Parathyroid glands disorders

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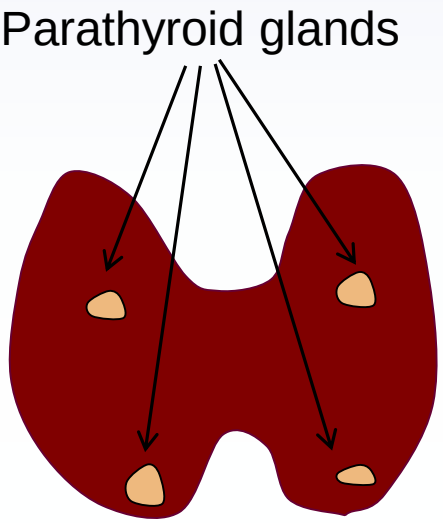
The parathyroid glands, around 4-6 in number, are usually located in the neck behind the thyroid. However, they are sometimes ectopically located elsewhere in the neck or chest. These glands are about the size of a grain of rice.

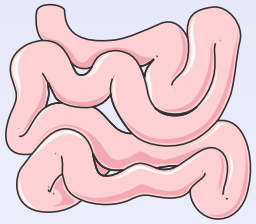
Thyroid gland (back view)



The parathyroid glands produce PTH, which is the main regulator of calcium level in the blood.

Proper calcium and phosphate balance is crucial to the normal functioning of the heart, nervous system, kidneys, and bones.

Calcium homeostatsis



Gastrointestinal system

Blood

Bones

calcium from food

1000 mg

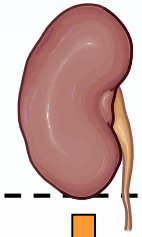
calcium from digestive juices

200 mg

intestinal absorption

400 mg/d

600 mg/d



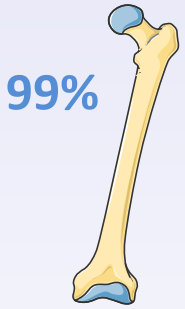
excretion in faeces

800 mg

urinary excretion

200 mg

Different forms of calcium



Most of the calcium in the body is stored in the bones as hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_{2)}$

Calcium in the serum:

- 45% - free ionised form ← physiologically active
- 45% - bound to proteins (predominantly albumins)
- 10% - complexed with anions (e.g. citrate, sulfate, phosphate)

Typically measured in routine blood tests

The total serum calcium concentration is adjusted to reflect any abnormality in albumin, the major calcium binding protein. The formula to use is:

corrected calcium = measured total serum calcium in mg/dL + 0.8 x (4.0 - patient's serum albumin concentration in g/dl).

Different forms of phosphate

- Most of the phosphate in the body is also stored in the bones as hydroxyapatite.
- Most of the remainder of the body's phosphate is intracellular (component of phospholipids in cell membranes, DNA and RNA, ATP and ADP).

- Small fraction in the serum:

  - circulating phospholipids

  - inorganic phosphate (HPO_4^{-2} and $H_2PO_4^-$) ➡ physiologically active and typically measured in routine blood tests

Normal laboratory values

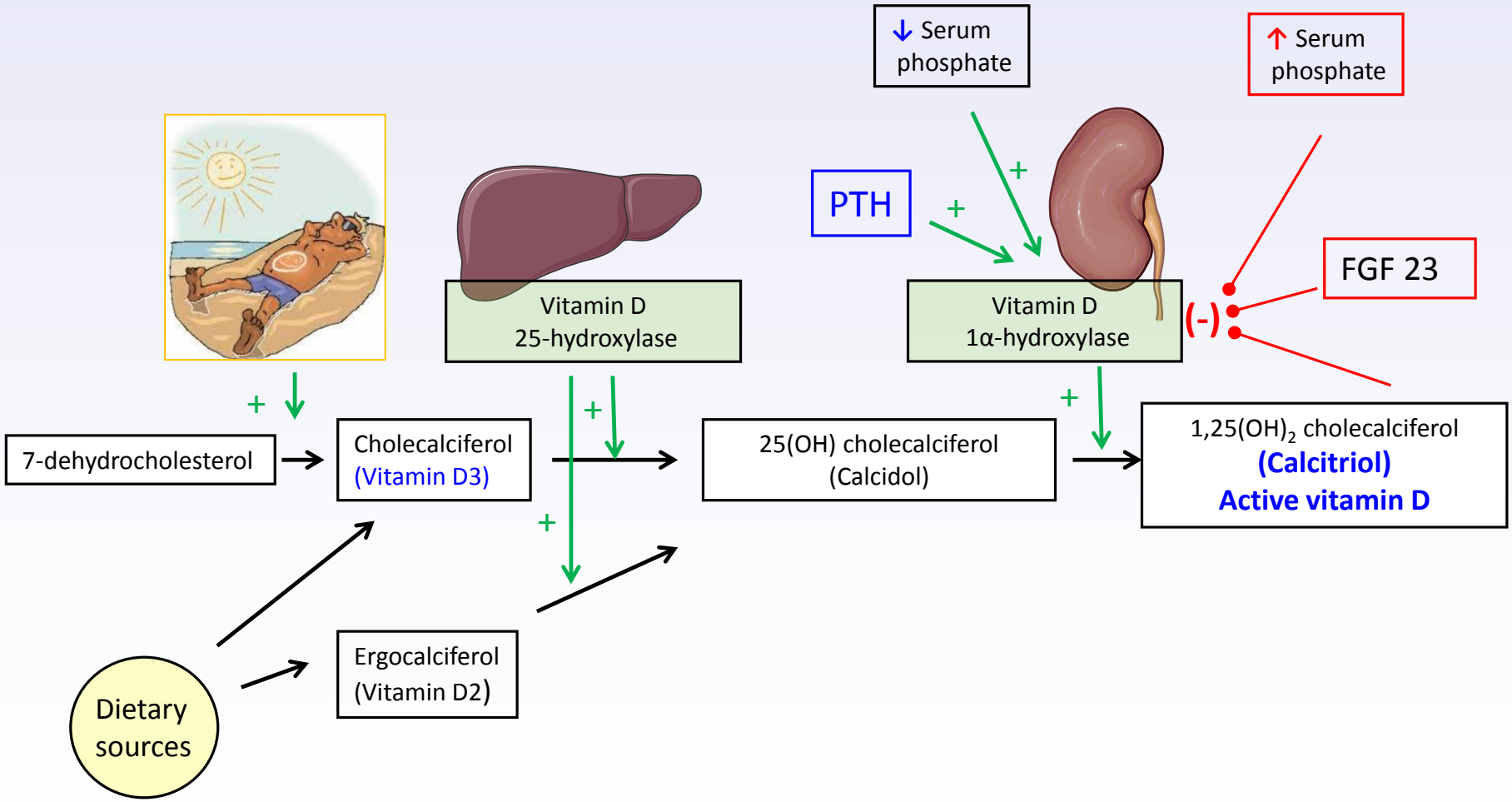
Test	Specimen	Conventional Units	SI Units
Calcium	serum	8.5-10.3 mg/dL	2.12-2.57 mmol/L
Ionised calcium	plasma	4-5.2 mg/dL	1.0-1.3 mmol/L
Calcium	urine	M < 300 mg/d F < 250 mg/d	M < 7.5 mmol/d F < 6.2 mmol/d
Phosphorus	serum	2.5-4.5 mg/dL	0.81-1.45 mmol/L
PTH (intact)	serum	11-67 pg/mL	

M-male, F-female

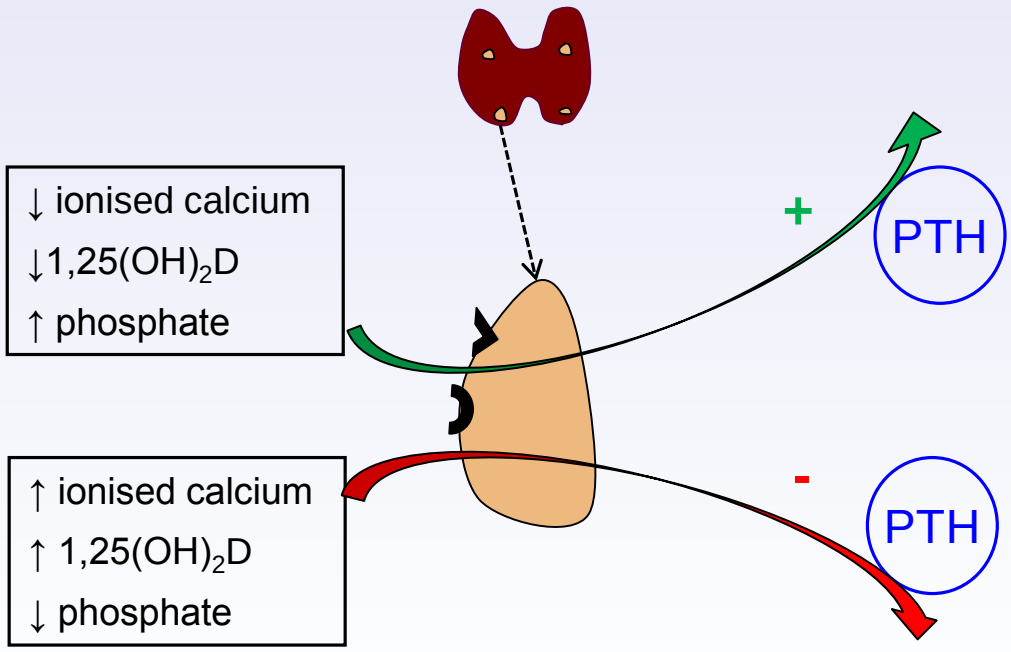
Major mediators of calcium and phosphate balance

