

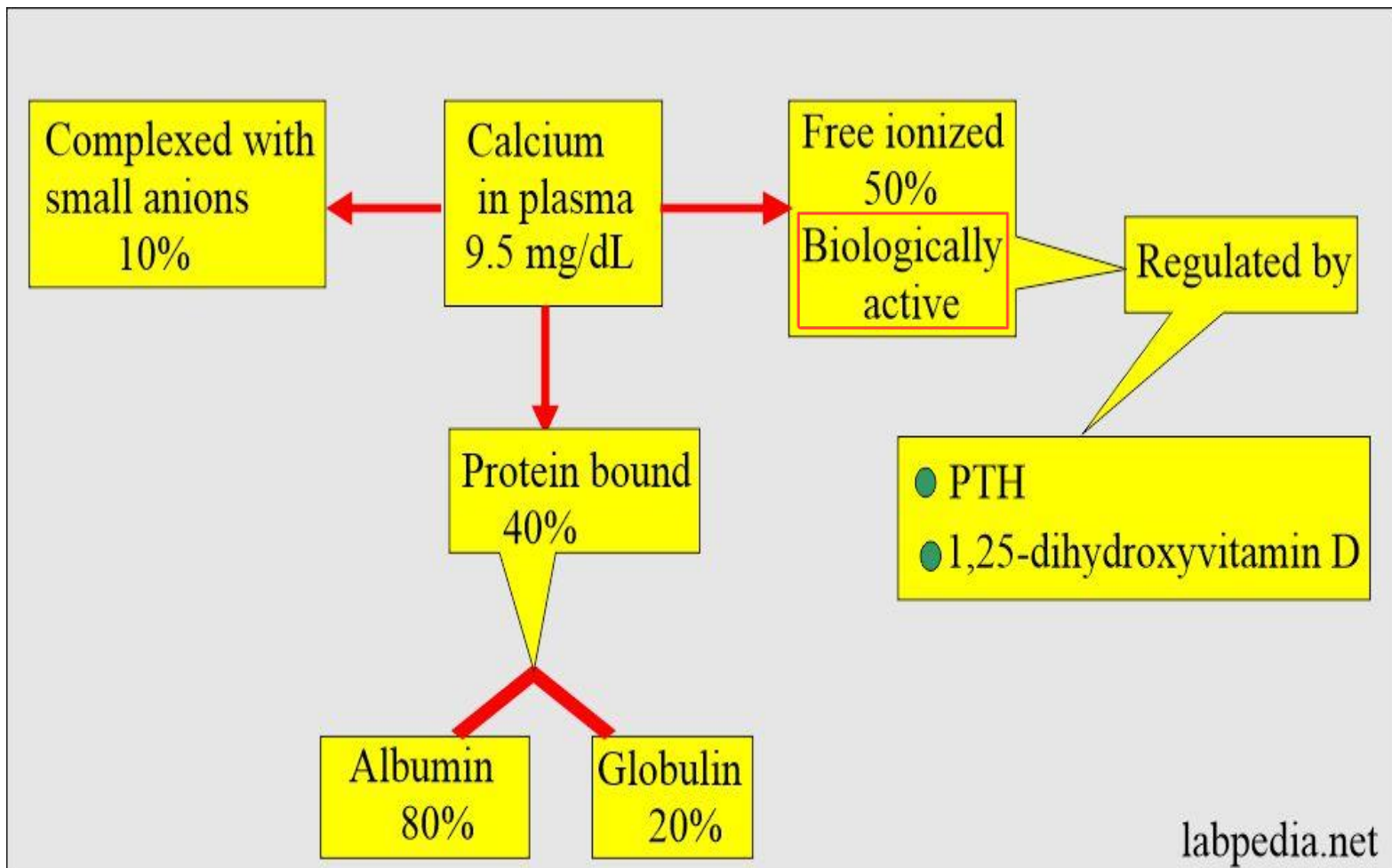
Parathyroid

parathyroid glands → 3-5
↳ maintain Ca^{++} levels

- 40 year old lady with Calcium 10.8 mg/dl

Normal values range from **8.5 to 10.2 mg/dL** •

↑ protein → ↑ bound Ca⁺⁺ → ↓ free ionized Ca⁺⁺



Corrected Calcium

↳ to know is 10.8 normal or abnormal
(to see how much Ca^{++} is free &
how much is bound)

