

Management of Parathyroid Adenoma: A Case of the Missing Parathyroid

M&M 8/23/2012

Long Island College Hospital

Verena Liu, MD

Case Report

- 61 F referred for primary hyperparathyroidism with hypercalcemia and elevated PTH, otherwise asymptomatic
- PMH- osteopenia, seasonal allergies
- PSH- none
- Meds- vitamin D, singulair PRN
- All- Sulfa
- PE-
 - NAD
 - Trachea midline, no neck masses palpable
 - Clear to auscultation b/l
 - Abdomen soft, nontender
 - Extremities warm, normal motor and sensory function

Case Report

- Labs: Ca²⁺ - 11.1 mg/dL (normal: 8.5 to 10.2 mg/dL)
PTH - 127 pg/mL (normal: 10 to 72 pg/mL)
- Sestamibi scan: small parathyroid adenoma next to inferior pole of right thyroid

Case Report

- Operation: Bilateral paratracheal exploration with right thyroid lobectomy and parathyroidectomy with intraoperative PTH monitoring
 - After extensive right cervical exploration including posterior to the trachea and the thyroid, as well as along the carotid sheath and in the tracheoesophageal groove, no parathyroid adenoma was identified
 - Tissue resembling a parathyroid was removed from the right lower paratracheal area, but was found to be a lymph node and normal parathyroid on frozen section. PTH did not drop after removal.
 - The superior right parathyroid was identified and protected

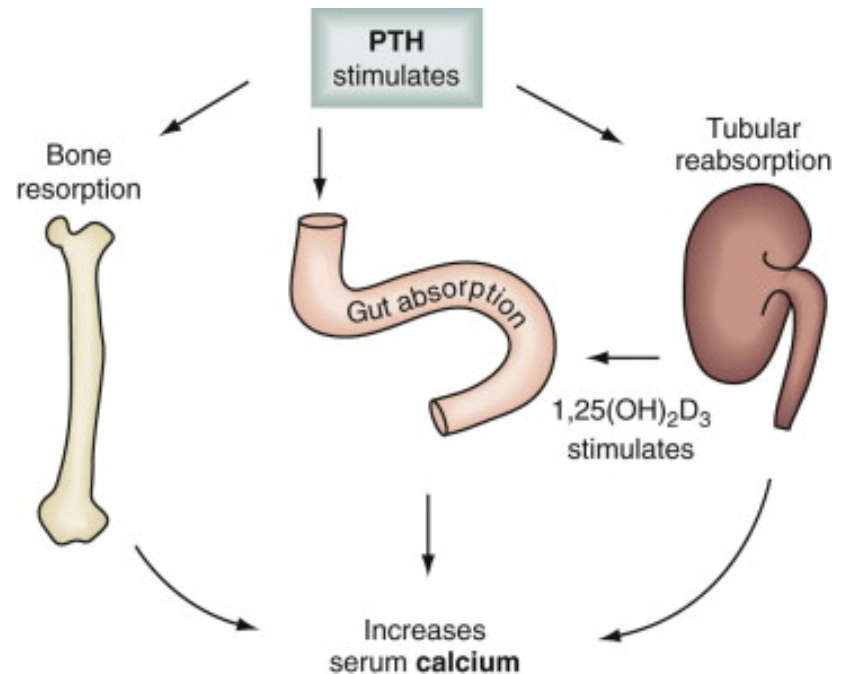
Case Report

- Left cervical exploration also did not yield any parathyroid adenoma, a normal appearing superior and inferior gland were identified
- Right thyroid lobectomy was performed
- Ectopic parathyroid adenoma was then identified in a retroesophageal superior mediastinal position and removed
- PTH dropped from 143 after anesthesia induction to 7 eight minutes after removal of the specimen
- Incision was closed, pathology confirmed parathyroid adenoma 2x0.8x0.8 cm (270 g)

Hyperparathyroidism: Pathophysiology

Hypersecretion of PTH, leading to Hypercalcemia:

- Classic pentad:
 - kidney stones, painful bones, abdominal groans, psychic moans, and fatigue overtones
- Nonspecific symptoms:
 - Bone pain, osteopenia/osteoporosis
 - Constipation
 - Pruritus
 - Decreased appetite, nausea, heartburn
 - Urinary frequency, incontinence
 - Muscle weakness, joint pain
 - Fatigue, lethargy, depression
- Truly asymptomatic patients are rare < 5%





Hyperparathyroidism: Classification

Primary Hyperparathyroidism:

- Adenoma 80%
- Double Adenoma 5-10%
- Four-Gland Hyperplasia 5-10%
- Parathyroid carcinoma 1%

Secondary and tertiary Hyperparathyroidism:

- Chronic hypocalcemia, which stimulates PTH secretion and parathyroid hyperplasia due to renal failure and other malabsorptive or metabolic disorders
- Autonomous hyperfunction can develop after long-standing secondary HPT/transplantation



Primary Hyperparathyroidism: Diagnosis

Patient Laboratory Values	Diagnosis of Primary Hyperparathyroidism?
Serum calcium = 11.0 mg/dL Intact PTH = 92 pg/mL	Yes, classic disease
Serum calcium = 11.2 mg/dL Intact PTH = 49 pg/mL	Yes, mild disease
Serum calcium = 9.9 mg/dL Intact PTH = 81 pg/mL	Probably mild disease, but rule out vitamin D deficiency

Normal serum calcium = 8.5 to 10.2 mg/dL; normal intact PTH = 10 to 72 pg/mL.



Primary Hyperparathyroidism: Indication for Parathyroidectomy

Criteria for surgical referral and parathyroidectomy:

- All symptomatic patients
- All asymptomatic patients with any of the following:
 - Serum calcium concentration >1 mg/dL (>0.25 mM/liter) above the upper limits of normal
 - Bone density at the lumbar spine, hip, or distal end of the radius that is >2 SD below peak bone mass (T-score <-2.5)
 - All individuals with primary hyperparathyroidism and <50 yr
 - Patients for whom medical surveillance is undesirable or impossible
- *In retrospective study of 3388 patients, only 40% of those meeting criteria were treated with parathyroidectomy*

Bilezikian et al: Guidelines for the management of asymptomatic primary hyperparathyroidism: summary statement from the third international workshop. J Clin Endocrinol Metab 94:335–339, 2009.