Serum		
Ca_s	P_s	**Parathormone (PTH)**
↑	↓	• increases the release of calcium and phosphate from bones • stimulates the formation of active vitamin D in the kidneys (activation of 1 α hydroxylase) • reduces calciuria and increases phosphaturia
		Vitamin D
↑	↑	• increases the uptake of Ca and P in the gastrointestinal tract
		Calcitonin (low physiological importance)
↓		• decreases the uptake of Ca in the gastrointestinal tract • increases calciuria • reduces bone resorption
		FGF 23 (Fibroblast Growth Factor 23)
	↓	• increases phosphaturia

Synthesis and regulation of active vitamin D (calcitriol)



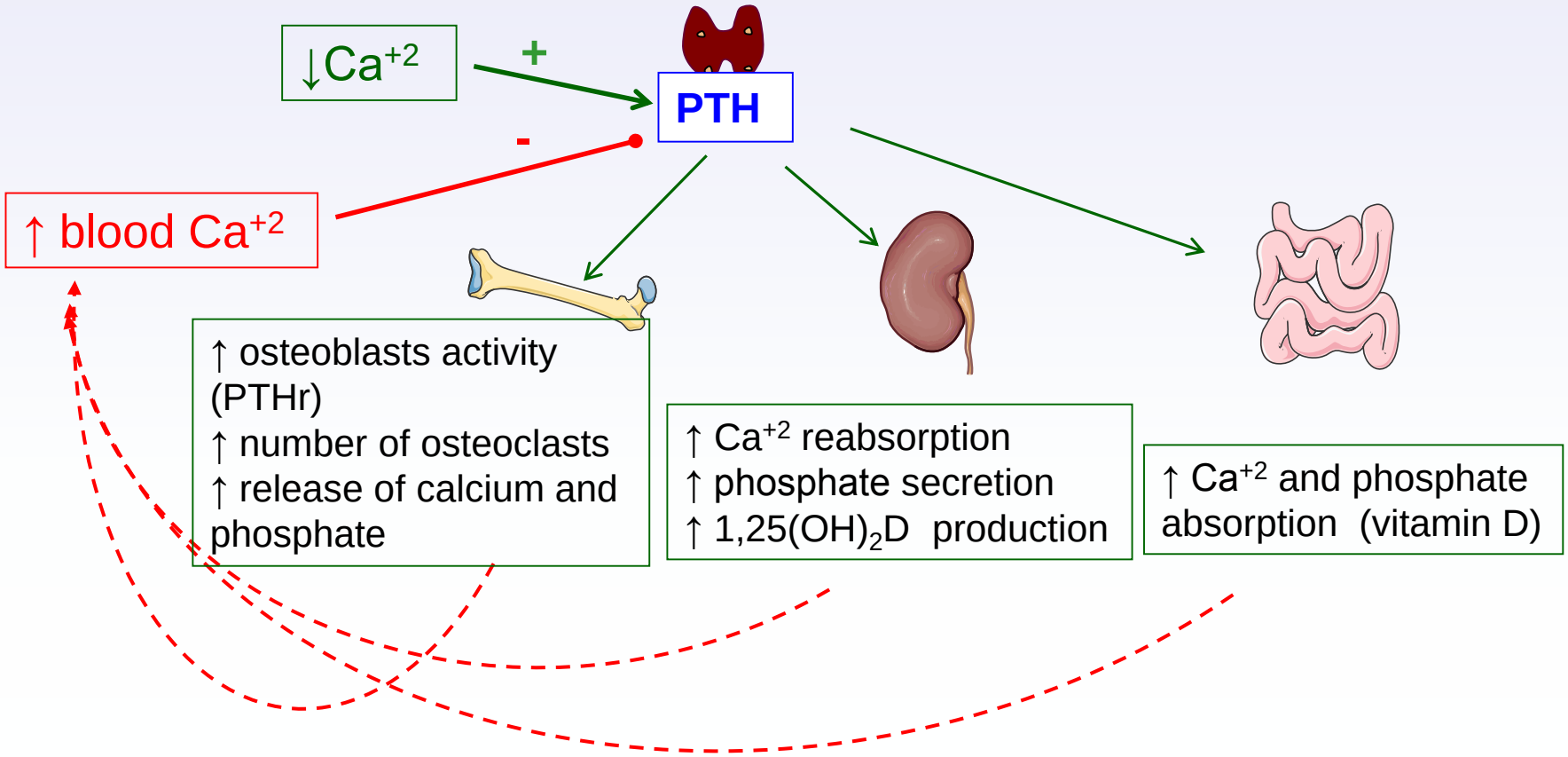
Regulation of PTH secretion



Ca SR - calcium-sensing receptor

VDR - vitamin D receptor

The effect of parathyroid hormone



Hyperparathyroidism

Primary - PTH secretion is disproportionately high in relation to the serum calcium concentration.

Secondary to kidney failure, severe vitamin D and calcium deficiency. Reversible, after removing the cause of the disorder.

Tertiary - is excessive autonomous secretion of parathyroid hormone after a long period of secondary hyperparathyroidism.

Primary hyperparathyroidism (PHPT)

Primary hyperparathyroidism is characterised by secretion of PTH that is excessively disproportionate to serum calcium levels, resulting from a primary defect of parathyroid cells.

PHPT results from:

- one or more adenomas (75-80% of cases)
- hyperplasia of all parathyroid glands (20%)
- parathyroid carcinoma (fewer than 1%)

The aetiology of 4-gland parathyroid hyperplasia is multi-factorial. It may be associated with a familial hereditary syndrome (5-10%), such as multiple endocrine neoplasia (MEN), types 1 (90%) and 2a (30%) or 2b (4%). As in the case of parathyroid adenomas, molecular mechanisms are heterogeneous.

PHPT - familial hereditary syndromes

Hereditary forms of PHPT account for 5–10% of cases:

- Multiple endocrine neoplasia (MEN)
- Familial non-MEN hyperparathyroidism
- Hereditary hyperparathyroidism – jaw tumor syndrome

Primary hyperparathyroidism (PHPT) - epidemiology

PHPT is the third most frequent endocrinopathy and it affects:

0.3-1.0%	of the general population
1-3%	of postmenopausal women.

women to men ratio is 3-4 : 1

Yu N et al.,QJM, 2011; Lundgren E. et al., Surgery, 1997; Fraser WD, Lancet 2009

Classical clinical consequences of PHPT

Bone destruction	Hypercalcemia	Hypercalciuria
Osteopenia	Peptic ulcer disease	Urolithiasis
Osteoporosis	Pancreatitis	Nephrocalcinosis
Bone deformities and fractures	Constipation, nausea, vomiting or loss of appetite	Nephrogenic diabetes insipidus
Osteitis fibrosa cystica, brown tumors	Polydipsia and polyuria	
	Renal failure	
	Cardiovascular features: hypertension, arrhythmia, ventricular hypertrophy, and vascular and valvular calcification	
	Tiring easily or weakness	
	Neuropsychiatric disorders	
	Parathyroid crisis	

The classical manifestations of PHPT:

"bones, stones, abdominal moans, and psychic groans„.

Primary hyperparathyroidism – clinical forms

- Symptomatic primary hyperparathyroidism nowadays tends to reduce the incidence in highly developed countries (20%).
- The most common clinical presentation of PHPT is asymptomatic or low symptomatic disease
- Atypical occurences include normocalcemic PHPT and parathyroid crisis.

The incidence of clinical consequences PHPT* (n=63)

	Percentage of patients	
Osteoporosis (DXA)	76	**96**
Osteopenia	20	
Urolithiasis	67	
Bone fractures	16	
Gastritis, peptic ulcer disease	22	
Cholelithiasis	28	
Pancretitis	2 persons	

*Dept. E D & IT, Wrocław Med.Univ. J. Szymczak

PHPT- skeletal changes

- Parathyroid hormone exerts anabolic and catabolic effects on bone. In PHPT bone turnover is increased with a predominance of resorption. This mobilises calcium salts and leads to the destruction of the bone and **reduction in bone mineral density** (BMD).
- In more severe cases, the cortex is grossly thinned, and the marrow contains increased amounts of fibrous tissue accompanied by foci of hemorrhage and cyst formation **(osteitis fibrosa cystica)**.
- Aggregates of osteoclasts, reactive giant cells, and hemorrhagic debris occasionally form masses that may be mistaken for neoplasms (**brown tumors** of hyperparathyroidism).

Primary hyperparathyroidism – bone fracture risk

PHPT, even when appearing as an asymptomatic disorder, is characterised by compromised cortical and trabecular compartments and increased fracture risk.

Normocalcemic primary hyperparathyroidism (a variant of PHPT)

- ↑PTH
- Normal serum total and ionized calcium concentration
- The features of PHPT may be present (e.g. low BMD)
- All secondary causes for hyperparathyroidism must be ruled out

Normocalcemic PHPT is considered to be an early form of asymptomatic PHPT or represent a unique phenotype of the disease.