$$\text{Ca}_{\text{Corr}} = \text{Ca} \left(\frac{\text{mg}}{\text{dL}} \right) + 0.8 * \left[4.0 - \text{Albumin} \left(\frac{\text{g}}{\text{dL}} \right) \right]$$

hyperparathyroidism depends on the
active Ca^{++} (free ionized)

- Albumin : 3 g/dl

- Corrected calcium: $10.8 + 0.8 * (4-3)$

11.6 mg/dl

Hypercalcemia

I. Hyperparathyroidism

- Primary hyperparathyroidism
- Tertiary HPT

II. Malignancy-related (some tumors secrete parathyroid related proteins → hypercalcemia)

- Solid tumor with metastases (breast)
- Solid tumor with humoral mediation of hypercalcemia (lung, kidney)
- Hematologic malignancies (multiple myeloma, lymphoma, leukemia)

III. Endocrine diseases: → ↑ metabolism → hypercalcemia

Hyperthyroidism. Addisonian crisis. pheochromocytoma

IV- Granulomatous diseases: Sarcoidosis.T.B.

IV. Iatrogenic:

- Excessive intake of Vit D or calcium
- Rx with lithium
- Thiazide diuretics

V. Associated with renal failure

- Tertiary hyperparathyroidism
- Aluminum intoxication

VI-Familial hypocalcuric hypercalcemia

- Milk-alkali syndrome

****Primary**

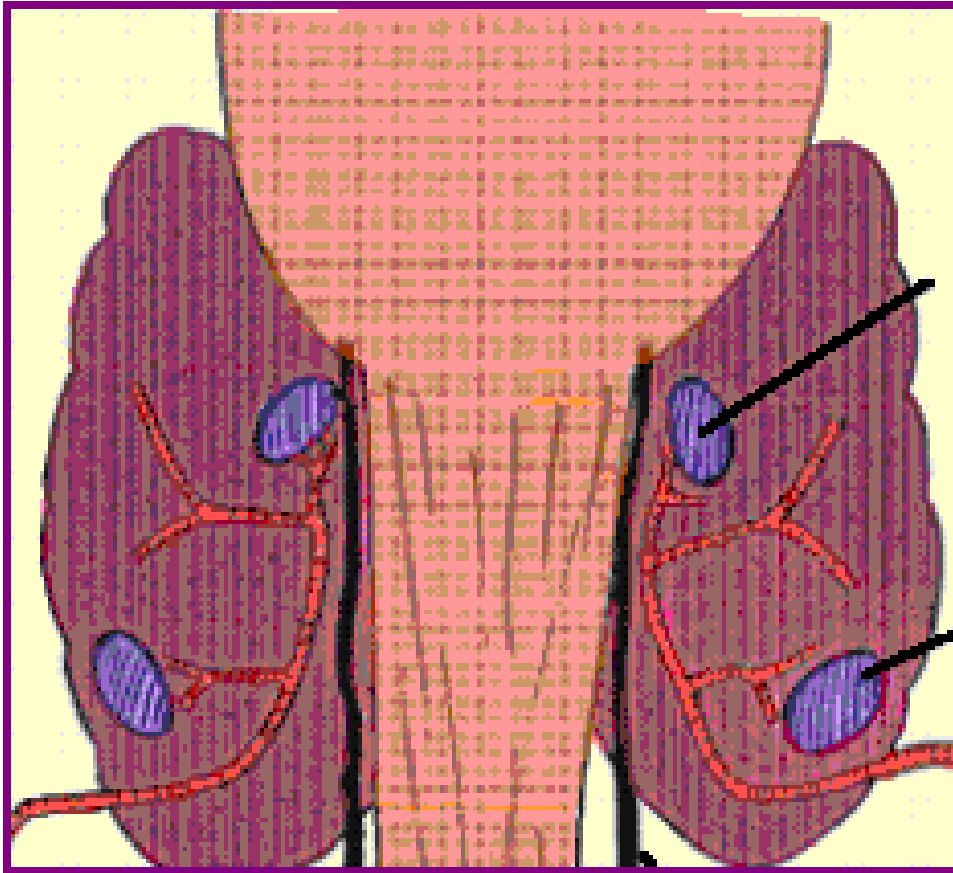
hyperparathyroidism and cancer account for 90% of cases of hypercalcemia

