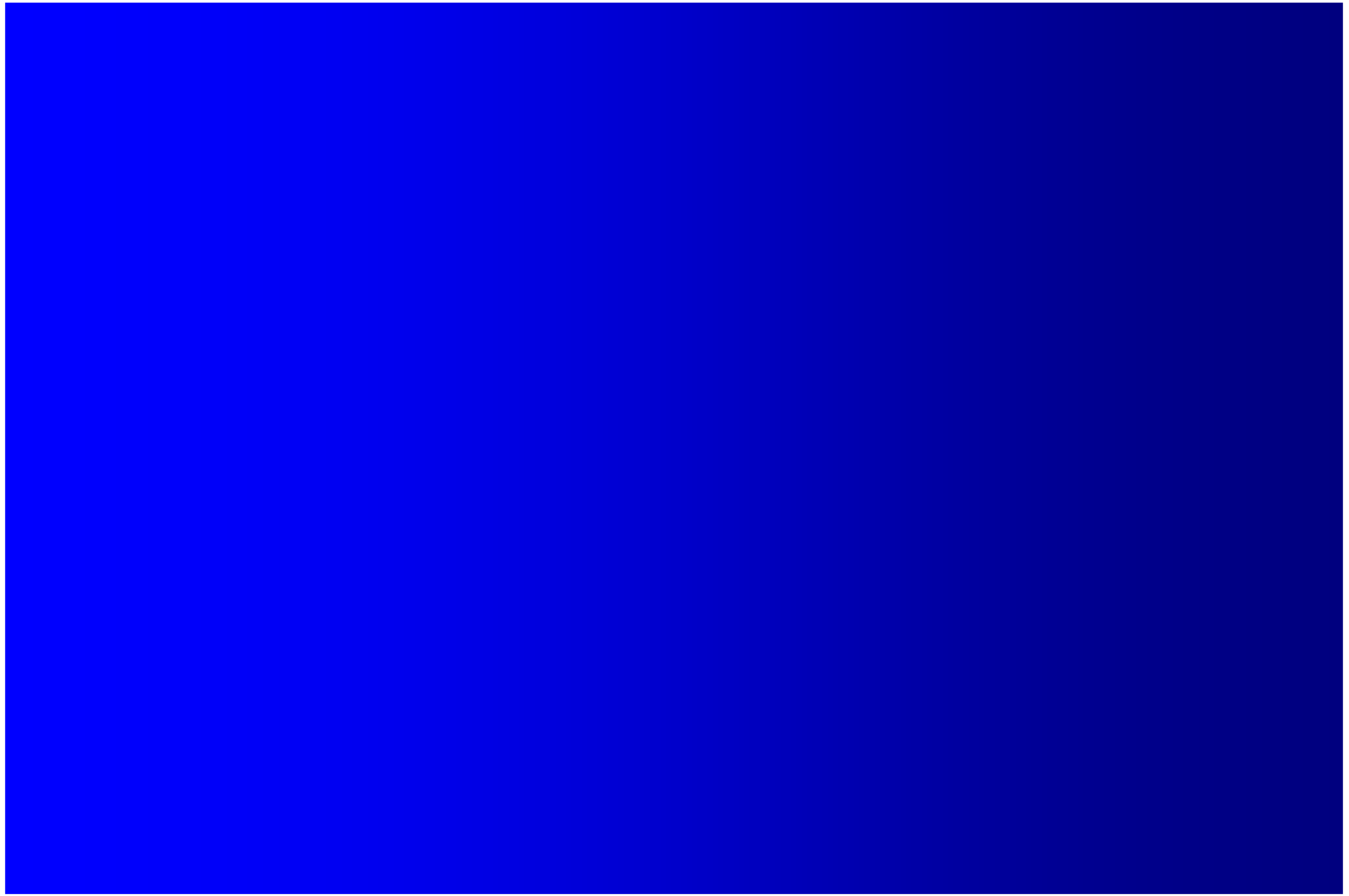
Calcitriol induces a synthesis of cytosolic **calbindin** (CaBP, calcium-binding protein). CaBP has high affinity to Ca^{2+} in cytosol. Therefore an increase of intracellular Ca^{2+} is limited and Ca is released from enterocytes.