Yeh et al: Surgery for Primary Hyperparathyroidism: Are the Consensus Guidelines being followed? Ann Surg 255(6):1179-83, 2012

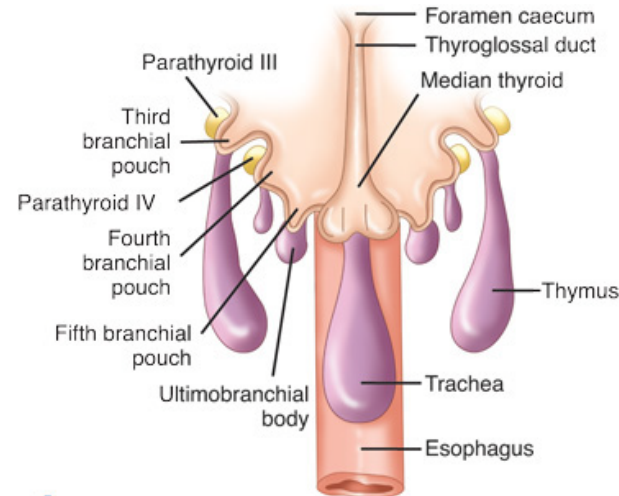
Primary Hyperparathyroidism: Benefits of Surgical Management

Benefits from surgical management of primary HPT:

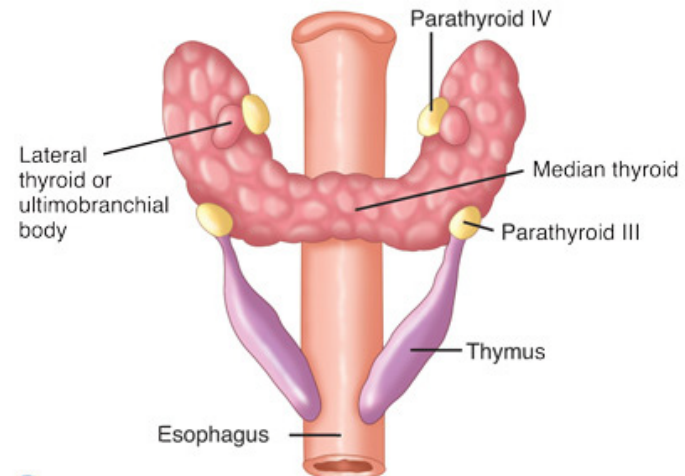
- Renal function and bone density improvement
- Resolution of neuropsychiatric symptoms
- Quality of life better
- Prolongs survival (10% reduction if untreated)
- Reduction in cardiovascular incidents
- Low complication rates
- Cost of parathyroidectomy at 5 years is less than the cost of surveillance

Parathyroid: Embryology

- Lower parathyroids are derived from the 3rd branchial pouch and migrate with the thymus
- Upper parathyroids are derived from the 4th branchial pouch and lie in close proximity to the ultimobranial bodies



A



B

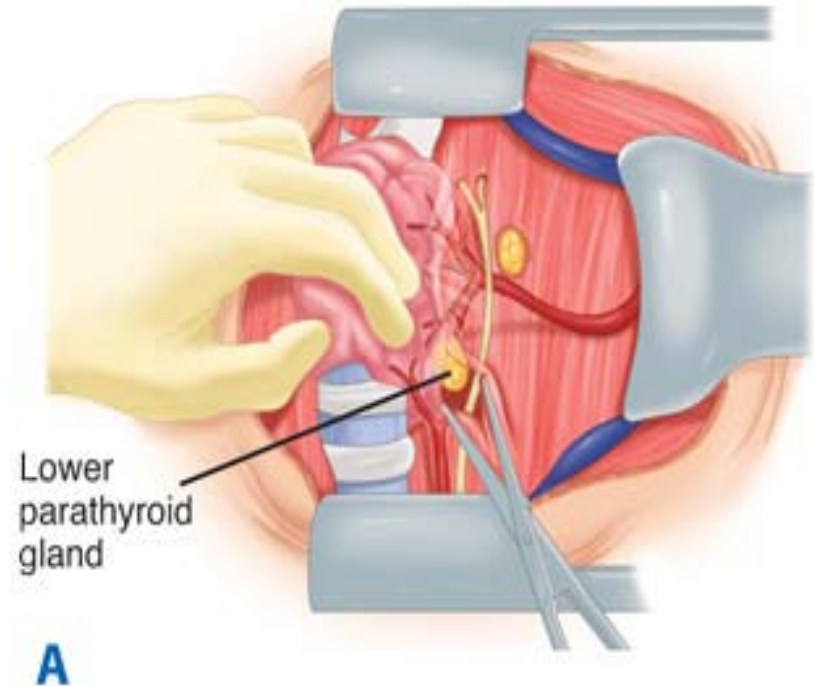
A- 8- to 10-mm embryo

B- 13- to 14-mm embryo

Parathyroid Anatomy

Anatomical Locations:

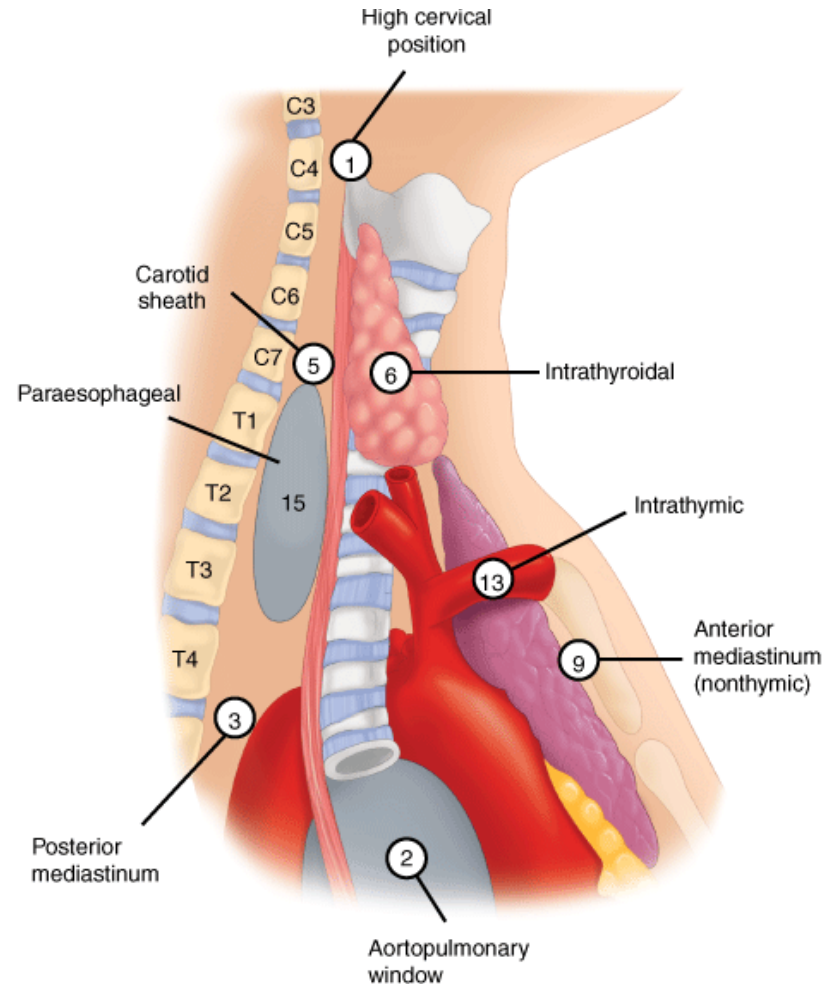
- Superior Glands:
posteromedial aspect of the thyroid, above junction of inferior thyroid artery and recurrent laryngeal nerve
- Inferior Glands:
posteriolateral aspect of the lower thyroid pole, below the inferior thyroid artery



Parathyroid Anatomy

Ectopic Locations (5-15%):

- Thyrothymic ligament
- Tracheoesophageal groove
- Retroesophageal space
- Retropharyngeal/high cervical
- Carotid sheath
- Intrathyroid
- Ant/post superior mediastinum
- Retropharyngeal
- Intrathymic
- Aorto-pulmonary window



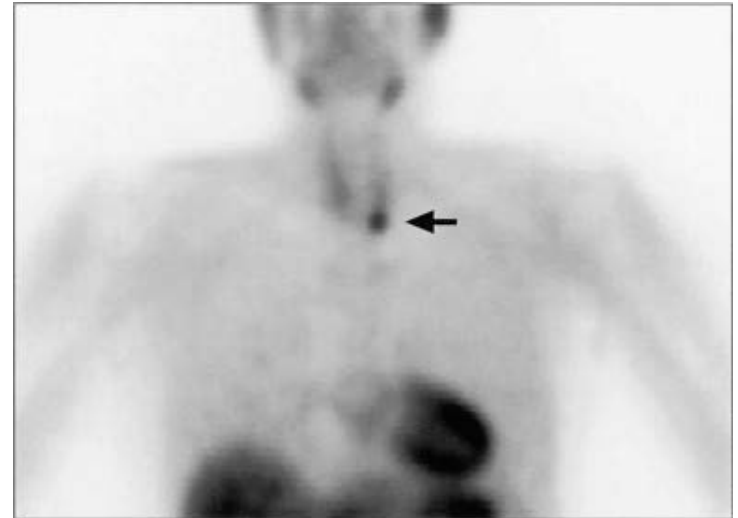
Preoperative Imaging

IMAGING MODALITY	SENSITIVITY	SPECIFICITY	COST	SAFETY
Noninvasive				
Sestamibi	Moderate	Moderate	Moderate	Safe
Sestamibi SPECT	High	High	Moderate	Safe
Ultrasound	Moderate	Moderate	Low	Safe
4D-CT	High	High	High	Radiation
MRI	Low	Moderate	Moderate	Safe
Invasive				
Angiography	Moderate	Moderate	Very high	Hematoma, CVA, nephropathy*
Venous localization	High	High	Very high	Hematoma, nephropathy*
Ultrasound, biopsy	High	High	Moderate	Hematoma, infection



Preoperative Imaging: Sestamibi Scan

- Intravenous injection of 25mCi of ^{99m}Tc
- AP and oblique views of thorax and neck with gamma camera immediately after injection and at 1h and 4h or SPECT (single photon emission computed tomography)
- Limitations with coexistence of thyroid pathology or other metabolically active tissue can be overcome with double-tracer subtraction technique