Hyperparathyroidism

- Affects approximately 100,000 patients a year
- Primary hyperparathyroidism occurs in 0.1 to 0.3% of the general population and is more common in women (1:500) than in men (1:2000).
- Primary hyperparathyroidism is characterized by increased parathyroid cell proliferation and PTH secretion which is independent of calcium levels.

Parathyroid

Usually supplied by inferior thyroid A (20% people have their Sup. parathyroids supplied by Sup. thyroid A)



- Four glands located behind the thyroid
- Length 6 millimeters
- Width 3 millimeters
- Thickness 2 millimeters
- Often accidentally removed
- Normal function with at least 2 glands

Anatomy

- The parathyroid glands are usually embedded between the posterior border of the thyroid gland and its fibrous capsule
- At times, the parathyroids may be intrathyroidal. They measure 6 x4x2 mm in maximum diameter and weigh 25-40 mg each.
- Number of glands can vary from 4-6

Anatomy

- Superior glands usually dorsal to the RLN at level of cricoid cartilage
- Inferior glands located ventral to nerve
- Usually derive most of blood supply from branches of **inferior thyroid artery**, although branches from superior thyroid supply at least 20% of upper glands.
- Glands drain ipsilaterally by superior, middle, and inferior thyroid veins.

Histology

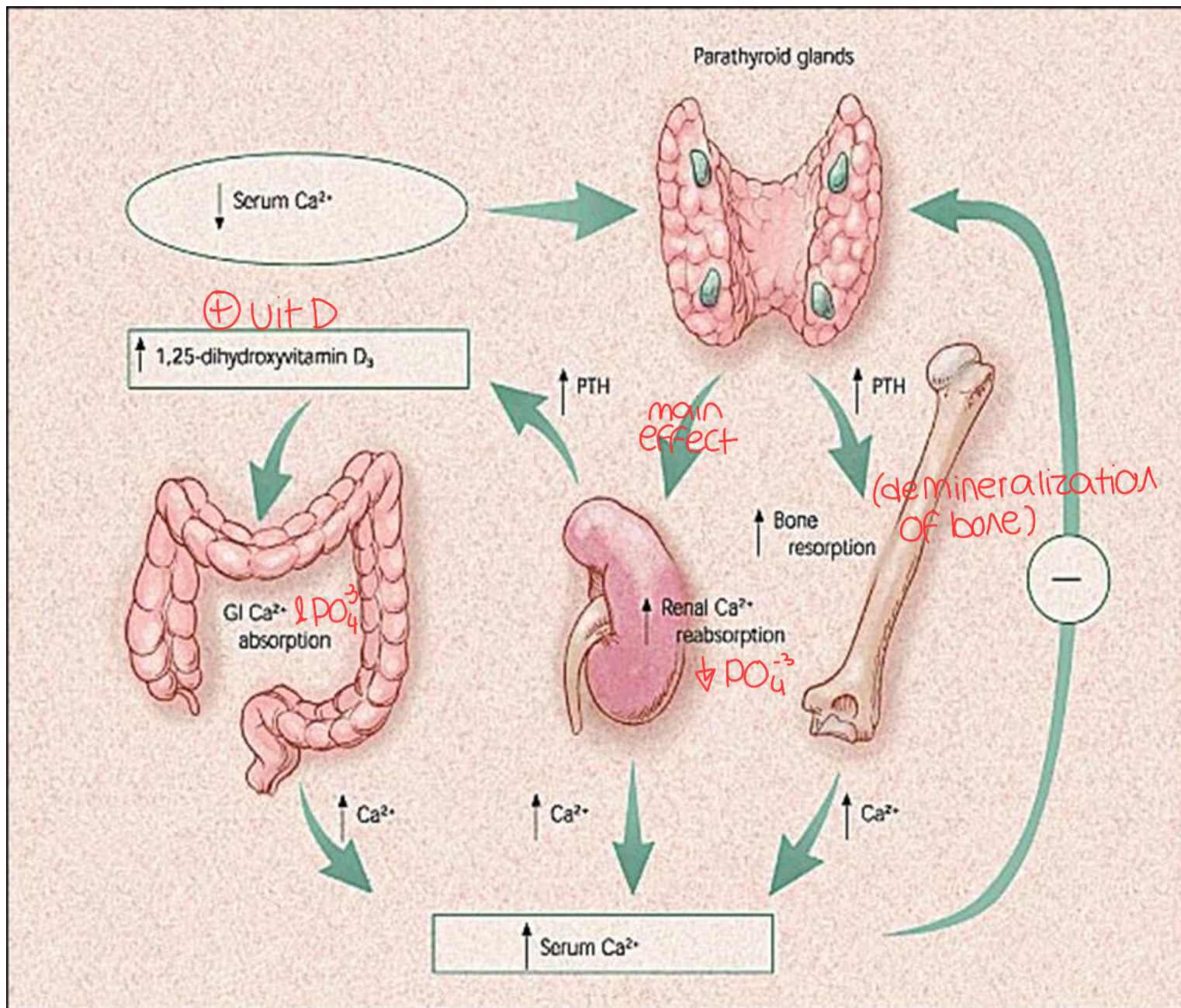
- Composed mostly of chief cells and oxyphil cells within an adipose stroma.
- Oxyphil cells derived from chief cells and increase as one ages
- Both types make Parathyroid hormone

Parath. Hormone

