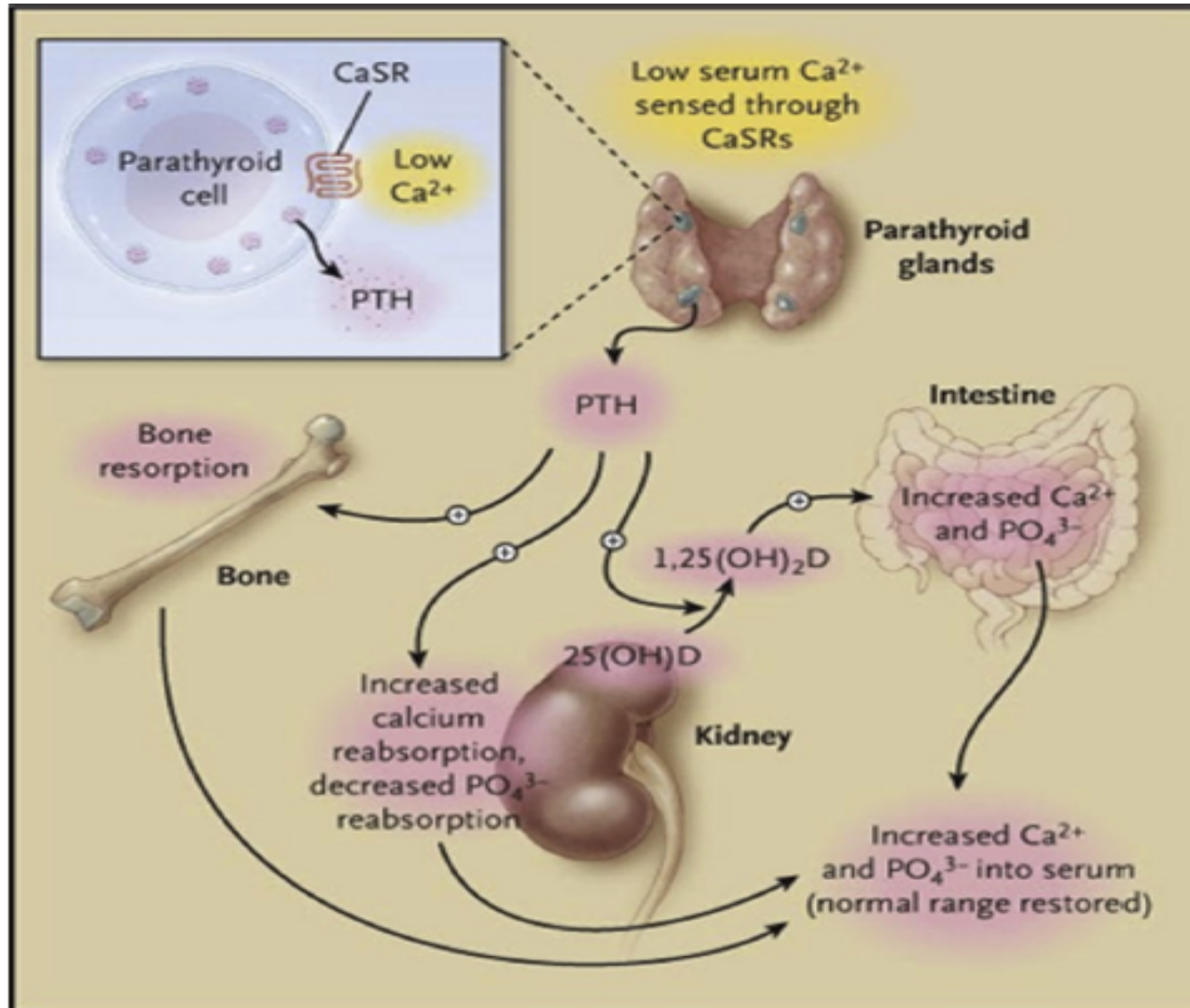


# Iperparatiroidismo primitivo: cosa fare prima della chirurgia?

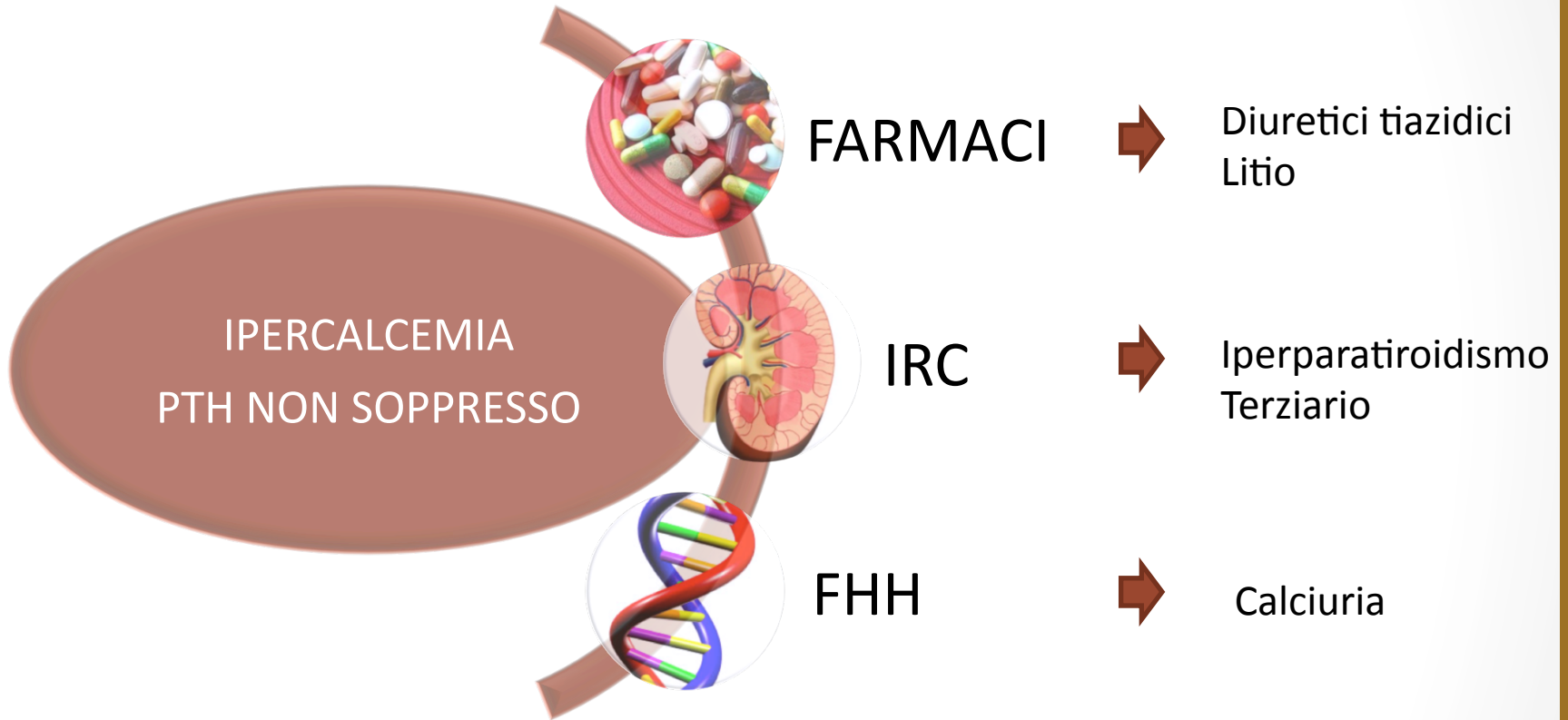


Dott. Alfredo Scillitani

# FISIOLOGIA



# DIAGNOSI



# Familial Hypocalciuric Hypercalcaemia (FHH)

**Jackson CE, Boonstra CE.**

Hereditary hypercalcemia and parathyroid hyperplasia without definite hyperparathyroidism

J Lab Clin Med **1966**;68:883 (Abstract 62)

*“Hereditary Hypercalcemia  
without Definite Hyperparathyroidism”*



**Foley TP, et al.**

Familial benign hypercalcemia

J Pediatr **1972**;81:1060–7

*“an inappropriate  
requirement of an unusually high concentration of  