Calcitriol induces a synthesis of **Ca^{2+}-ATPase**, from Ca^{2+} transport from enterocyte do extracellular fluid.

Conclusion

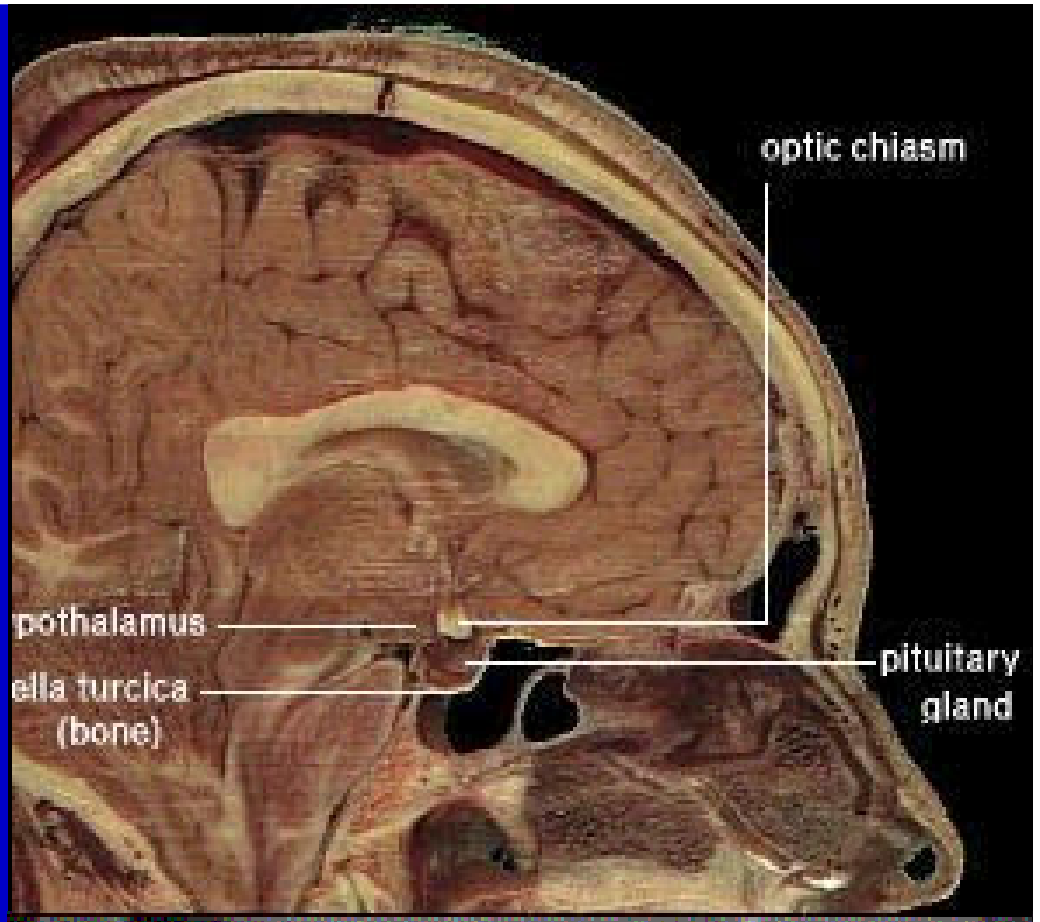
Idiopathic impaired calcium intestinal resorption