- PTH is synthesized in the parathyroid gland as a precursor hormone, **preproparathyroid** hormone, which is cleaved first to **proparathyroid** hormone and then to the final 84-amino-acid PTH.
- Secreted PTH has a **half-life of 2 to 4 minutes**. In the liver, PTH is metabolized into the active N-terminal component and the relatively inactive C-terminal fraction

PTH-Calcium regulation

- The **calcium-sensing receptor (CASR)** is expressed on the surface of the parathyroid cell and senses fluctuations in the concentration of extracellular calcium.
- **Increased PTH secretion** leads to an increase in **serum calcium** levels by increasing **bone resorption** and enhancing renal calcium reabsorption.
- PTH also stimulates renal **1- α Hydroxylase activity**, leading to an increase in **1,25-dihydroxy vitamin D**, which also exerts a negative feedback on PTH secretion



usually incidental finding, but if you dig deep in history you'll find that 70% have manifestations

Hyperparathyroidism Clinical

→ Classical manifestations

- **Kidney stones, painful bones, abdominal groans, psychic moans, and fatigue overtones**
- Kidney stones (calcium phosphate and oxalate)
- Osteopenia, osteoporosis, and osteitis fibrosa cystica. Increased bone turnover can usually be determined by documenting an elevated blood alkaline phosphatase level.
- Peptic ulcer disease, pancreatitis, constipation
- Psychiatric manifestations such as florid psychosis, obtundation, coma, depression, anxiety, fatigue
- Polyurea, polydipsia

OSTEOPOROSIS STAGES



Table 1: Diagnostic criteria for osteoporosis according to WHO.

