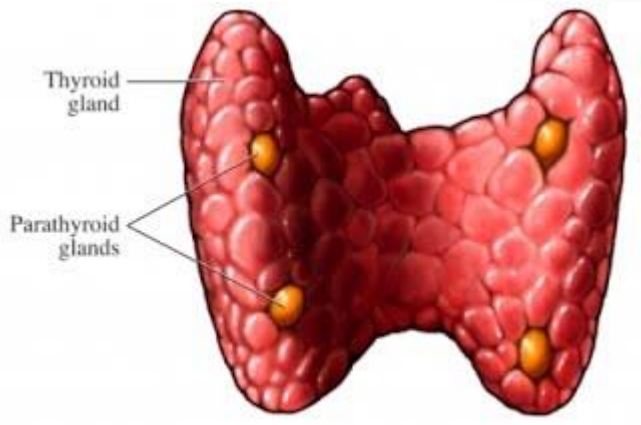
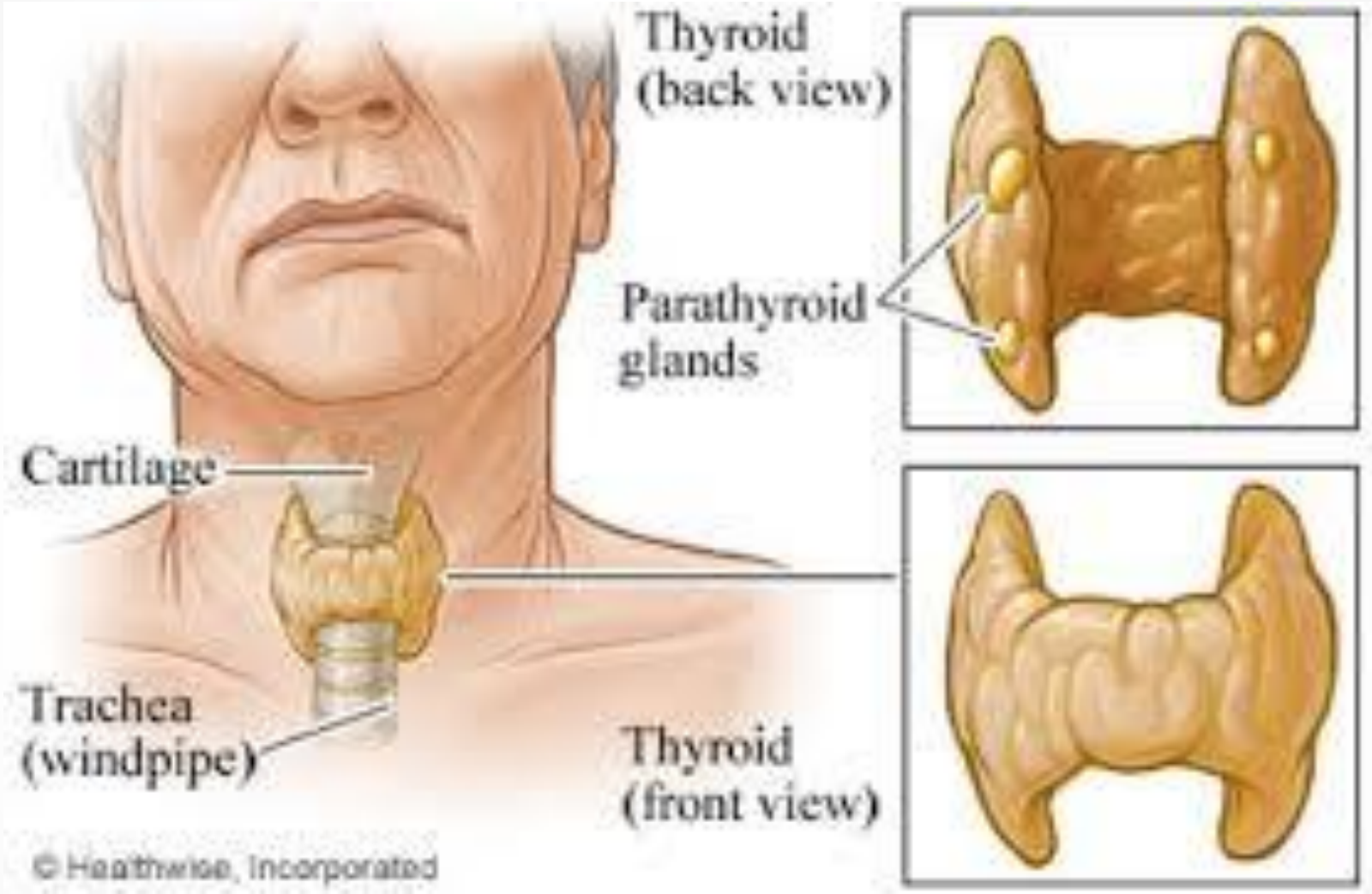
Persistent post transplant hyperparathyroidism