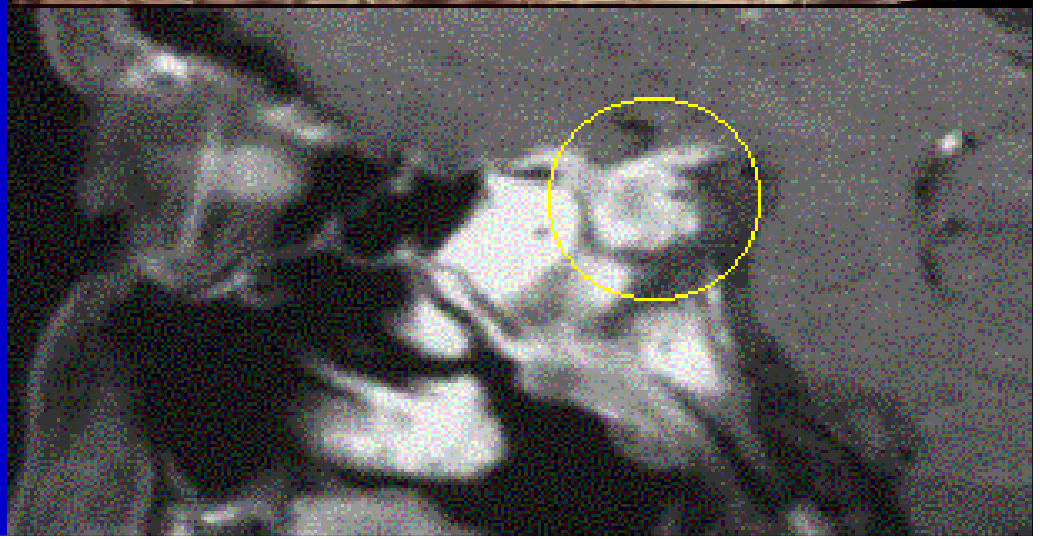
- **Recommended nutritional support by „sipping“.**
- **Therapy: Ca 1,5 g / day, Alpha-D3 1 ug / day.**
- **Follow up in out-patient department of osteology**



Case report No. 3

Hypopituitarism





Female, 38 yr.

1990 umbilical herniotomy
1998 cholecystectomy for gallbladder stones
2004 sectio cesarea

Without regular medication
Abuse - negative
Allergy - negative

Social status: teacher, 3 children

Gynecology: 3 deliveries, 3 aborts

June 26, 2009, sectio cesarea as a 3rd delivery

One week after delivery, severe weakness, headache and impaired lateral vision revealed.

June 26, 2009, sectio cesarea as a 3rd delivery

One week after delivery, severe weakness, headache and impaired lateral vision revealed.

Perimeter

Bitemporal hemianopsia

MRI of pituitary (September 14, 2009)

Macroadenoma of pituitary gland with suprasellar propagation, in a near contact with chiasma n. optici.

Laboratory

Prolactin	117 mIU/l	(<630)
LH	0,62 IU/l	(0,7-5,0)
FSH	2,22 IU/l	(0,5-8,0)
Estradiol	11,0 pg/ml	(25-75)
free T4	6,2 pmol/l	(11,0-21,0)
TSH	0,6 mIU/l	(0,5-5,0)
Cortisol	81,0 nmol/l	(200-750)

All described hormones are borderline or bellow normal limits.

Laboratory findings respond to combined pituitary insufficiency:

- hypogonadism,
- hypothyroidism,
- hypocortisolism

Hospitalization at internal department

Substitution therapy of hypopituitarism

High doses of corticoids $\rightarrow$ hypokalemia

October 04, 2009 – paroxysm of ventricular fibrillation

Hospitalization at internal department

Substitution therapy of hypopituitarism

High doses of corticoids $\rightarrow$ hypokalemia

October 04, 2009 – paroxysm of ventricular fibrillation

Transport to ICU of the 3rd Internal clinic, General Faculty Hospital in Prague

Stabilization, correction of hypokalemia and hypophosphatemia

Indicated to neurosurgical treatment of pituitary adenoma

Hospitalization at internal department

Substitution therapy of hypopituitarism

High doses of corticoids → hypokalemia

October 04, 2009 – paroxysm of ventricular fibrillation

Tra[illegible]ICU of the 3rd Internal clinic, General [illegible]Prague

[illegible]hypokalemia and

[illegible]reatment of pituitary

Hydrocortison 25-15-5 mg / d.

Euthyrox 125 μg / d.

Omeprazol (Helicid) 20 mg / d.

January 25, 2010 – admission to Neurosurgical dept.

Perimeter

Normal finding !!

MRI of pituitary (January 26, 2010, Prague)

Hypophysis 12x6 mm, without signs of adenoma !!

Infundibulum without dislocation.

No signs of bleeding.

Normal size of ventricular system.

Conclusion:

Actual finding is not an indication to surgery.

Pituitary apoplexy ?