Diagnostic criteria	T - score range	Bone mineral density
Osteoporosis	T Score \leq -2.5	2.5 SD or more below that of the mean level for a young-adult reference population
Osteopenia	-2.5 < T-Score < -1.0	Between 1.0 and 2.5 SD below that of the mean level for a young-adult reference population
Severe Osteoporosis	T Score \leq -2.5 with fragility fracture	2.5 SD or more below that of the mean level for a young-adult reference population with fractures
Normal	T-Score \geq -1.0	Within 1 SD of the mean level for a young-adult reference population

Osteitis fibrosa cystica

↳ brown tumor مايو ميس جاس ل

not seen anymore (very advanced)



Biochemical features of prim HPT

Serum tests	Alteration
Calcium	Increased (20% people normal Ca^{++})
Intact PTH	Increased(>0.5mg/L)
Phosphate	↓
P Chloride	↑
CL:PO4	↑ (>33)
Alkaline phosphatase	N or ↑(in the presence of bone disease)
Acid-base status	Mild hyperchloremic metabolic acidosis
Ca-:creatinine clearance ratio	>0.02(vs<0.01 in BFHH)
Urine Test: 24h urinary Ca	N or ↑ (>250mg/24h)

Hyperparathyroidism

Surgical Management

Slightly \uparrow Ca^{++} ,
old age,
asymptomatic,
no morbidities
(observation
only)

Surgery indications:

- Serum calcium > 11.5 mg/dl
(\uparrow risk of complications: pancreatitis, peptic ulcer, calcifications of vessels, fractures)
- Presence of signs and symptoms
 - Nephrolithiasis
 - Osteitis fibrosa cystica
 - Neuromuscular symptoms
 - abd. pain, bone pain
 - Psychological abnormality
 - Overtones
- Markedly reduced cortical bone density (DEXA scan)
- Decreased creatinine clearance (risk of renal failure)
- Patient age < 50 years
- Markedly reduced cancellous bone density
 - Spine

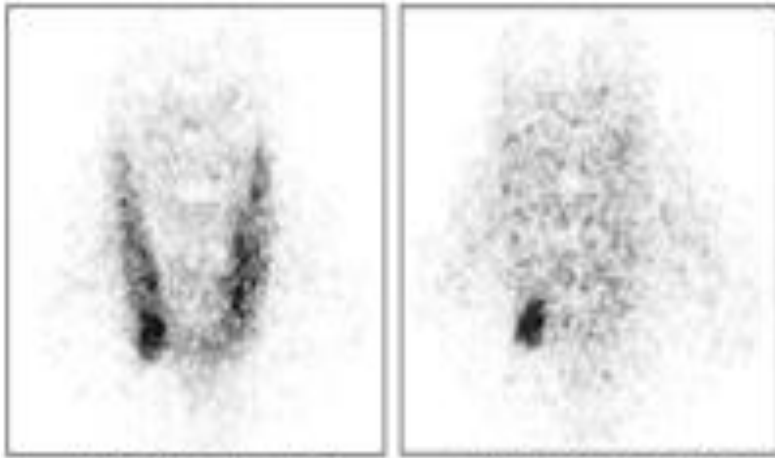
most cases are
uniglandular disease
(أغلبية حالات المرض هي
مرض الغدة الوحيدة)

Pre-Operative Imaging- Localization

- High-resolution ultrasound
 - Sensitivity 65-85% for adenoma
 - Results suboptimal in pts with multinodular thyroid disease, pts with short thick neck, ectopic glands (15-20%)
 - May be useful in detecting sestamibi scan negative adenomas
- CT with contrast/thin section
 - Sensitivity of 46-87%
 - Good for ectopic glands in the chest
- MRI
 - Sensitivity of 65-80%
 - Good for ectopic glands
- Sestamibi → most sensitive most specific
 - 85-95% accurate in localizing adenoma in primary HPT
- Sestamibi-SPECT(single photone emission CT)
 - Sensitivity 60% for enlarged gland and 98% for solitary adenomas