Parathyroid crisis

Parathyroid crisis, which is rare, is characterised by severe hypercalcemia, with the serum calcium concentration usually above 15 mg/dl and marked symptoms of hypercalcemia:

- dehydration (hypercalciuria)
- central nervous system dysfunction (confusion, daze, nausea and vomiting)
- constipation, paralytic ileus
- bradycardia (ECG - QT shortening)

Diagnosis of primary hyperparathyroidism

The diagnosis of primary hyperparathyroidism is established by appropriate biochemical testing.

PHPT is associated with hypercalcemia and elevated levels of parathyroid hormone.

Diagnosis of primary hyperparathyroidism (1)

Laboratory tests		
	Results	
Blood tests	↑	Calcium
	↑	PTH
	↓, N	Inorganic phosphate
	N, ↓	Vitamin 25(OH)D (but $1,25(OH)_2D$ - ↑ or N)
	↑	ALP (alkaline phosphatase)
	N (↑)	Creatinine
24 hour urine collection	↑ (N)	Calciuria
	N	Creatinine excretion

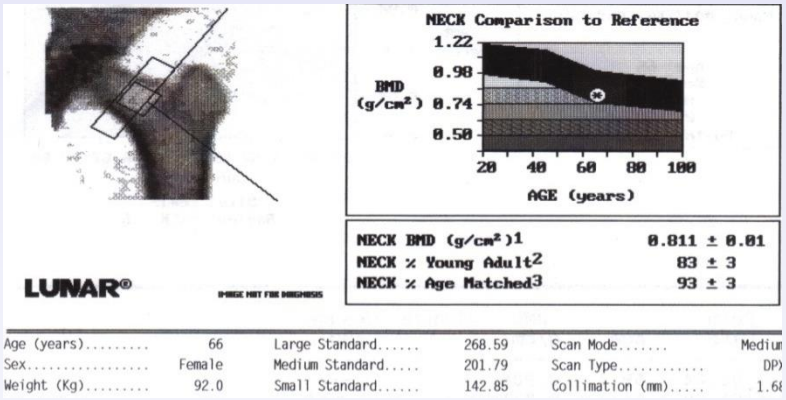
Diagnosis of primary hyperparathyroidism (2)

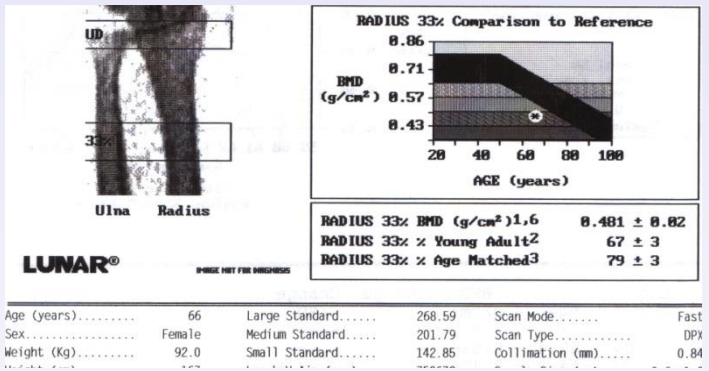
additional evaluation to determine management

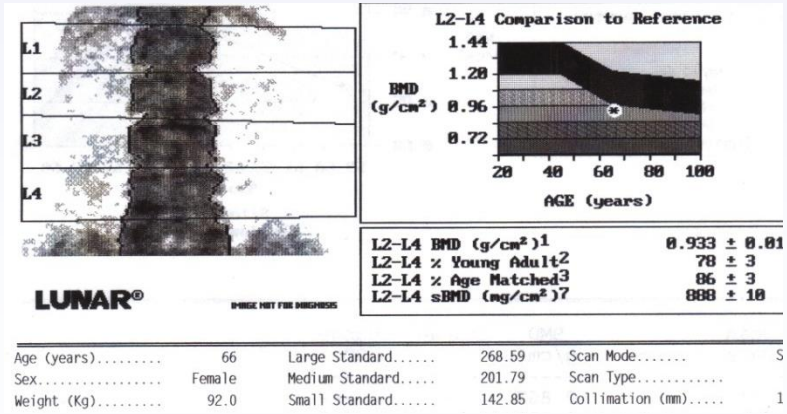
Bone densitometry (DXA)	• lumbar spine • hip (total or femoral neck) • radius (distal 1/3 site)
Ultrasound abdominal examination	renal imaging
X-ray of painful or deformed parts of the skeleton	
Vertebral **F**racture **A**ssessment (**VFA**) by DXA or x-ray *	In order to diagnose asymptomatic vertebral compression fractures in asymptomatic patients who do not have osteoporosis in DXA
Detection of genetic disease	

* optional

Primary hyperparathyroidism - bone mineral density (DXA)



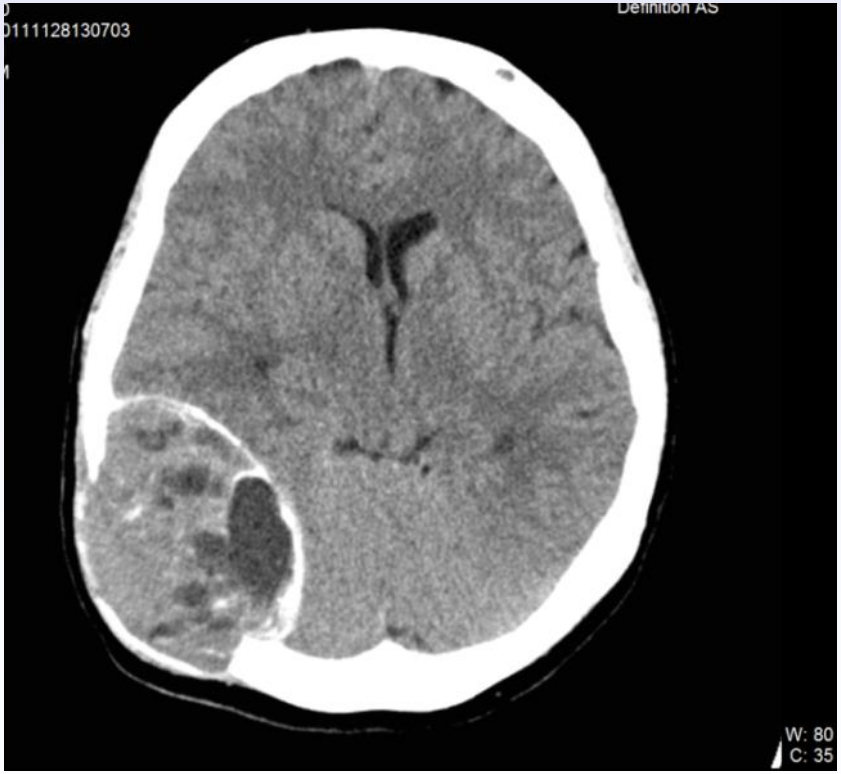




	T- score
Femoral neck	-1.41
Lumbar spine	-2.23
Forearm (1/3 distal)	-3.26

Patients with asymptomatic PHPT may have decreased BMD, in particular at more cortical sites (forearm) as compared with more trabecular sites (spine).

Primary hyperparathyroidism – bone destruction



Brown tumor of the skull of a young woman (CT)

Primary hyperparathyroidism - differential diagnostics
Hypercalcemia: etiologies by mechanism

PTH excess	PTH independent bone resorption	Vitamin D excess	Excessive dietary intake of calcium	Thiazides
Hyperparathyroidism: • primary • secondary • tertiary	**PTHrP secreting malignancy**	↑ intake of Vit. D	Milk alkali syndrome (calcium-alkali syndrome - ↑ intake of $CaCO_3$)	
Familial hypocalciuric hypercalcemia (FHH) - (inactivating mutation in the calcium sensing receptor gene)	Osteolytic bone metastases	Ectopic $1,25(OH)_2D$ production (lymphoma, granuloma)		
Lithium (reduces sensitivity of PTH secretion to inhibition by calcium)	Paget's disease			
	Immobilisation			
	Hyperthyroidism			

Common causes of secondary hyperparathyroidism

Disorder	**Comment**
Chronic kidney disease (CKD) (GFR below 60 ml/min)	Impaired 1,25$(OH)_2$D production, hyperphosphatemia
Decreased calcium intake	
Calcium malabsorption	Vitamin D deficiency, celiac disease, chronic pancreatitis, post gastrectomy syndrome, bariatric surgery
Renal calcium loos	Renal hypercalciuria
Drugs	Bisphosphonates (inhibiton of bone resorption), anticonvulsants, furosemide, phosphorus

Familial Hypocalciuric Hypercalcemia (FHH)

The reason of FHH is inactivating mutation of the calcium sensing receptor in parathyroid glands.

