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Geriatric Endocrinology
CALCIUM-PHOSPHATE

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Learning Objectives

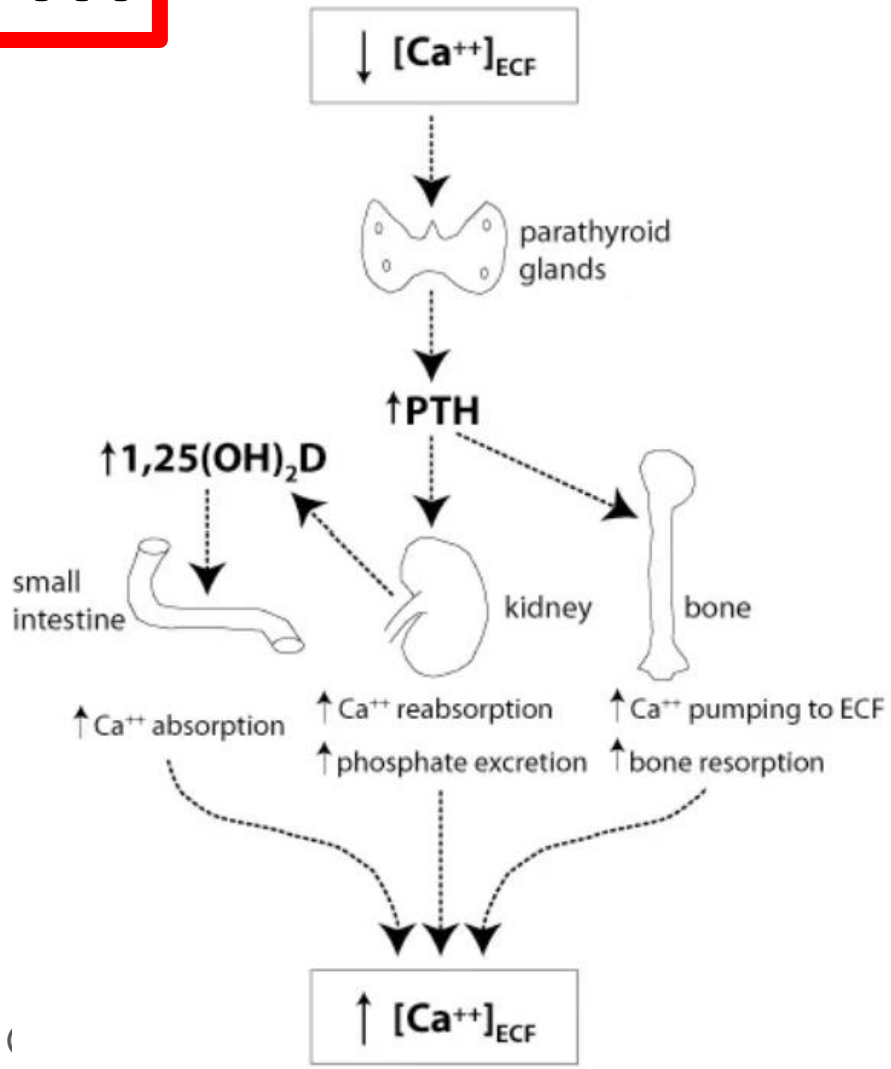
- Hypercalcemia (causes, diagnosis and treatment)
- Primary *hyper*parathyroidism (PHPT) incl. complications and challenges

- *Hypo*parathyroidism (causes and treatment)
- Hypocalcemia

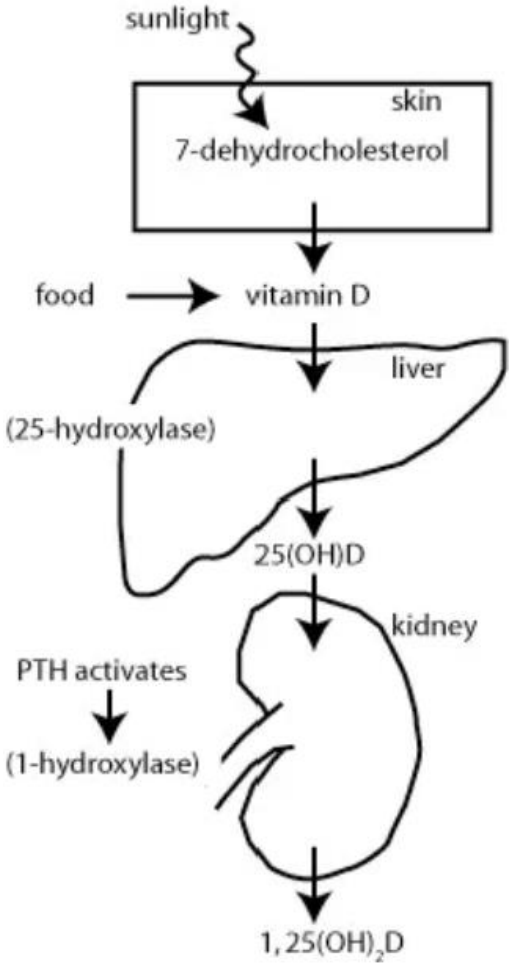
- Hypo-and hyperphosphatemia
- Tumor-induced osteomalacia

Pathophysiology

iPTH



Vitamin D



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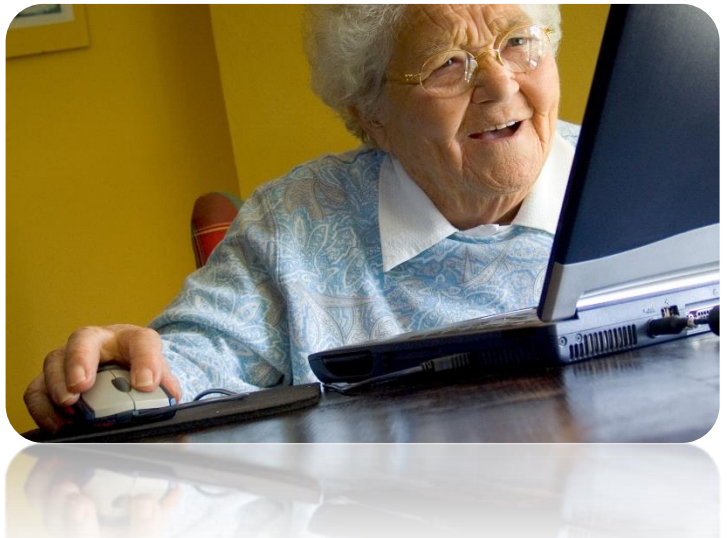
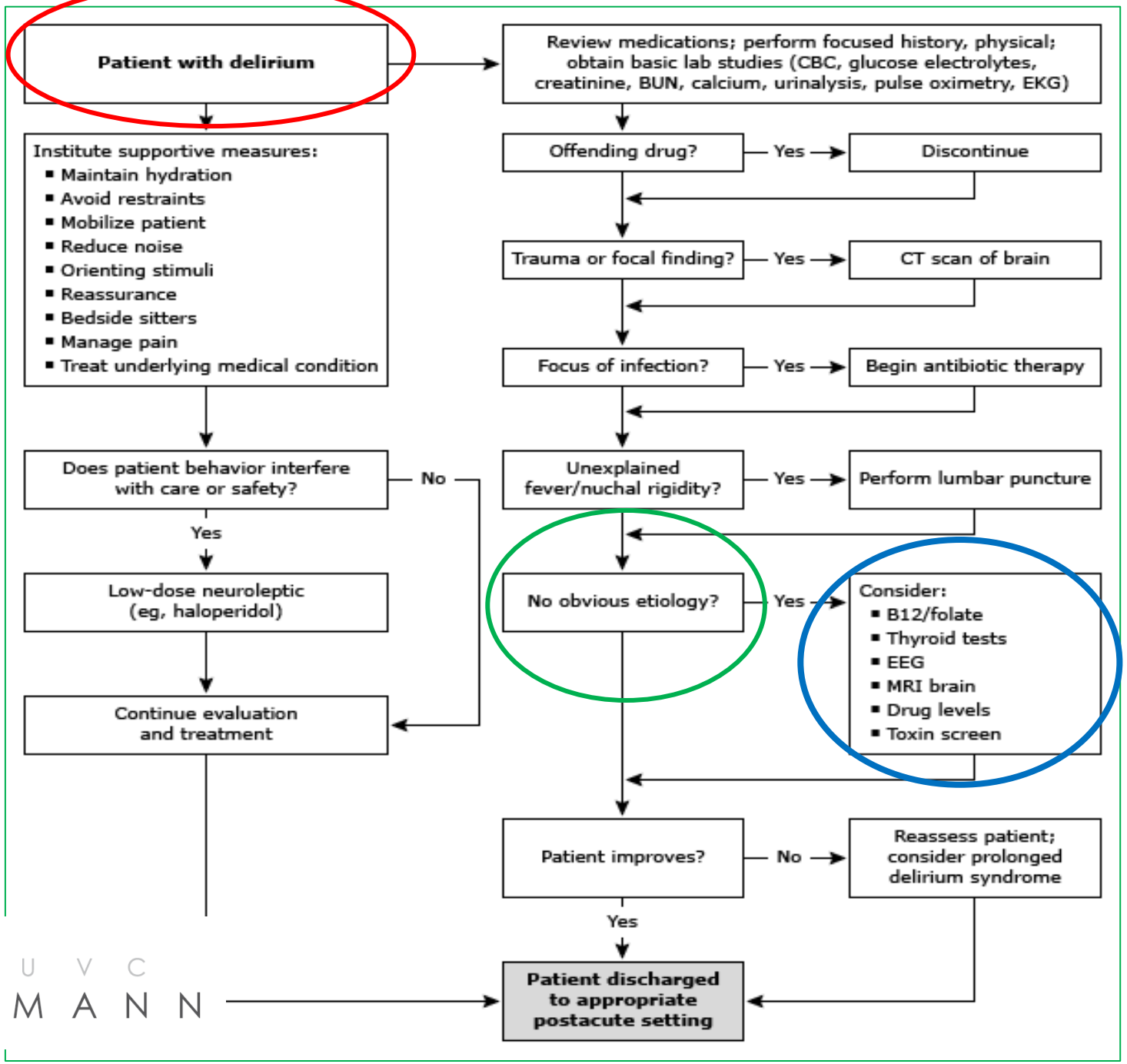
Case

- 84-yo patient ♀
- H in Geriatric dpt for asthenia, fatigue, difficulty walking, falls …
- “Cognitive decline” according to her daughter

- Previous HX:
  - Breast cancer (tumorectomy), CVA (frontal ischemic, 2013), AHT, hypercholesterolemia, osteoporosis
- Social :
  - Lives alone (3rd floor with elevator)
  - 2 children whom she visits very often