Preoperative Imaging: Ultrasound

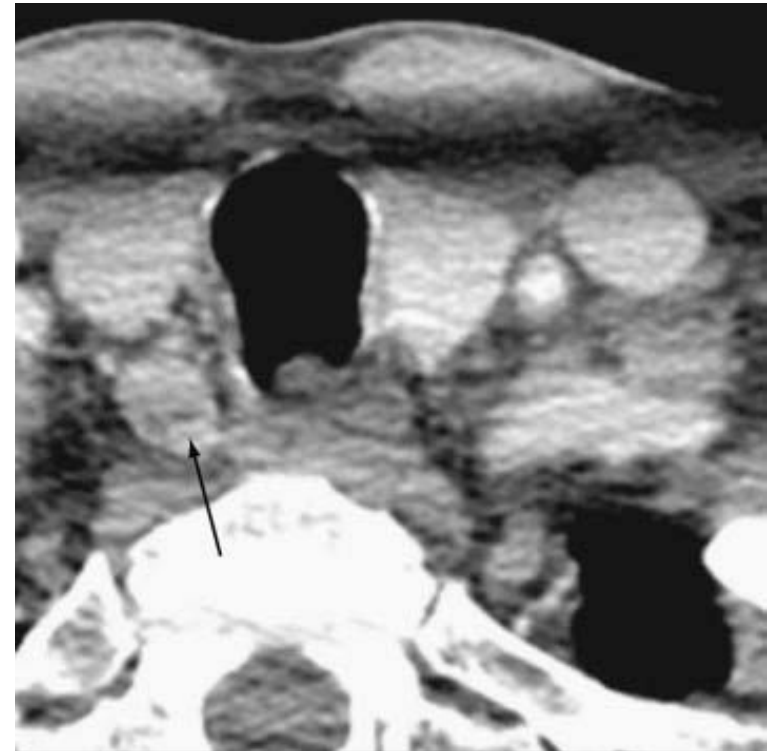
- Effective, noninvasive and inexpensive
- Limitations are operator dependent, restriction to lesions in the neck
- Often combined with sestamibi





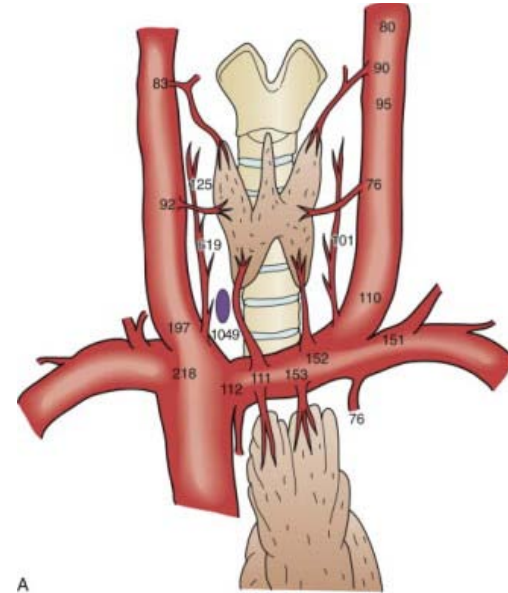
Preoperative Imaging: CT

- Higher sensitivity than ultrasound, but involves radiation
- 4D-CT is derived from 3D CT scanning, with added dimension from changes in perfusion of contrast over time, which allows to characterize hyperfunctioning parathyroid glands



Preoperative Imaging: Venous Sampling

- Selective arteriography in conjunction with venous sampling for PTH
- Requires catheterization of multiple veins in the neck and mediastinum, from which blood samples are obtained with rapid PTH measurement in angio suite
- Parathyroid adenomas have increased vascularity, demonstrating a characteristic blush on arteriography
- Indicated for patients requiring re-exploration with negative or discordant imaging studies





Parathyroidectomy

Bilateral Neck exploration

- 4 gland exploration, removal of enlarged parathyroid
- Intraoperative, histopathologic frozen section examination of excised parathyroid tissue
- Complication rate 1-3%
- Cure rate 95-99%

Classic approach, now used when:

- 4 gland hyperplasia is suspected
- Family history of MEN1, MEN2A, PHPT
- Concomitant thyroid disorder
- Parathyroid localization studies are negative
- ioPTH does not fall after unilateral exploration

Focused Parathyroidectomy (Minimally-Invasive Parathyroidectomy)

- Preoperative localization
- Unilateral exploration
- Intraoperative PTH monitoring
- Local/ regional anesthesia
- Ambulatory surgery
- Complication rate 1.2%
- Cure rate 93-99%

Widely used when positive localization available, patients with sporadic PHPT

www.downstatesurgery.org

Bilateral Exploration vs Focused Parathyroidectomy

- Most studies show equal results in terms of complications, operative failure and cure rate, but large prospective trials with long-term follow-up are lacking
- RCT with 5-year follow-up comparing unilateral vs. bilateral neck exploration did not note any difference in the rates of recurrent or persistent disease in the two groups of patients

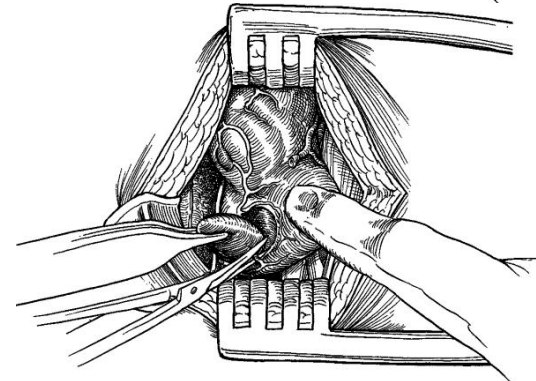
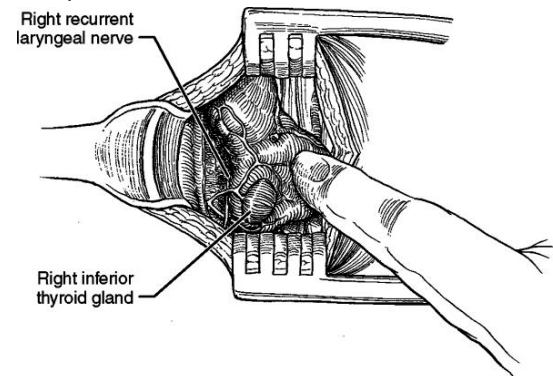
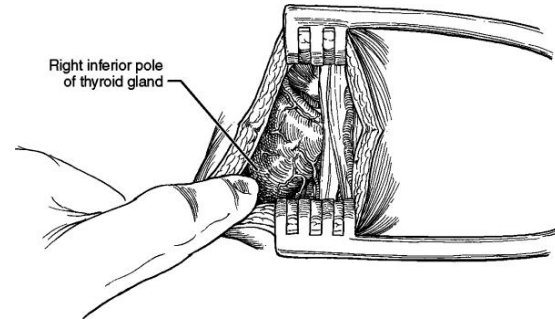
TABLE 1. Biochemical Data 1 Year and 5 Years after Surgery for Primary Hyperparathyroidism