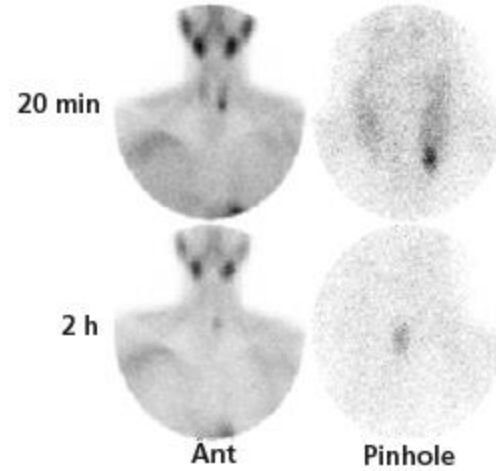
Pre-operative localization

- ^{99m}Techneium-labeled Sestamibi was initially introduced for cardiac imaging and is concentrated in mitochondria-rich tissue.
- It was subsequently noted to be useful for parathyroid localization because of the delayed washout of the radionuclide from hypercellular parathyroid tissue when compared to thyroid tissue.
- In one prospective study of 387 patients the sensitivity for single adenomas was 90 percent, but 27 percent of double adenomas and 55 percent of hyperplastic glands were missed



^{99m}Tc -Sestamibi
15 min

^{99m}Tc -Sestamibi
2.5 hr



Clearance
except from
affected
parathyroid

Pre-operative localization

- Single-photon emission computed tomography (SPECT), when used with planar sestamibi, has particular utility in the evaluation of ectopic parathyroid adenomas, such as those located deep in the neck or in the mediastinum. Specifically, SPECT can indicate whether an adenoma is located in the anterior or posterior mediastinum.

Intraoperative parathyroid hormone testing

- Intraoperative parathyroid hormone testing
 - introduced 1993
 - Used to determine the adequacy of parathyroid resection.
 - When the PTH falls by 50% or more in 10 minutes after removal of a parathyroid tumor, as compared to the highest preremoval value, the test is considered positive and the operation is terminated.
- if post parathyroidectomy values didn't drop to 50%. (for ex: 80%) that means there is another diseased parathyroid gland

Surgery

- Bilateral neck exploration is the traditional method.
(neck collar incision)
- Pre-operative imaging techniques permitted minimally invasive focused surgery towards adenoma
↳ (we remove the diseased gland (that appeared in imaging) without comparing other parathyroids to it)
- In some centers: 99-Tc Sestamibi timed within 3 hours of surgery to intra-operatively localize parathyroid adenoma using hand held geiger probe

Not successful surgery → complications:

↳ persistent hyperparathyroidism

↳ recurrent hyperparathyroidism

Surgery

- Rush medical Center, 2007
- 220 patients,
- 49 had BNE,
- 60 had BNE w/ ioPTH level monitoring
- 110 had MIPS with io PTH level monitoring
- At 3 months postoperatively, mean serum calcium and intact PTH levels were similar between groups, and eucalcemia rates were same
- The ultimate rates of persistent disease and recurrence were also similar.
- Operative time was shorter in group 3 compared to group 2 ($P < .001$) but not group 1.
- Frozen sections and patient charges were significantly lower in group 3 compared to groups 1 and 2 ($P < .005$).

hyperplasia vs. adenoma
all glands are ↳ one gland is big
big
(2° to ↓ Ca⁺⁺) (no difference pathologically)

→ Aggressive (poor prognosis)