Case – lab results

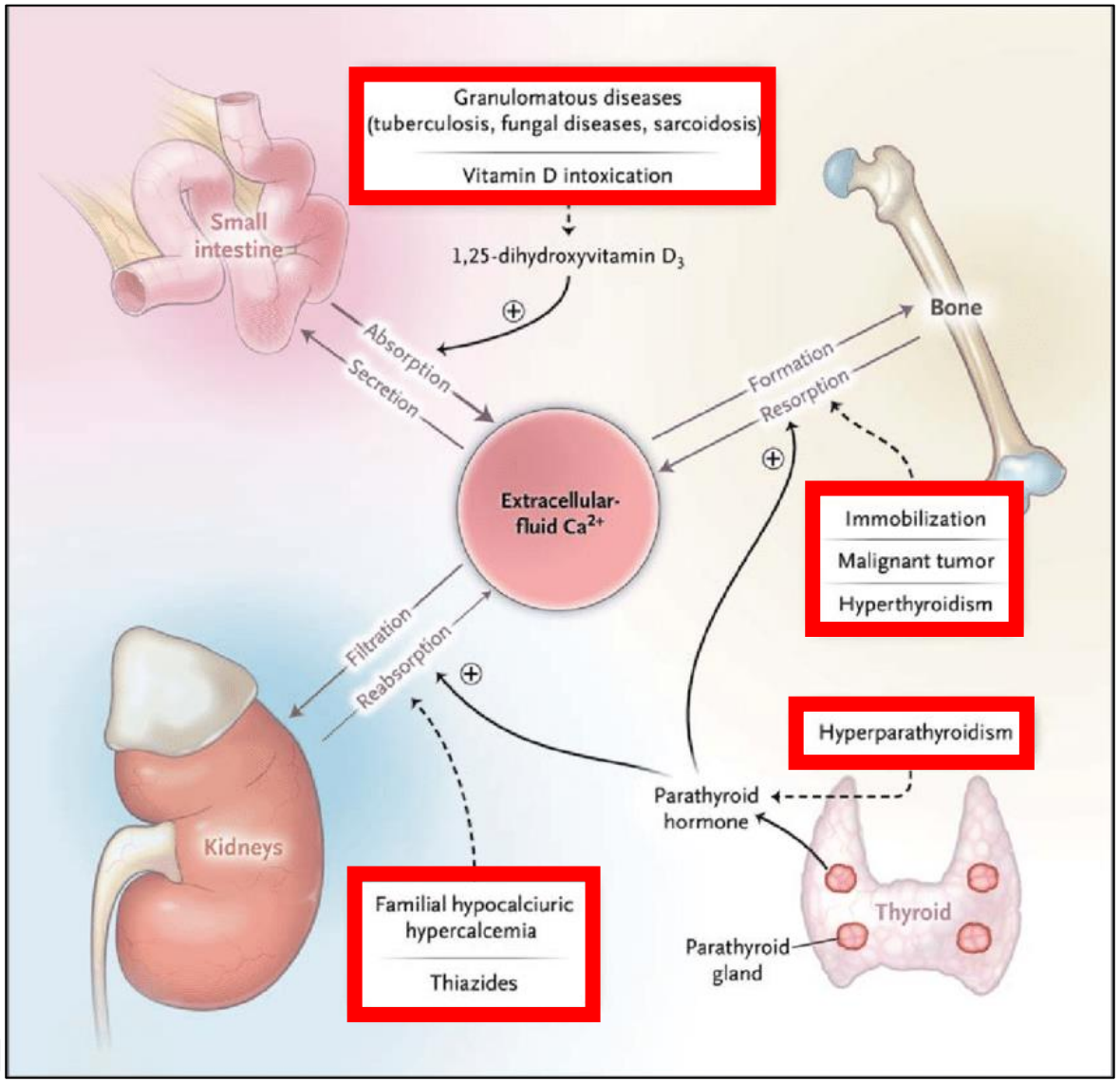
• Calcium 3,75 mmol/L ↗	N 2,20-2,55
• Phosphate 0,72 mmol/L ↘	N 0,75-1,39
• Mg^{2+} 0,60 mmol/L	N 0,63-1,05
• Albumin 36 g/L	N 40-49

→ Calcemia of 3,8 mmol/L corrected for albumin

What to do next ?

- **A** 25-OH Vitamin D
- **B** iPTH
- **C** 1,25-dihydroxy Vitamin D
- **D** Thyroid ultrasound
- **E** Bone scan
- **F** Combination of the above

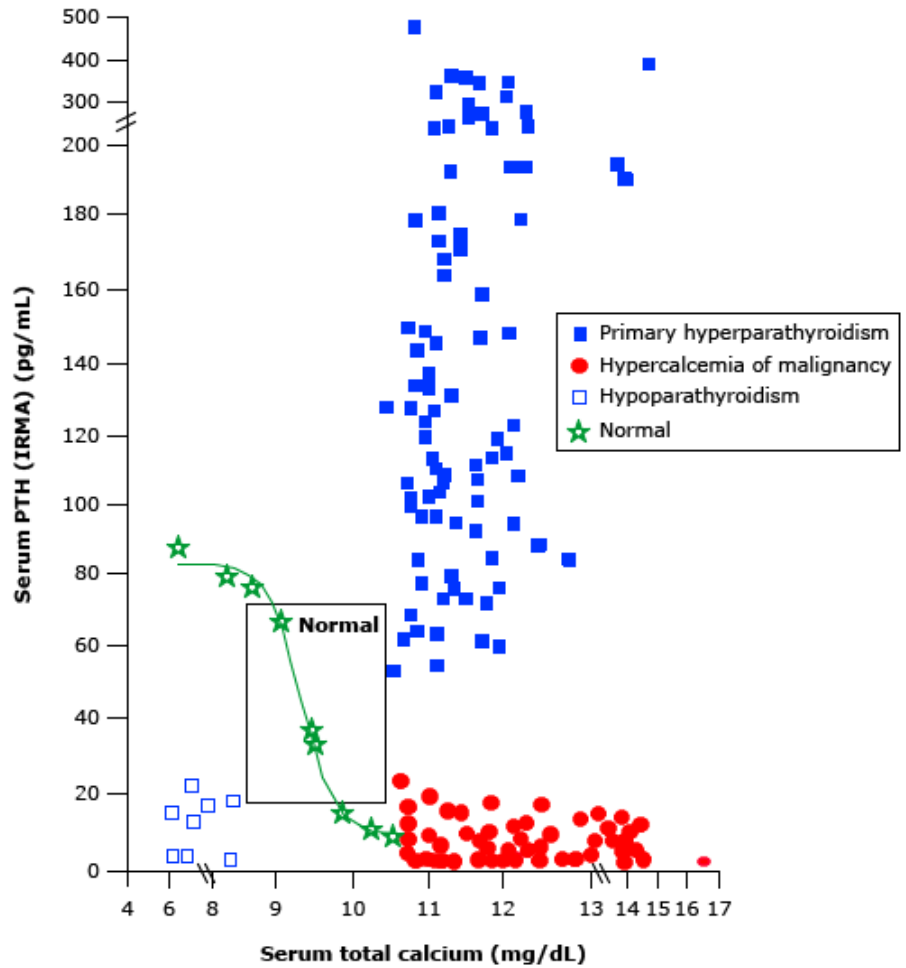
Causes of hypercalcemia

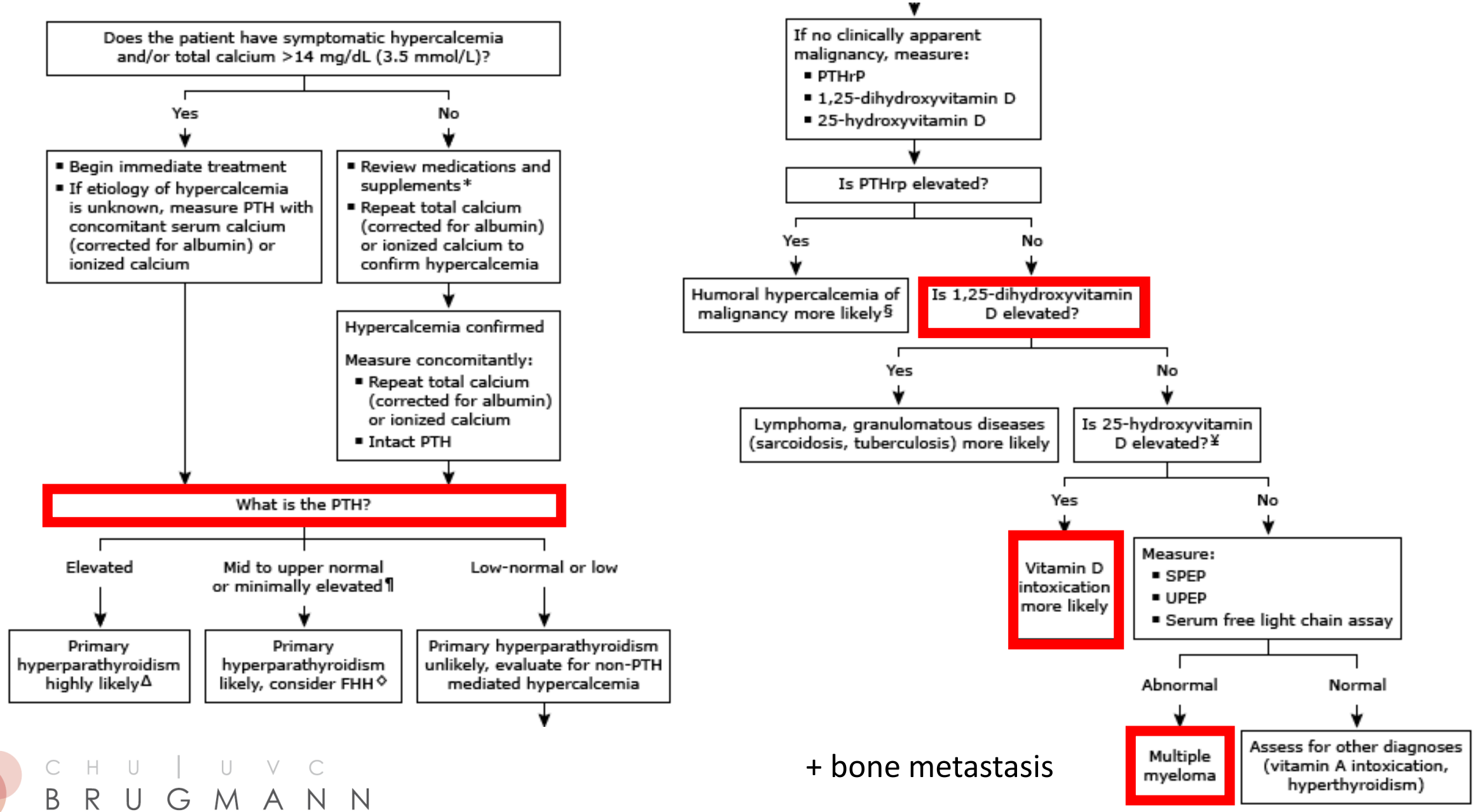


Causes of hypercalcemia

80-90% either PHPT or malignancy

Serum parathyroid hormone (PTH) concentrations in hypercalcemia and hypocalcemia





+ bone metastasis

Case

• Calcium 3,75 mmol/L ↗	N 2,20-2,55
• Phosphate 0,72 mmol/L ↘	N 0,75-1,39
• Mg^{2+} 0,60 mmol/L	N 0,63-1,05
• Albumin 36 g/L	N 40-49
• PTH 133 ng/L ↗	N < 49
• 25-OH Vitamine D 39,6 mcg/L	N 30-80

→ PTH-related hypercalcemia

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The voice for endocrinology

PARAT: An ESE Educational programme on Parathyroid Disorders

Managing Parathyroid Disorders: Primary Hyperparathyroidism

European Society of Endocrinology

This guide summarizes the 13 primary hyperparathyroidism (PHPT) consensus recommendations published within "European Expert Consensus on Practical Management of Specific Aspects of Parathyroid Disorders in Adults and in Pregnancy". *European Journal of Endocrinology* 186 (2) February 2022'. Please access the article for full disclosure.

Q1 How do we differentially diagnose familial hypercalcemic hypocalciuria (FHH)?

Calcium creatinine clearance ratio (CCCR) <0.01 is a screening tool for FHH, but the 'cut-off' is of limited clinical value due to low diagnostic sensitivity and specificity.

A positive family history is a key feature of FHH. Historic calcium values are important to exclude progressive hypercalcemia as in primary hyperparathyroidism (PHPT). PTH levels >2-fold above upper limit of normal are suggestive of PHPT.

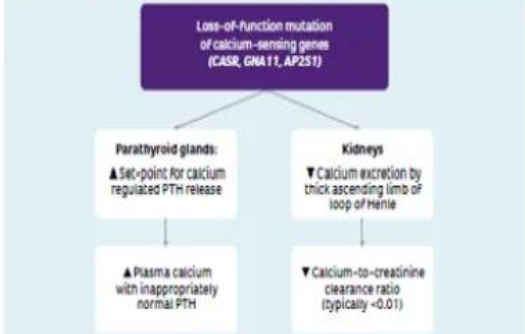


Figure 1. Alterations in calcium metabolism caused by FHH

Genetic testing is recommended for all patients with suspected FHH, but negative genetic testing does not exclude FHH, and ongoing follow-up of mutation negative patients is recommended.