Variable	1-Year Follow-up					5-Year Follow-up				
	Unilateral Group (n = 45)		Bilateral Group (n = 43)		P	Unilateral Group (n = 38)		Bilateral Group (n = 33)		P
Serum ionized calcium (mmol/L)	1.22	1.11–1.55	1.20	1.05–1.39	0.13	1.23	1.10–1.39	1.23	1.11–1.38	0.54
Serum PTH (pmol/L)	4.2	1.4–14.0	4.6	0.7–7.2	0.90	4.6	2.3–12.0	5.3	2.1–12.0	0.36
Serum phosphate (mmol/L)	1.04	0.69–1.39	1.09	0.67–1.43	0.29	1.08	0.84–1.53	1.07	0.75–1.56	0.51
Serum creatinine (μmol/L)	72	29–209	72	48–174	0.51	72	45–149	74	40–424	0.56
GFR (mL/min)	68	25–117	77	25–120	0.65	*	*	*	*	*
Serum alkaline phosphatase (μkat/L)	3.2	1.1–5.8	2.9	1.6–6.4	0.65	*	*	*	*	*
25 (OH) vitamin D ₃ (nmol/L)	39	13–91	47	10–140	0.33	*	*	*	*	*
1.25 (OH) ₂ vitamin D ₃ (pmol/L)	47	19–240	52	12–116	0.24	*	*	*	*	*

*Data are not available for 5 years after surgery.

Focused Parathyroidectomy

- 2-4 cm transverse incision just below cricoid cartilage, division of platysma +/- flaps, strap muscles divided in midline
- Identification and mobilization of thyroid pole according to preop localization
- Dissection of parathyroid adenoma, control of blood supply
- ioPTH monitoring to confirm removal of hyperfunctioning adenoma
- Closure in layers



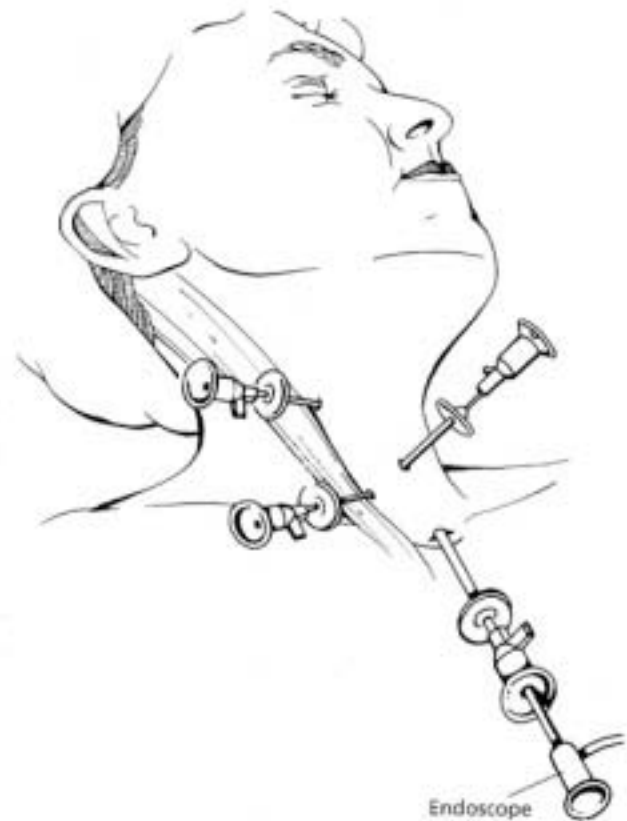


www.downstatesurgery.org

Focused Parathyroidectomy: Other Techniques

Video-Assisted Parathyroidectomy and Endoscopic Parathyroidectomy

- Creation of working space in the neck with CO₂ insufflation (5-8 mmHg)
- Variable port placement
- Operative space created between platysma and strap muscles
- Increased operative time and expenses
- Small amount of blood often diminishes view
- Metabolic derangements due to absorption of CO₂
- Greatest use for thoracoscopic resection of mediastinal parathyroid adenomas

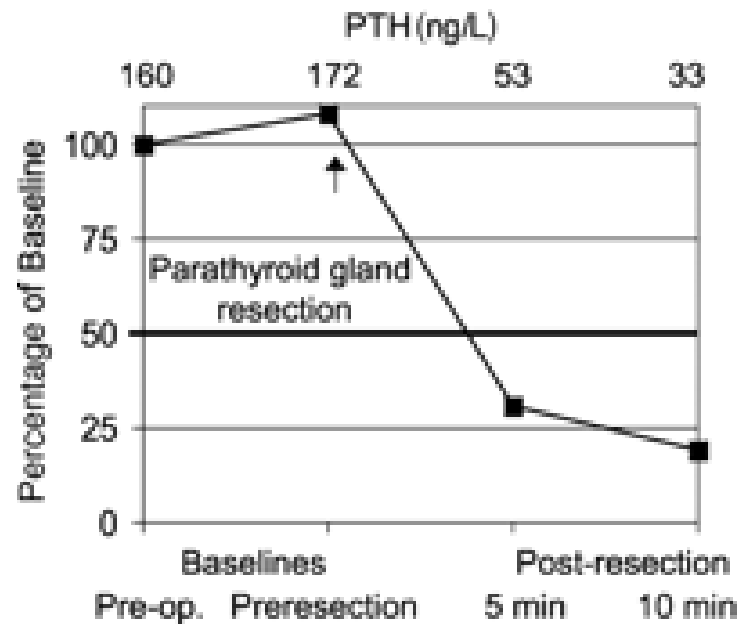




Intraoperative Monitoring: PTH

Rapid PTH assay:

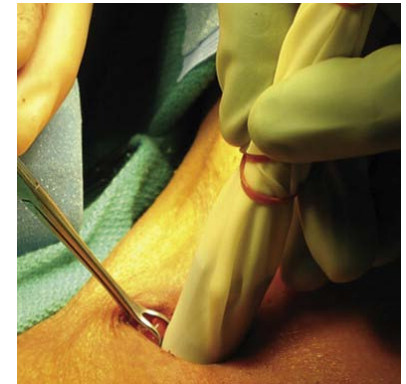
- PTH level is sent before induction of anesthesia, at resection of adenoma and 5 and 10 minutes after resection of adenoma
- 50% reduction at 10 minutes compared to original level confirms removal of parathyroid adenoma



Intraoperative Monitoring: Gamma Probe

Radioguided parathyroidectomy:

- Injection of sestamibi 1-4h prior to procedure
- Background count by scanning the thyroid isthmus with the γ -probe
- Resected parathyroid tissue is placed on the probe for an ex vivo count
- Ratio of ex vivo to in vivo background counts is $> 20\%$ confirms hyperfunctioning parathyroid tissue
- Not widely used because yields little additional information over that obtained by adequate preoperative localization and the intraoperative PTH assay

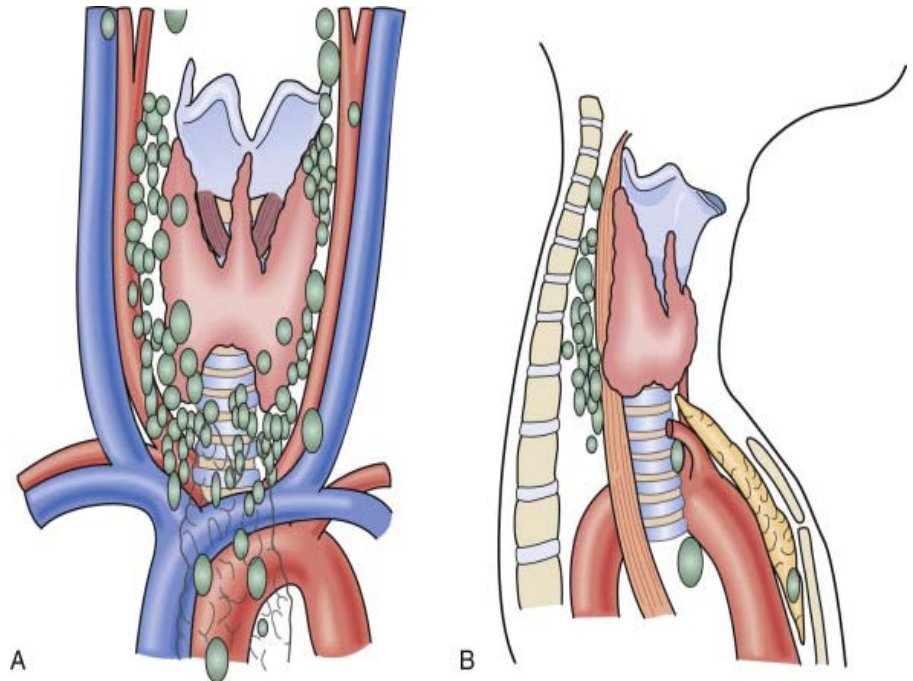


Steps to Find a Missing Parathyroid

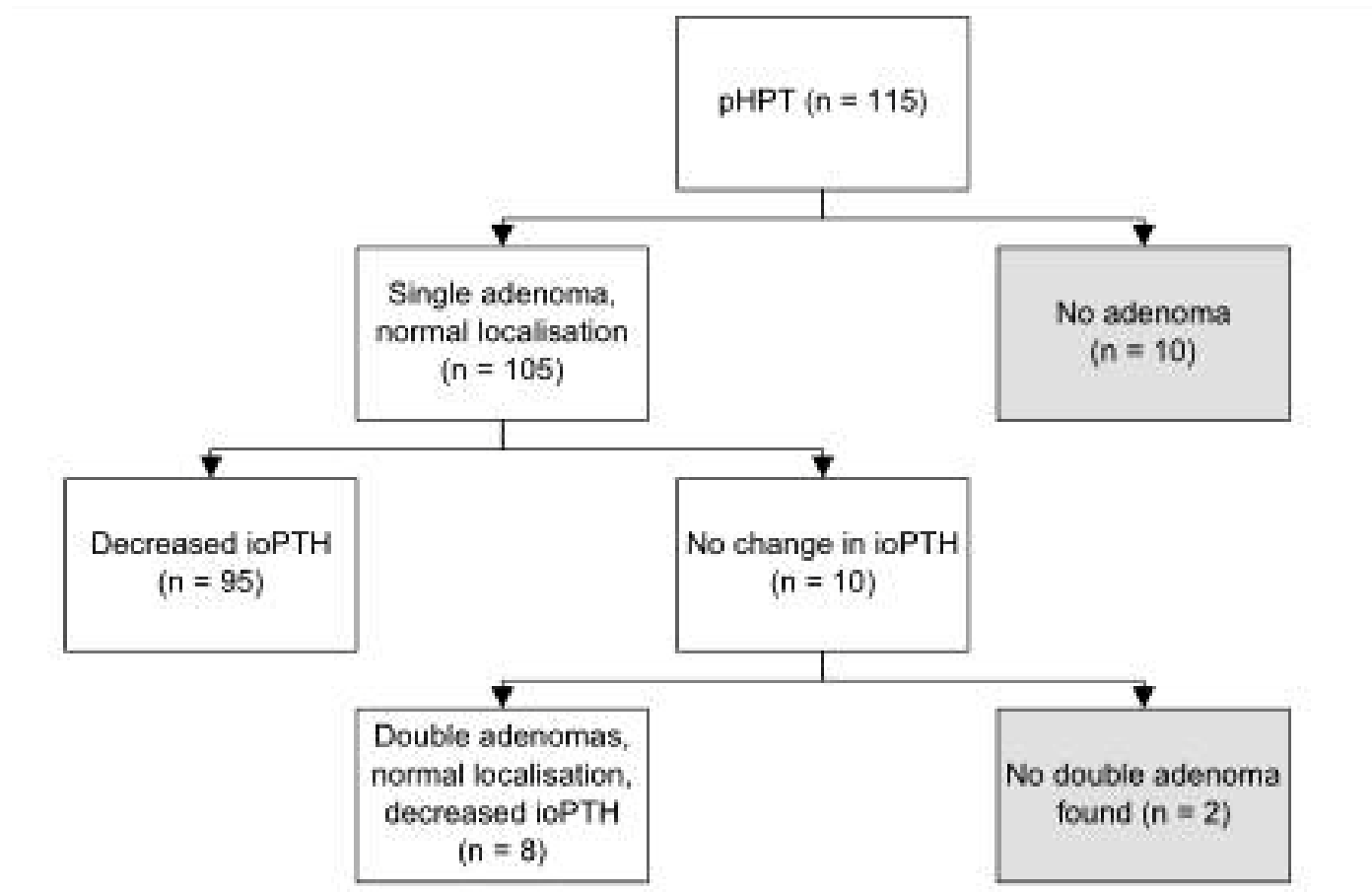
Retrospective analysis of 115 patients (2003-2005):