Shiva Seyrafian
IUMS-97/10/18-
8/1/2019



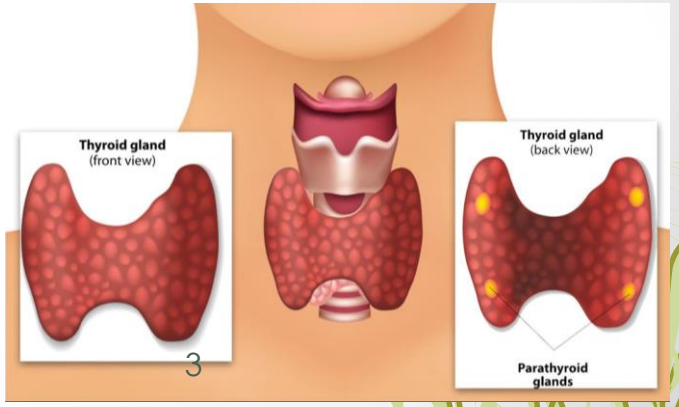


normal weight =18-160 mg
In HPT= 500-1000 mg

Epidemiology

Mild 2nd hyperparathyroidism (HPT) resolve after renal transplantation (TX) as early as 3 months, as more normal GFR restores.

Persistent HPT in 15-50 % following TX lasting more than 1 year, because of hyperplasia , adenoma formation.



uptodate® 2018-12-19, Persistent HPT

Risk Factors

- **Degree of pretransplant hyperparathyroidism**
- **Duration of dialysis**
- Inadequate vitamin D stores
- Poor allograft function (de novo secondary hyperparathyroidism)

Clinical manifestations

- ↑Ca, ↓P, sometimes only ↑PTH
- **Bone pain, pruritus, nephrolithiasis, myopathy** generally not observed in TX patients.

Hypercalcemia, hypercalciuria:

- Symptomatic: mostly in the first 3 months post TX.

Hypophosphatemia:

- In early post TX 40% -90%, in first year(P<2.5): 40%

- Additional causes of hypercalcemia after TX:

1. Increased calcitriol production
2. Resorption of soft-tissue calcium phosphate deposition
3. Increase in plasma albumin (mild increase in total Ca)

- Additional causes of hypophosphatemia after TX:

1. Continuing of excess FGF-23 (released by osteocyte and osteoblasts in response to PTH, calcitriol, high dietary phosphate and calcium).

After TX: FGF-23 rapidly decrease but may persists.

Outcome

- **Increased mortality:** PTH>65, HR:1.46, 95% CI

  Mechanism: not known, vascular calcification

- **Allograft loss:** PTH > 65, 85% increase in death-censored graft loss, mechanism not known, increased fracture.

Management-1

Before transplantation

1. Optimal management of HPT
2. Parathyroidectomy (PTX)(refractory, moderate to severe symptoms, TX not imminent),
3. Subtotal PTX: PTH>800, regardless of symptoms despite medical therapy.
4. PTH>800: 80% risk of graft failure, unlikely respond to vit D or vit D derivatives, hypercalcemia and hypercalciuria, decreased allograft survival

Management-2

Before transplantation

PTX: safer if done before TX.