Q2 What is normocalcemic primary hyperparathyroidism (PHPT)?

Normocalcemic PHPT is characterised by persistently (>3 months) increased PTH levels in the setting of consistently normal total, albumin-adjusted and / or free ionized serum calcium. Normocalcemic PHPT is a diagnosis of exclusion.

Q3 What are the causes of hyperparathyroidism with normal calcium that should be excluded before considering a diagnosis of normocalcemic PHPT?

Secondary causes of hyperparathyroidism include medications, hypercalciuria, hypovitaminosis D, renal insufficiency, malabsorption syndromes, phosphate metabolism disorders or low dietary calcium

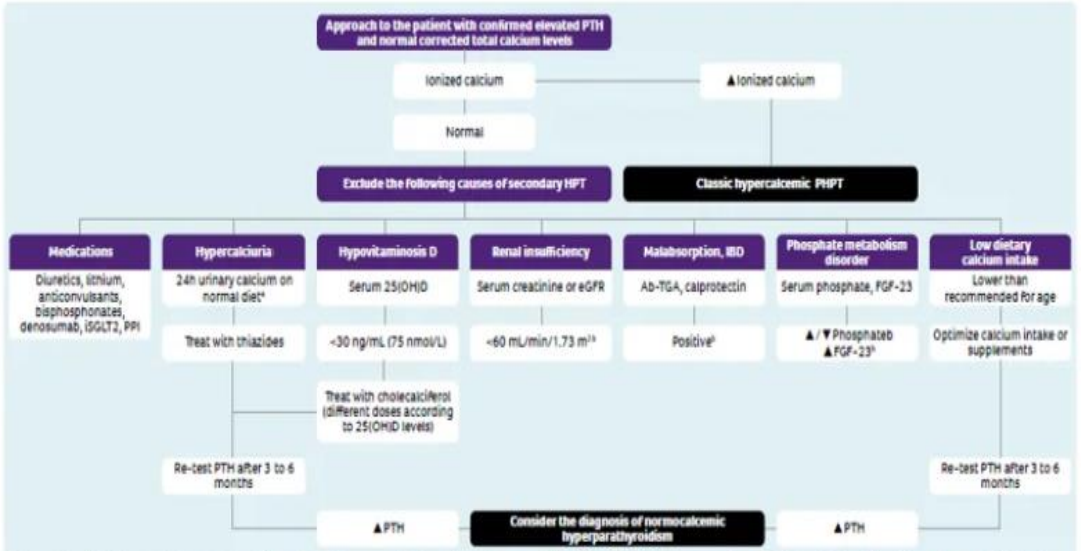


Figure 2. A clinical approach to patients with confirmed normocalcemic primary hyperparathyroidism. *Reference range >4 mg/kg/ day, >250 mg/day in females, and >300 mg/ day in males. ‡Evaluate for these disorders and manage as appropriate. 25(OH) D, serum 25-hydroxyvitamin D; Ab-TGA, anti-tissue transglutaminase antibodies; eGFR, estimated glomerular filtration rate; FGF-23, fibroblast growth factor-23; HPT, hyperparathyroidism; IBD, inflammatory bowel disease; iSGLT2, sodium-glucose cotransporter-2 inhibitors; PHPT, primary hyperparathyroidism; PPI, proton pump inhibitors; PTH, parathyroid hormone.

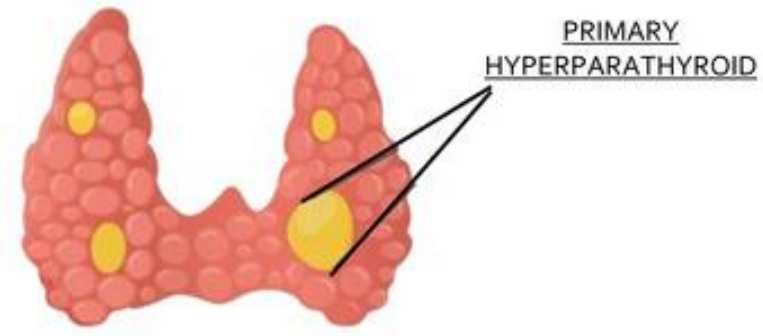
Cause of secondary hyperparathyroidism	Proposed intervention thresholds	Comments
Vitamin D deficiency	Aim for 25(OH)D concentrations of 30 ng/mL (75 nmol/L) to avoid secondary hyperparathyroidism	Re-test PTH when vitamin D replete. PTH concentrations may remain elevated for 6–12 months and optimization of calcium intake is mandatory
Low-dietary calcium intake	1200 mg/day for postmenopausal women 1000 mg/day for men 51–70 years and 1200 mg/day for older men	Evaluate calcium intake using a dietary questionnaire. Patients should increase calcium intake or use calcium supplements
Hypercalciuria due to renal abnormalities	Urinary calcium excretion >250 mg/24 h (6.25 mmol/24 h) in females, >300 mg/24 h (7.5 mmol/24 h) in males, or >4 mg/kg/24 h (0.1 mmol/kg/24 h)	'Thiazide challenge' test (administer hydrochlorothiazide 25 mg twice a day for 2 weeks; check PTH levels prior to starting thiazide and after 2 weeks of therapy). PTH normalization supports renal secondary causes of PHPT
Renal insufficiency	eGFR <60 mL/min/1.73 m²	As kidney function declines, 1α-hydroxylation activity decreases and, consequently, active vitamin D levels fall, calcium levels decline, and PTH levels increase
Gastrointestinal disorders associated with calcium malabsorption	Celiac disease, inflammatory bowel disease, and bariatric surgery	Measure anti-tissue transglutaminase antibodies and fecal calprotectin to consider celiac disease and inflammatory bowel disease, respectively
Medications	1200 mg/day for postmenopausal women 1000 mg/day for men 51–70 years and 1200 mg/day for older men	Non-thiazide diuretics can increase PTH levels (if possible, discontinue and reevaluate PTH). Lithium therapy can raise PTH levels (decision to withdraw from therapy is difficult and should be made by a psychiatrist). Treatment with bisphosphonates or denosumab can raise PTH levels as a result of positive calcium signaling to the parathyroid glands in the context of inhibited bone resorption. Bisphosphonate effects may last for a long time after discontinuation. Denosumab discontinuation should be avoided to prevent excessive bone loss. Recent studies showed that SGLT2 inhibitors have complex interactions with bone metabolism, including an increase in PTH
Phosphate metabolism disorders	Hyperphosphatemia and FGF-23–mediated hypophosphatemia are both associated with secondary hyperparathyroidism	Extracellular phosphate regulation involves changes in PTH levels. Both high and low phosphate levels may be associated with secondary hyperparathyroidism

25(OH)D, 25-hydroxyvitamin D; eGFR, estimated glomerular filtration rate; FGF-23, fibroblast growth factor 23; PTH, parathyroid hormone; SGLT2 inhibitors, sodium-glucose cotransporter-2 inhibitors.

Primary hyperparathyroidism

- Third most common endocrine disorder
- Incompletely regulated, chronic, excessive secretion of parathyroid hormone (PTH)
- Hypercalcemia with elevated PTH

- Causes :
  - Single benign adenoma (85%)
  - Multiglandular disease (15%)
  - Parathyroid carcinoma (1%)



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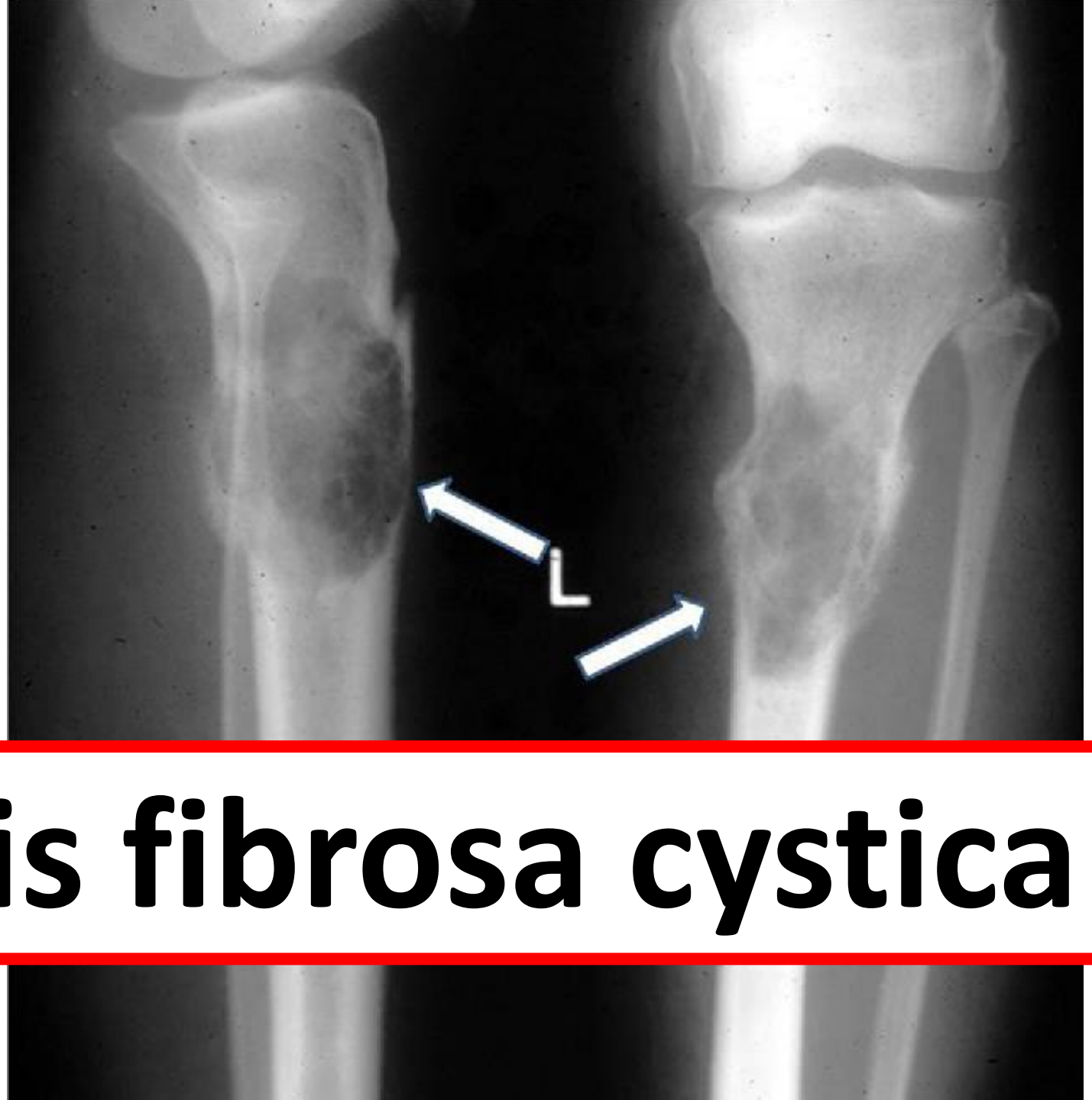
Primary hyperparathyroidism

- Historically,

disease of bones, stones, and groans…

= skeletal disorder resulting in a loss of bone mass, a weakening of the bones as their calcified supporting structures are replaced with fibrous tissue (peritrabecular fibrosis), and the formation of cyst-like tumors in and around the bone

= **osteitis fibrosa**, **osteodystrophia fibrosa**, and **von Recklinghausen's disease of bone**