alcium to suppress the production of parathormone.”*

**Marx SJ, et al.**

Family studies in patients with primary parathyroid hyperplasia.

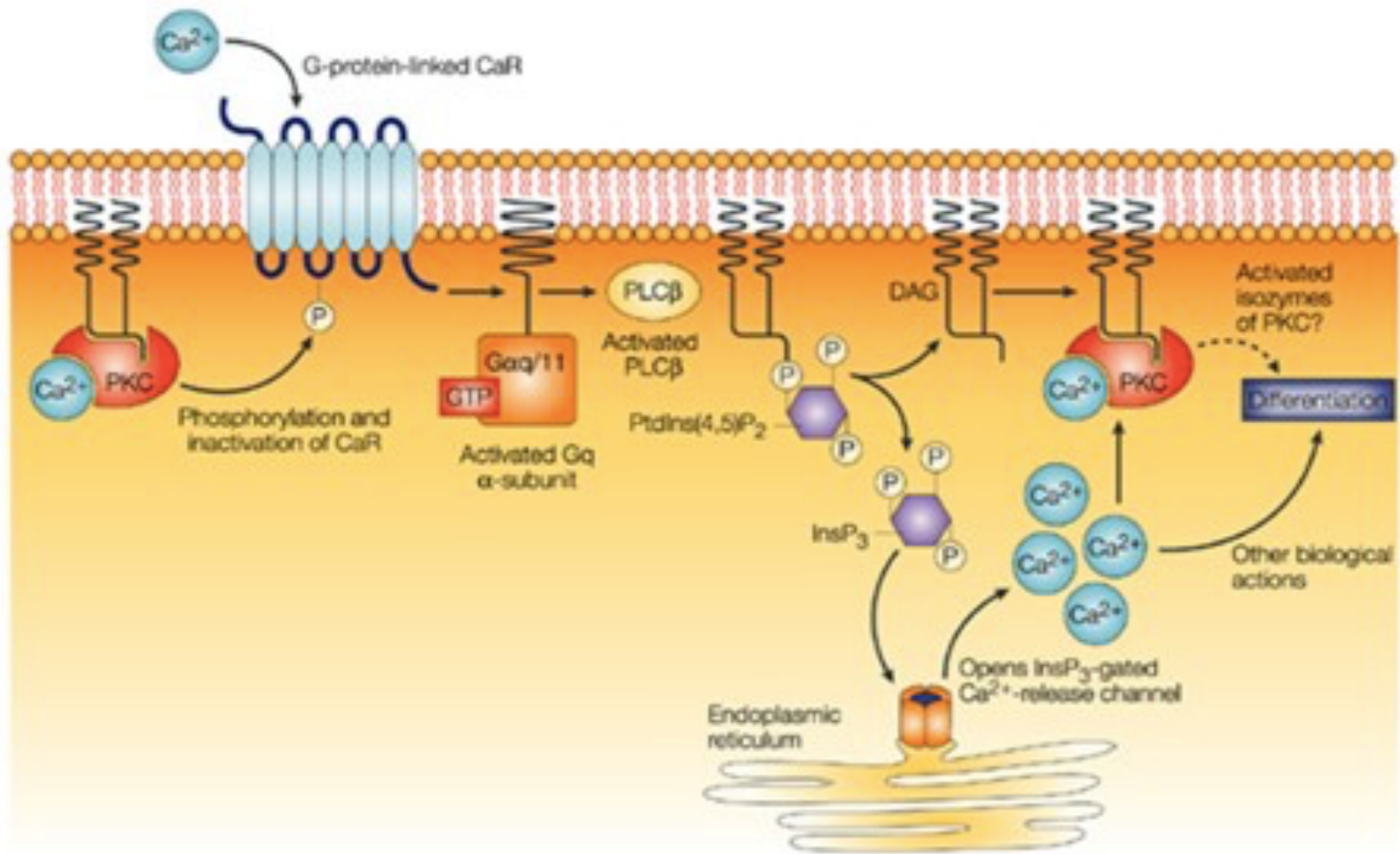
Am J Med **1977**;62:698–706.

*“Familial Hypocalciuric Hypercalcemia”*

*in recognition of  
the unexpectedly low urinary excretion of  
calcium relative to the hypercalcemia of  
affected persons*



# Familial Hypocalciuric Hypercalcaemia (FHH)



Nature Reviews | Cancer

*Cloning and characterization of an extracellular Ca<sup>2+</sup>-sensing receptor from bovine parathyroid cells. Brown EM, et al. Nature 1993;366:577–80.*