↑Serum calcium and ↑PTH

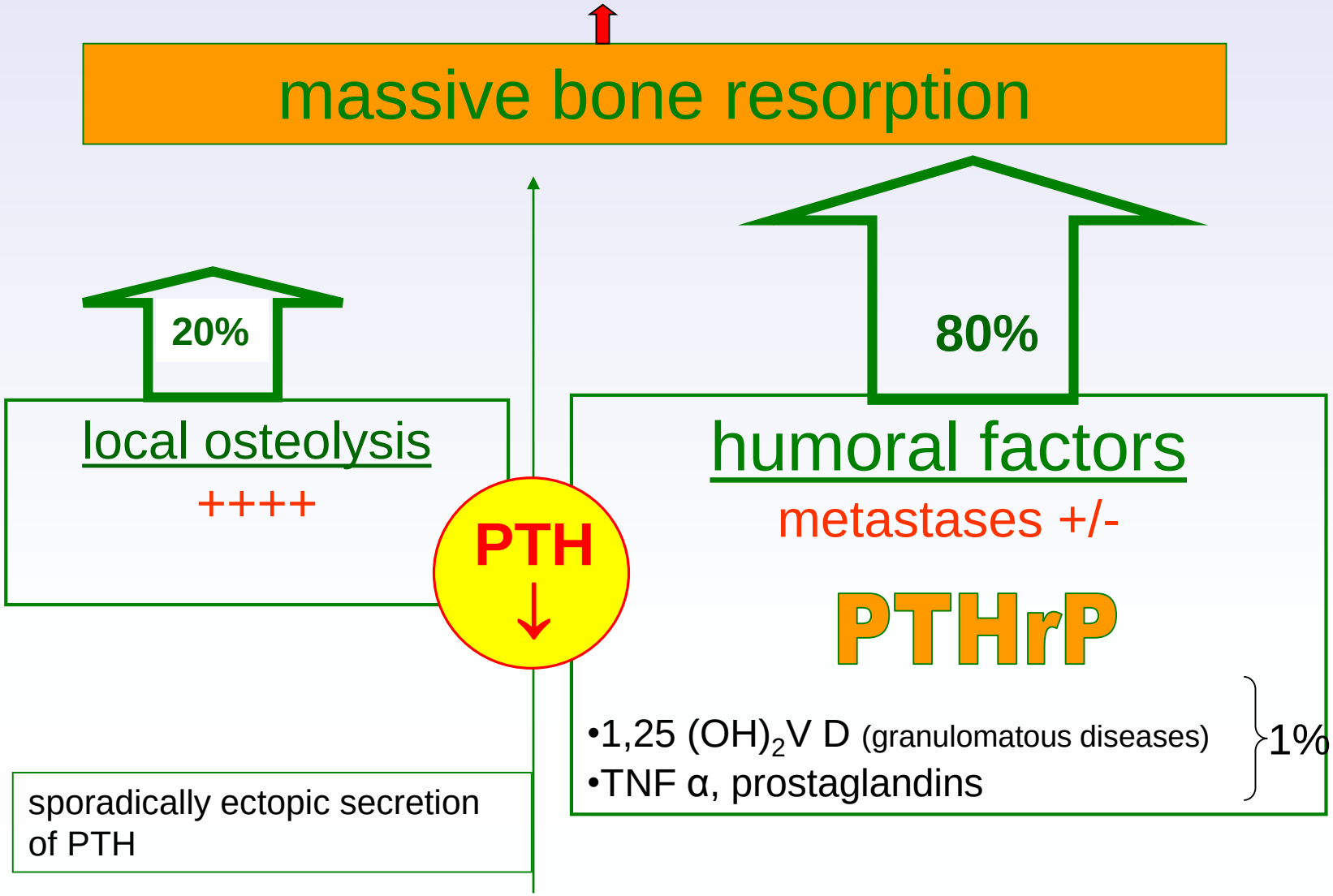
but

- Urine calcium is low (< 100 mg/24H)

- Calcium-creatinine clearance ratio =< 0.01
(24 H urine Ca/serum Ca x serum Cr/24 H urine Cr)

FHH is a rare, lifelong, benign condition.

Hypercalcemia in neoplastic disorders



PTHrP - *PTH related protein*

Primary hyperparathyroidism - differential diagnostics

	PHPT (Primary hyperpara-thyroidism)	FHH (Familial Hypocalciuric Hypercalcemia)	Secondary hyperparathyroidism		Malignancy
			Chronic renal failure	Malabsorption, Ca & Vit.D deficiency	
PTH	↑↑	↑	↑↑↑	↑, N	↓
Ca_s	↑↑	↑	↓, N	↓, N	↑
Ca_{u24h}	↑↑	↓	↓	↓	↑↑
$Phosphate_s$	↓	N	↑	↓, N	↓, N
BMD (DXA)	↓↓	N	↓	↓	↓, N

Primary hyperparathyroidism - treatment

1. Selective parathyroidectomy

- The treatment of choice for symptomatic disease is surgical removal of the hyperactive parathyroid glands along with intraoperative PTH monitoring.
- Surgery may be also recommended in some asymptomatic or low symptomatic patients.
- Parathyroidectomy (PTX) should only be performed by highly experienced surgeons.

2. Pharmacotheraphy

In many people, the disease may remain mild or asymptomatic for a long period. In these patients, as well as in those after an unsuccessful PTX, who are unwilling to undergo or considered unsuitable for surgery it attempts to apply a symptomatic pharmacotherapy.

So far treatment with calcimimetics or bisphosphonates seems to be the most promising.

Primary hyperparathyroidism - indications for surgery in asymptomatic PHPT* 2014

Measurement	Surgery Recommended [a]
Serum Calcium	**> 1.0 mg/dl (0.25 mmol/L) above normal**
Skeletal	**A. Bone Mineral Density** by DXA **T score < -2.5** SD at lumbar spine, hip (total or femoral neck) or radius (distal 1/3 site)[b] or presence of **fragility fracture** **B. Vertebral fracture** by X-ray, CT, MRI or VFA
Renal	**A.** Creatinine clearance < 60 ml/min **B.** 24h urine for calcium > 400 mg/d (>10 mmol/d) and increased stone risk by biochemical stone risk analysis **C. Presence of nephrolithasis** or nephrocalcinosis by X-ray, US, or CT
Age	< 50 years

[a] Surgery is also indicated in patients for whom medical surveillance is neither desired nor possible.
[b] the use of Z-scores instead of T scores is recommended in evaluating BMD in premenopausal women and men younger than 50 y

**According to: Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop. Bilezikian et al.,JCEM,2014,99*

Localisation studies

Localisation studies should not be used to establish the diagnosis of PHPT or to determine management.

They should be done after a decision for surgery has been made. Localisation studies, in conjunction with intraoperative parathyroid hormone testing, can help minimise the extent of surgical dissection, and can help detect ectopic parathyroid tissue.

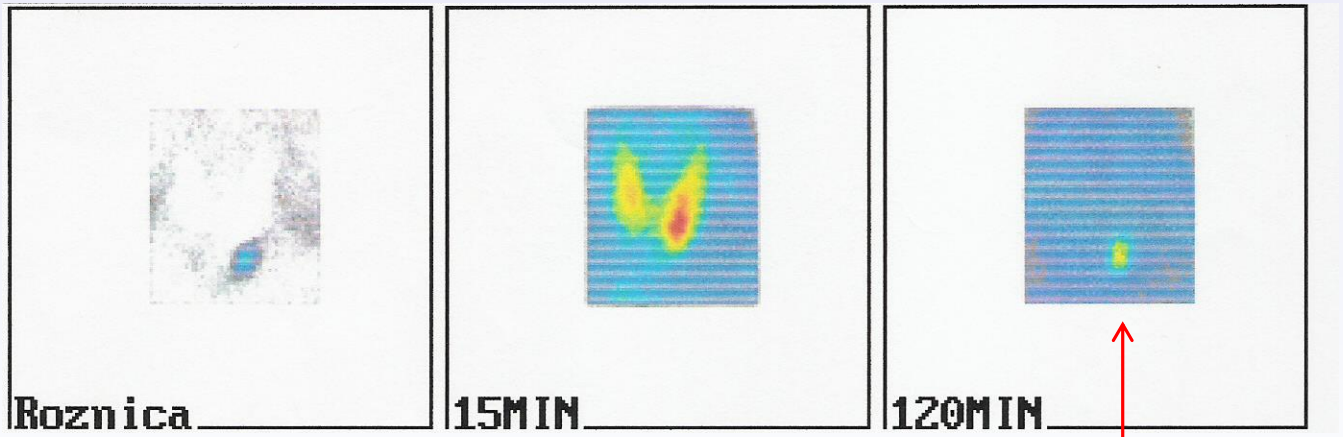
No imaging technique, even in combination, accurately predicts multiglandular disease, and a bilateral neck exploration should be strongly considered when the studies are discordant, equivocal, or negative.