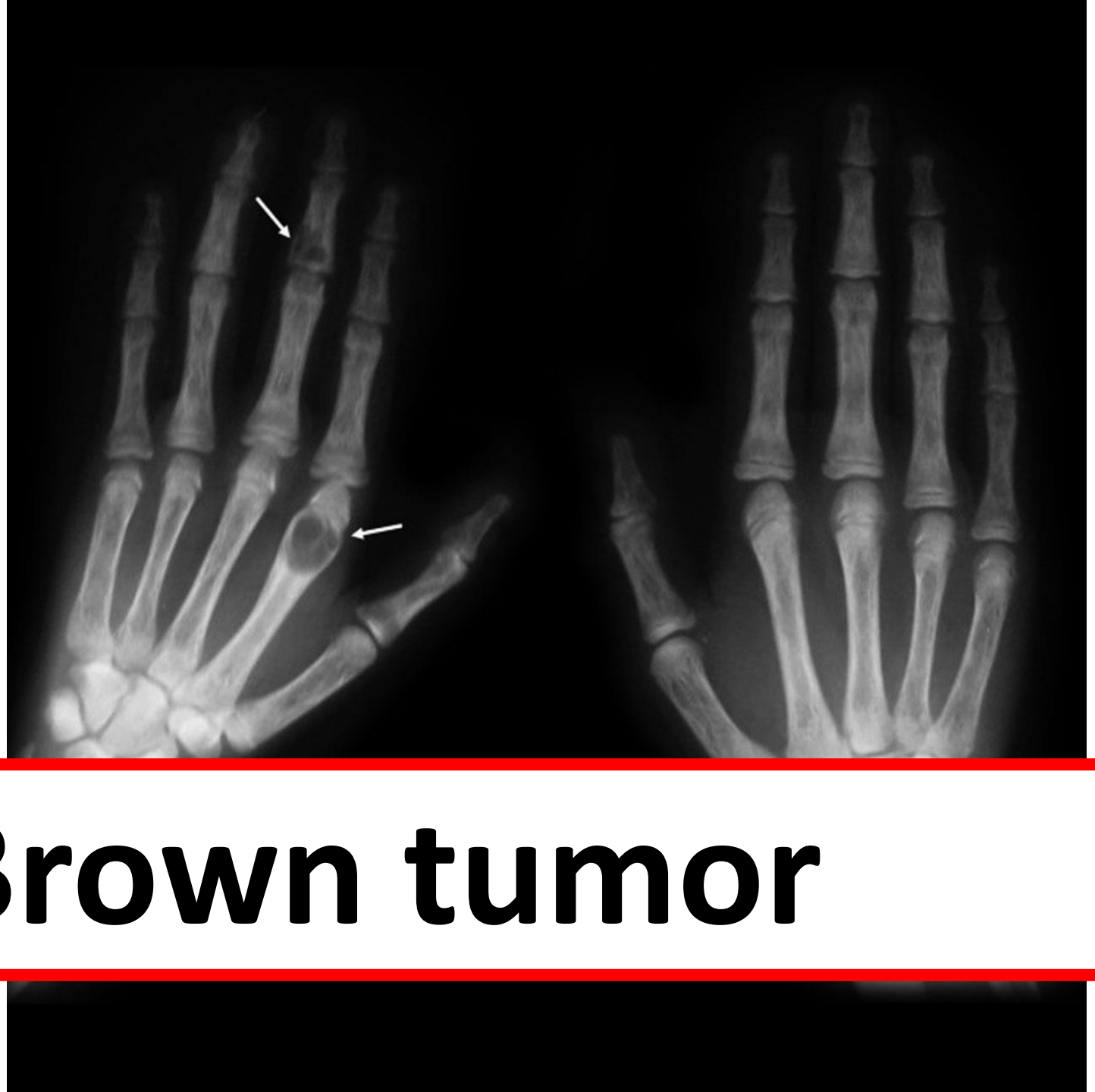
Osteitis fibrosa cystica

- Excess osteoclast activity, such as PHPT

- A form of osteitis fibrosa cystica
- Not a neoplasm, but rather simply a mass.

- Most commonly affects the maxilla and mandible, though any bone may be affected

- Radiolucent on x-ray



Brown tumor

Symptomatic PHPT

Asymptomatic PHPT

Normocalcemic PHPT
(routine screening)

The disease did not change, we did !

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Primary hyperparathyroidism

- 3x > in ♀; incidence **increases with age**
- 80% initially lack symptoms
  - nephrolithiasis
  - kidney dysfunction
  - gastrointestinal upset
  - neuropsychiatric effects
- PHPT accelerates bone turnover → fragility fractures

Habib 2021, JAMA

Treatment of (severe) hypercalcemia

- IV hydration
- IV hydration
- IV hydration

Treatment of (severe) hypercalcemia

- IV hydration
- + Diuretics (avoid fluid overload)
- Calcitonin (early use, tachyphylaxis)
- Antiresorptives (Pam, IV Zol, Dmab)
- Corticosteroids (*1a-hydroxylase*)
- Dialysis in extreme hyperCa^{2+} or in CKD

Case

Recurrent hypercalcemia *1 month* after discharge

* Calcium 3,19 mmol/L N 2,20-2,55

→ Start Mimpara (Cinacalcet) 60mg daily

Two weeks later …

* Calcium 3,78 mmol/L N 2,20-2,55
* Albumin 45 g/L N 40-49
* PTH 209 ng/L N < 49

Case

Treatment regimen:

- IV hydration
- Calcitonin
- Cinacalcet (Mimpara) 60 mg daily
- Bisphosphonate

However, **no clinical nor biological response** …

Parathyroidectomy

- **Surgery** → most effective & only curative treatment for PHPT

Types:

- Unilateral parathyroid exploration (single parathyroid adenoma)
- Bilateral parathyroid exploration (multigland disease, intraoperative parathyroid hormone (IOPTH) monitoring unavailable)

Wilhelm, JAMA Surg. (2016)

Parathyroidectomy in elderly patients

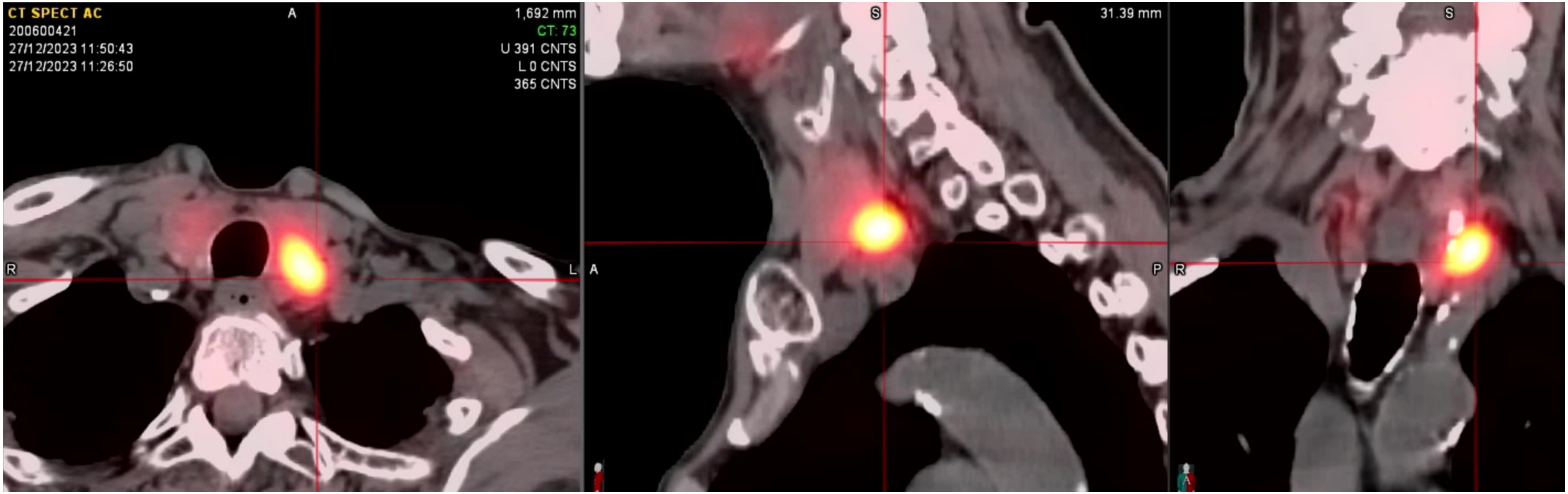
- **Safe, effective, feasible & beneficial**

<u>Complications in the elderly:</u>

- Conversion to bilateral exploration, multiglandular disease
- Some studies - respiratory infections, cardiac problems
- Other studies - similar complications to general population
- Longer length of stay

Calo, Aging Clin Exp Res (2017)

Scintigraphy MIBI-Tc99m



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Case

- Localization of an adenoma
- Lack of response to medical treatment
- Clinical deterioration of the patient

→ parathyroidectomy

<u>Post-op follow up</u>:

- Normalization of serum calcemia and iPTH
- Rapid clinical recovery

Q10-13 Parathyroidectomy (PTX)

Q12 What causes hypocalcemia after PTX?

- Postoperative hypocalcemia can be related to hypoparathyroidism (inappropriate low PTH in relation to calcium concentration), accompanied by a high phosphate concentration.

Q10-13 Parathyroidectomy (PTX)

Hungry Bone Syndrome (HBS)

- HBS: Massive transfer of calcium to bone – is characterized by normal or high PTH, low phosphate, and magnesium.

= sudden withdrawal of PTH

- **increased osteoblast-mediated bone formation**
- **bone uptake of calcium, phosphate and magnesium**

Table 2 Potential risk factors for hungry bone syndrome.

Potential risk factors for hungry bone syndrome	Explanation
High preoperative PTH level	Sudden removal of the effect of high circulating levels of PTH on osteoclastic resorption leads to increased influx of calcium into bone (new remodeling sites) (94)
Large volume (weight and mass) of parathyroid adenoma	Positive correlation between PTH levels and volume of adenoma (93, 95)
High preoperative calcium levels	Explained as increased calcium resorption from bone and calcium reabsorption from renal tubules in case of preoperatively elevated PTH levels (95)
Radiological evidence of PHPT-related bone disease	Brown tumors, multiple fractures, osteitis fibrosa cystica as an effect of long-lasting high circulating levels of PTH on the skeleton (91, 94)
Significantly elevated alkaline phosphatase	Reflects osteoblast activity and bone formation, thus overall the state of bone turnover (91, 94)
Preoperatively low 25(OH)D concentrations	HBS develops indirectly by skeletal demineralization due to low circulating levels of $1,25(OH)_2D$ with postoperative increased skeletal calcium requirements (95)

$1,25(OH)_2D$, 1,25-dihydroxyvitamin D; 25(OH)D, 25-hydroxyvitamin D; HBS, hungry bone syndrome; PHPT, primary hyperparathyroidism; PTH, parathyroid hormone.

