Parathyroid Diseases

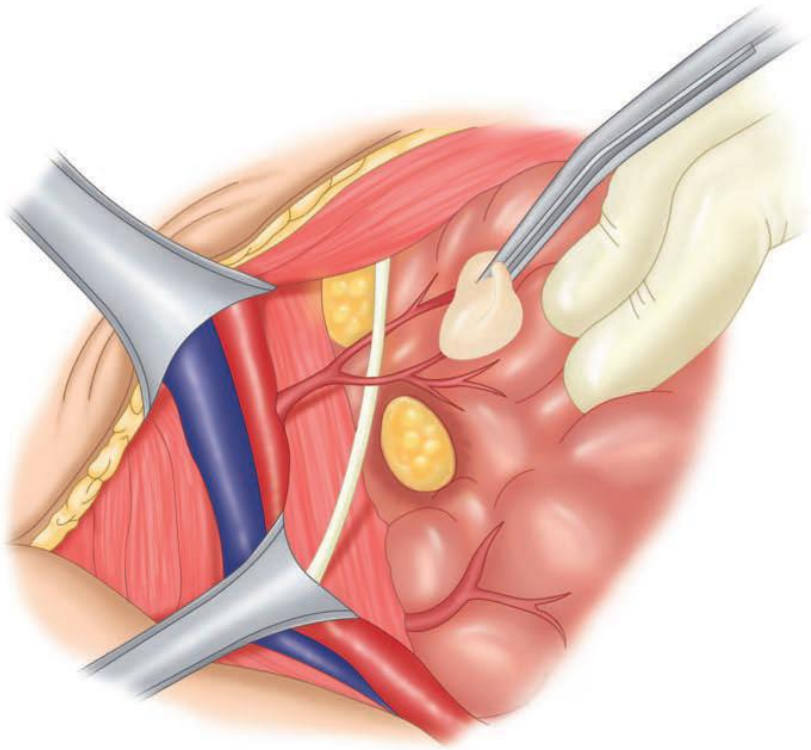
DR. ALI JAD ABDELWAHAB

Embryology and Surgical Anatomy

- Four parathyroid glands develop from the 3rd and 4th pharyngeal pouches between the 5th and 12 weeks of gestation
- Yellow brown in color
- Wt. 30 mg
- 5% supernumerary

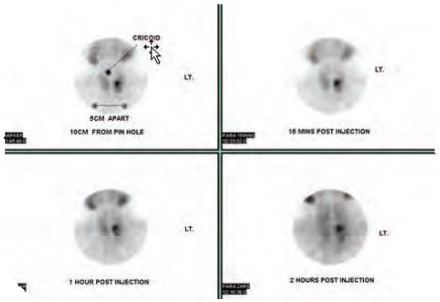
- The blood supply of both the superior and inferior parathyroid glands arises from the **inferior thyroid artery**
- The inferior parathyroid gland and the thymus arise from the third pharyngeal pouch: More variation in position
- The superior parathyroid glands arise from the dorsal portion of the fourth pharyngeal pouch.

Relation to RLN

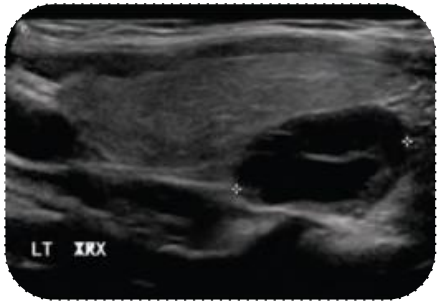


- 80% of patients
- S. parathyroid glands are at the posterior aspect of the thyroid lobe in an area 2 cm in diameter, centered 1 cm around the junction of the inferior thyroid artery and the recurrent laryngeal nerve in strict proximity to the cricothyroid junction