PTX after TX, abrupt deterioration of renal allograft function,

Cinacalcet:

- commonly in nontransplant- candidate ESRD,
- not used in TX candidate unless PTX is contraindicated
- Risk of rebound hypercalcemia
- If treated should have stopped before TX to determine rebound ⬆Ca, and benefit from pre-TX PTX.

Management-3

After transplantation

All TX recipients:

- Ca and P at each visit during first year.

-

PTH and alkaline phosphatase quarterly or more if hypercalcemia or hyperphosphatemia.

Management-4

After transplantation

Hypercalcemia:

- Severe Hypercalcemia: PTX or subtotal PTX+ cinacalcet
- Ca > 11 for more than 6 months = PTX
- Mild hypercalcemia and hyperparathyroidism (2-3 times)= cinacalcet

- Not respond to cinacalcet after 6-12 ms: all referred to subtotal PTX
- Cinacalcet is not approved for transplant patients in USA.

Management-5

After transplantation

Hypercalcemia:

- One week of cinacalcet therapy causes a moderate but significant decrease in systemic exposure of tacrolimus while cyclosporine and mycophenolate pharmacokinetics not affected

  (Falck P, etal. Cinacalcet effects on the pharmacokinetics of tacrolimus and mycophenolate.., Nephrol Dial Transplant 2008; 23:1048).

Management-6

After transplantation

Hypophosphatemia:

Mild or moderate (1-2.3 mg/dl): if PTH ~ 2-3 ULN,

1. Treat HPT,
2. if ⬇P persists following successful treatment of HPT, increase intake of phosphate-rich foods.

Management-7

After transplantation

Hypophosphatemia:

Severe (< 1 mg/dl):

1. Oral phosphate regardless of PTH or Ca concentration+ vitamin D deriv., if not hypercalcemic.
2. If HPT: PTX.
3. Dipyridamole enhances renal tubular phosphate reabsorption.

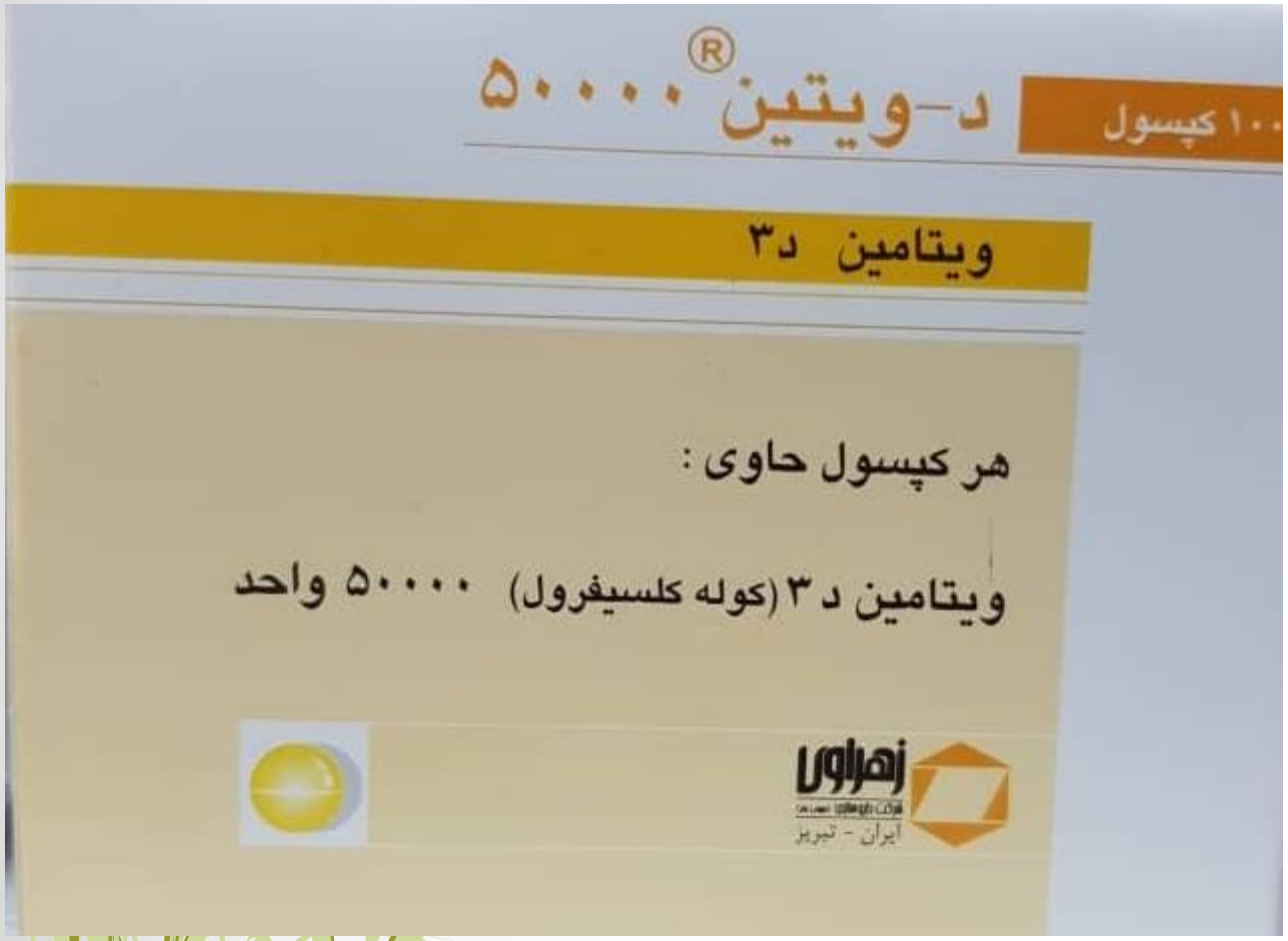
In a study 3 weeks of dipyridamole elevated P from 1.94 to 2.73. (balal M. et al, dipyridamole for renal phosphate leak..., Clin Nephrol 2005; 63:87)