Challenges in PHPT

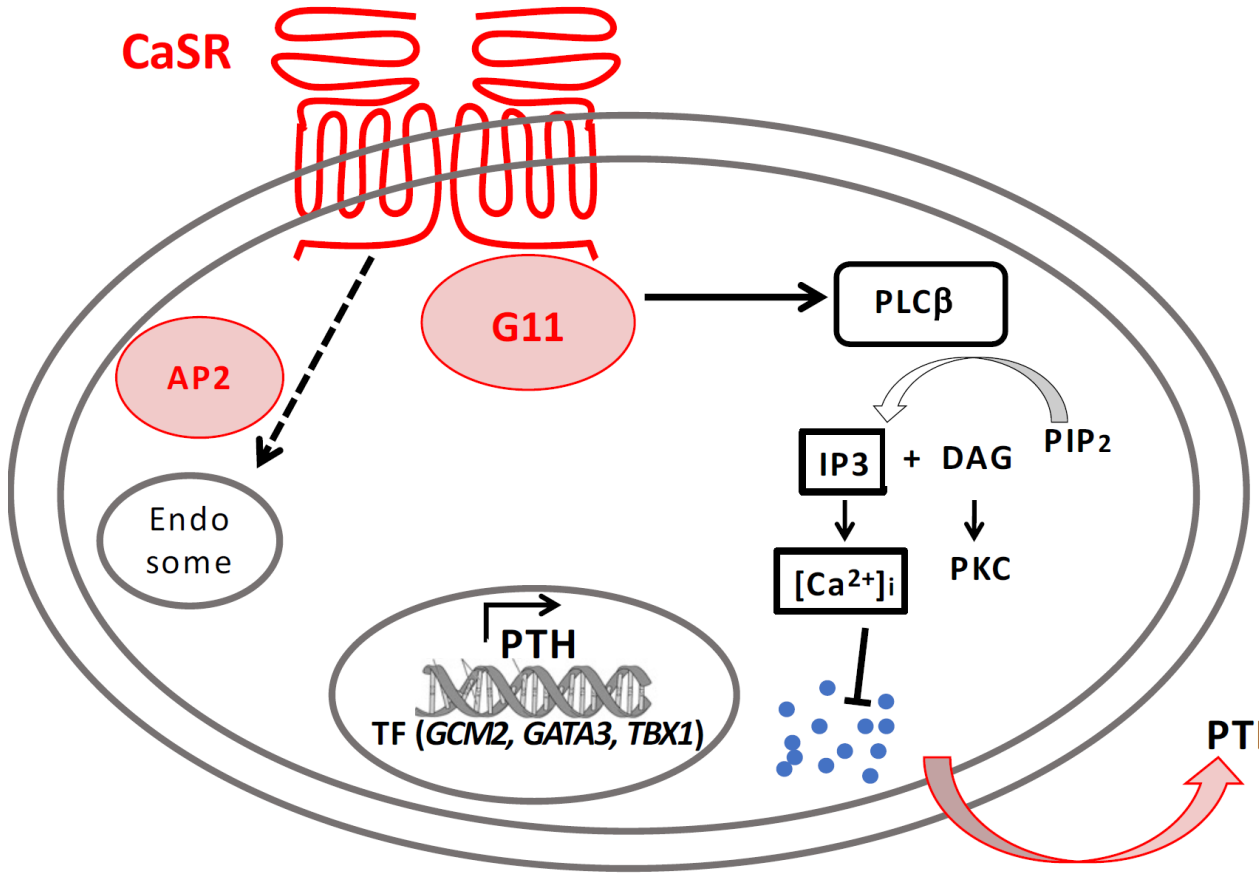
- DDx with familial hypocalciuric hypercalcemia (FHH)
- Normocalcemic PHPT – DDx secondary HPT
- Optimal management of recurrence/persistence after surgery
- Syndromes (MEN-1, MEN-2, ...)

DDx Familial hypocalciuric hypercalcemia (FHH)

= autosomal dominant disorder of CaSR

- Positive family history
- Non-progressive elevation of calcium
- Normal or mildly raised PTH
- Low urinary calcium excretion <0,01
- **Does not require surgical intervention**

FHH mechanism



FHH1: CASR LoF
FHH2: GNA11 LoF
FHH3: AP2S1 LoF

Parathyroid cell

LoF; loss of function

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Dr. Michael Mannstadt, 2024

Q2-3-4 Normocalcemic PHPT

Q2 What is normocalcemic PHPT?

- Normocalcemic PHPT is a biochemical signature of persistently (>3 months) increased PTH levels in the setting of consistently normal calcium concentrations.
- Normocalcemic PHPT represents a diagnosis of exclusion and can only be considered following a careful evaluation of causes of secondary

Is it secondary hyperparathyroidism ?

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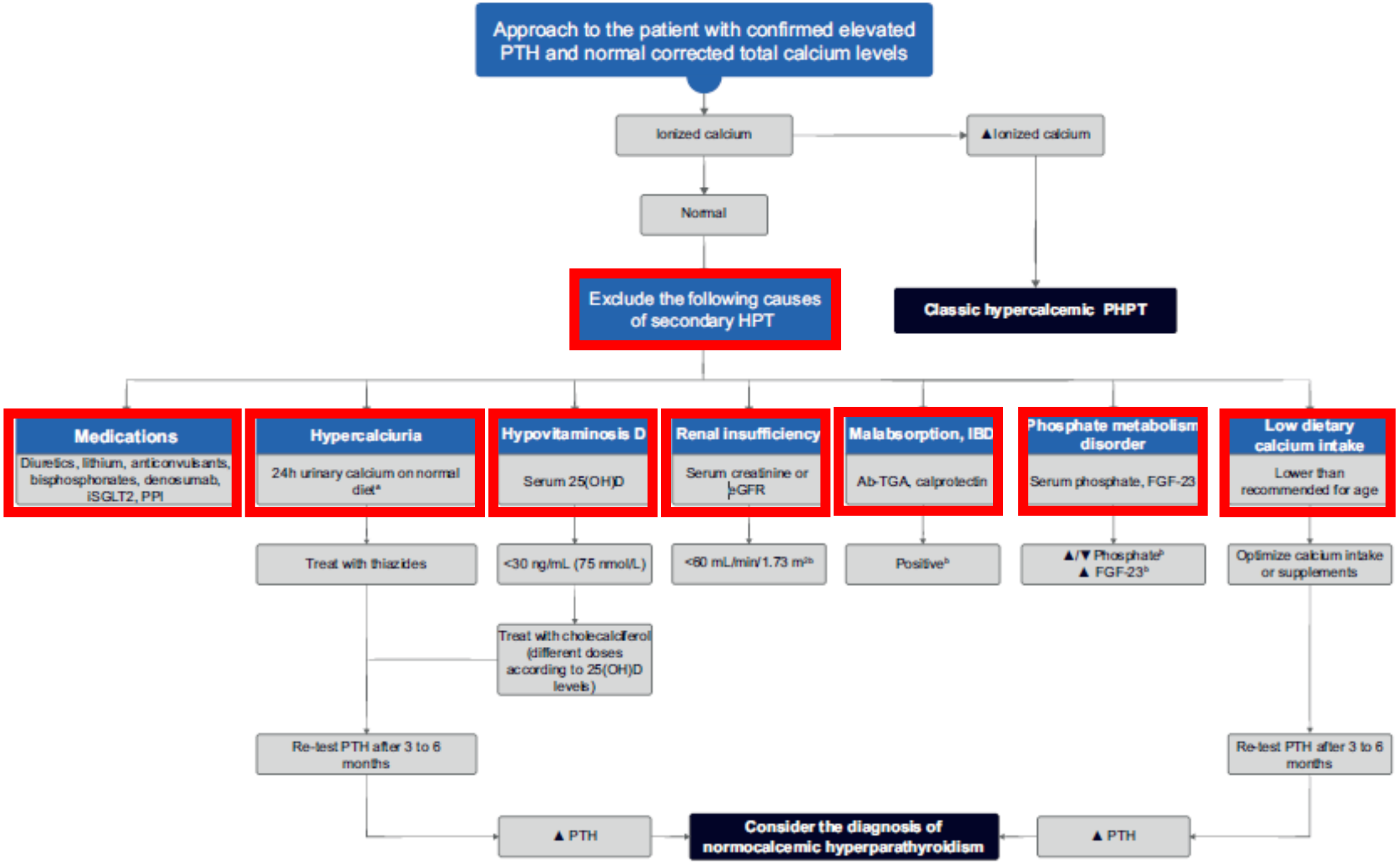
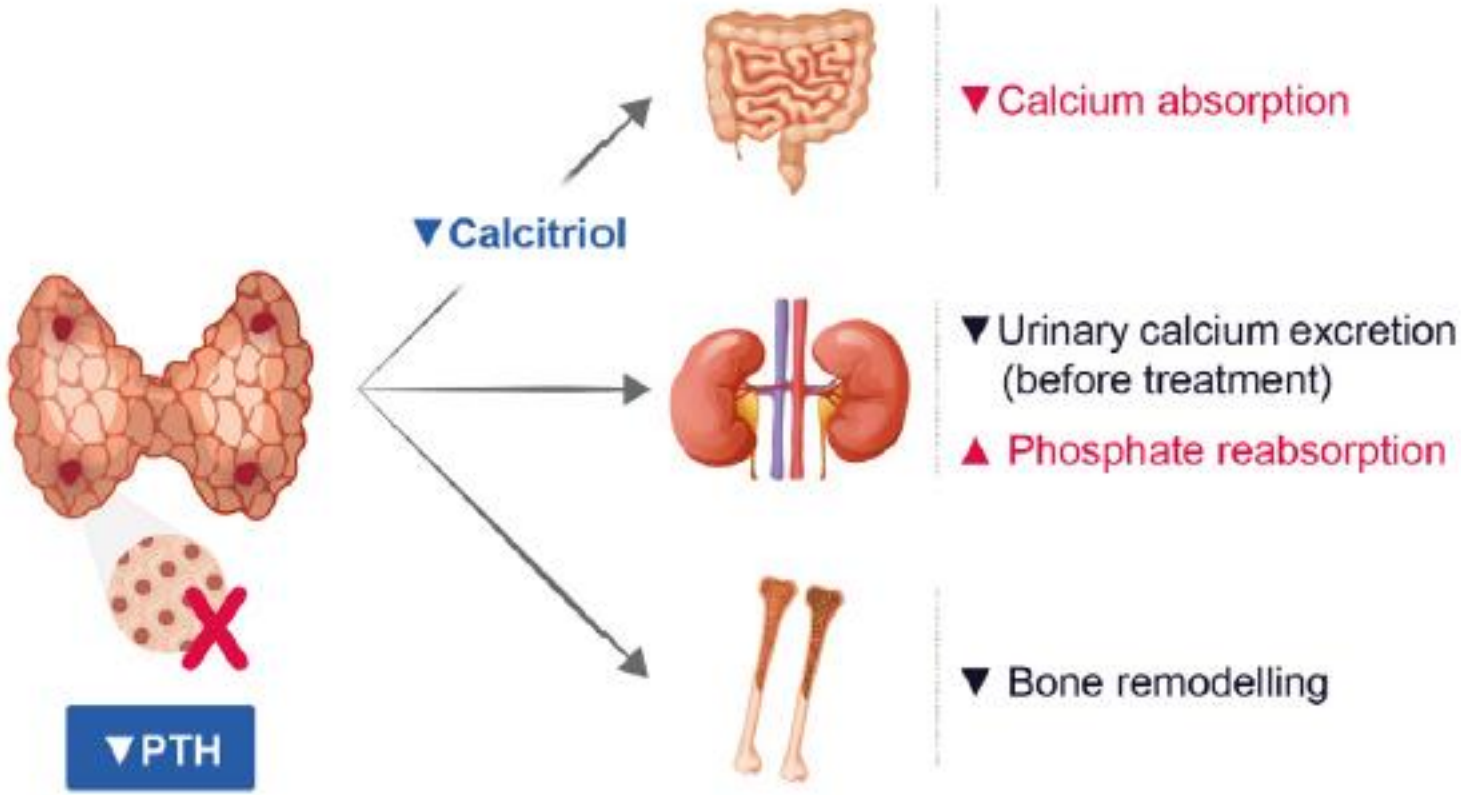

Approach to the patient with confirmed elevated PTH and normal corrected total calcium levels
Ionized calcium
▲Ionized calcium
Normal
Exclude the following causes of secondary HPT
Classic hypercalcemic PHPT
Medications
Diuretics, lithium, anticonvulsants, bisphosphonates, denosumab, iSGLT2, PPI
Hypercalciuria
24h urinary calcium on normal diet[a]
Hypovitaminosis D
Serum 25(OH)D
Renal insufficiency
Serum creatinine or eGFR
Malabsorption, IBD
Ab-TGA, calprotectin
Phosphate metabolism disorder
Serum phosphate, FGF-23
Low dietary calcium intake
Lower than recommended for age
Treat with thiazides
<30 ng/mL (75 nmol/L)
<60 mL/min/1.73 m²[b]
Positive[b]
▲/▼ Phosphate[b] ▲ FGF-23[b]
Optimize calcium intake or supplements
Treat with cholecalciferol (different doses according to 25(OH)D levels)
Re-test PTH after 3 to 6 months
Re-test PTH after 3 to 6 months
▲ PTH
Consider the diagnosis of normocalcemic hyperparathyroidism
▲ PTH

*Hypo*parathyroidism

- Orphan disease
- Hypocalcemia (symptomatic or asymptomatic) with insufficient PTH secretion

- Causes :
  - Neck surgery (75%) : chronic if > 6 months after surgery
  - Genetic, auto-immune, infiltrative, Mg^{2+}


