Parathyroid Gland and Hyperparathyroidism

Prof. Dr Arun Jamkar
MS. Ph D( Surgical Oncology), FICS, FIAGES, FMAS, FAIMER fellow
Director,
Post graduate programme, Research and Development,
MIT Group of Medical colleges Pune
- Ex Vice Chancellor, Maharashtra University of Health Sciences, Nashik
- Consultant, Persistent System Pvt. Ltd
- Chair, National Bioethics Curriculum Implementation, UNESCO Chair in Bioethics, Haifa
- Ex Dean, B J Medical College Pune and RCSM Govt. Medical College, Kolhapur
- Ex Professor of Surgery, B J Medical College Pune
Anatomy of Parathyroid gland

- Small, oval in shape 0.5 to 6x3x1.5mm
- Yellowish brown colour 30 to 40 mgs
- Size and appearance resembles a `Tur dal
- **Exact no.** of parathyroid may vary
- Gilmour (1936)

  - 88% 4 glands
  - 6% 5 glands
  - 6% Glands: might be due to fusion

- Small fat lobules usually bruised on operation table may look like parathyroid
- Sink test
  Sink in water parathyroid will sink – fat lobule will float
Position of Parathyroid

- Upper two Parathyroid glands fairly constant,
- closely embedded in thyroid at Postero Lateral border of thyroid Gland immediately above entry of inf. thyroid artery.
- Rarely it might vary above and within substance of thyroid gland along the of thyroid gland.
- with approximately 75% being located either cricothyroidal or juxtathyroidal, and the remainder are located primarily behind the upper pole of the thyroid gland.
- Common embryological origin from IV th bronchial arch. Parathyroid IV

- Inferior Thyroid gland varies in position.
- Usually situated at the lower pole of thyroid gland.
- May be found any where in this situation downwards to the upper pole Thymus.
- 5% found in upper anterior Mediastinum.
- Embryo logically Inferior. thyroid gland shows origin with Thymus – 3rd bronchial arch Parathyroid III

Di George Syndrome – Congenital absence of parathyroid gland Thymus and pharyngeal derivatives
Fig. 38.1 Parathyroid gland. Normal and uncommon sites.

Right side
Normal sites

Left side
Variations of normal

Above and within substance of thyroid:
Rare

Inferior thyroid artery

Behind trachea and behind great vessels:
Not uncommon

Subclavian artery

Alongside and within substance of thymus:
Not uncommon

Thymus
Histology:

- Rich sinusoidal capillary net work with islands of secretary cells.
- Glandular cells
- Chief (Principle cells) Small, vasicular nuclei and poorly staining cytoplasm
- Clear cells: Found in hyperplastic Neoplastic Tumours.
NORMAL HUMAN PARATHYROID GLAND; H. AND E. STAIN, X 350
A=LIGHT AND DARK CHIEF CELLS; B=OXYPHIL CELLS

NORMAL HUMAN PARATHYROID GLAND; H. AND E. STAIN, X 17½

PAS STAIN, X 675
GLYCOGEN IN CHIEF CELLS

BODIAN STAIN, X 1800
SECRETORY GRANULES IN CHIEF CELLS

BAAF STAIN, X 1350
MITOCHONDRIA IN OXYPHIL CELLS
Fig. 38.1 Parathyroid gland. Normal and uncommon sites.

Fig. 38.2 The blood supply of a parathyroid gland.
Physiology:

1. Stimulates osteoclastic activity. Increasing bone Reabsorption by mobilizing Ca PO4 from bone.

2) Increases Reabsorption of calcium from renal tubules Thus reducing urinary excretion of calcium.

3) Augments absorption of Ca from gut.

4) Renal tubular excretion PO4 \(\downarrow\) increases Ca
Physiology of Parathyroid
Hyperparathyroidism

1) Primary
   a) Hyperplasia
      • Chief Cell Alone
      MEN I
      MEN II a
      FHHH
      • Water Clear Cell (WCCH)
   b) Neoplasia
      Carcinoma
      Adenoma (MEN I, MEN II a)
2) Secondary:
- Chronic renal failure with Renal osteodystrophy
  (Serum Ca lowers leading to Compensatory parathyroid Hyperplasia of all 4 glands)
- Malabsorption syndrome

3) Tertiary HPT:
- Persistent HPT after Renal Transplantation in Renal osteodystrophy
Primary Hyperthyroidism