CALCEMIA 10,8 mg/dL

ALBUMINA 3,7 g/dL



CALCEMIA 11 mg/dL  
corretta per albumina

CREATININEMIA 0,82 mg/dL



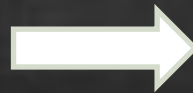
0,074

CALCEMIA 11 mg/dL  
corretta per albumina



0,06

CALCIURIA 88 mg/die



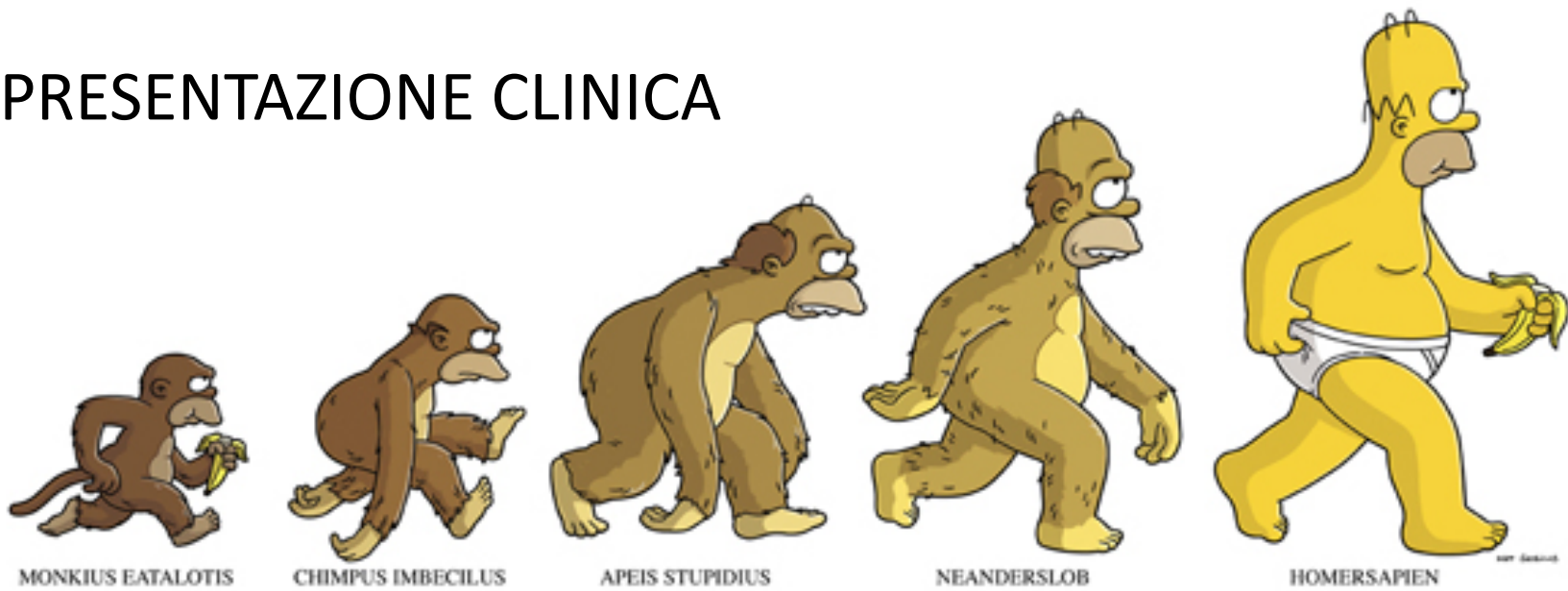
0,81

CREATININURIA 108 mg/dL

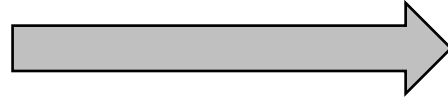
$ClCa / ClCr = 0,06$  valori indicativi di FHH  $< 0,010$



# PRESENTAZIONE CLINICA



Sintomatica



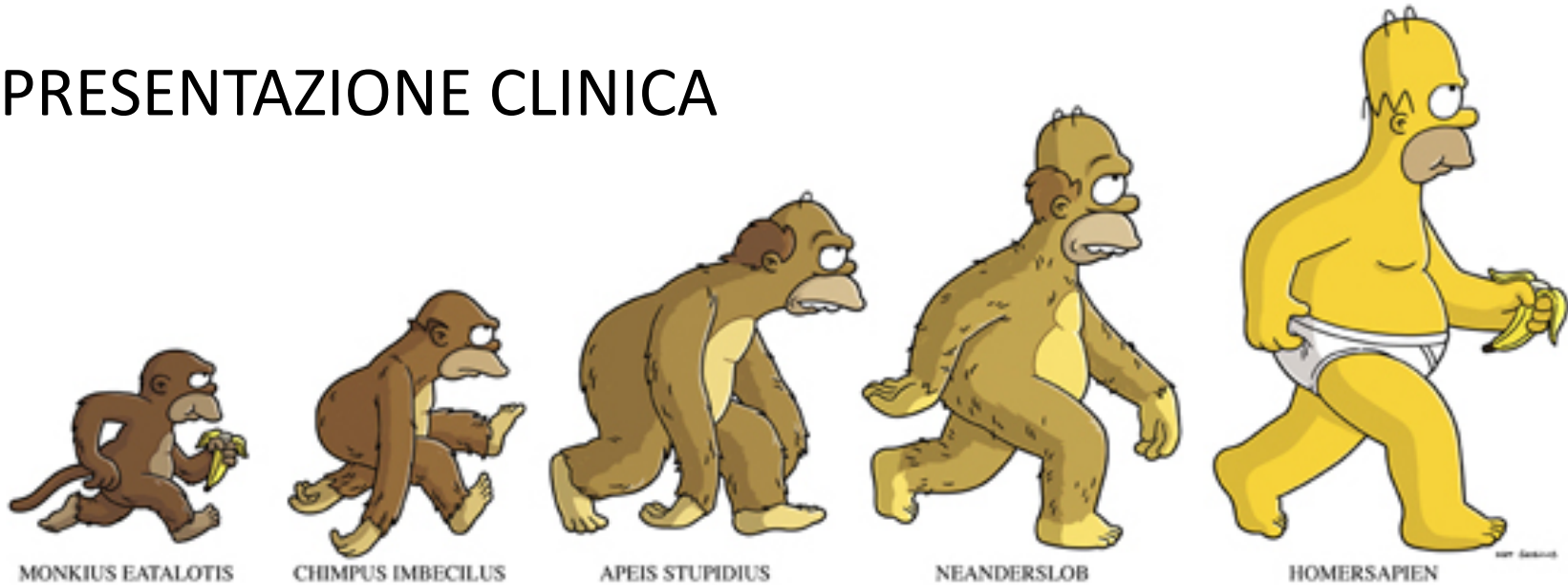
Asintomatica



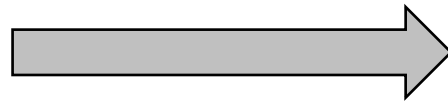
In the first 343 cases of PHPT seen at Massachusetts General Hospital, 57% had urolithiasis, 23% had parathyroid bone disease, and 8% had peptic ulcer disease.