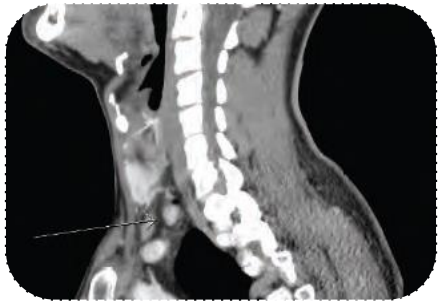
Localization Studies



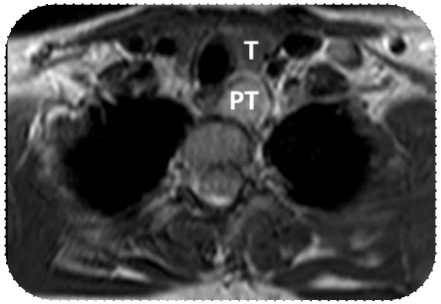
Nuclear medicine-based studies (sestamibi scanning)



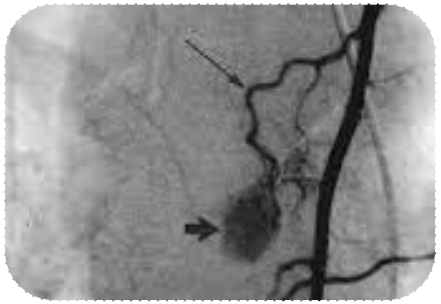
Ultrasonography



4D-CT



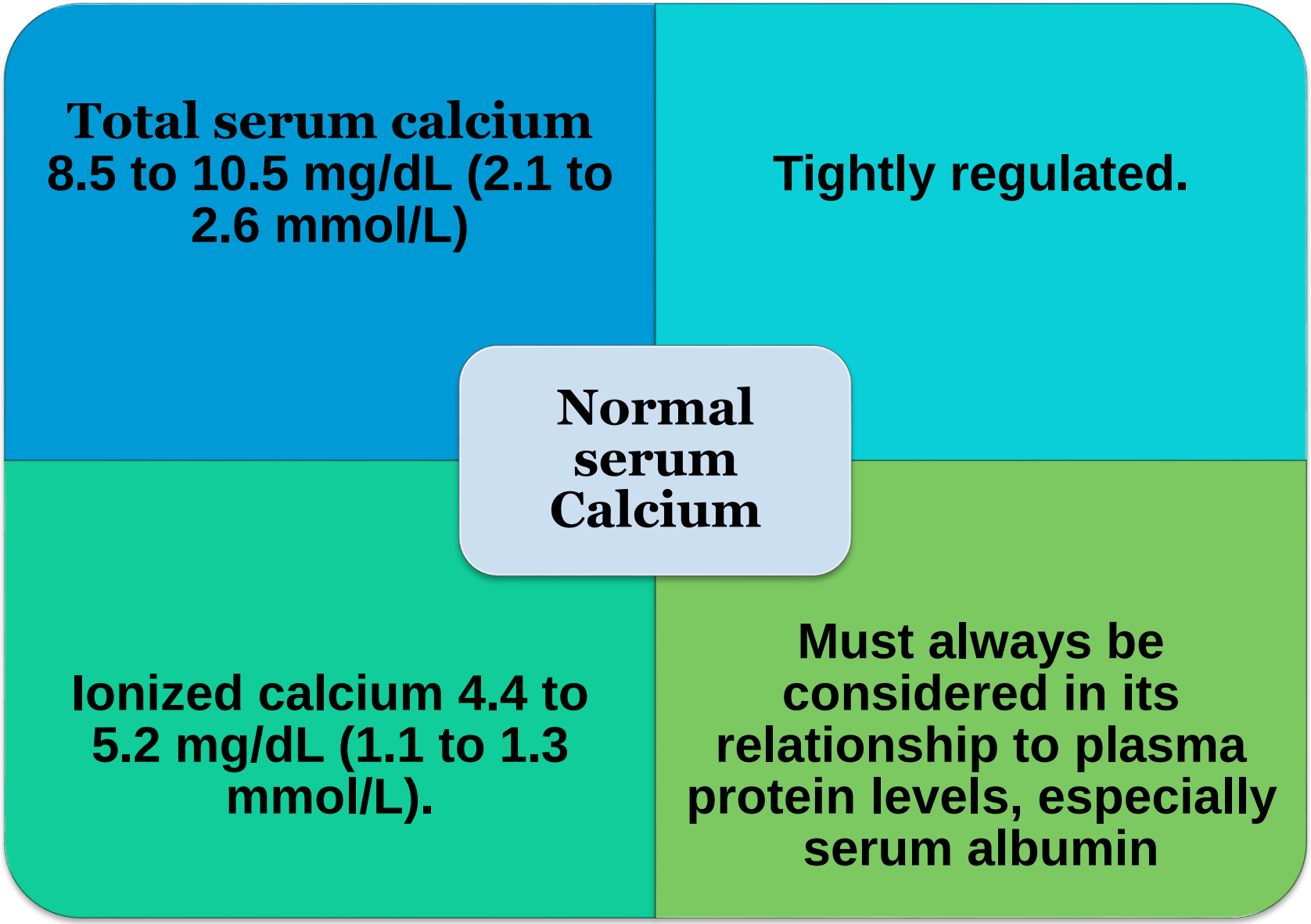
MRI



Parathyroid angiography and venous sampling for PTH

Hypercalcemia

CALCIUM IS THE MOST ABUNDANT CATION IN HUMAN BEINGS


Total serum calcium 8.5 to 10.5 mg/dL (2.1 to 2.6 mmol/L)
Tightly regulated.
Normal serum Calcium
Ionized calcium 4.4 to 5.2 mg/dL (1.1 to 1.3 mmol/L).
Must always be considered in its relationship to plasma protein levels, especially serum albumin

D.Dx of Hypercalcemia

- Primary hyperparathyroidism
- Tertiary hyperparathyroidism
- Familial hypercalcemic hypocalciuria
- Lithium therapy
- Paraneoplastic syndrome (humoral hypercalcemia of malignancy)
- Osteolytic metastases
- Multiple myeloma
- Drug-induced hypercalcemia
- Granulomatous disease
- Hypervitaminosis D
- Milk-alkali syndrome
- Nonparathyroid endocrine disease
- Immobilization
- Idiopathic

Primary Hyperparathyroidism (PHPT)

- **Occurs in 0.1% to 0.3% of the general population**
- **More common in women (1:500) than in men (1:2000).**

Disease Mechanisms

Increased PTH production → Hypercalcemia via:

- **Increased GI absorption of calcium**
- **Increased production of vitamin D3**
- **Reduced renal calcium clearance**

Primary Hyperparathyroidism

- **PTH is elevated relative to the serum calcium level.**
- **Serum phosphate is often low**
- **Renal function is normal**

Causes

- **Parathyroid adenoma (85%)**
- **Parathyroid hyperplasia (15%)**
- **Parathyroid carcinoma (<1%).**