Key:
- Ca = Calcium (Ca++)
- P = Phosphate (HPO$_4$-)
- D = Dihydroxy (hydroxyapatite)

Adenoma (usually single, occasionally multiple) about 80% of cases
Primary "Water Clear" Cell Hyperplasia about 10% of cases
Primary Chief Cell Hyperplasia about 5% of cases
Carcinoma about 2% of cases

G.I. Tract
Parathyroid Hormone Increased

Serum Ca: Moderately or Markedly Elevated
Serum P: Often Low but may be Normal

High Intake of Ca and P (e.g., Milk) tends to reverse bone resorption process and to normalize serum P and alkaline phosphatase levels

Increased Inhibition of P Re-Absorption
Increased Stimulation of Osteoclastic Activity and Resorption of Calcium and Phosphate

Nephrocalcinosis (+ infection)
Renal Stones

Key:
- Fracture
- Variously Diminished Bone Density, Cysts, Fractures
- Osteitis Fibrosa Cystica
- Osteoclast, Osteoblast
- Superosteal Resorption
- Bone Cyst

Circulation: Ca x P = K
Secondary Hyperthyroidism
Clinical Features

Bones,

Stones,

Abdominal groans

and Psychic moans
- Rarely found in first decade of life.
- 20 to 60 years.
- Common in females than males

Vague bony pain and joint pains D/D Rheumatism

Generalized decalcification of skeleton Von-Reclinginghausen’s disease (Osteitis cystica fibrosa)

Early Skull, Phalanges
Loss of density
Sub Periosteal erosion

- Late: Generalized calcification
- Multiple bone cyst
- Psuedo tumours of Jaw

Pathological fractures
Multiple, Recurrent Renal Stones.
Nephrolithiasis – Nephrocalcinosis
Ectopic Calcification.

Investigate all patients of Multiple and recurrent stones for Hyperparathyroidism.
Abdominal groans

- Dyspeptic cases: Nauseas, vomiting, anorexia.
- Peptic Ulcer
- Pancreatitis
Psychic Moans

- Uncommon, Lethargy
- Tiredness, Listlessness, irrational behavior
- Wrongly Labeled as Neurotic or Menopausal

Only 50% present with these symptoms
Hypercalcemic Syndrome:

- Minor mental changes, Lethargy
- Polydypsia, Polyurea
- Dehydration, Persistent Irritable GIT
- Weigh loss

Acute HPT syndrome
- Nausea, vomiting
- Abdominal pain
- Oliguria
- Coma

Asymptomatic: Detected during biochemical check up.
Parathyroid adenoma is seldom palpable
Corneal calcification may be seen
Hypertension is seen in 50% cases
Shortened QT interval
Diagnosis is Bio chemical
Laboratory Studies

- Serum Calcium: Serial reading for 3 occasions. (9.5 to 11 mg)
- >11 mg% Suspicious of HPT. >12 definite for HPT
  - No tourniquet
  - Long storage
  - Low PO4 diet
  - Diurnal variation 1 to 4%

Cortisone Test
150mg/day/10 days
No effect Primary HPT
Calcium levels reduced all other causes

Secondary in bone
Carcinoma with endocrine potential
(bronchus, kidney, ovary)
Multiple Myeloma
Sarcoidosis
Thyrotoxicosis, Hypervitaminosis D

Sulkowitch Test: The patient is given a diet containing 125 mg of calcium daily, for three successive days. In hyperparathyroidism more than 200 mg of calcium is excreted in the urine daily (in a normal subject this level will be less than 100 mg).
**D/D of Hypercalcaemia**

<table>
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<tr>
<th>Condition</th>
<th>Serum Ca</th>
<th>Serum P</th>
<th>ALK.P.ASE</th>
<th>Urine Ca</th>
<th>TRP</th>
<th>Misc. Findings</th>
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<td>↓</td>
<td>&quot;</td>
<td>↓</td>
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<td>OR ↑</td>
<td>↑</td>
<td>N OR</td>
<td>↑</td>
<td>Serum Globulin Elevated</td>
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<tr>
<td>Multiple Myeloma</td>
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<td>N OR</td>
<td>↑</td>
<td>N</td>
<td>Bence Jones Protein in Urine; Serum Globulin Elevated</td>
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<td>N OR</td>
<td>↑</td>
<td>N OR</td>
<td>↑</td>
<td>Destructive Lesion on X-Ray</td>
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<td>N OR</td>
<td>↑</td>
<td>N</td>
<td>Primary Lesion, X-Ray, Bronchoscopy</td>
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<td>Disuse Atrophy (Osteoporosis)</td>
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<td>N OR</td>
<td>↑</td>
<td>History of Immobilization</td>
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<td>Thyrotoxicosis</td>
<td>↑</td>
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<td>N OR</td>
<td>↑</td>
<td>N</td>
<td>Long-Standing Hyperparathyroidism</td>
</tr>
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</table>
Laboratory Studies II