Operative strategy:

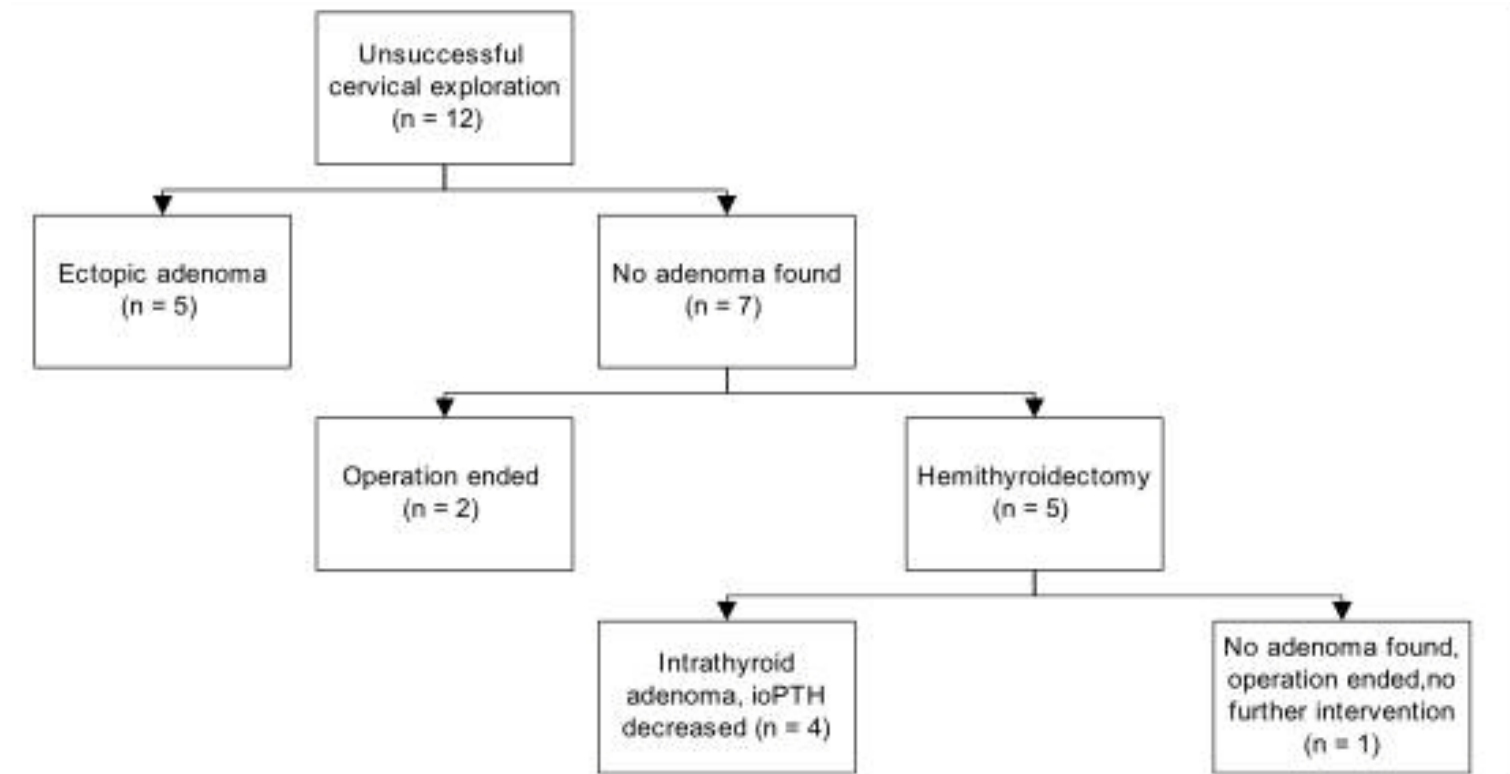
- Systematic perithyroid exploration, PTH monitoring
- Extended cervical exploration: bilateral exploration along thyrothymic ligament, esophagotracheal sulcus, carotid sheath, retropharyngeal/esophageal region, cranial ventral and dorsal mediastinum
- Hemithyroidectomy: on the side with higher suspicion/preop localization