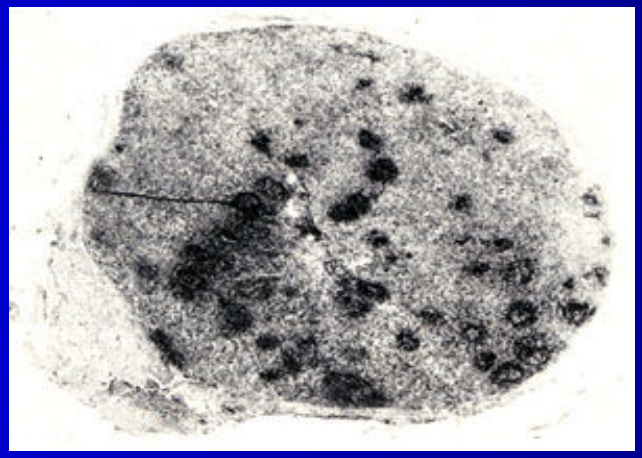
Persisting panhypopituitarism, requiring substitution.

Following revision of previous MRI images

The finding, regarded to be a pituitary macroadenoma, is a typical image of lymphocyte (autoimmune) hypophysitis.

Development of MRI image as well as clinical course confirm this diagnosis.

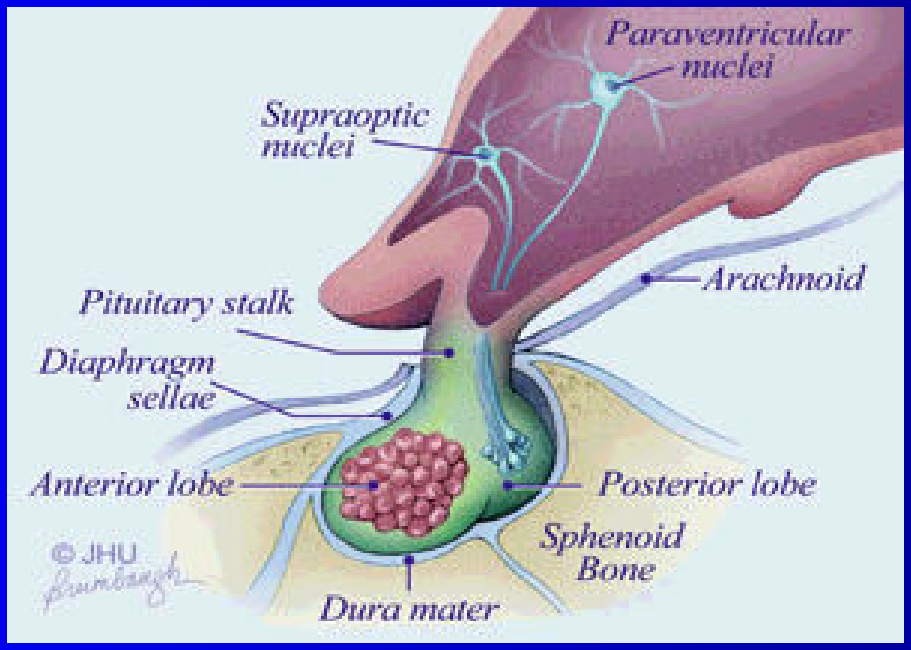
Prof. J. Marek, 3rd Internal Dept., 1st Faculty of Medicine