Management-8

After transplantation

Increased PTH without hypercalcemia:

- If vit D <20 ng/ml: vit D3 (cholecalciferol) 800 -2000 U daily.
- If PTH persistently ⬆ despite normal vit D with CKD = calcitriol
- Subtotal PTX or cinacalcet not indicated to treat HPT in the absence of hypercalcemia.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مکمل رژیمی - غذایی
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ویتامین د۳
اطلاعات مکمل
مقدار مصرف: روزانه یک قرص
مقدار در هر قرص
ویتامین د۳ (بصورت کوله کلسیفرول) ۱۰۰۰ واحد بین المللی (۲۵ میکرو گرم)
فرآورده شرکت داروسازی حکیم (سهامی عام) تهران - ایران

Indications of parathyroidectomy

- Progressive elevation of parathyroid hormone (PTH) and alkaline phosphatase levels
- New metabolic bone disease, osteonecrosis, metastatic calcifcation,
- Severe symptoms of pruritus
- Proximal myopathy.
- Severe symptomatic hypercalcemia and persistent hypercalcemia in association with elevated PTH for longer than 6 to 12 months (4% to 10%).

Indications of parathyroidectomy

- The plasma calcium concentration > 12.5 mg/dl (3.1 mmol per liter) for more than 1 year, particularly if associated with a radiologic evidence of increased bone resorption.

- Persistent mild hypercalcemia: generally managed conservatively.

Transplantation Proceedings

Volume 49, Issue 1, January–February 2017, Pages 53-56

The Transplantation Science Symposium Asian Regional Meeting

Kidney transplantation

Incidence and Risk Factors of Persistent Hyperparathyroidism After Kidney Transplantation

K. Nakai [a, b], H. Fujii [a], T. Ishimura [c], M. Fujisawa [c], S. Nishi [a]

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https://doi.org/10.1016/j.transproceed.2016.10.011

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Incidence and risk factors of persistent hyperparathyroidism after kidney transplantation

86 kidney transplantation between 2008 and 2014.

Nine patients showed **persistent hyperparathyroidism**:

1) PTH levels > 65 pg/mL and calcium levels >10.5 mg/dL at 1 year
2) Parathyroidectomy after kidney transplantation; and
3) Reintroduction of cinacalcet after kidney transplantation.