▼Calcium absorption
▼Calcitriol
▼Urinary calcium excretion
(before treatment)
▲ Phosphate reabsorption
▼ Bone remodelling
▼PTH

Treatment of chronic HypoPT

- 0,5-2 mcg/day of **alfacalcidiol** once a day

  OR

  0,5-1 mcg/day of **calcitriol** (Rocaltrol®) twice a day

- **Calcium supplements** if dietary intake is insufficient
- **25(OH)D >20ng/ml**

Treatment of chronic HypoPT

Calcium levels:

Lower part or slightly below the **lower limit** of the reference range, without symptoms of hypocalcemia

Treatment of chronic HypoPT

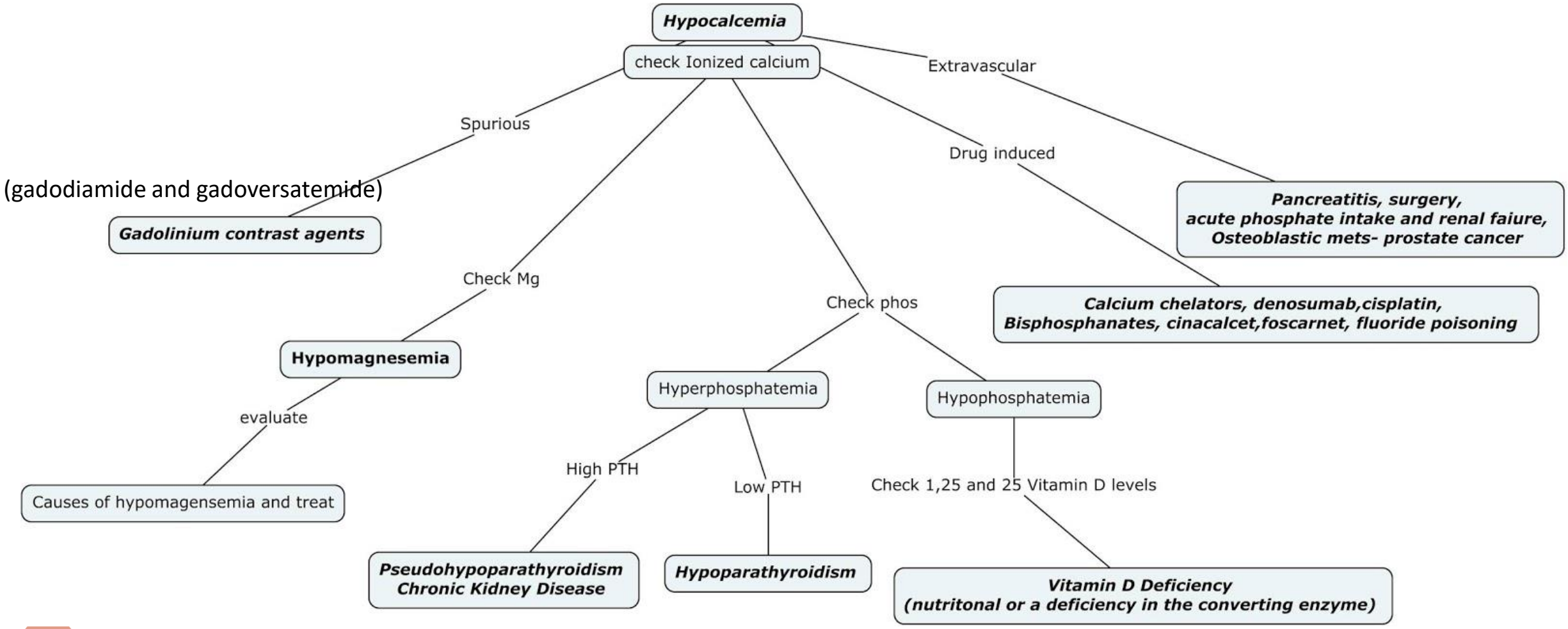
- Problems:
  - Hypercalcemia
  - Hypercalciuria

Table 5 Imaging in hypoparathyroidism.

Organ	Looking for	Interval	Comments
Kidney	Nephrolithiasis, nephrocalcinosis	At diagnosis; As clinically indicated; Every 5 years	Ultrasound + no radiation - highly operator-dependent Non-contrast renal CT + accurate - accumulation of radiation exposure *Sensitivity of CT vs ultrasound in nephrocalcinosis detection uncertain*
Brain	Intracerebral calcifications	As clinically indicated	Non-contrast CT MRI (only special MRIs usable for this assessment). *Sensitivity of even specialized MRI for detection of calcifications uncertain*
Bone	Changes in bone density/quality, vertebral fx	As clinically indicated	DXA + cheap + low radiation + Vertebral fracture assessment (VFA) X-ray spine and VFA + detection of unknown vertebral fracture
Eyes	Cataract	At diagnosis; As clinically indicated	Ophthalmologist check in non-surgical patients

CT, computed tomography; DXA, dual-energy X-ray absorptiometry; HypoPT, chronic hypoparathyroidism; MRI, magnetic resonance imaging; Fx, fractures.

Hypocalcemia



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B R U G M A N N

Dr. Gerald Diaz, 2024

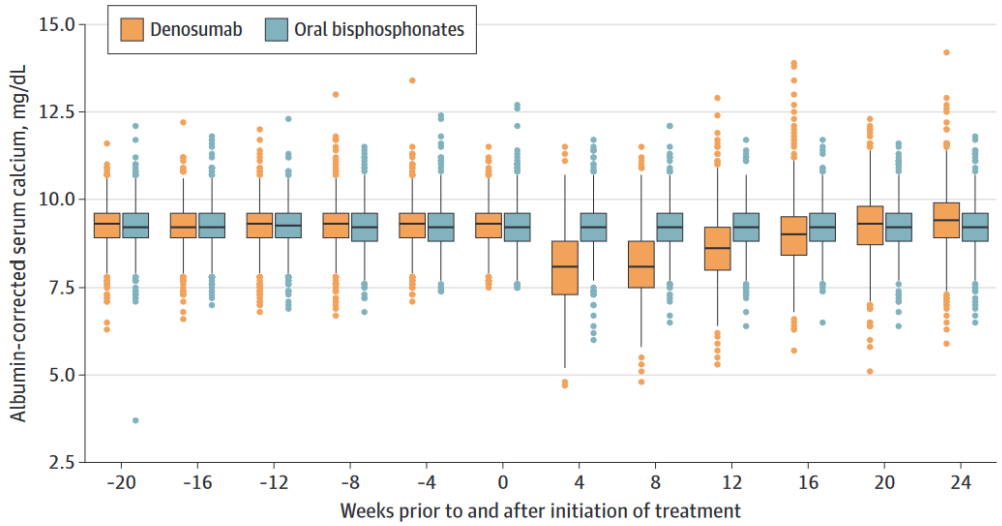
Denosumab and hemodialysis

JAMA | Original Investigation

Severe Hypocalcemia With Denosumab Among Older Female Dialysis-Dependent Patients

Steven T. Bird, PhD, PharmD; Elizabeth R. Smith, BS; Kate Gelperin, MD, MPH; Tae Hyun Jung, PhD; Aliza Thompson, MD; Rekha Kambhampati, MD; Hai Lyu, MS; Henu Zhao, PhD; Yueqin Zhao, PhD; Yunfan Zhu, MA; Olivia Easley, MD; Ali Niak, MD; Michael Wernecke, BA; Yoganand Chillarige, MPA; Marina Zemskova, MD; Jeffrey A. Kelman, MD; David J. Graham, MD, MPH

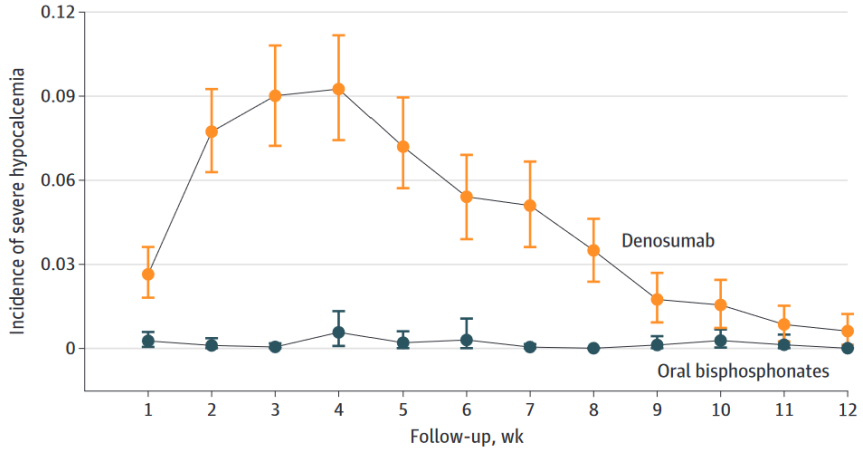
Figure 1. Total Albumin-Corrected Serum Calcium Levels 6 Months Before and After Initiation of Denosumab or Oral Bisphosphonate Treatment



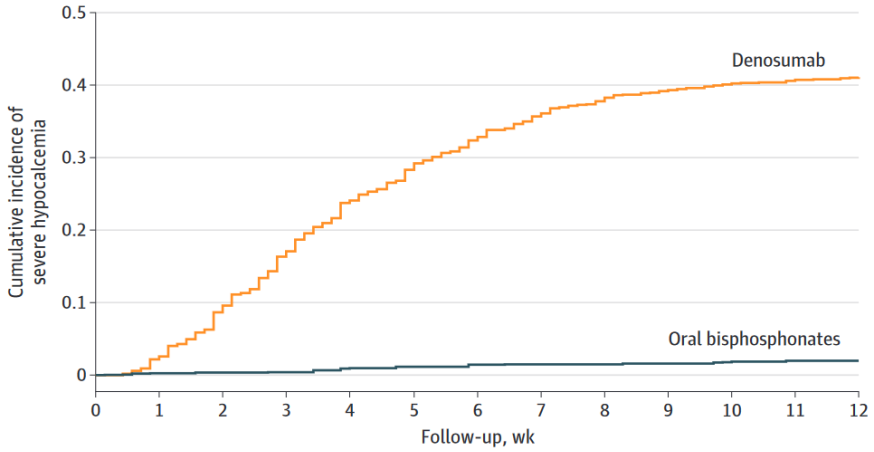
No. of patients												
Denosumab	1280	1291	1287	1324	1347	1337	1184	1246	1188	1166	1144	1135
Oral bisphosphonates	1036	1070	1072	1099	1112	1137	1073	1038	1020	977	952	942

Figure 2. Severe Hypocalcemia Incidence Among Patients Treated With Denosumab and Oral Bisphosphonat

A Weekly incidence of severe hypocalcemia



B Cumulative incidence of severe hypocalcemia



Phosphate metabolism

- Essential for many biological functions
  - energy production (component of ATP)
  - cellular signaling
  - structural roles in nucleic acids and membranes

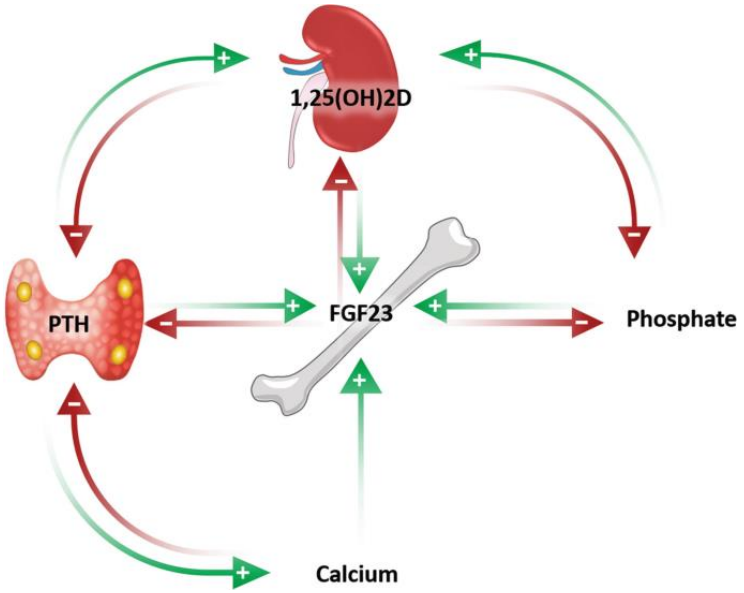
- **Distribution and Storage**
  - 85% in bones and teeth as hydroxyapatite
  - 15% in extracellular fluids and soft tissues
  - Critical for structural rigidity and metabolic functions