PHPT - localisation tests

The type of imaging	Comments	Sensitivity*
Ultrasonography	Usually a hypoechoic parathyroid adenoma posterior to the thyroid parenchyma with peripheral vascularity seen on colour Doppler. US provides additional anatomic information about the thyroid gland.	up to 80%
Technetium-99m sestamibi scintigraphy	Planar image	60-90%
SPECT — Sestamibi-single photon emission computed tomography	Is a three-dimensional sestamibi scan. The multidimensional images illustrate the depth of the parathyroid gland or glands in relation to the thyroid.	~ 90%
SPECT-CT	SPECT and CT fusion. Adds the ability to discriminate parathyroid adenomas from other anatomic landmarks.	
Computed tomography (CT)	Low sensitivity	
Magnetic resonance imaging (MRI)	For reoperative surgery. Provides a non-invasive imaging to localise abnormal parathyroid tissue	40-85%

* Sensivity for detecting solitary adenoma. No imaging technique accurately predicts multiglandular disase

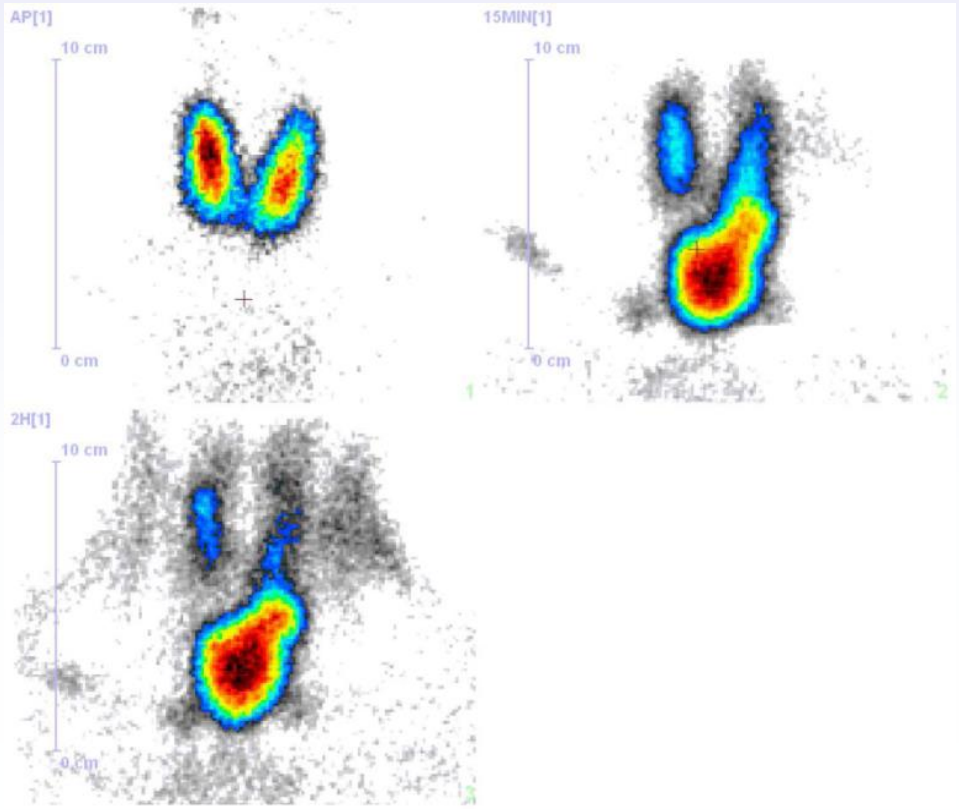
Parathyroid scintigraphy (Tc99 + MIBI)



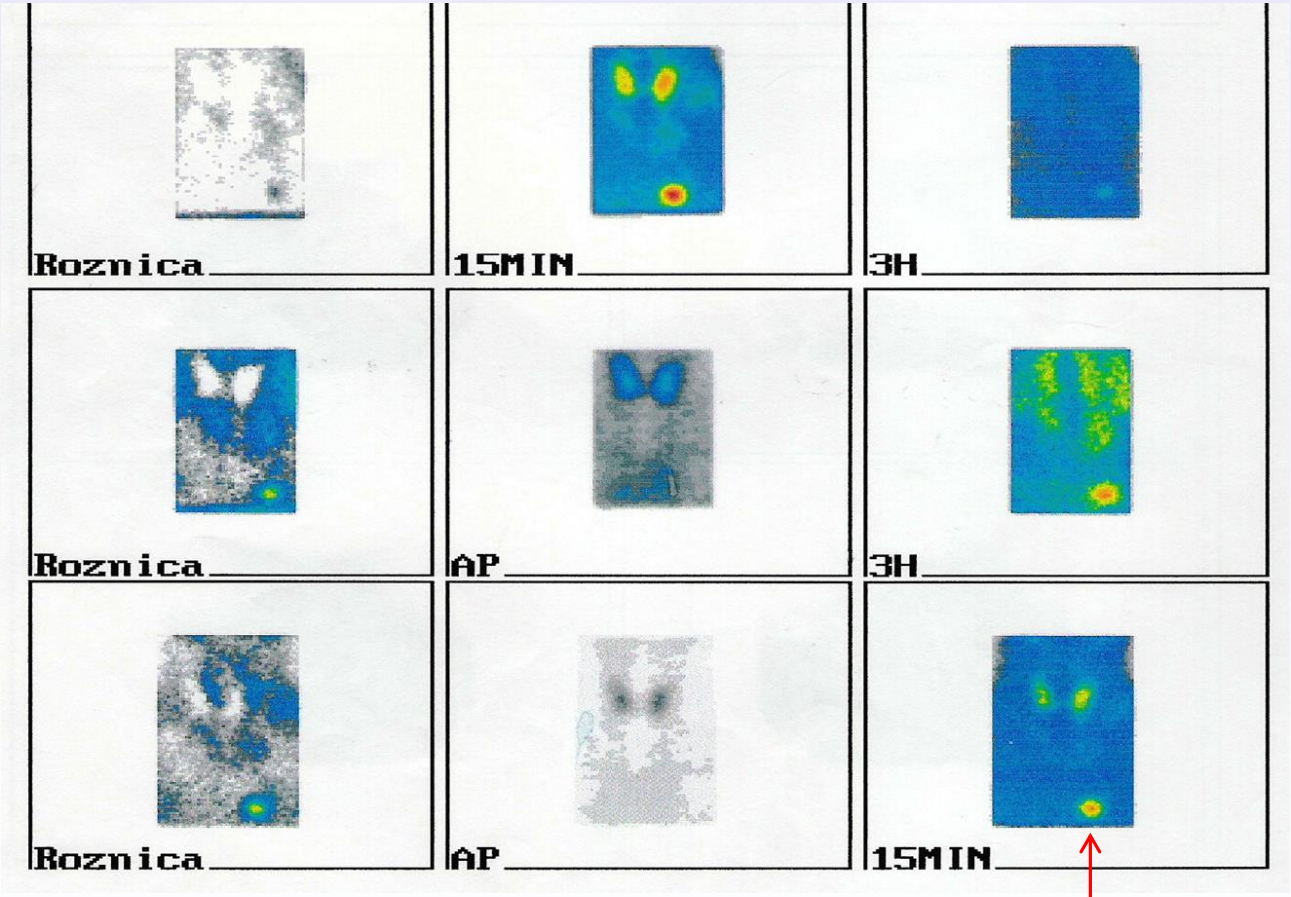
Adenoma of left inferior parathyroid gland

99mTc-sestamibi is taken up by the mitochondria in thyroid and parathyroid tissue; however, the radiotracer is retained by the mitochondria-rich oxyphil cells in parathyroid glands longer than in thyroid tissue. Radionuclid usually washes out of normal thyroid tissue in under an hour. It persists in abnormal parathyroid tissue.

Parathyroid scintigraphy
(99mTc+MIBI and 99mTc)

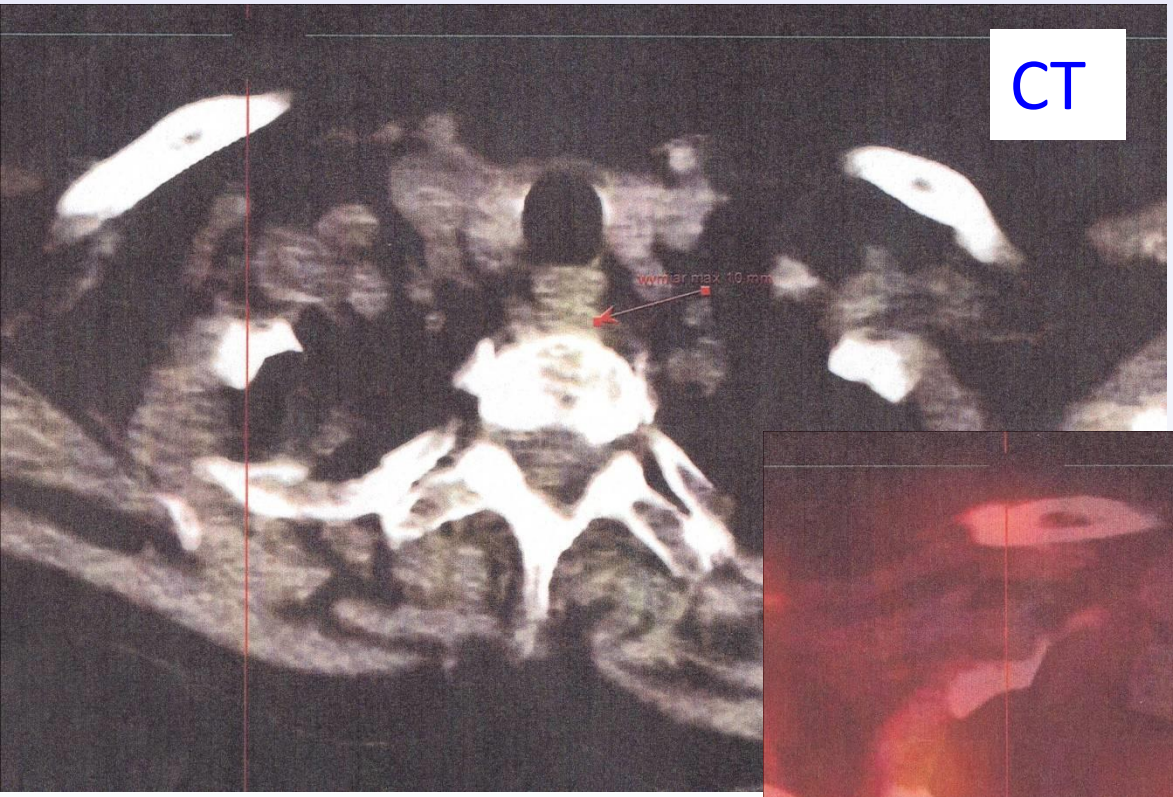


Parathyroid scintigraphy (Tc99 + MIBI)