Parathyroid carcinoma

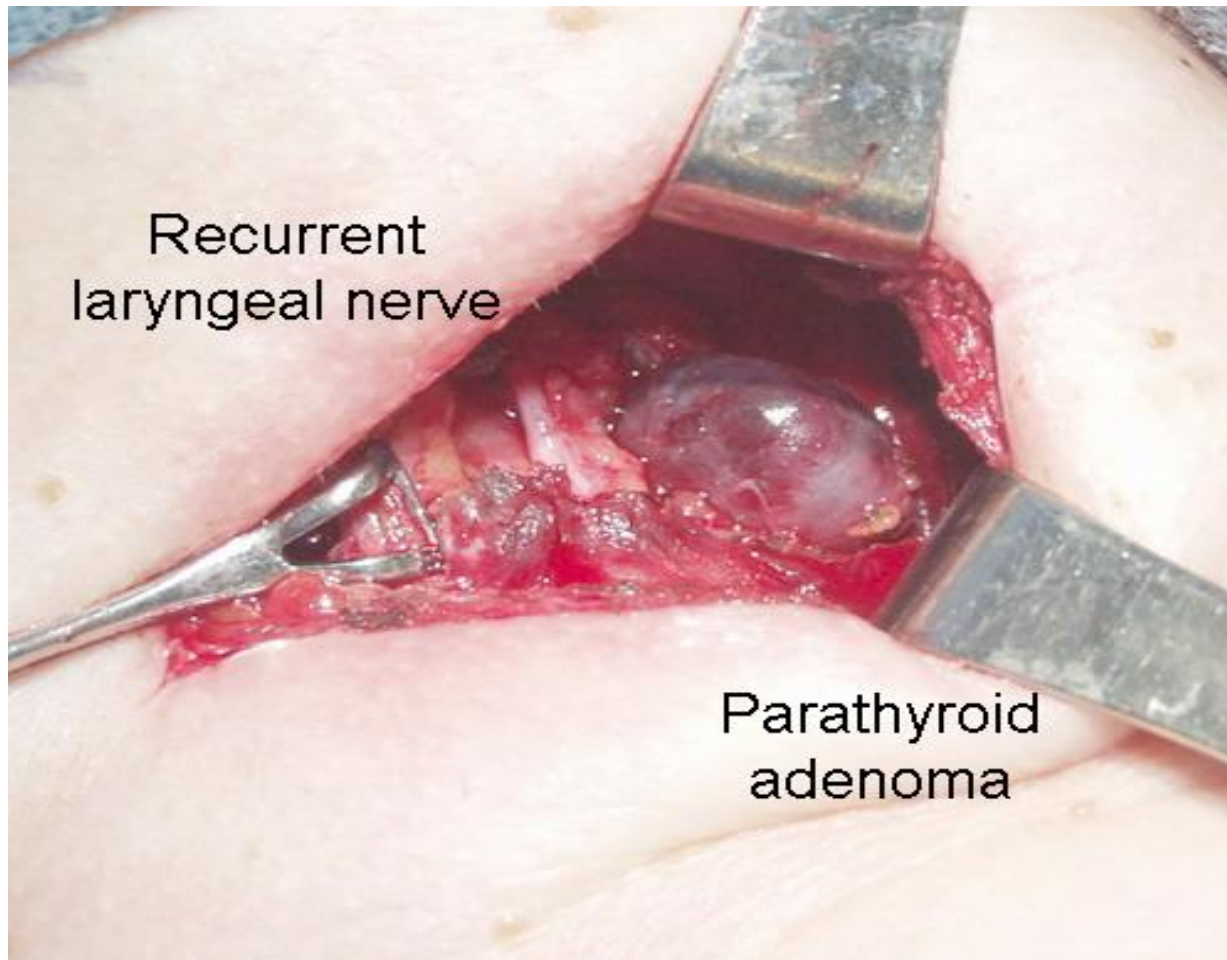
characterized by invasion of adjacent structure (± mets & LN involvement) → so we excise adjacent tissue to make sure is it

- 1% of cases of primary hyperparathyroidism benign or malignant
- 15% of patients have lymph node metastases and 33% have distant metastases at presentation.
- Intraoperatively, cancer is suggested by the presence of a large, gray-white to gray-brown parathyroid tumor that is adherent to or invasive into surrounding tissues
- bilateral neck exploration, with en bloc excision of the tumor and the ipsilateral thyroid lobe.
- Modified radical neck dissection is recommended in the presence of lymph node metastases