- Serum PO₄: Lower than normal (<300 mg/dl)
- Alkaline PO₄: increases if there is bone involvement

- Urinary Calcium
  - Low Ca⁺ diet
  - Useful with only high Serum Ca
  - Ser. Ca: Renal Stones.
  - Upper Limit: 250 mg in Males/day 300 mg in Females/day

- Serum Parathormone levels

- Bone biopsy from iliac crest
- CAT Scan
- Ultra Sonogram
- X-Ray Studies.
Localization of Parathyroid Pathology:

Potential locations for the left parathyroid glands
Preoperative:
Minimum invasive:

- Ultra Sound operator dependant
- Computed tomography –For localization outside neck
- Barium swallow, and Cine oesophagogram
- Neck massage PTH, urinary cyclic AMP
- Technetium Tc 99m Sestamibi radionuclide 91% to 100% accuracy
- Thallium Technicium isotope Substraction scanning useful for Adenoma but not for Hyperplasia
- MRI: 64% detection rate Low signal is obtained on T1 weighted images, T2 weighed images give contrast resolution
Localization of Parathyroid Pathology:

- **Preoperative:**
  - Invasive:
  - Selective venous sampling of PTH
  - Selective Angiography
  - Arterial injection of selenomethionine 15
  - Needle aspiration

- **Intraoperative:**
  - Methylene blue
  - 0-Toludine blue,
  - Urinary Cyclic AMP
  - Intraoperative assessment of PTH
  - Intraoperative gamma probes for nuclear mapping
MIBI scan

CT scan
SESTAMIBI Scan

Parathyroid Adenoma
Thyroid Scan with 99m Tc

Thallium scan taken up by both Thyroid and Parathyroid

Both Images captured by gamma camera and by Computer subtraction. The “hot spot” remaining is of parathyroid.
MRI For Parathyroid Adenoma: T2 weighted image
Parathyroidectomy: Indications

1) Primary HPT
   - Hyperplasia – 3.1/2
   - Adenoma --- one
   - Carcinoma – Local Radical Diss.

2) Secondary HPT
   - If bone decalcification
   - Severe pain.

3) Tertiary HPT

4) Re operative.
Parathyroidectomy History

- Felix Mandl in Vienna, Austria performed the first successful Parathyroidectomy in 1925.
- Endoscopic Parathyroidectomy was pioneered by Dr Michel Gagner at the Cleveland Clinic in 1996
Surgical techniques

- Open Parathyroidectomy
- Minimally invasive *Radioguided* Parathyroidectomy
- Endoscopic Parathyroidectomy
Parathyroidectomy
Parathyroidectomy
Radioguided Parathyroidectomy

- The gamma probe is used to localize the maximal area of radioactivity. This correlates with the location of the enlarged parathyroid gland as shown on the sestamibi scan.
Marking the incision site. Administration of local anesthesia

Utilization of the gamma probe to guide the surgical dissection.
- Excision of the enlarged parathyroid gland

- Measuring the radioactivity (counts/sec) in the specimen to confirm it is parathyroid issue.
Auto Transplantation of Parathyroid

- Primary Thyroid hyperplasia
- Secondary HPT
- Re operative HPT
- Total Thyroidectomy for Ca Thyroid
Deferred parathyroid Autotransplantation

- Immediately placed in sterile saline or tissue culture
- Sliced into 1x1x3mm silvers.
- 3ml Glass vials will accommodate 10 silvers
  - 1 to 1.5 ml
  - 10% DMSO dimethyl sulfoxide
  - 10% autologus serum
  - 80% Tissue culture media
- Frozen 1 degree centigrade per minute
- Till you reach -80 degree Centigrade
- -190 oC Vapour phase Liquid nitrogen freezer
- Linde BF 4/6 biological freezing system
- Thawing rapidly to 57oC
- Implant in Thigh subcutaneously