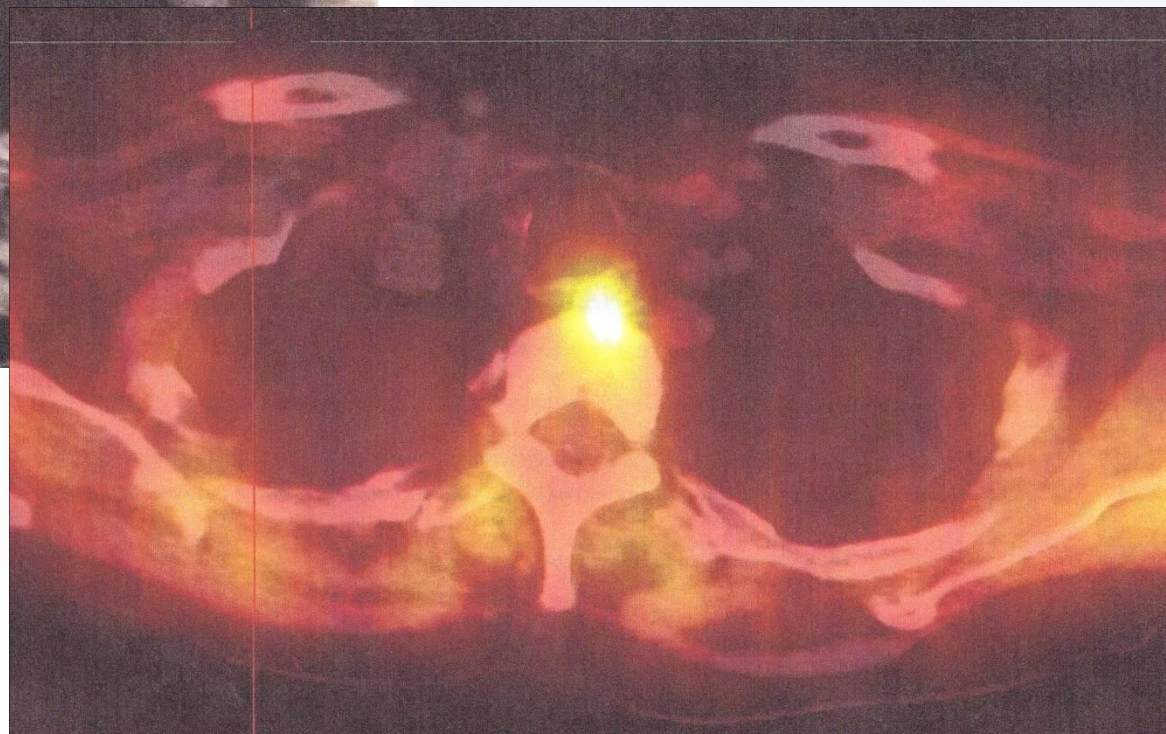


Ectopic parathyroid located in the chest

PHPT-parathyroid imaging



CPECT/CT



“The most important preoperative localisation challenge in PHPT is to locate the parathyroid surgeon!”

John Doppman, 1975

Surgical techniques applied in PHPT

1) Minimally invasive techniques of parathyroidectomy (MIP) are appropriate for most patients. These techniques require adequate imaging, experienced surgeons, and an intraoperative PTH assay*. They are not appropriate for a patients who have multigland disease especially those who have familial forms of PHPT.

2) Bilateral cervical exploration is the ideal operation for most patients with multigland disease, including those with genetic disease. In patients with hereditary PHPT all parathyroid cells are mutated. The extent of resection is „not too much and not too little". Recommended operation for MEN 1 patients with is a subtotal PTX removing $3^1/_2$ glands and leaving a viable 30 to 50 mg remnant from the most normal-appearing gland.

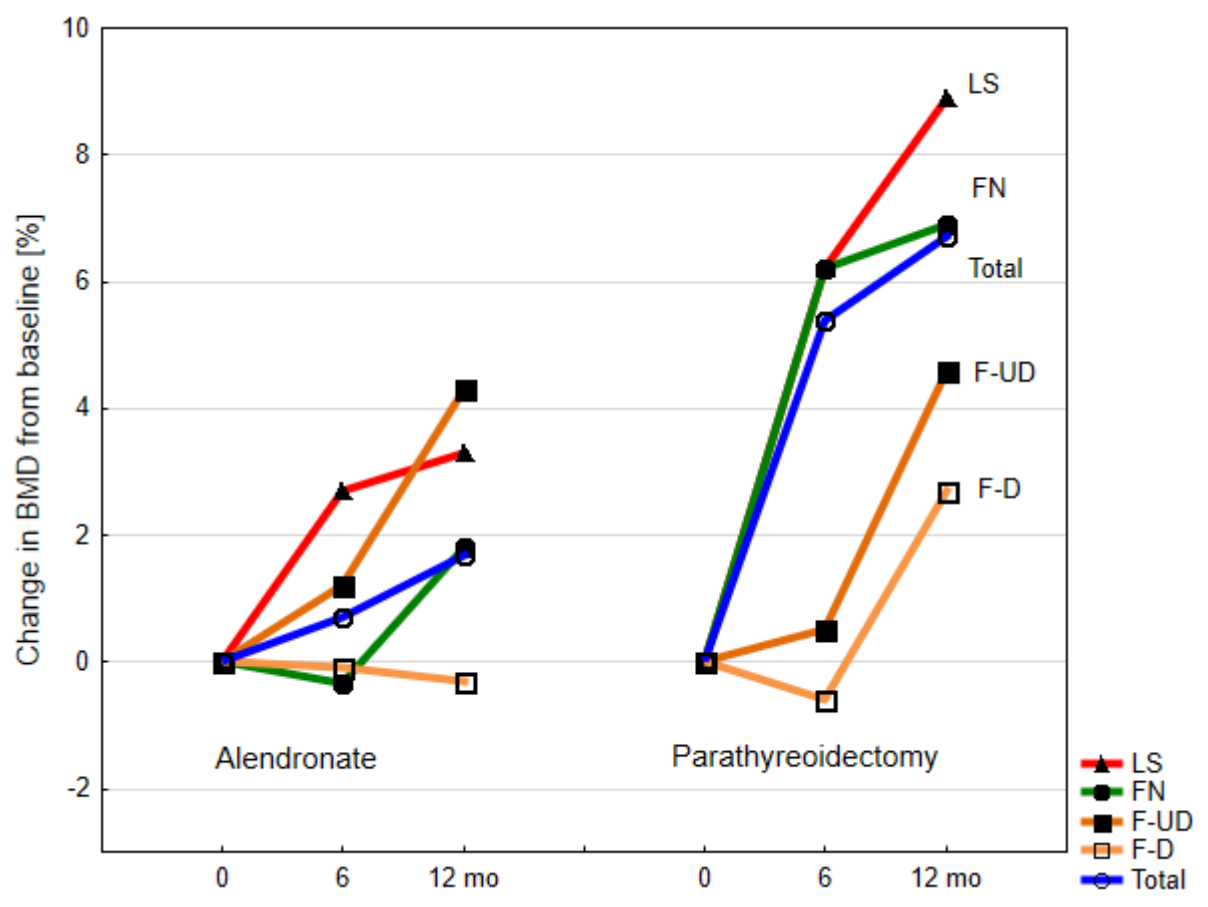
*Intraoperative PTH (half life ~ 3-4 minutes) - biochemical cure is drop by 50% from the preexcision level, at 10 minutes

The effect of successful parathyroidectomy in PHPT

1. Normalisation of biochemical disorders
2. Reduction of nephrolithiasis
3. Improvement in bone mineral density, bone reconstruction

The increase in BMD after PTX depends more on bone turnover than on age. Is greater the more severe was the disease before treatment, and the most intense in the first few months after surgery.