Surgery

- If on exploration, hyperplasia found, can remove and reimplant, or subtotal parathyroidectomy leaving approx 50 mg of tissue (as reimplantation has 5% failure rate).
- Bilateral upper cervical thymectomy also performed with hyperplasia because of supernumerary glands occur in 20% of patients
- With autotransplantation, 12 to 14 pieces inserted into belly of brachioradialis muscle
- Sternotomy may be needed to find a missing gland, generally not at initial operation, and after localizing studies performed, thyroidectomy may be also performed.
- Intra-op PTH measuring helpful as well during sternotomy to make sure got the gland

Parathyroid



Secondary Hyperparathyroidism

↳ responding to hypocalcemia

- In pts with chronic renal failure
- Deficiency of 1,25-dihydroxy vitamin D as a result of loss of renal tissue, low calcium intake, decreased calcium absorption, and abnormal parathyroid cell response
- Normally treated medically (treat 1^o cause)

Secondary Hyperparathyroidism

- Surgical treatment is indicated and recommended for patients with
 - bone pain, → CUZ OF PTH, PO_4^{-3}
 - pruritus, and a calcium-phosphate product ≥ 70 ,
 - Ca greater than 11 mg/dL with markedly elevated PTH
 - Calciphylaxis
 - soft-tissue calcification

Tertiary Hyperparathyroidism

↳ treatment : surgery

- Long standing renal failure s/p renal transplant
- autonomous parathyroid gland function and tertiary HPT.
- Can cause problems similar to primary hyperparathyroidism
- Operative intervention
 - symptomatic disease
 - autonomous PTH secretion persists for more than 1 year after a successful transplant
 - subtotal or total parathyroidectomy with autotransplantation

Post Operative Complications

- Hypocalcemia (Chvostek's and Trousseau's sign)
- Vocal cord paralysis after RLN injury
- Bone Hunger syndrome
(bone uptakes all Ca^{++} → acute hypocalcemia)

Hypoparathyroidism

Deficient secretion of PTH which manifests itself biochemically by hypocalcemia, hyperphosphatemia diminished or absent circulating iPTH and clinically the symptoms of neuromuscular hyperactivity.

Hypoparathyroidism

Causes:

- Surgical hypoparathyroidism – the commonest
 - After anterior neck exploration for thyroidectomy, abnormal parathyroid gland removal, excision of a neck lesion. It could be due to the removal of the parathyroid glands or due to interruption of blood supply to the glands.

Hypoparathyroidism

Causes:

- Idiopathic hypoparathyroidism
 - A form occurring at an early age (genetic origin) with autosomal recessive mode of transmission “multiple endocrine deficiency –autoimmune-candidiasis (MEDAC) syndrome”
 - “Juvenile familial endocrinopathy”
 - “Hypoparathyroidism – Addison’s disease – mucocutaneous candidiasis (HAM) syndrome”

Hypoparathyroidism

Causes:

- Idiopathic hypoparathyroidism
 - The late onset form occurs sporadically without circulating glandular autoantibodies.
- Functional hypoparathyroidism
 - In patients who has chronic hypomagesaemia of various causes.
 - Magnesium is necessary for the PTH release from the glands and also for the peripheral action of the PTH.

Hypoparathyroidism

Clinical Features:

A. Neuromuscular

- The rate of decrease in serum calcium is the major determinant for the development of neuromuscular complications.
- When nerves are exposed to low levels of calcium they show abnormal neuronal function which may include decrease threshold of excitation, repetitive response to a single stimulus and rarely continuous activity.

Hypoparathyroidism

Clinical Features:

B. Other clinical manifestation

1. Posterior lenticular cataract

2. Cardiac manifestation:

Prolonged QT interval in the ECG

Resistance to digitalis

Hypotension

Refractory heart failure with cardiomegaly can occur.

Hypoparathyroidism

Treatment:

The mainstay of treatment is a combination of oral calcium with pharmacological doses of vitamin D or its potent analogues.

Phosphate restriction in diet may also be useful with or without aluminum hydroxide gel to lower serum phosphate level.

Emergency Treatment for Hypocalcaemic

Tetany:

Calcium should be given parenterally till adequate serum calcium level is obtained and then vitamin D supplementation with oral calcium should be initiated.