*Cope O. N Engl J Med 1966*

# PRESENTAZIONE CLINICA



Sintomatica

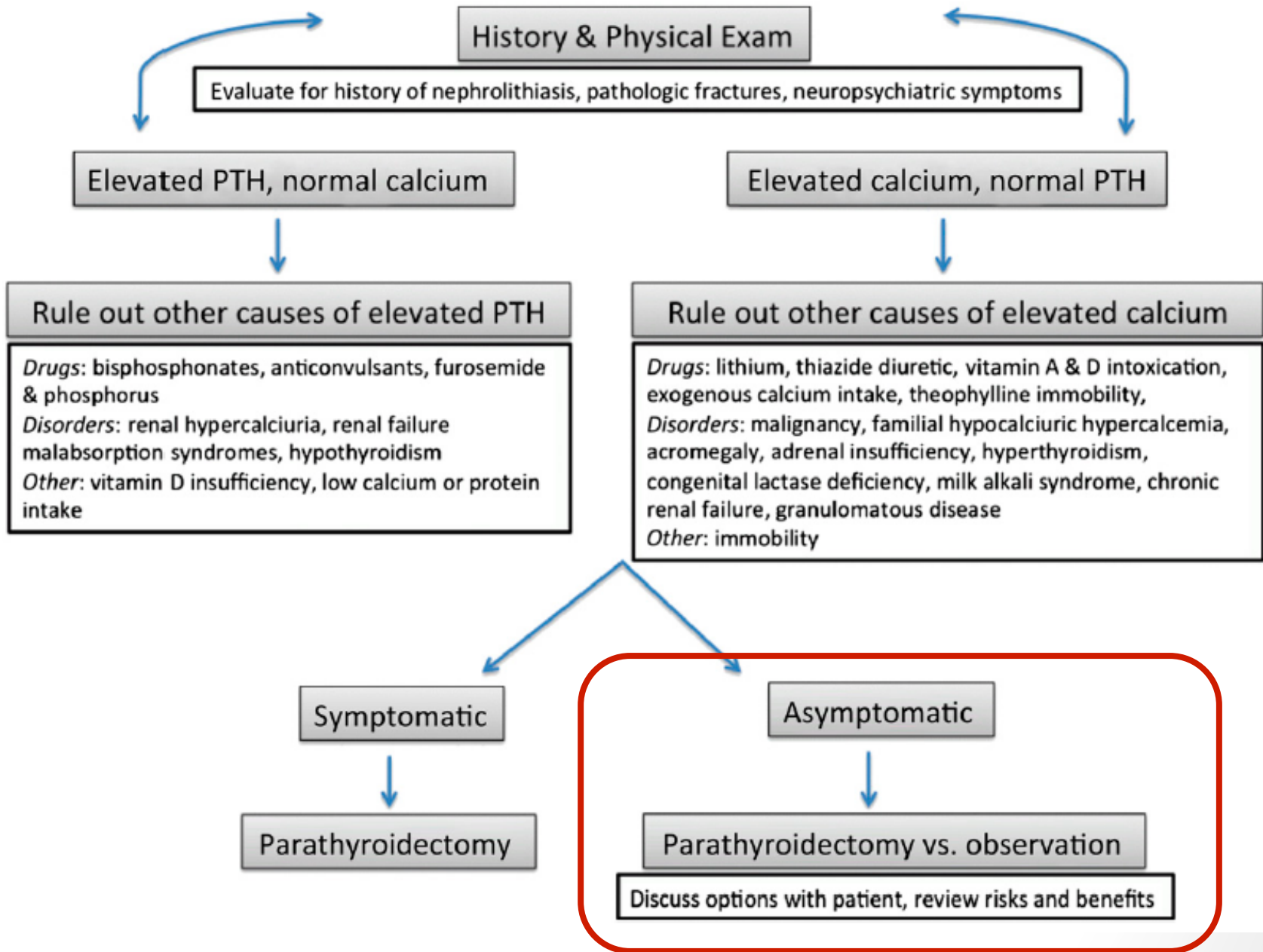


Asintomatica

Oggi circa  
l'80% dei pazienti con PHPT  
sono asintomatici







Parameter

Serum calcium:

1 mg/dL (0.25 mmol/L) > upper limit of normal

BMD by DXA:

*T* score < -2.5 at lumbar spine, femoral neck, total hip, or distal 1/3 radius

Detection of vertebral fractures

by X-rays, VFA, MRI or CT

Serum creatinine

Estimated creatinine clearance (eGFR) <60 mL/min

24-h urine:

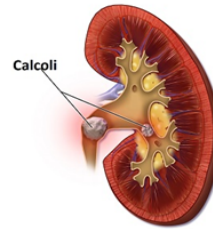
Daily urinary calcium excretion >400 mg/day and increased stone risk by the urinary biochemical stone risk profile

Presence of nephrolithiasis or nephrocalcinosis (by X-ray, ultrasound or CT)

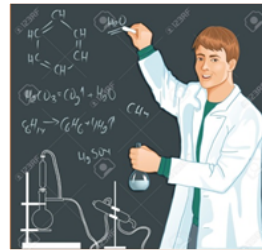
Age <50 years

---

# DIAGNOSI



Litiasi



Calcolo eGFR



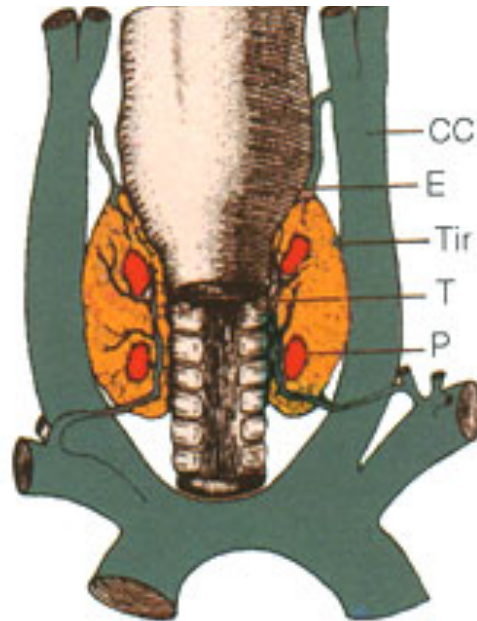
Osteoporosi



Fratture

# SEDI DI LOCALIZZAZIONE

Le paratiroidi superiori si trovano adiacenti alla faccia dorso laterale della tiroide, all'altezza dell'istmo.

