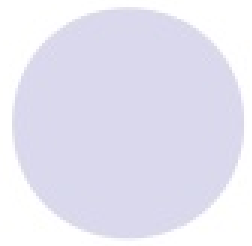
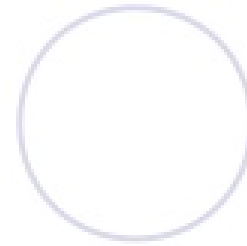
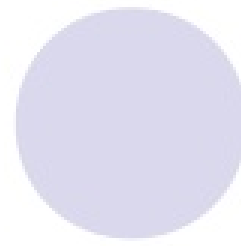
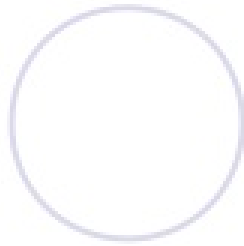
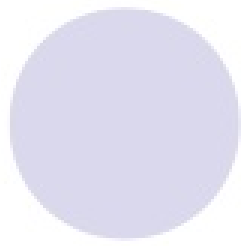
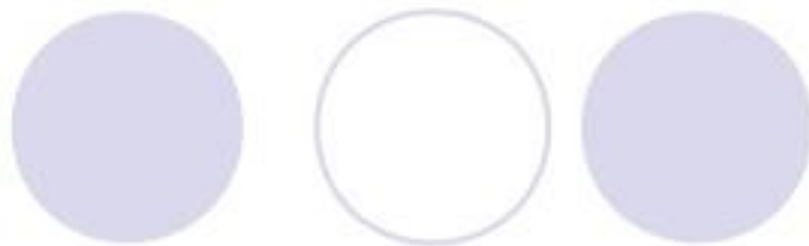


# PARATHYROID GLANDS

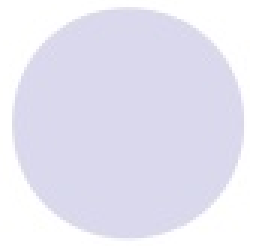
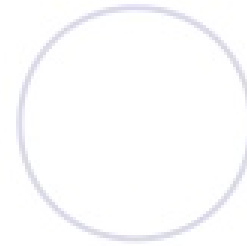
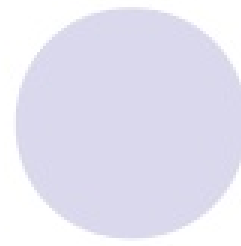
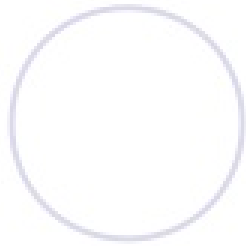
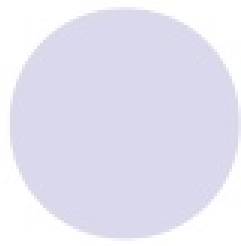
**BY DR.OMAR TARIK ALHEETI**