These 9 patients had significantly **longer duration of dialysis** therapy (186 ± 74 mo vs 57 ± 78 mo) and more frequent **treatment with cinacalcet during dialysis** (89% vs 12%).

Incidence and risk factors of persistent hyperparathyroidism after kidney transplantation

In conclusion, dialysis vintage > 6 years, calcium phosphate products >55 $(mg/dL)^2$, and cinacalcet use before kidney transplantation are strong **predictors of persistent hyperparathyroidism.**

High-risk patients should be evaluated for parathyroid enlargement, and parathyroidectomy must be considered before kidney transplantation.

Official Journal of The Transplantation Society & International Liver Transplantation Society

Transplantation

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Total Parathyroidectomy with Autograft in Persistent Hyperparathyroidism After Renal Transplantation

Okada, Manabu[1,4]; Minami, Masato[2]; Futamura, Kenta[2]; Tsujita, Makoto[2]; Hiramitsu, Takahisa[1]; Goto, Norihiko[2]; Narumi, Shunji[1]; Watarai, Yoshihiko[1]; Ichimori, Toshihiro[1]; Tominaga, Yoshihiro[3]

Transplantation: July 2018 - Volume 102 - Issue - p S564
doi: 10.1097/01.tp.0000543431.25986.d1
P.188: PDF Only

Total Parathyroidectomy with Autograft in Persistent Hyperparathyroidism After Renal Transplantation

- **Retrospective study: 53** renal transplant with persistent HPT received total PTx-AT between January 2000 and May 2017.

- Total PTx-AT: persistent hypercalcemia (**calcium ≥ 11.**0 mg/dL) or **symptoms related to HPT**.
  11 (20.8%) patients receiving cinacalcet before surgery.

Total Parathyroidectomy with Autograft in Persistent Hyperparathyroidism After Renal Transplantation

- **Results:** significant decrease in serum calcium and PTH levels (11.3 mg/dL vs 9.0 mg/dL, P<0.001; 185 pg/mL vs 47.5 pg/mL, P<0.001), 1 year after surgery.

- Serum phosphorus and creatinine levels increased significantly (2.4 mg/dL vs 3.6 mg/dL, P<0.001; 1.16 mg/dL vs 1.20 mg/dL, P<0.001). **Hypercalcemia corrected** in 52 (**98.1%**) patients.
- **But persistent hypocalcemia** in 16 (**30.2%**) patients.

JASN Journal of the American Society of Nephrology

Clinical Research

Paricalcitol for Secondary Hyperparathyroidism in Renal Transplantation

Matias Trillini, Monica Cortinovis, Piero Ruggenenti, Jorge Reyes Loaeza, Karen Courville, Claudia Ferrer-Siles, Silvia Prandini, Flavio Gaspari, Antonio Cannata, Annalisa Perna, Eliana Gotti, Maria Rosa Caruso, Davide Martinetti, Giuseppe Remuzzi and Norberto Perico

JASN May 2015, 26 (5) 1205-1214; DOI: https://doi.org/10.1681/ASN.2013111185

Paricalcitol for Secondary Hyperparathyroidism in Renal Transplantation

Paricalcitol, a selective vitamin D receptor activator

- A single-center, prospective, randomized study
- 43 renal transplants with secondary hyperparathyroidism.
- Compared the effect of paricalcitol or nonparicalcitol therapy
- On serum PTH levels and proteinuria
- Dose: 1 μg/d for 3 months then uptitrated to 2 μg/d if tolerated,
- Duration: 6-month treatment

Paricalcitol for Secondary Hyperparathyroidism in Renal Transplantation

- Result: Serum PTH levels significantly declined on paricalcitol from 115.6 (94.8–152.0) to 63.3 (52.0–79.7) pg/ml (P<0.001) but not on nonparicalcitol therapy.
- Serum bone-specific alkaline phosphatase and osteocalcin decreased on paricalcitol therapy significantly (P<0.001.

- 24-hour proteinuria level decreased only on paricalcitol (P<0.05).
- L3 and L4 vertebral mineral bone density, assessed by dual-energy x-ray absorption, significantly improved with paricalcitol (P<0.05).