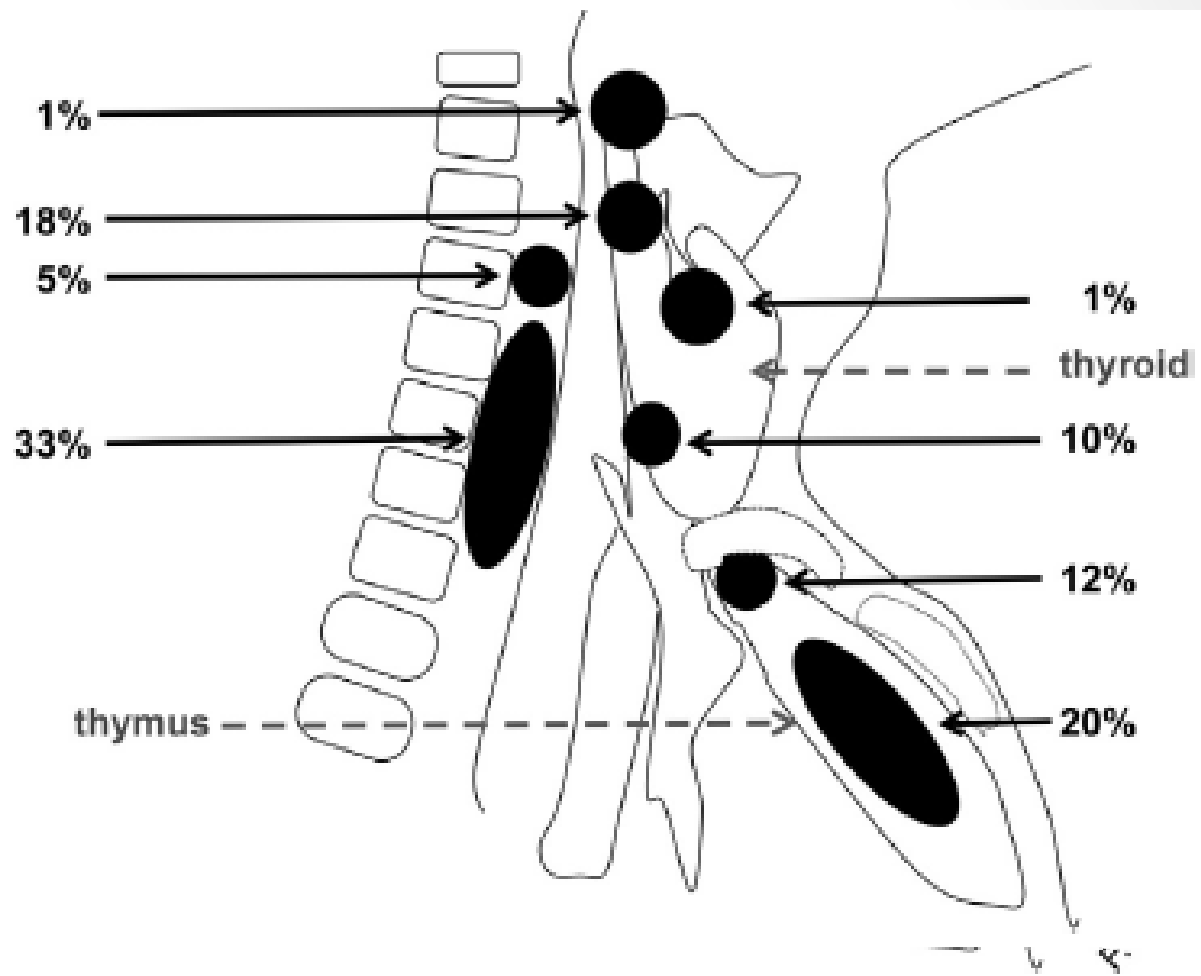


Le paratiroidi inferiori sono di norma posizionate in prossimità della faccia infero-laterale dei poli tiroidei inferiori

**80 – 85 %**

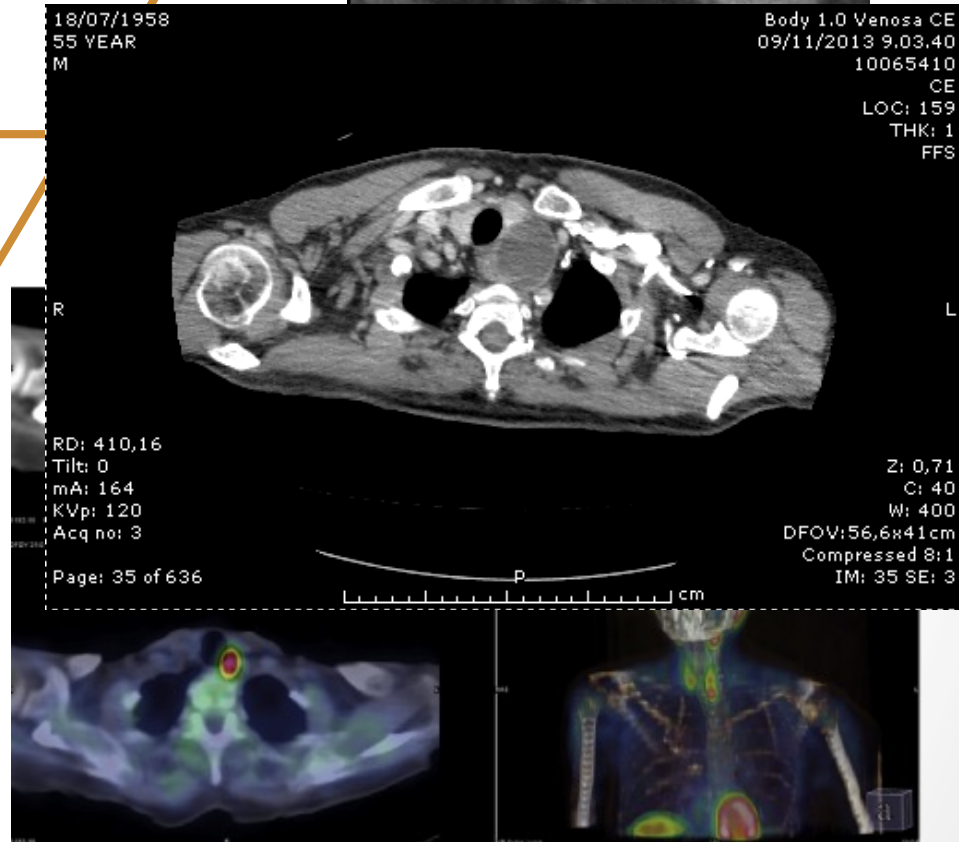
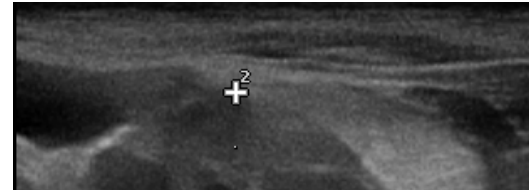
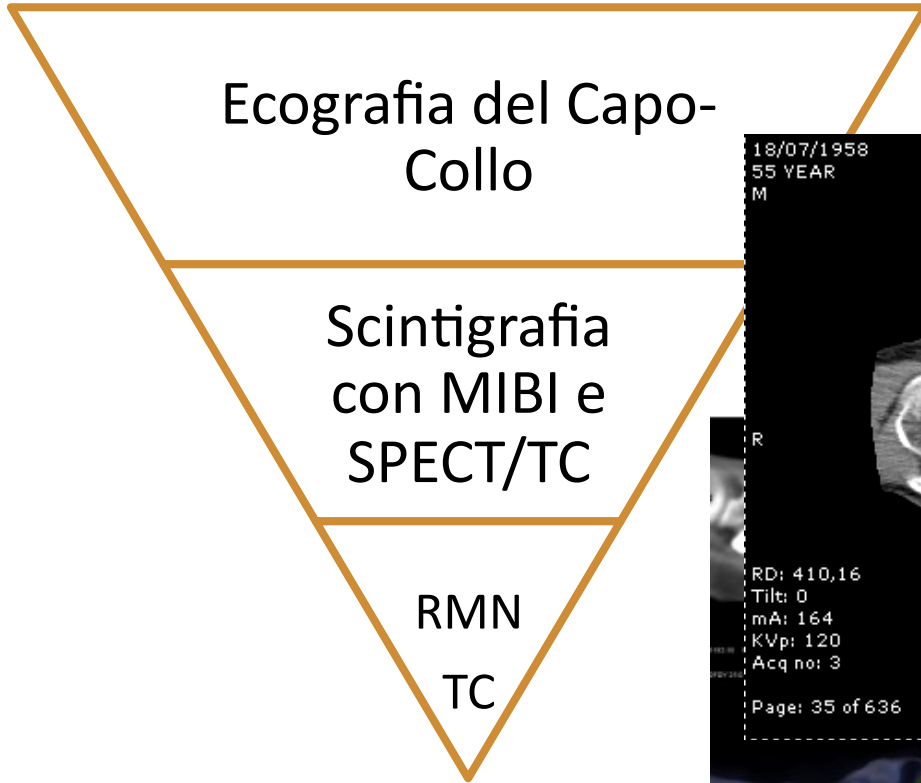
delle lesioni paratirodee si trovano nella loro sede abituale