Berndt & Kumar, 2009

Phosphate regulation

Parathyroid Hormone (PTH)

- master regulator of both calcium (Ca2+) and phosphate (Pi) homeostasis
  - → **↑ blood Ca2+ + ↑ Pi renal excretion**
  - → ↑ FGF23 secretion from bone & ↑ synthesis of calcitriol in the kidney
  - →Since PTH action releases Pi from bone & stimulation of intestinal Ca2+ and Pi absorption enhances the Pi load



PTH compensates by ↑ **phosphaturia** (downregulation of renal Pi transporters – 85% of Pi reabsorption in proximal tubules)

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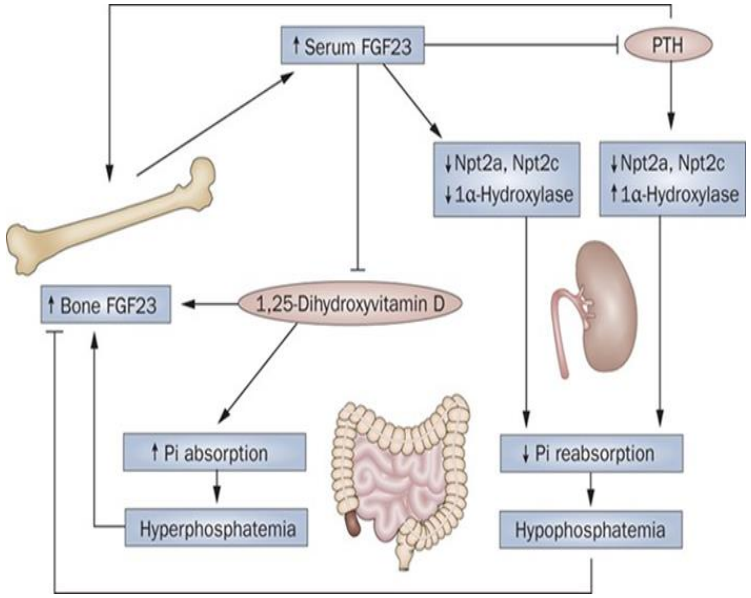
Wagner, *Nephrol Dial Transplant.* 2024

Phosphate regulation

- **Fibroblast Growth Factor 23 (FGF23)**
  - Physiologically, produced mainly by osteocytes, but in diseased organs, it can be secreted by different cell
  - Stimulated upon increased Pi intake
  - acts primarily on the kidneys to stimulate renal clearance of Pi
  - reduces circulating calcitriol (which stimulates Pi absorption in the kidney)



Increase in Pi →production of **FGF23** by osteocytes → stimulates Pi renal clearance + reduces absorption (by ↓ calcitriol)

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Wagner, *Nephrol Dial Transplant.* 2024

Hyperphosphatemia

Causes of hyperphosphatemia

Acute phosphate load
Endogenous
Cell lysis (tumor lysis syndrome, rhabdomyolysis)
Exogenous
Phosphate-containing medications (laxatives, fosphenytoin)
Intestinal uptake (vitamin D toxicity)
Cellular shift
Lactic or ketoacidosis
Decreased renal clearance
Reduced glomerular filtration rate
Acute kidney injury
Chronic kidney disease
Increased tubular reabsorption
Hypoparathyroidism or pseudohypoparathyroidism
Acromegaly
Bisphosphonates
Cinacalcet
Vitamin D toxicity (also increases intestinal absorption)
Familial tumoral calcinosis
Fibroblast growth factor receptor inhibitors
Pseudohyperphosphatemia
Endogenous
Hyperglobulinemia (multiple myeloma, Waldenström macroglobulinemia)
Hyperlipidemia
Hemolysis
Hyperbilirubinemia
Exogenous
Medications (amphotericin B, heparin, tissue plasminogen activator)

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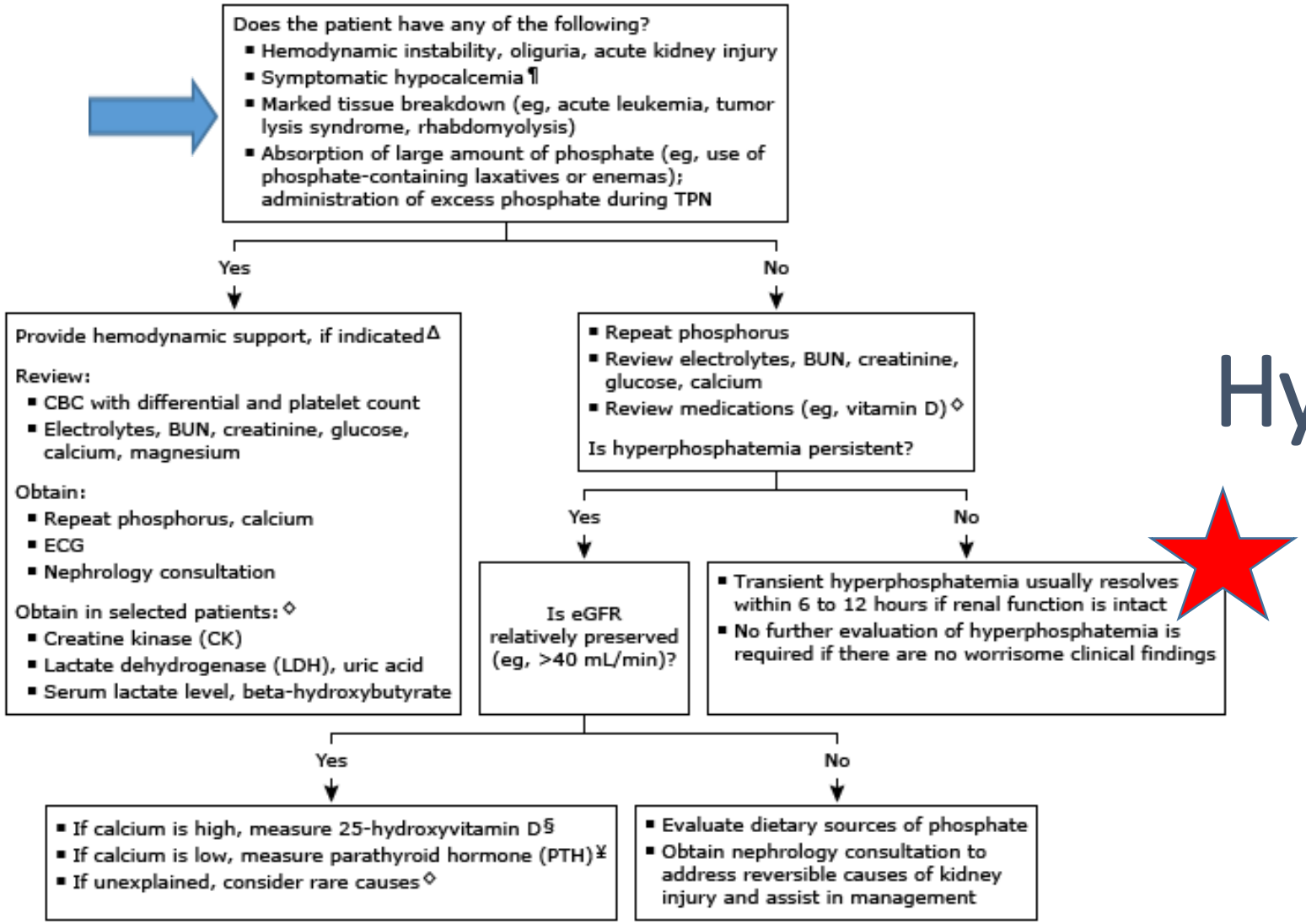
Hyperphosphatemia symptoms

- **Symptoms related to Hypocalcemia** (excess blood Pi binds to Ca2+)
  - Muscle cramps and spasms
  - Tetany
  - Perioral numbness or tingling
  - Seizures
- **Calcification in Soft Tissues**
  - Joint pain and stiffness - calcifications in joints
- **Vascular calcifications** → increase in risk of cardiovascular disease
- **Renal Symptoms**
  - Nephrocalcinosis: calcification in the kidney →impair kidney function
  - Renal failure → high Pi levels → worsen kidney function in preexisting kidney disease
- **Bone Pain**
  - Secondary to osteomalacia or renal osteodystrophy in CKD patients

Koumakis, *calcif tissue int*, 2021

Hyperphosphatemia



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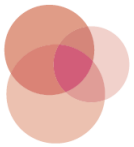
Treatment of hyperphosphatemia

- Treatment of underlying disorder!
- **No treatment** is usually needed in the setting of normal renal function as hyperPi is self-resolving
- **Limiting dietary phosphate intake** (by reducing protein intake)
- blocking intestinal phosphate absorption with **phosphate binders** (mild persistent asymptomatic hyperPi in the setting of mild to moderate renal failure)
  - calcium carbonate, calcium acetate, and sevelamer (Renvela)
- **Hemodialysis** may be required for severe hyperPi with symptomatic hypoCa2+



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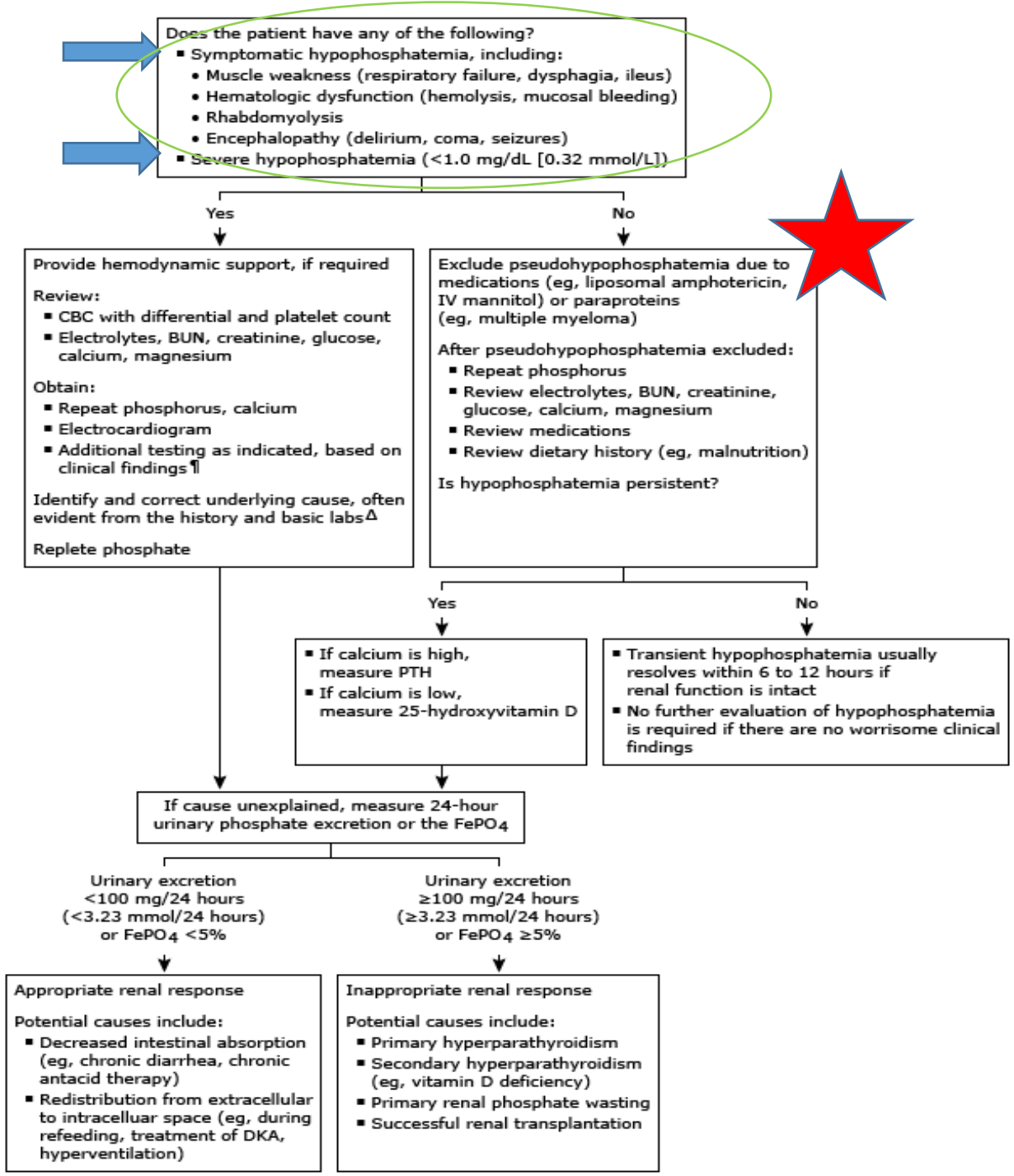
Shiber and Mattu, 2002