Clinical Picture

Classical mnemonic :“stones, bones, groans, moans, and psych overtones,”	
Stones	**Urolithiasis**
bones	**Bone diseases including bone resorption with cyst (osteitis cystica) and brown tumor formation**
groans	**Abdominal pain from peptic ulcers or pancreatitis**
moans	**Diffuse joint and muscle pains, fatigue and lethargy**
psych overtones	**Neuropsychiatric abnormalities including depression or worsening psychosis**

Currently most patients are found incidentally from investigating hypercalcemia

In outpatients

- **The most common cause of hypercalcemia is primary hyperparathyroidism**

In inpatients

- **The most common cause is malignancy, either via paraneoplastic syndrome or bony metastases**

Treatment

Medical

- Acute, severe hypercalcemia : large-volume saline infusion
- There is no definitive medical treatment for primary or tertiary hyperparathyroidism

Surgical

- Patient selection criteria for parathyroidectomy include asymptomatic patients <50 years of age

NIH Criteria for Parathyroidectomy

Age < 50 OR Any age with any of the following:
Nephrolithiasis
Osteitis fibrosa cystica
Serum calcium >1.0 mg/dL above reference range (typically >11.2)
Hypercalciuria (>400 mg/day)
Bone mineral density T score reduced by >2.5 SD measured at one or more sites
Creatinine clearance reduced by 30% compared to age-matched normal range
History of an episode of life-threatening hypercalcemia
Neuromuscular symptoms: documented proximal weakness, atrophy, hyperreflexia, and gait disturbance

Observation Vs. Operation

Observation rather than operation is not safe for noncompliant patients.