Differential diagnostics of pituitary expansions

Tumors — 90 %

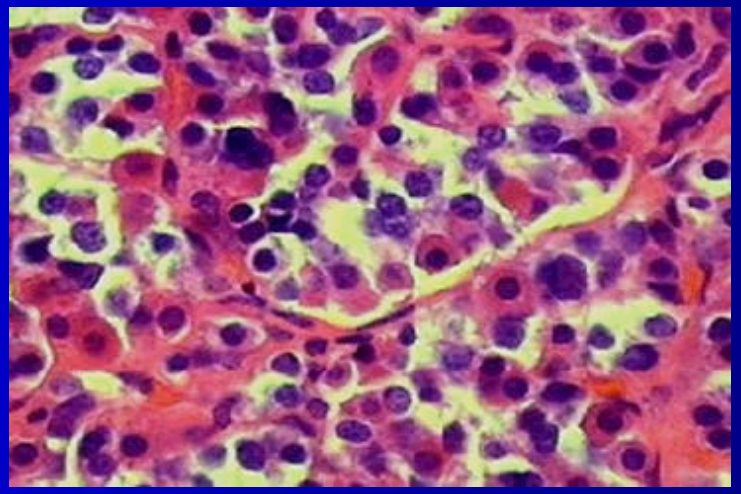
Other — 10 %



Differential diagnostics of pituitary expansions

- Tumors
  - Adenome
- Other

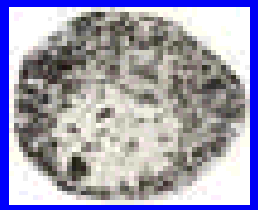
35 % hormonally afunctional
30 % PRL ... prolactinoma
25 % STH ... acromegaly
10 % ACTH ... Cushing sy
< 1 % other (TSH, LH, FSH)



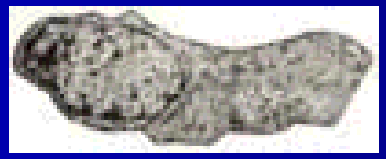
Differential diagnostics of pituitary expansions

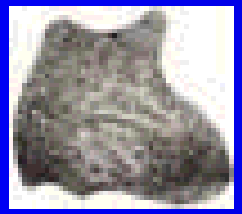
Tumors

Other



Craniopharyngeoma





Glioma

Chordom

Meningeoma

Metastasis

Hamartoma

Dysgerminoma

Differential diagnostics of pituitary expansions

Tumors

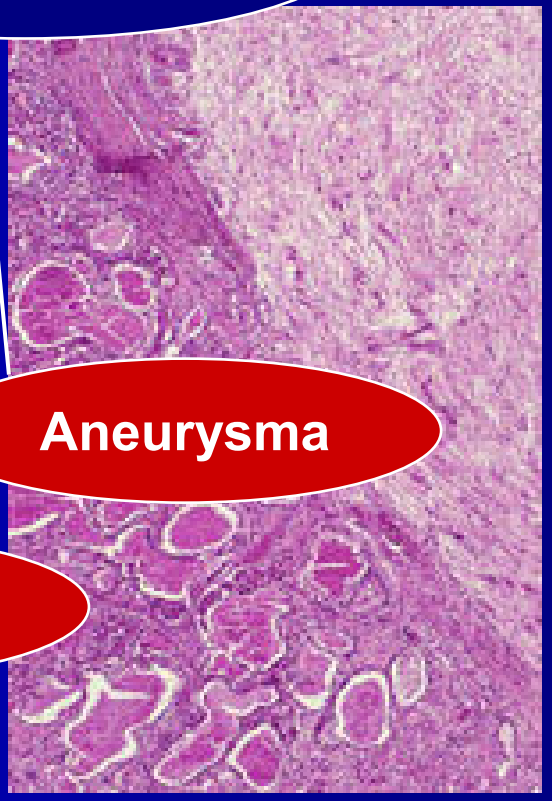
Other

Hereditary disorders

Cysts

Hypofysitis

Aneurysma

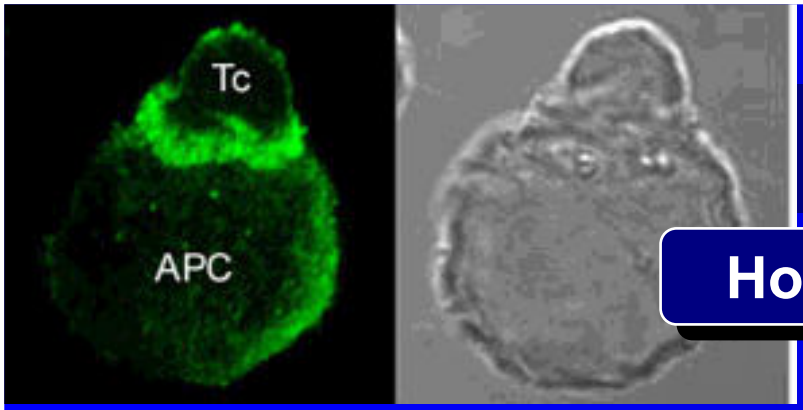


Autoimmune hypophysitis

The most often type of chronic pituitary inflammation
Prevalence: females – mainly during pregnancy + shortly after delivery