Steps to Find a Missing Parathyroid

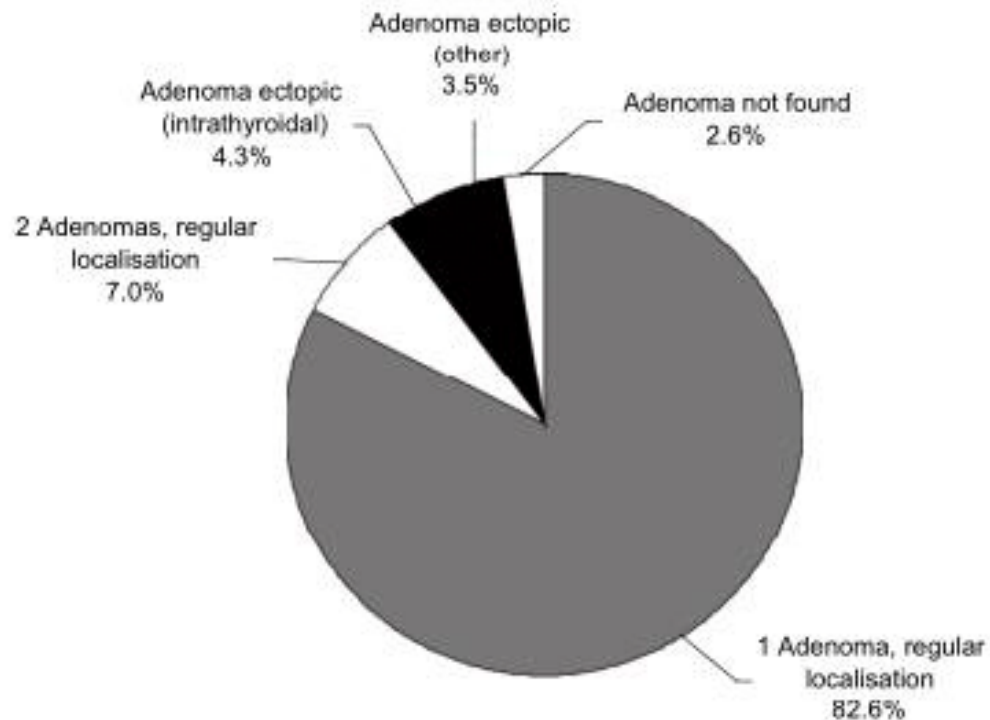


Steps to Find a Missing Parathyroid



Herden et al: Intrathyroid adenomas in primary hyperparathyroidism: are they frequent enough to guide surgical strategy? Surg Innov. 18(4):373-8. 2011

Steps to find a missing Parathyroid



Herden et al: Intrathyroid adenomas in primary hyperparathyroidism: are they frequent enough to guide surgical strategy? Surg Innov. 18(4):373-8. 2011



Other Steps to Find a Missing Parathyroid

- Perform bilateral internal jugular venous sampling for PTH
- Perform a cervical thymectomy
- Open the carotid sheath
- Search for an undescended gland, occasionally found in undescended thymic tissue
- Perform intraoperative ultrasound of the thyroid gland
- Sternotomy is not recommended during initial exploration
- If the gland cannot be found, terminate the operation, leaving normal parathyroid gland intact



Summary

- Patients with symptomatic and asymptomatic primary hyperparathyroidism benefit from parathyroidectomy
- After biochemical diagnosis of HPT, technique of choice for PHPT due to parathyroid adenoma is focused parathyroidectomy with preoperative localization (sestamibi scan most widely used) and intraoperative PTH monitoring
- Drop of ioPTH to under 50% of preop value 10 minutes after resection confirms resection of hyperfunctioning parathyroid adenoma
- If adenoma cannot be found and/or ioPTH does not drop appropriately, bilateral extended cervical exploration and if needed hemithyroidectomy on the side of localization should ensue (10-15% of parathyroid adenomas are ectopic, 5-10% double adenoma)
- If adenoma still cannot be found after extended cervical exploration and hemithyroidectomy, the procedure should be aborted and further localization studies performed

References

- Townsend: Sabiston Textbook of Surgery, 19th ed.: Chapter 39 – The Parathyroid Glands
- Cameron: Current Surgical Therapy, 10th ed.: Primary Hyperparathyroidism
- Townsend: Atlas of General Surgical Techniques, 1st ed.: Chapter 3 – Parathyroidectomy
- Schwartz's Principles of Surgery, 9e: Chapter 38. Thyroid, Parathyroid, and Adrenal
- Westerdahl et al: Unilateral vs Bilateral Neck Exploration for Primary Hyperparathyroidism. Ann Surg. 2007;246(6):976-81
- Herden et al: Intrathyroid adenomas in primary hyperparathyroidism: are they frequent enough to guide surgical strategy? Surg Innov. 18(4):373-8. 2011
- Bilezikian JP, Potts JT Jr, Fuleihan GH, et al. Summary statement from a workshop on asymptomatic primary hyperparathyroidism: a perspective for the 21st century. J Clin Endocrinol Metab 2002;87(12):5353-5361.
- Yeh et al: Surgery for Primary Hyperparathyroidism: Are the Consensus Guidelines being followed ? Ann Surg 255(6):1179-83, 2012
- From Wang C-A. A clinical and pathological study of 112 cases. Ann Surg 1977;186:140-145.)

Questions

A 47 year old female develops symptoms of hypercalcemia and further workup demonstrates her to have primary hyperparathyroidism. What is the most likely etiology of her disease?

- ☒ A- single adenoma
- ☐ B- double adenoma
- ☐ C- hyperplasia
- ☐ D- carcinoma

Questions

A 45 year old female without history of previous hospitalization or significant medical history presents to her primary care physician with complaints of headache, lethargy and constipation. EKG shows shortended QT interval and a widened T wave. Which of the following is the most likely etiology of her disease?

A- vitamin D toxicity

B- malignancy

☒ C- primary hyperparathyroidism

D- sarcoidosis

E- secondary hyperparathyroidism

Questions

A 55 year old woman with primary hyperparathyroidism is noted to have an asymptomatic kidney stone on an abdominal radiograph. What is the next step in management?

- A- cystoscopy
- B- serum oxalate measurement
- ☒ C- parathyroid localization studies
- D- bilateral neck exploration
- E- observation

Questions

Surgical exploration for a patient with primary hyperparathyroidism reveals all 4 glands to be enlarged. What is the most appropriate way to manage this?

- A- closure with localization study
- B- incisional biopsy of all glands
- ☒ C- subtotal parathyroidectomy
- D- excision of the largest enlarged gland
- E- selective venous PTH sampling