The mean percentage changes in BMD in PHPT patients after parathyroidectomy or alendronate treatment

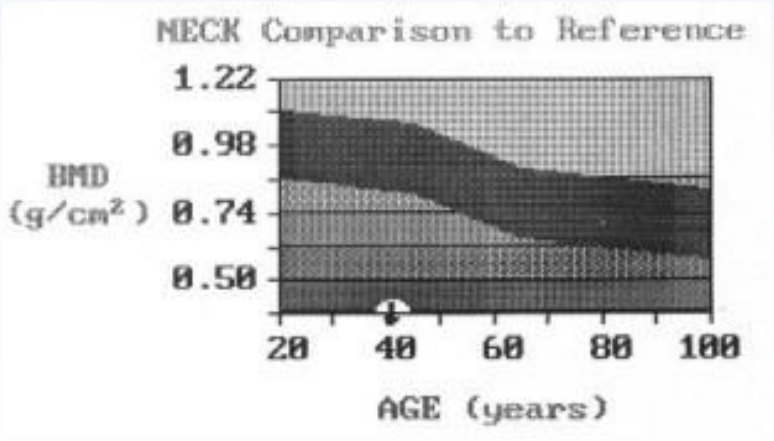


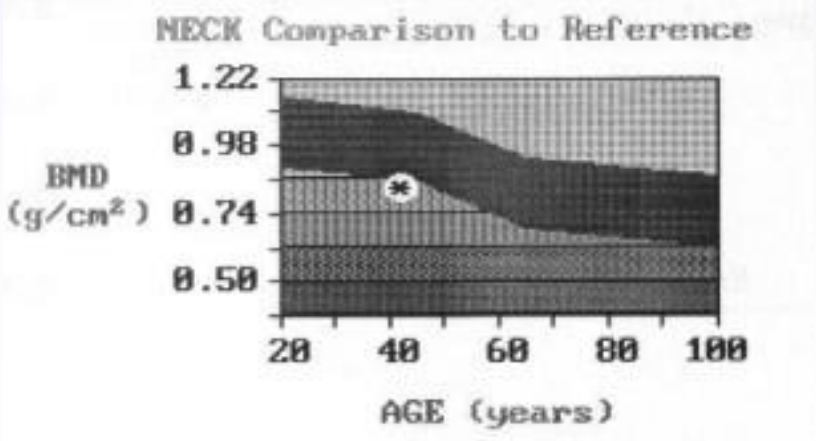
LS-lumbar spine, FN-femoral neck, F-D- forearm 1/3 distal, F-UD-forearm ultradistal, total -total body

According to: Szymczak J, Bohdanowicz-Pawlak A. HMR 2013

Increase in BMD in woman (42 y) with severe PHPT within 6 months after PTX

	Z-score before	Z-score after 6 months	Change [%]
Lumbar spine	(-) 2,42	(-) 1,46	17,9
Femoral neck	(-) 4,67	(-) 1,21	121,7
Forearm 1/3 distal	(-) 5,38	(-) 3,72	31,6

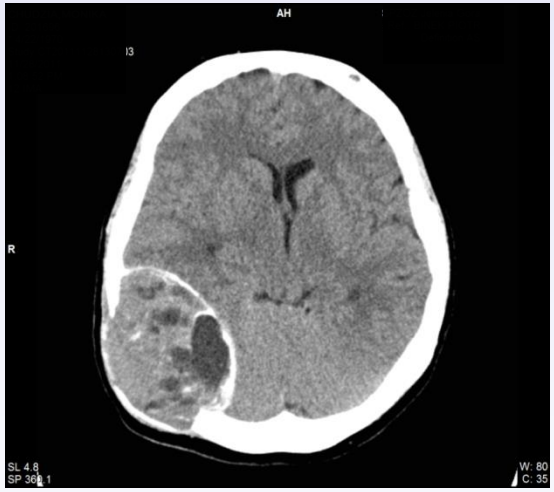


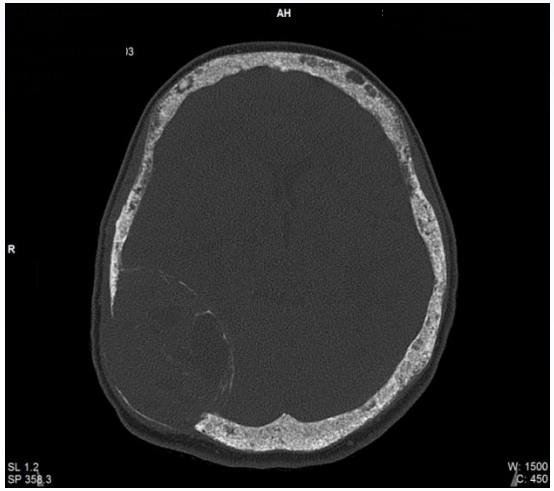


Before PTX: PTH 1000-2000 ng/ml, Ca_s – 12-18 md/dl, Cau_{24}- 920-2000 mg

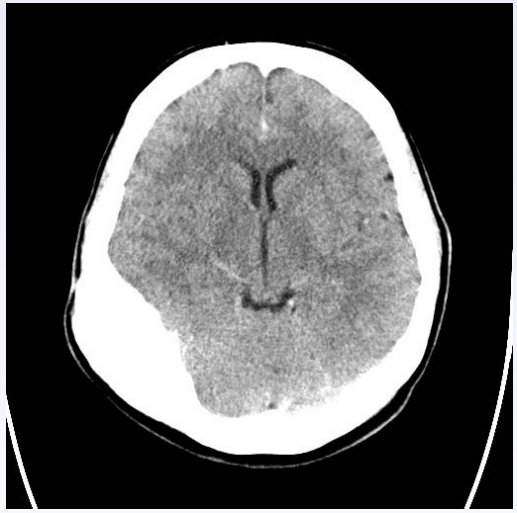
Brown tumor of the skull of a young woman (CT)

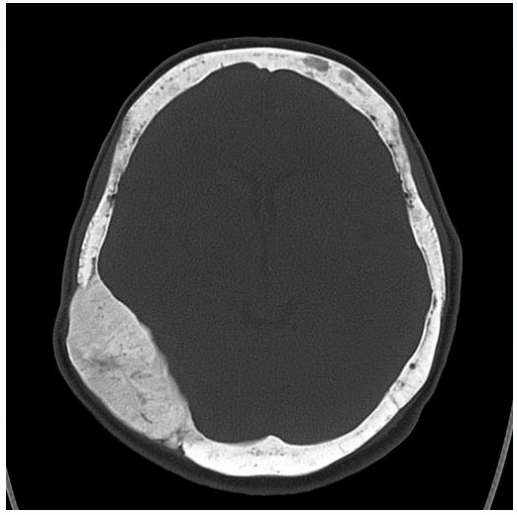
before PTX





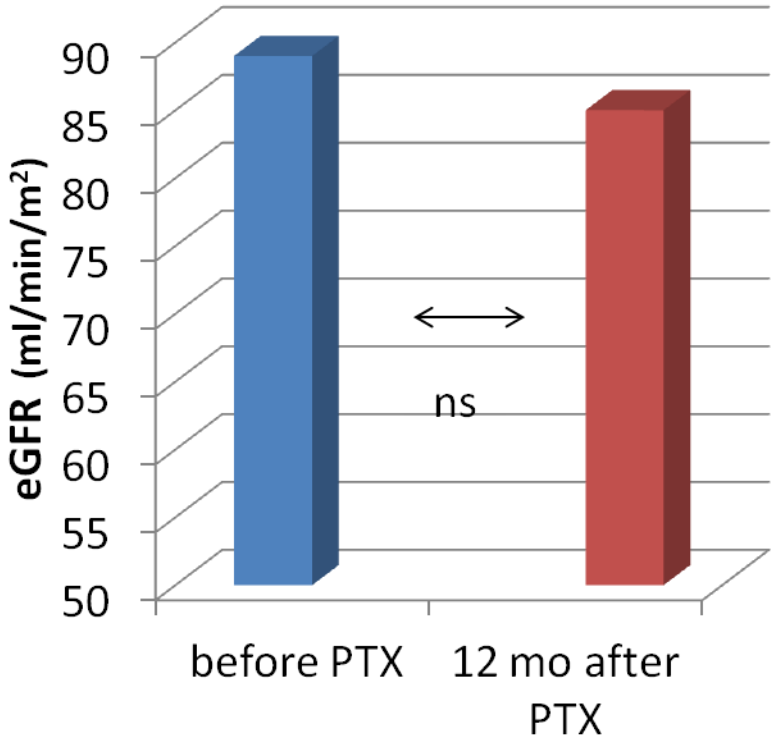
6 months after PTX



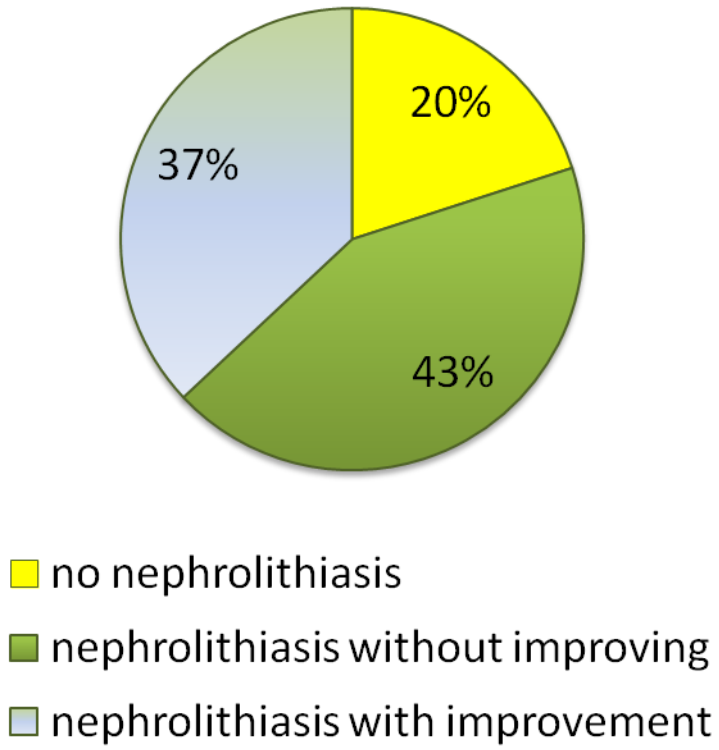


The effect of parathyroidectomy on GFR and severity of nephrolithiasis in patients with PHPT (n=30)

GFR



Nephrolithiasis or nephrocalcinosis



J.Szymczak

PHPT - postoperative hypocalcemia

Hypocalcemia	**The cause of hypocalcemia**
Transient and mild	suppression of the remaining normal parathyroid tissue
Prolonged and accompanied by hypo- or euphosphatemia and high PTH levels (hungry bone syndrome)	rapid deposition of serum calcium into demineralised bone
Accompanied by hyperphosphatemia and low PTH levels	hypoparathyroidism

Medical Management of Primary Hyperparathyroidism

Pharmacotherapy may be used in mild or asymptomatic PHPT and in in patients after an unsuccessful parathyroidectomy (PTX), or in those who are unwilling to undergo or considered unsuitable for surgery.

