

# Normocalcemic Primary Hyperparathroidism

Joe Hassin Cordero, MD, FACS  
Professor, Chairman  
Dept. of Otolaryngology – Head & Neck Surgery  
Texas Tech University Health Sciences Center

---

---

---

---

---

---

---

---

## Disclosure

- Nothing to disclose

---

---

---

---

---

---

---

---

## Objectives

---

---

---

---

---

---

---

---

### Primary Hyperparathyroidism (PHPT)

- Disorder of calcium, phosphate and bone metabolism due to increase in parathyroid hormone (PTH).
- Characterized by hypercalcemia and elevated iPTH.
- Isolated or familial syndrome.
- 80% of pts are asymptomatic or nonspecific symptoms.

---

---

---

---

---

---

---

---

### PHPT symptoms

- Due to hypercalcemia
- Anorexia, nausea, constipation, polydipsia, polyuria
- Bone loss and nephrolithiasis

---

---

---

---

---

---

---

---

### PHPT Management

- Surgery for adenoma or hyperplasia
- Improves health-related quality of life:
  - Bone density
  - Neurocognition
  - Reduction of fracture incidence and kidney stones

---

---

---

---

---

---

---

---

### Normocalcemic PHP (NCHPT)

- New clinical phenotype
- Normal total and ionized serum calcium + elevated iPTH
- In absent of secondary causes of HPT
- Unknown prevalence

---

---

---

---

---

---

---

---

### Pathophysiology

- Early or milder form of traditional PHPT
- Narrow range of normal serum calcium
- Hypersecretion of PTH less in normocalcemic
- Partial tissue resistance to PTH (Maruani et al, 2003)

---

---

---

---

---

---

---

---

### Diagnosis of NCHPT

- Elevation of iPTH on at least two occasions 3-6 months
- Normal albumin-adjusted and ionized calcium
- Must rule out secondary causes of elevated PTH

---

---

---

---

---

---

---

---

### Secondary Causes of Elevated iPTH

- Vitamin D deficiency (<30 ng/ml)
- Stage 3-5 chronic kidney disease
  - eGRF < 60 mL/min
- Medications
  - Loops diuretics
  - Thiazides
  - Lithium
  - Bisphosphonates or denosumab
- Hypercalciuria
- Calcium deficiency or malabsorption

---

---

---

---

---

---

---

---

### Epidemiology

- Prevalence ranges 0.4 to 8.9% depending on population studied and criteria used for exclusion of 2<sup>nd</sup> causes of hyperparathyroidism

---

---

---

---

---

---

---

---

### Clinical Features

- High rates of osteoporosis, fracture and nephrolithiasis
- No adverse cardiovascular outcomes

---

---

---

---

---

---

---

---

### Sequelae of Disease

- Bone Disease
  - Common to have low T-score at one site
  - Typically not at cortical bone site as in PHPT
  - One report of fragility fractures in 11% of patients
- Kidney
  - 9-35% reported incidence of nephrolithiasis

---

---

---

---

---

---

---

---

### Management

- No data regarding optimal treatment strategies
- Guidelines available from the **Fourth International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism** (J Clin Endocrine Metabol 2014)
  - Surgery considered if complications of disease, ie fractures/stones
  - Monitor those without complications with yearly total/ionized calcium and iPTH and bone density 1-2 yrs. If worsening, surgery considered.

---

---

---

---

---

---

---

---

Consensus Statement

### Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Fourth International Workshop

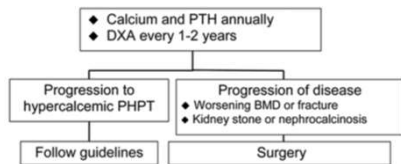


Figure 1. Algorithm for monitoring patients with normocalcemic PHPT.

---

---

---

---

---

---

---

---

### Medical Management

- **Alendronate** improvement in bone density in PHPT (Khan et al, 2004) and NCHPT (Cesareo et al, 2014)
- N = 30, NCHPT and osteoporosis, females
  - alendronate 70 mg + Vit D 2800 intl units wkl vs. Vit D alone x 1 yr
  - Alendronate group = improvement in bone densities at lumbar + hip
  - Vit D = ongoing declines

---

---

---

---

---

---

---

---

### Medical Management

- **Cinacalcet** (Brardi et al, 2015) reduced number and diameter of kidney stones in PHPT and NCHPT over 10 months therapy

---

---

---

---

---

---

---

---

### Localization

- Less likely to localize in NPHPT
- Sestamibi imaging: 14% localized during normocalcemic period, 73% adenomas found after patient became hypercalcemic (Siprova, et al. 2016).
- 4-D CT best: 56% vs 75%, US 22% vs 58%, scintigraphy 11% vs. 75% (Cunha-Bezerra, et al. 2018)
- Multiglandular: sestamibi – 57% in NCHPT, 72% in PHPT (Traini, et al, 2018)

---

---

---

---

---

---

---

---

### Multiglandular Disease

- Kiriakopoulos, et al, 2018
  - N = 154
  - PHPT, 115: 16.5%
  - High Calcium, normal PTH, 11: 9.1%
  - NCHPT, 23: 21.7%
- Lim, et al, 2018
  - N = 573
  - PHPT, 405: 9%
  - Normohormonal, 96: 10%
  - NCHPT, 72: 45%
- NCHPT 8X to have multiglandular disease

---

---

---

---

---

---

---

---

### Surgical Intervention

- Consider when clinical symptoms
- Use ionized calcium (< 1.35 mmol/L)
- Consider two preoperative imaging studies
- If discordant or negative = bilateral exploration with intraoperative PTH (IOPTH)
- IOPTH drawn in preop, t0, t5, t10 and t20
- Identify additional glands if not drop by >50%

---

---

---

---

---

---

---

---

### What to Expect with NCHPT (Tufano, et al, 2018)

- Baseline IOPTH significant lower in NCHPT than PHPT
- Higher rate to intraop conversion to bilateral exploration
- Weight of gland less
- Hyperplasia had the slowest rate of IOPTH decline

---

---

---

---

---

---

---

---

### Technical Challenges

- Cure determined by postop PTH levels
  - Use intraop PTH
- Frequently multigland disease
  - 45% multigland
  - Vs 10% in normohormonal HPT Vs 8% in PHPT
- Typically smaller adenomas when present

---

---

---

---

---

---

---

---

### Conclusions

---

---

---

---

---

---

---

---

Galileo Galilei

• "You can't teach anybody anything, only make them realize the answers are already inside them."

---

---

---

---

---

---

---

---





---

---

---

---

---

---

---

---