PARATIROIDI  
ECTOPICHE

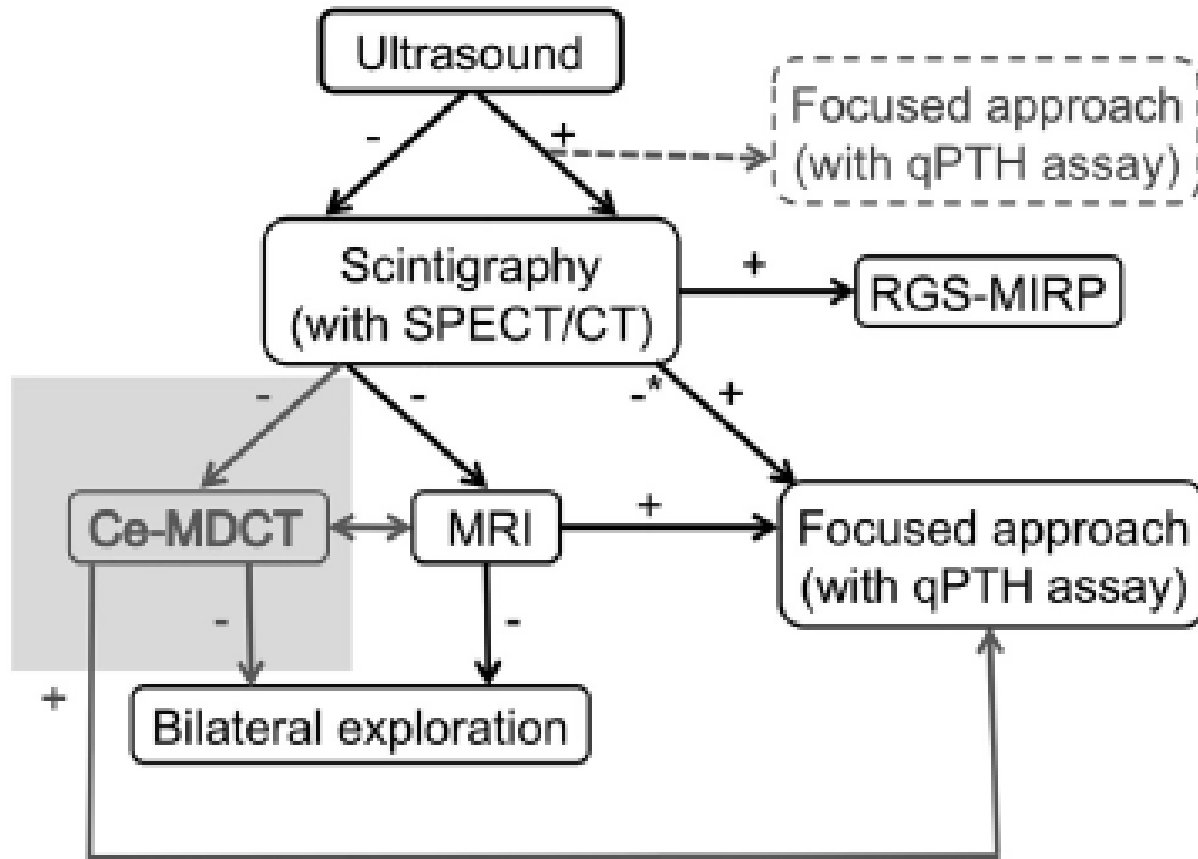


**FIGURE 35.1** Distribution of hyperfunctioning parathyroid glands according to anatomic location. A total of 104 lesions found at re-operation in a single institution (Massachusetts General Hospital, Harvard Medical School, Boston, MA) because of recurrent PHPT after prior conventional four-gland exploration surgery from 1930 to 1975. The most common ectopic sites (about 65% of the total) mirror the route of descent of the lower parathyroid glands, with a long migration path associated with descent of the thymus.