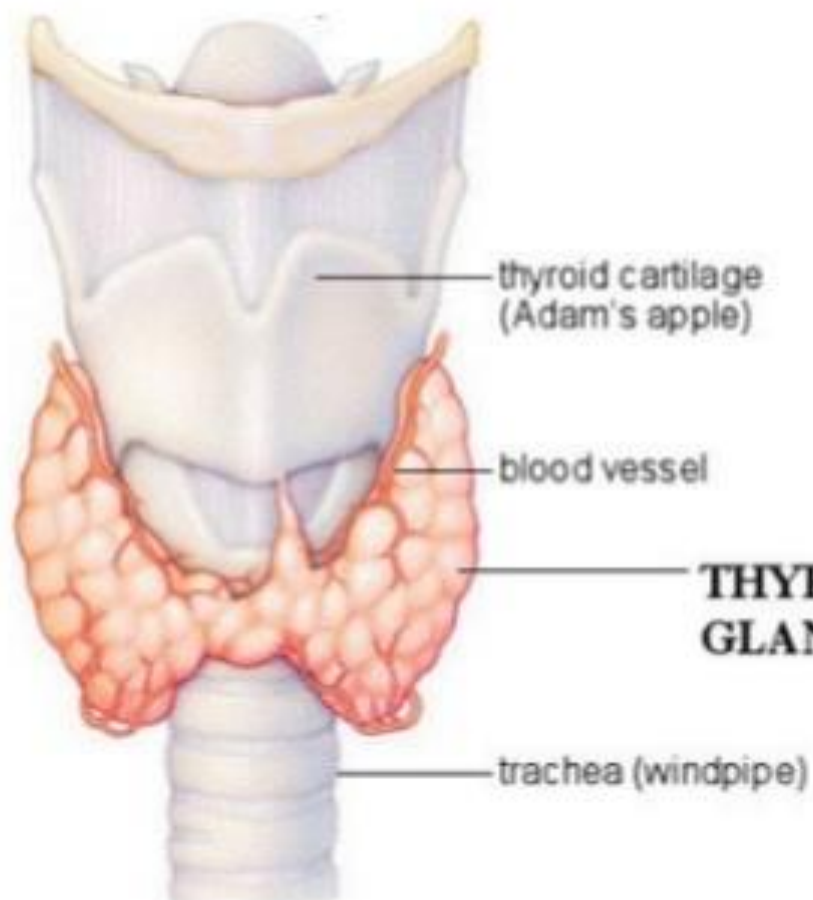
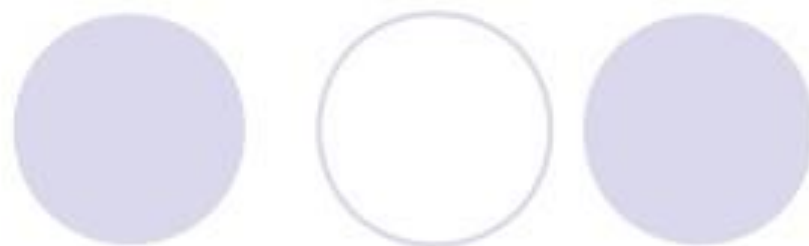
- The **endocrine system** regulates body activities by releasing **hormones** (chemical messengers) into the bloodstream, where they are carried throughout the entire body
- secrete their products (**hormones**) into the extracellular space around the secretory cells. The secretions diffuse into capillaries and are carried throughout the body by the circulatory system



- The specific cells which are affected by a hormone are called **target cells**.
- Circulating hormones may linger in the blood for minutes to hours, exerting their effects for a prolonged period of time



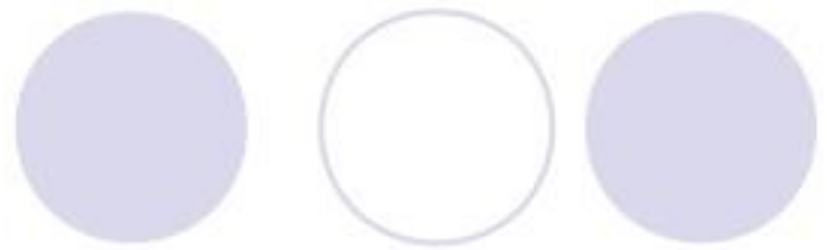
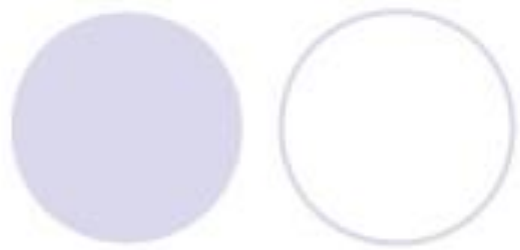
- Parathyroids are two paired endocrine glands located on the thyroid glands
- Hence the name



# DEVELOPMENT



- Endodermal proliferation of 3<sup>rd</sup> and 4<sup>th</sup> pharyngeal pouches
- Dorsal aspect of 3<sup>rd</sup> – inferior parathyroid
- Ventral – thymus
- Inferior parathyroid migrates inferiorly along with the development of thymus
- 7<sup>th</sup> week – normal position