Paricalcitol for Secondary Hyperparathyroidism in Renal Transplantation

Overall:

- 6-month paricalcitol supplementation reduced parathyroid hormone levels and proteinuria,
- attenuated bone remodeling and mineral loss, and reduced eGFR in renal transplant recipients with secondary hyperparathyroidism.

Kidney & Blood Pressure Research

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1423-0143/15/0404-0386$39.50/0

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Original Paper

Long-term Outcomes of Parathyroidectomy in Kidney Transplant Recipients with Persistent Hyperparathyroidism

Po-Yu Tseng Wu-Chang Yang Chih-Yu Yang Der-Cherng Tarng

Division of Nephrology, Department of Medicine, Taipei Veterans General Hospital and School of Medicine, National Yang-Ming University, Taipei, Taiwan

Long-term Outcomes of Parathyroidectomy in Kidney Transplant Recipients

- the long-term effects of parathyroidectomy (PTX) on blood pressure (BP) and graft function in patients with persistent post-transplant HPT
- retrospective study
- 19 patients at the Taipei Veterans General Hospital
- Between 2004 and 2012

Long-term Outcomes of Parathyroidectomy in Kidney Transplant Recipients

- Systolic BP and PP reduced 2 years after PTX
- There was no significant difference between the peri-operative all-cause hospitalization rates.
- eGFR decreased significantly from 74.0 ± 20.5 mL/min/1.73m^2 preoperatively to 68.2 ± 24.8 mL/min/1.73 m^2 12 months after PTX but recovered at 15 months and lasted to 2 years after PTX.