Frequent mismatch with macroadenoma

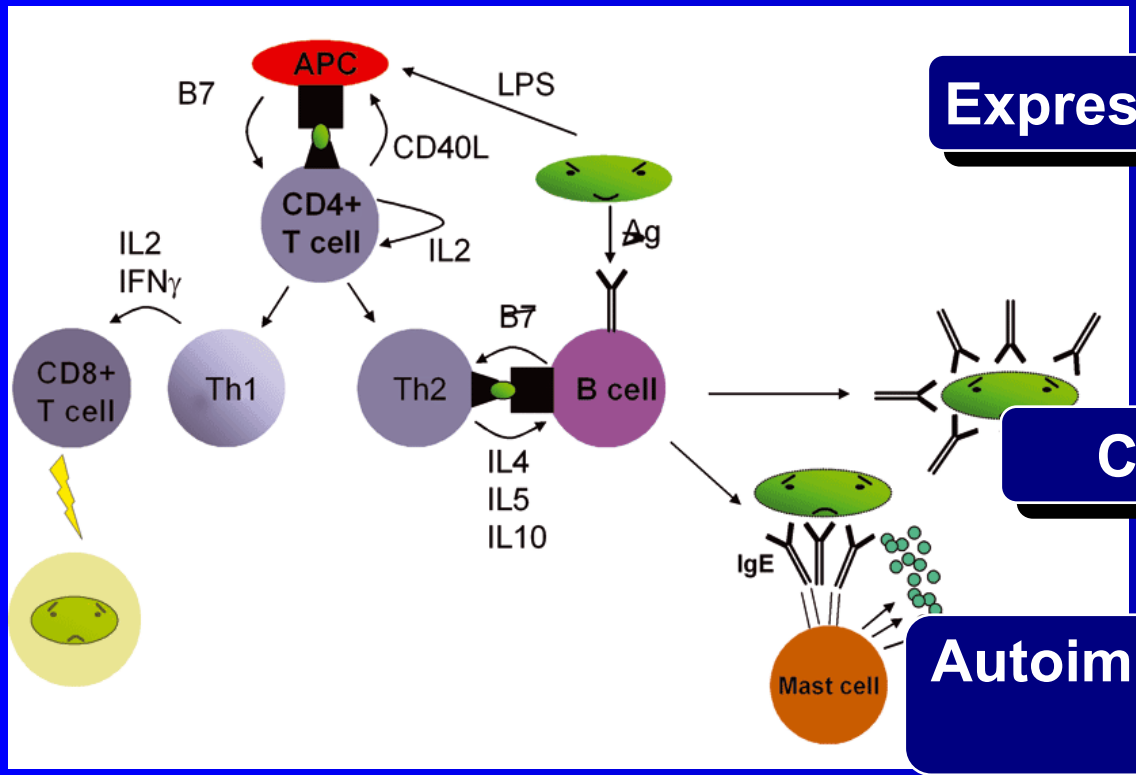
Good prognosis with tendency to spontaneous regression.



Patogenesis of hypophysitis

Hormonal dysbalance (gravidity, post-delivery)