Hypophosphatemia

Major causes of hypophosphatemia

Internal redistribution
Increased insulin secretion, particularly during refeeding
Acute respiratory alkalosis
Hungry bone syndrome
Decreased intestinal absorption
Inadequate intake
Inhibition of phosphate absorption (eg, antacids, phosphate binders, niacin)
Steatorrhea and chronic diarrhea
Vitamin D deficiency or resistance
Increased urinary excretion
Primary and secondary hyperparathyroidism
Vitamin D deficiency or resistance
Hereditary hypophosphatemic rickets
Oncogenic osteomalacia
Fanconi syndrome
Other - acetazolamide, tenofovir, IV iron, chemotherapeutic agents
Removal by kidney replacement therapies



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Hypophosphatemia

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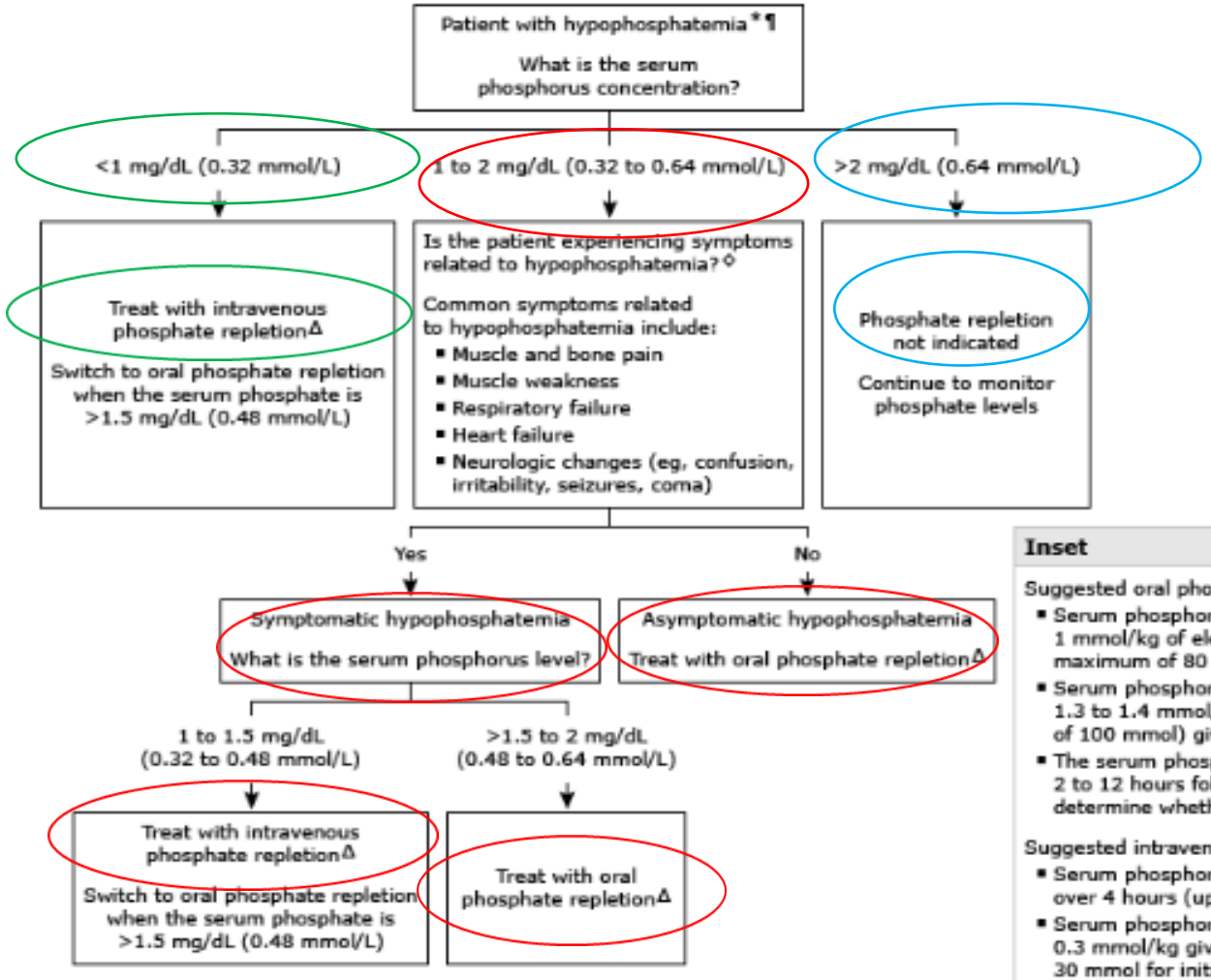
Hypophosphatemia



Inset

Suggested oral phosphate dosing:§

- Serum phosphorus >1.5 mg/dL to 2 mg/dL (0.48 to 0.64 mmol/L): 1 mmol/kg of elemental phosphorus (minimum of 40 mmol and a maximum of 80 mmol) given in 3 to 4 divided doses over 24 hours.
- Serum phosphorus 1 to 1.5 mg/dL (0.32 to 0.48 mmol/L): 1.3 to 1.4 mmol/kg of elemental phosphorus (up to a maximum of 100 mmol) given in 3 to 4 divided doses over 24 hours.
- The serum phosphorus concentration should be rechecked 2 to 12 hours following administration of the last dose to determine whether repeat doses are required.

Suggested intravenous phosphate dosing:¥

- Serum phosphorus ≥1.4 mg/dL (0.45 mmol/L): 0.2 mmol/kg given over 4 hours (up to a maximum dose of 20 mmol for initial dosing).
- Serum phosphorus ≥1.1 to 1.3 mg/dL (0.36 to 0.42 mmol/L): 0.3 mmol/kg given over 4 hours (up to a maximum dose of 30 mmol for initial dosing).
- Serum phosphorus ≤1 mg/dL (0.32 mmol/L): 0.4 mmol/kg given over 6 hours (up to a maximum dose of 50 mmol for initial dosing).
- The serum phosphorus concentration should be monitored every 6 hours when intravenous phosphate is given.

Tumor-induced osteomalacia

- rare paraneoplastic sd
- characterized by **bone pai**n, **fractures** and **muscle weakness**
- caused by tumoral overproduction of fibroblast growth factor 23 (FGF23) → acts at the proximal renal tubule → ↓ Pi reabsorption → hypophosphatemia & osteomalacia
- small, **benign mesenchymal tumors** - found in bone or soft tissue, anywhere in the body

- Locating the tumor is critical → complete removal is curative

- If the tumor is not localized, or surgical resection is not possible

→ phosphate and active vitamin D supplementation (successful in healing the osteomalacia & ↓ symptoms)

Florenzano et al, Bone Rep (2017)

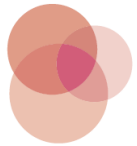

Thank you !
C H U | U V C
B R U G M A N N

Case - Imaging

- Head CT: absence of hemorrhage, mass effect, hydrocephalus
- History of tumorectomy of left breast > induration left breast
  > US of L&R breasts : sequellar appearance, no suspicious lesion
- Bone scintigraphy: no hyperfixation suspicious of bone metastasis

Indications for parathyroidectomy

- Symptomatic
- Asymptomatic
  - Age < 50 years
  - Serum calcium level >1 mg/dL above URL
  - Skeletal involvement
    - Fracture by VFA or vertebral X-ray, or bone mineral density (BMD) by T-score ≤ -2.5 at any site
  - Renal involvement
    - eGFR or creatinine clearance <60 mL/min
    - Nephrocalcinosis or nephrolithiasis by X-ray, ultrasound, or other imaging modality
    - Hypercalciuria (eg, >250 mg/day in women; >300 mg/day in men)
  - Patient preference



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Bilezikian et al., JBMR. (2022)

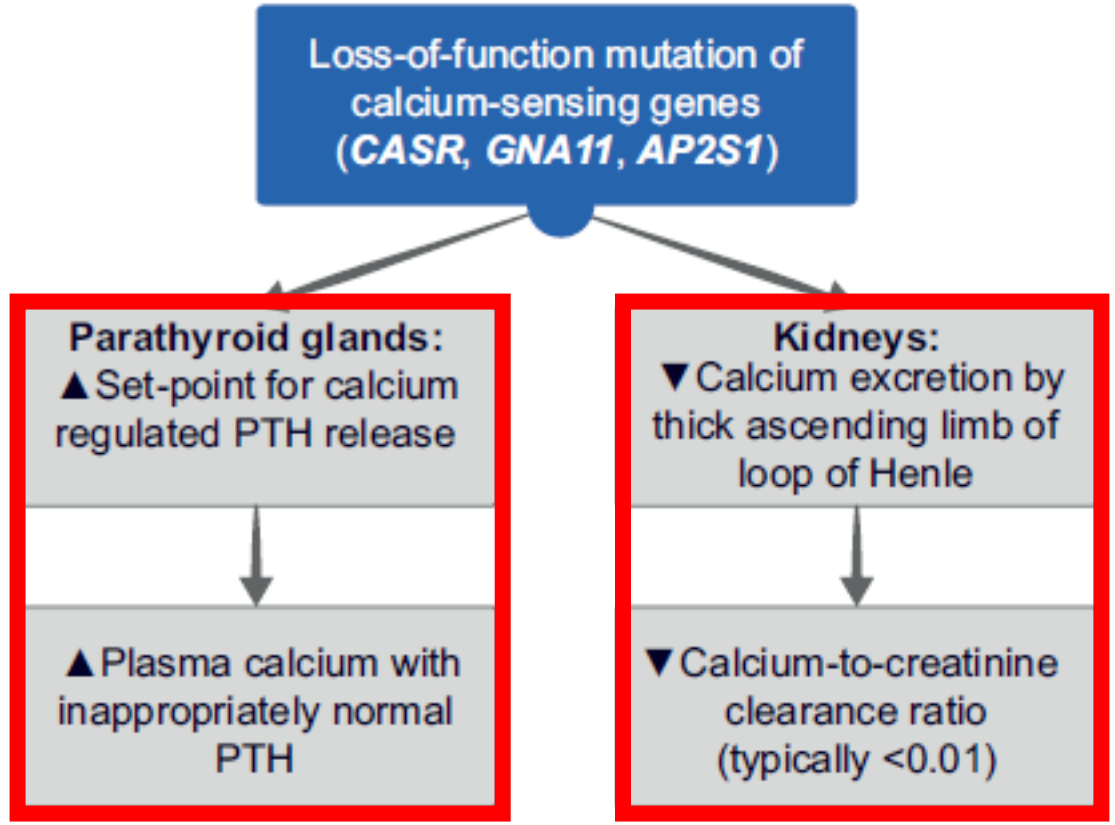

Figure 1

Alterations in calcium metabolism caused by familial hypocalciuric hypercalcemia (FHH). Hypercalcemia arises due to an increase in the parathyroid set-point for parathyroid hormone (PTH) release and possibly also from decreased renal calcium excretion (11, 12). Alterations in bone metabolism are not usually observed in FHH (13).