# IMAGING



## Unequivocal Biochemical Diagnosis with Clear Indication to Surgery

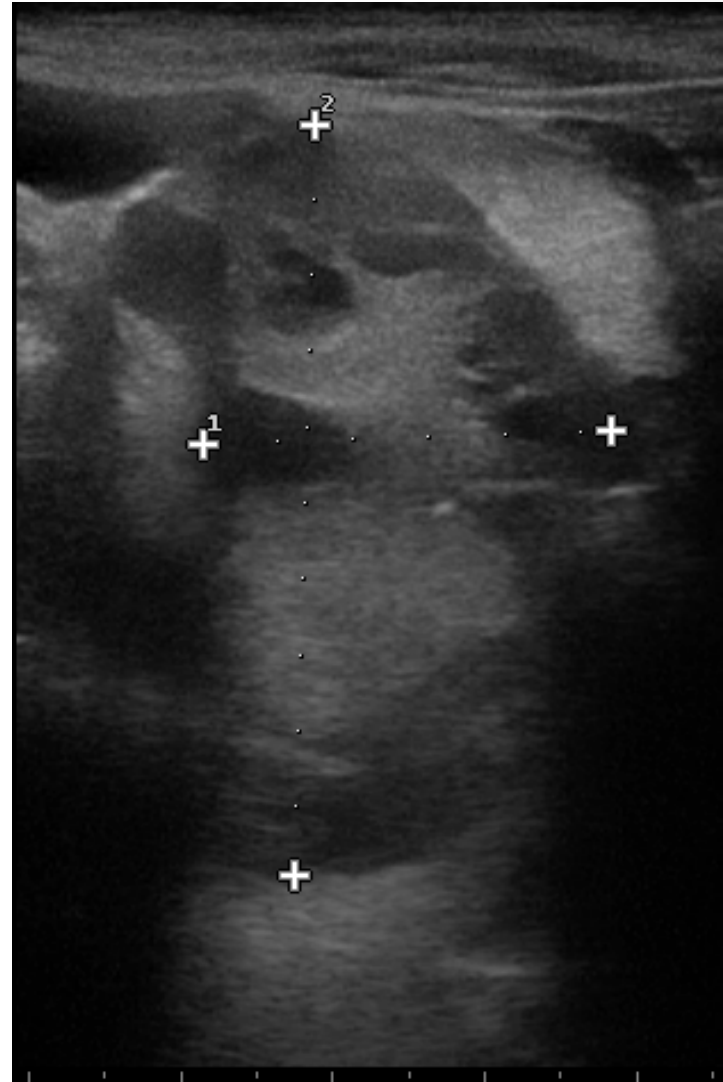


qPTH= intraoperative quick PTH assay

RGS\_MIRP= RadioGuided Surgery-Minimally Invasive Radioguided Parathyroidectomy

Ce\_MDTC= Contrast-enhanced Multi detector Computed Tomography

# FNA ?





# COSTI

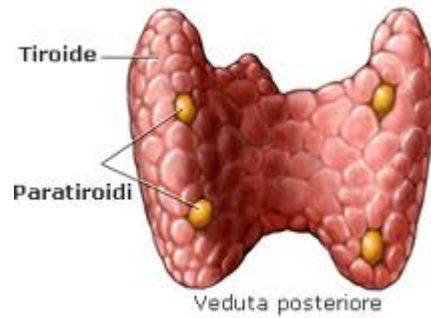
Service	Center for Medicare & Medicaid Services (CMS); Fee Schedule Amounts (US dollars)	Medicaid Services amounts (US dollars)
Serum calcium	\$7.09	
Serum phosphorus	\$6.52	
Serum parathyroid hormone (PTH)	\$56.74	
Serum albumin	\$6.80	
Serum creatinine	\$7.04	
25-Hydroxyvitamin D	\$40.70	
24-hour urine calcium and creatinine	\$8.29	
Dual-energy X-ray absorptiometry bone mineral density of spine and hip	\$55.01-\$84.65	
Dual-energy X-ray absorptiometry bone mineral density of radius	\$31.22-\$47.13	
Consultation with endocrinologist—clinic	\$81.40-\$222.65	
Return visit with established patient	\$79.54	
Surgery consultation	\$81.40-\$222.65	
Computed tomography (CT) of abdomen and pelvis without contrast (range)	\$253.87-\$397.86	
Renal ultrasound (range)	\$121.17-\$138.35	
Kidney ureters bladder (KUB) plain film radiographs with tomography (range)	\$27.13-\$82.01	
Parathyroid scan (range)	\$335.27-\$407.53	
Ultrasound of neck (range)	\$136.41-\$129.06	
Dynamic parathyroid computed tomography (CT) (range)	\$354.60-\$405.54	
Parathyroidectomy (range)	\$4344.93-\$6287.56	

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Dynamic parathyroid computed tomography (CT) (range)	\$354.60-\$405.54
Parathyroidectomy (range)	\$4344.93-\$6287.56



Sporadico



Iperparatiroidismo  
Primitivo

Familial Isolated  
HyperParathyroidism  
(**FIHP**)

Multiple Endocrine  
Neoplasia Type-1  
(**MEN1**)

Familial Hypocalciuric  
Hypercalcemia  
(**FHH**)

**ANAMNESI**

**ESAMI**

**GENETICA**

Familiare



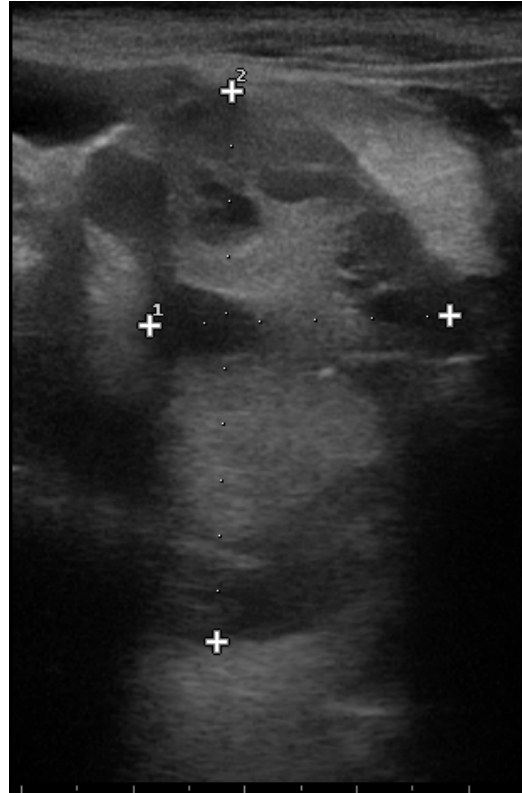
Multiple Endocrine  
Neoplasia Type-2A  
(**MEN2A**)

Hyperparathyroidism-  
Jaw Tumor  
(**HPT-JT**)

# CARCINOMA PARATIROIDEO



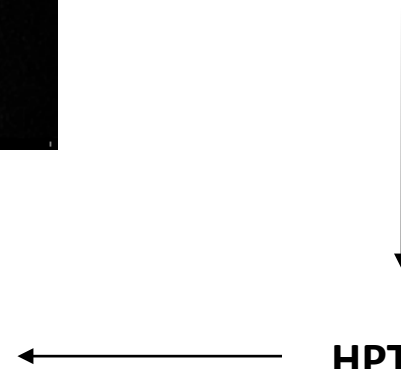
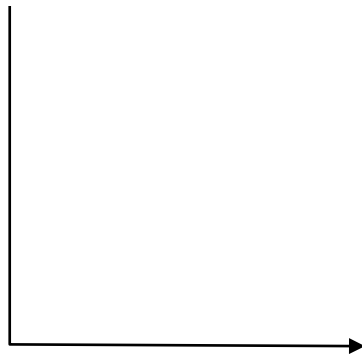
Sporadico



Familiare

**HRPT2/CDC73**

HPT-JT

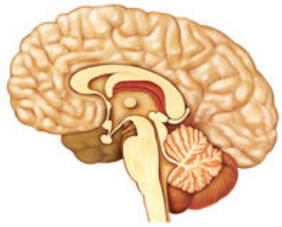


SIAMO PRONTI PER L'INTERVENTO CHIRURGICO ??