Pharmacological treatment should be reserved for those patients in whom it is desirable to lower the serum calcium or increase BMD.

Medical Management of Primary Hyperparathyroidism

Medicine	Effect
Calcimimetics (cinacalcet)	• Decrease calcemia and calciuria • Reduce, but not normalise PTH • Do not affect BMD
Bisphosphonates (alendronate)	• Improve BMD • Do not alter serum calcium
Denosumab (?)	• RANKL antagonist - decrases bone resorption

Patients with low serum 25-hydroxyvitamin D should be repeatedely administered with doses of vitamin D that bring its serum levels to 20 ng/ml at a minimum (with caution, so as not to aggravate hypercalcemia).

Treatment of severe hypercalcemia (parathyroid crisis)

- Hydration with normal saline
- Furosemide (after hydration)
- Bisphosphonates iv. (pamidronate, zoledronic acid)
- Glucocorticoids (prednisone 10-40 mg/d)
- Calcitonin sc., im.
- Calcimimetics (cinacalcet) – 10-80 mg/d

Monitoring patients with primary hyperpararathyroidism who do not undergo parathyroid surgery*

Measurement	Frequency
Serum calcium	**Annually**
Renal	Serum creatinine, eGFR **annually.** If renal stones suspected: 24-h biochemical stone profile, renal imaging by x-ray, ultrasound, or CT
Bone Mineral Density	DXA - every 1–2 y (3 sites), x-ray or VFA of spine if clinically indicated (e.g.: height loss, back pain)

*According to : Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop. JCEM,2014,99

Hypoparathyroidism

Hypoparathyroidism is the state of decreased secretion or activity of parathyroid hormone (PTH). This leads to decreased blood levels of calcium (hypocalcemia) and increased levels of blood phosphorus (hyperphosphatemia).

Causes of deficient PTH secretion or activity in hypoparathyroid disease states

1. **Acquired** deficiency of parathyroid hormone secretion (> 99% of all cases):

- Surgical removal of the parathyroid glands (usually unintentionally)
- Radiation therapy to the neck, infiltration of parathyroids
- Hypomagnesemia
- Calcimimetics
- Autoimmune:
  - isolated hypoparathyroidism
  - APS 1 (autoimmune polyendocrine syndrome caused by mutations of the autoimmune regulator (AIRE) gene) → antibodies anty CaSR
- Neonatal hypocalcemia

2. **Congenital** lack of PTH secretion due to absent, hypoplastic or ectopic parathyroid glands (e.g. DiGeorge syndrome), (extremely rare)

3. **Resistance to parathyroid hormone** (pseudo-hypoparathyroidism), (extremely rare). Inability of the kidneys and bones to respond to the PTH being produced by normal parathyroids.

Diagnostics of hypoparathyroidism

1. Blood tests:

↓ calcium levels
↑ phosphorus levels
↓ PTH levels (but normal or elevated in pseudohypoparathyroidism)
↔ ALP
↔ magnesium
↔ creatinine
↓ $1,25(OH)_2D$

2. 24 urine low calcium excretion

3. Imaging tests if necessary:

- X-ray and CT may reveal calcifications in the basal ganglia of the brain and other soft tissue and the density of the bone structure
- Renal ultrasoud

4. Consultations with an ophthalmologist (cataract) and neurologist
5. ECG: prolonged QT interval

Hypoparathyroidismus - differential diagnostics (Hypocalcemia - etiologies by mechanism)

Hypoparathyroidism	Vitamin D deficiency	Low dietary intake of Ca^{+2}	Miscellaneous mechanisms
PTH ↓, N	PTH ↑		
Thyroidectomy or other neck surgery	Low calcitriol: • ↓ intake of dietary Vit. D • Inadequate sunlight exposure • Malabsorption syndrome		Osteoblastic bone metastases
I 131 therapy for G-B disease or thyroid cancer			Pancreatitis
Autoimmune hypoparathyroidism	↓ conversion of 25OHD to $1,25(OH)_2D$ • Renal failure • Hyperphosphatemia • Vitamin D dependent rickets, type 1		Hungry bones syndrome
Infiltration of parathyroids			Hyperphosphatemia
Hypomagnesemia	Calcitriol resistance • Vitamin D resistant rickets		Multiple transfusions
Congenital /genetic			Acute respiratory alkalosis
PTH resistance (pseudo hypoparathyroidism) PTH ↑)	↑ inactivation of vit. D (e.g. carbamazepine, phenytoin)		

The symptoms of hypoparathyroidism result from:

1. Hypocalcemia:
   tetany, paresthesias, neurological disorders, epileptic seizures

2. Deposits of calcium phosphate in soft tissues
   due to an excess of phosphate (basal ganglia, joint capsules, subcutaneous tissue, vitreous humor of the eye, muscles, bones).

Hypoparathyroidism – symptoms (1)

The major clinical manifestations of hypoparathyroidism are referable to hypocalcemia and are related to the severity and chronicity of the hypocalcemia.

Subjects who develop severe hypoparathyroidism quickly (for example, after neck surgery) can feel tired, irritable, anxious or depressed and demonstrate spontaneous or latent tetany.

Tetany

Tetany is a syndrome of increased neuromuscular excitability usually associated with hypocalcemia.

Three subtypes of tetany can appear in isolation, but all three can occur simultaneously in the same subject. These are:

- **Tetanic attack**
  - Sensory symptoms: paresthesias of the lips, tongue, fingers and feet
  - Carpopedal spasm
  - Spasm of facial musculature
  - Generalised muscle aching and spasm
- **Latent tetany** which requires stimuli to elicid (Chvostek's and Trousseau's signs are easily performed to elicid latent tetany).
- **Tetanic equivalents**

  The involved of autonomic nervous system may be present as: diplopia, blepharospasmus, laryngospasms, spasm of the bronchi, cardia and sphincter of the bladder. In similar manner blood vessels may be affected causing migraine, angina pectoris, abdominal angina or Raynaud syndrome.

Hypoparathyroidism – symptoms (2)

Patients with gradually developing hypoparathyroidism and long standing hypocalcemia associated with hyperphosphatemia may also exhibit:

- Calcification of the basal ganglia (Fahr's syndrome) with symptoms such as deterioration of motor functions and speech, seizures, headaches, dementia, and vision impairment.
- Ocular cataracts (mineral deposits in the lens)
- Dry and thick skin, coarse breaking hair, brittle nails
- Defects of the tooth enamel

The occurrence of hypoparathyroidism in early childhood may be the cause of short stature and mental retardation as well as dental abnormalities (hypoplasia, failure of eruption, defective enamel and root).

The aims of treatment in hypoparathyroidism

- Keep the serum calcium in the lower normal range, so that the patient feels well and does not exhibit tetany (1.8-2.25 mmol/l while normal calcium range is around 2.1-2.5 mmol/l)
- Reduce serum phosphate levels at least to the upper limits of normal (prevention of calcifications in the soft tissues)
- Calciuria should not be higher than normal (prevention of kidney stones)

The methods of treatment of hypoparathyroidism:

- A high-calcium and low-phosphorous diet
- Calcium carbonate 1-4 g/d orally, during and between meals
- Activated vitamin D analogues e.g. alfacalcidolum 1-3 µg/d
- Vitamin D supplementation 400–800 IU/d to patients treated with activated vitamin D analogues
- In a patient with hypercalciuria, consider a reduction in calcium intake, a sodium-restricted diet, and/or treatment with a thiazide diuretic
- Magnesium supplementation in case of deficiency
- Recombinant human parathyroid hormone (rhPTH, Natpara) is commercially available in the United States and is indicated as an adjunct to calcium and vitamin D (caution! may cause osteosercoma)
- Implants of stem cells (trials are in progress)

Tetany attack should be treated with iv infusion of calcium salts.
Calcium gluconate may be given as 10 ml of 10% solution over 10 min, and if necessary next infusion with 20-30 ml of 10% calcium gluconate in 5% glucose.