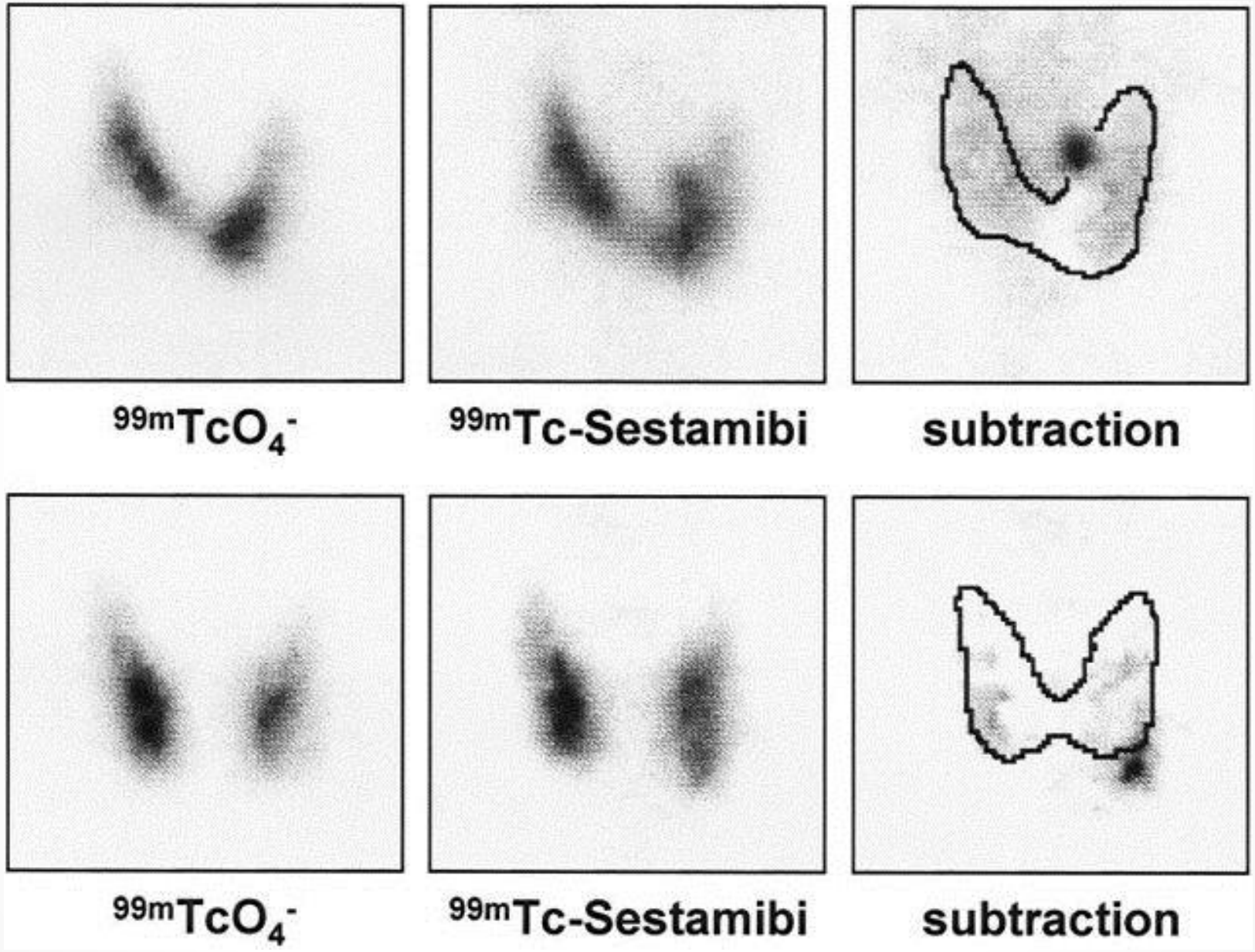
Summary-1

- Persistent HPT in 15-50 % following TX lasting more than 1 year
- HPT: degree of pretransplant HPT, duration of dialysis
- PTH> 65: increased mortality and allograft loss
- Before TX: Subtotal PTX: PTH>800, despite medical therapy
- Ca > 11 for more than 6 months = PTX

Summary-2

- Mild hypercalcemia and hyperparathyroidism (2-3 times)= cinacalcet
- Not respond to cinacalcet after 6-12 ms: all referred to subtotal PTX
- Severe hypophosphatemia (< 1 mg/dl) + HPT: PTX.

- Subtotal PTX or cinacalcet not indicated to treat HPT in the absence of hypercalcemia.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^{99m}Tc-Sestamibi
subtraction
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^{99m}Tc-Sestamibi
subtraction

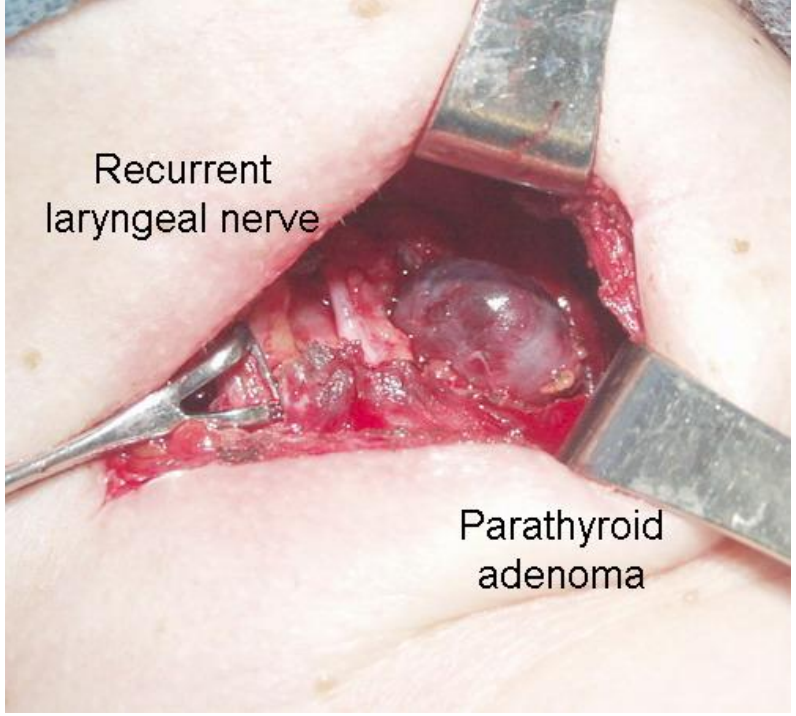

Figure 2 Excised ectopic parathyroid adenoma in a 65-year-old female.

Figure 3 – Implant in a single site.

Have a nice time and beautiful winter