Observation requires active surveillance :

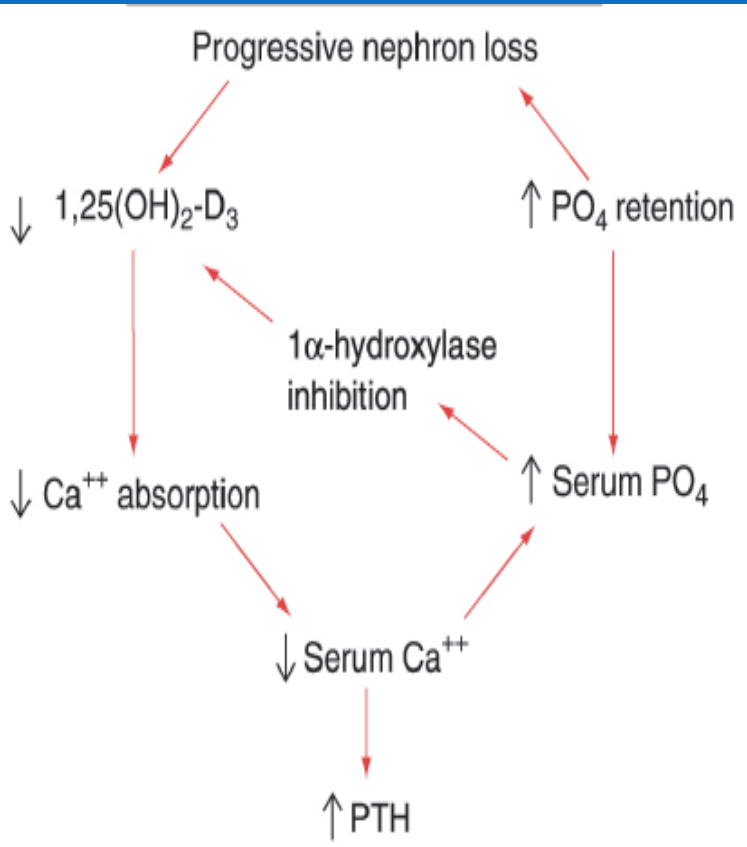
- **biannual serum calcium levels**
- **annual serum creatinine measurement**
- **annual bone mineral density determination**

Secondary Hyperparathyroidism

Causes

- **Chronic renal failure**
- **Inadequate calcium intake**
- **Decreased vitamin D**
- **Malabsorption**

Pathophysiology



Secondary Hyperparathyroidism

Clinical Picture

- **Bone pain,**
- **Soft tissue calcifications (calcinosis)**
- **Pruritus**

Lab. Results

- **Increased PTH**
- **Normal calcium**
- **Raised phosphate**

Treatment

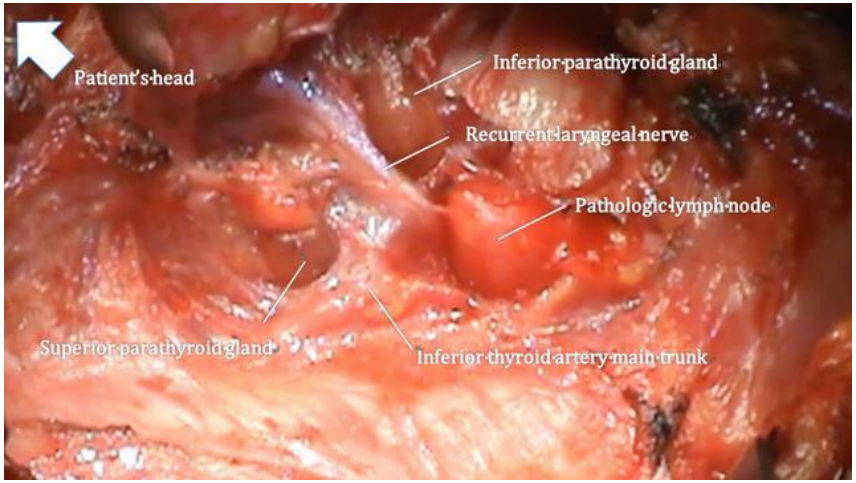
Medical

- **For end-stage renal disease**
  - Dialysis
  - Vitamin D supplements
  - Oral phosphate binders
- Cinacalcet (Sensipar): lowers calcium by activating the calcium-sensing receptor