„Dysbalance“ of T_{H1} / T_{H2} responses



Expression of MHC II

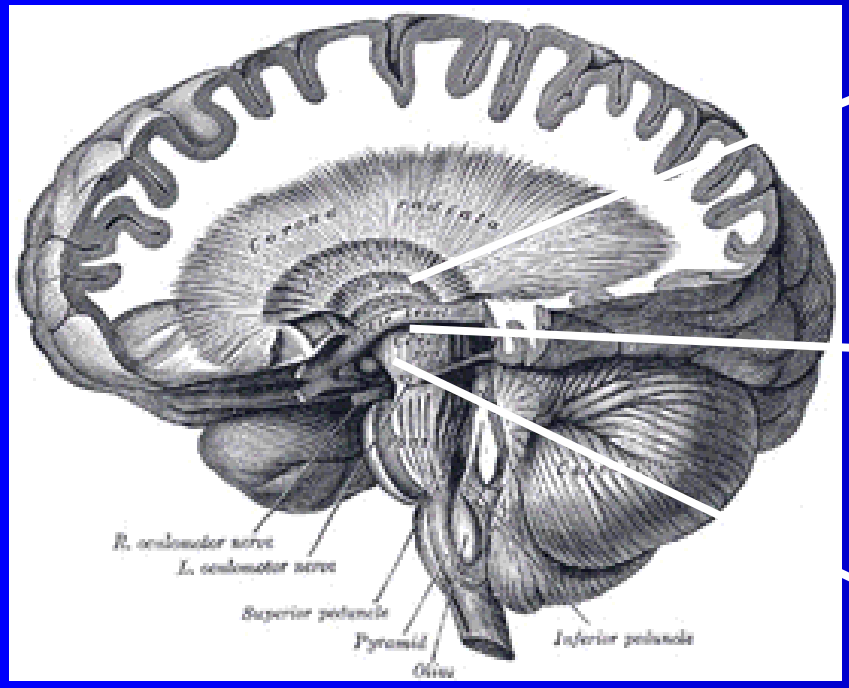
+

CD 4+ T Ly

CD 8+ T Ly

Autoimmune reaction type 4

Clinical findings



Local changes
47 % headache
33 % vision alteration

Hypopituitarism
33 % ↓ ACTH
13 % ↓ TSH

Hypothalamic - pituitary dysfunction
27 % diabetes insipidus
23 % ↑ PRL

Dif. dg. between hypophysitis and pituitary adenoma

Young females

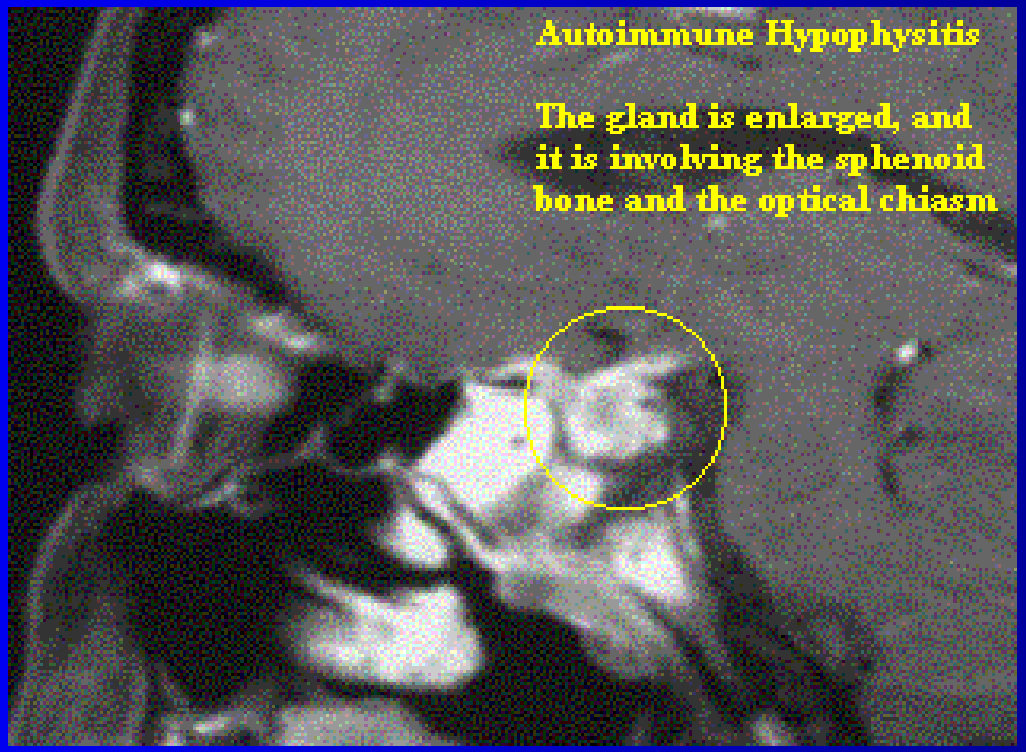
Onset usually before or early after delivery

Early symptoms - headache, vision alteration

Spontaneous regression

Dif. dg. between hypophysitis and pituitary adenoma

MRI image ... elongated, pyriform shape of pituitary in hypophysitis



Dif. dg. between hypophysitis and pituitary adenoma

„Selective“ hypopituitarism:

Pituitary destruction caused by tumor leads usually to subsequent dysfunction in following order:

↓
- LH, FSH
- STH, TSH
- ACTH

In a case of lymphocyte hypophysitis, the decrease of ACTH is usually the first sign.