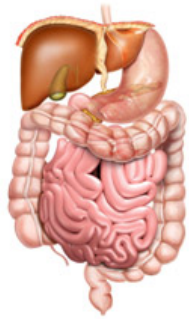
DOVREMMO  
RIDURRE LA  
CALCEMIA.....





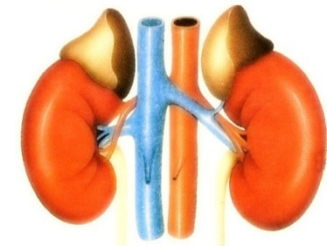
## CENTRAL NERVOUS SYSTEM

- Impaired concentration and memory
- Fatigue
- Muscle weakness
- Cognitive impairment
- Depression
- Psychosis
- Altered consciousness (confusion, lethargy, stupor, coma)



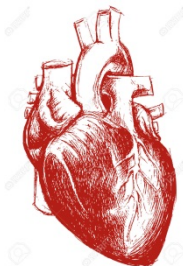
## GASTROINTESTINAL TRACT

- Polydipsia
- Anorexia
- Nausea
- Vomiting
- Abdominal pain (pancreatitis, peptic ulcer)
- Constipation



## RENAL SYSTEM

- Polyuria
- Dehydration
- Low urinary specific gravity
- Reduced glomerular filtration rate
- Renal failure



## CARDIOVASCULAR SYSTEM

- Hypertension
- ECG alterations: shortened QT interval, prolonged PR interval, widened QRS complex, bundle branch block, Brugada syndrome (in predisposed individuals), and bradyarrhythmias
- Cardiac arrest

Intervention	Mode of action	Onset of action	Duration of action
Isotonic saline hydration	Restoration of intravascular volume Increases urinary calcium excretion	Hours	During infusion
Calcitonin	Inhibits bone resorption via interference with osteoclast function Promotes urinary calcium excretion	4 to 6 hours	48 hours
Bisphosphonates	Inhibit bone resorption via interference with osteoclast recruitment and function	24 to 72 hours	2 to 4 weeks
Loop diuretics*	Increase urinary calcium excretion via inhibition of calcium reabsorption in the loop of Henle	Hours	During therapy
Glucocorticoids	Decrease intestinal calcium absorption Decrease 1,25-dihydroxyvitamin D production by activated mononuclear cells in patients with granulomatous diseases or lymphoma	2 to 5 days	Days to weeks
Denosumab	Inhibits bone resorption via inhibition of RANKL	4 to 10 days	4 to 15 weeks
Calcimimetics	Calcium sensing receptor agonist, reduces PTH (parathyroid carcinoma, secondary hyperparathyroidism in CKD)	2 to 3 days	During therapy
Dialysis	Low or no calcium dialysate	Hours	During treatment

## IPERCALCEMIA LIEVE



10,2/10,4 – 12 mg/dL

Ipercalcemia asintomatica o lieve  
(calcemia < 12 mg/dL)

- Non richiede trattamento immediato.
- Evitare fattori che possano aggravare l'ipercalcemia
- Diuretici tiazidici, carbonato di litio, deplezione di volume, prolungato allettamento
- Idratazione adeguata (almeno dai 6 agli 8 bicchieri di acqua al giorno) per minimizzare il rischio di nefrolitiasi.



## IPERCALCEMIA MODERATA



12 – 14 mg/dL

Ipercalcemia cronica moderata asintomatica o lievemente sintomatica

(calcemia compresa tra 12 e 14 mg/dL)

- potrebbe non richiedere un trattamento immediato
- Stesse precauzioni descritte per l'ipercalcemia lieve

Aumento acuto della calcemia

- potrebbe causare un'alterazione del sensorio e potrebbe richiedere una terapia più aggressiva simile all'ipercalcemia grave
- Trattamento con soluzione fisiologica e bisfosfonati come nell'ipercalcemia grave

# IPERCALCEMIA GRAVE



> 14 mg/dL

**Disidratazione progressiva**

CASR

AQP2

TRPV5

aumento del volume  
urinario dovuto  
all'inibizione diretta del  
riassorbimento tubulare  
renale del sodio e  
dell'acqua



alla riduzione  
dell'apporto di liquidi  
dovuta all'anoressia,  
alla nausea e al  
vomito

# IPERCALCEMIA GRAVE

## IDRATAZIONE

Espansione del volume con una soluzione salina isotonica



Velocità di infusione  
iniziale di 200 – 300 mL/h



3 – 4 Litri  
nelle prime 24 h



2 – 3 Litri  
nei giorni successivi

Diuresi = 100 – 150 mL /h

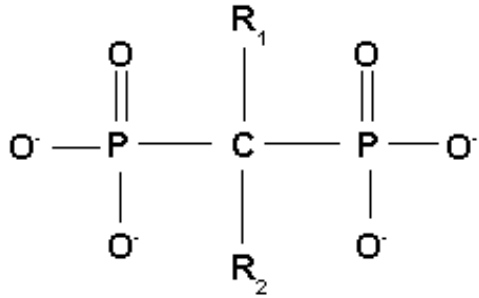
**IPERCALCEMIA GRAVE**

**IDRATAZIONE**



# IPERCALCEMIA GRAVE

## BISFOSFONATI



Derivati del pirofosfato a cui il ponte P-O-P è stato sostituito con un ponte P-C-P non idrolizzabile.

Inibiscono l'azione degli osteoclasti

## Acido Zoledronico



- Più potente
- 1 fl da 4 mg in 100cc di soluzione fisiologica in 15 minuti
- Riduzione della calcemia più velocemente e più a lungo



Reazione di fase acuta



Filtrato glomerulare

< 30 ml/min



DENOSUMAB?

# Vitamina D ?

Clinical Endocrinology (2014) 80, 797–803

ORIGINAL ARTICLE

**Effect of 25 (OH) D replacements in patients with primary hyperparathyroidism (PHPT) and coexistent vitamin D deficiency on serum 25(OH) D, calcium and PTH levels: a meta-analysis and review of literature**

Viral N. Shah\*, Chirag S. Shaht, Sanjay K. Bhadada† and D. Sudhakar Rao§

**Conclusion** Vitamin D replacement in subjects with PHPT and coexistent vitamin D deficiency increase 25 (OH) D and reduce serum PTH significantly without causing hypercalcaemia and hypercalciuria. The finding of the study needs to be confirmed by a large randomized trial in patient with PHPT and coexistent vitamin D deficiency.





**GRAZIE PER  
L'ATTENZIONE**