Surgical

- For end-stage renal disease: transplantation
- Parathyroidectomy for
  - Ongoing bone loss
  - Soft tissue calcifications
  - Severe pruritus
  - Patients on lithium who develop hypercalcemia and cannot be managed with other medications

- **Since secondary hyperparathyroidism is always multiglandular, at least subtotal parathyroidectomy (three and one-half gland) should be performed**



Tertiary Hyperparathyroidism

Definition

- One or more of the hyperplastic glands of a patient with secondary hyperparathyroidism becomes an autonomous producer of PTH

Suspicion

- PTH levels remain high despite successful renal transplantation in most cases
- Patients who remain on dialysis and spontaneously progress from secondary to tertiary hyperparathyroidism marked by the onset of hypercalcemia.

Elevated intact PTH plus Hypercalcemia

Primary and tertiary hyperparathyroidism	**Familial hypercalcemic hypocalciuria (FHH, also called familial benign hypercalcemia),**	**Vitamin D deficiency**	**Lithium induced hypercalcemia**

PTHrP

Serum parathyroid hormone–related peptide (PTHrP) level might be useful when occult malignancy is a concern:

-Bronchial squamous cell carcinoma is the commonest. – Other sources: breast, renal, and ovarian	Bone destruction by primary cancers (e.g., multiple myeloma) or lytic bony metastases causes hypercalcemia without PTHrP elevation	Vitamin D analogues are secreted by some tumors (e.g., lymphoma) and can produce hypercalcemia without PTH or PTHrP elevations

Surgery for Tertiary Hyperparathyroidism

- **Guided by the intraoperative findings, most often multiglandular disease.**
- **Total parathyroidectomy with forearm autotransplant or subtotal parathyroidectomy**

MULTIPLE ENDOCRINE NEOPLASIA SYNDROMES

- Familial endocrine tumor syndromes
- Inherited as autosomal dominant
- Divided into three types

MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 (MEN-1)

Glands and Sites Involved	Type of Disease
Parathyroid	Hyperplasia
Pancreas	Islet cell tumors
Pituitary	Adenoma
Adrenal	Adenoma or carcinoma
Enterochromaffin system	Carcinoid tumor
Soft tissue	Lipoma Facial angiofibroma Collagenoma

Screening

Should begin during the 2nd or 3rd decade

Screening tests include	**Calcium, prolactin, fasting glucose and insulin, gastrin**

Calcium and PTH levels should be measured in all patients

The absence of hyperparathyroidism virtually excludes MEN-1

Parathyroid Disease in MEN-1

Primary hyperparathyroidism is the most common endocrine disorder in MEN-1

- **In over 90% of cases**
- **Only3% of all cases of primary hyperparathyroidism.**

Mean age of onset is 25 years

- **Much younger than for sporadic primary hyperparathyroidism**
- **Affects all parathyroid glands**

Patients with hypercalcemia and hypergastrinemia should undergo parathyroidectomy first for optimal control of gastrin secretion

- **Either total (four gland) parathyroidectomy with forearm autotransplant or subtotal (three and one-half gland) parathyroidectomy is appropriate**
- **The cervical thymus should always be removed because supernumerary glands can occur and are usually within the thymus**

Treatment

Therapeutic goals :controlling symptoms of hormonal excess and malignancy excision

Gastrinomas are usually multiple, malignant and resection requires pancreaticoduodenectomy	**Surgery is appropriate for all insulinomas**	**Parathyroidectomy should precede operation for gastrinoma in hypercalcemic patients**

Multiple Endocrine Neoplasia Type 2A, Type 2B, And Familial Medullary Thyroid Carcinoma

- **Medullary thyroid cancer (MTC) is the primary component for each.**

MEN-2A	MEN-2B	Familial Medullary Thyroid Carcinoma (FMTC)
• MTC • Adrenal pheochromocytoma • Primary hyperparathyroidism	• MTC • Adrenal pheochromocytoma	• MTC

Screening

Genetic screening(RET DNA analysis) has largely replaced calcitonin screening

Performed soon after birth and is performed once in a lifetime.	**Patients at risk but with negative RET testing do not require further screening.**	**Positive RET results lead to thyroidectomy and further evaluation**

THANK YOU