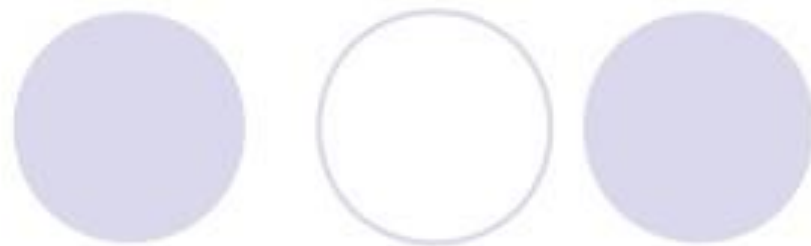
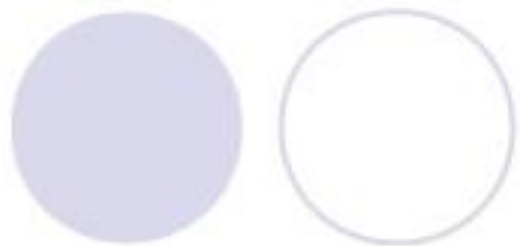
- Dorsal aspect of 4<sup>th</sup> pouch – superior parathyroid
- Ventral aspect and remnant of 5<sup>th</sup> pharyngeal pouch – ultimobranchial bodies
- Sup parathyroid migrates caudally and medially
- 5<sup>th</sup> week – normal position



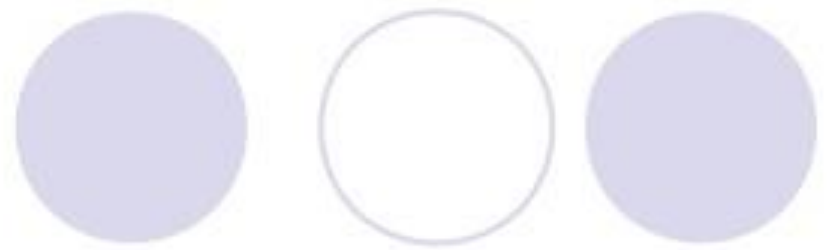
# ANATOMY

- Two pairs of glands 80 – 97%
- >4 – 13%, 3 – 3%
- Light yellowish to reddish brown
- Oval or lentiform shaped
- Bilobed 5%, multilobed 1%
- 5x3x2 mm
- 40 – 50 gms





- Superior parathyroids – more consistent in location
- Subcapsular
- Posterior part of upper half of thyroid lobe at the cricothyroid junction
- 1cm above the intersection between inferior thyroid artery and the recurrent laryngeal nerve

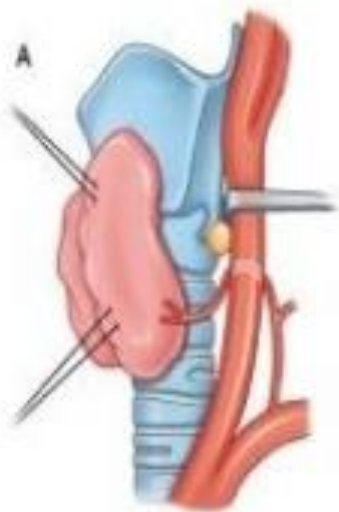


- Inferior parathyroids variable in location
- inferior, posterior or lateral to the lower pole 61%
- Inferior to lower pole in close relation to the thyrothymic ligament
- 26% within cervical part of thymus

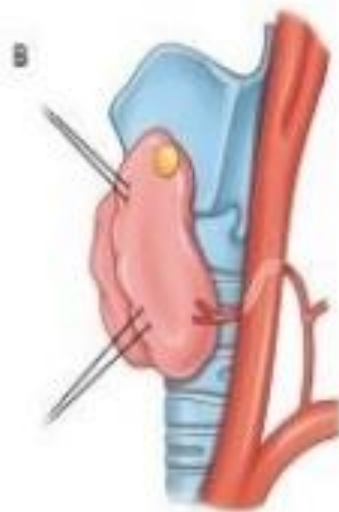




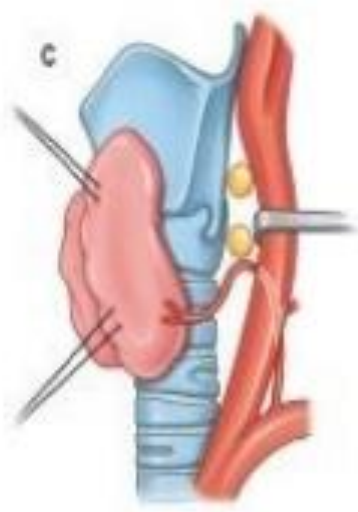
- 2% in the mediastinal portion of thymus
- 0.2% in the mediastinum
- Failure of descent – located above the superior parathyroid glands surrounded by remnants of thymic tissue
- Superior parathyroids lie posterior and inferior parathyroid lie anterior to recurrent laryngeal nerves



Cricothyroidal and juxtacricoid 77%



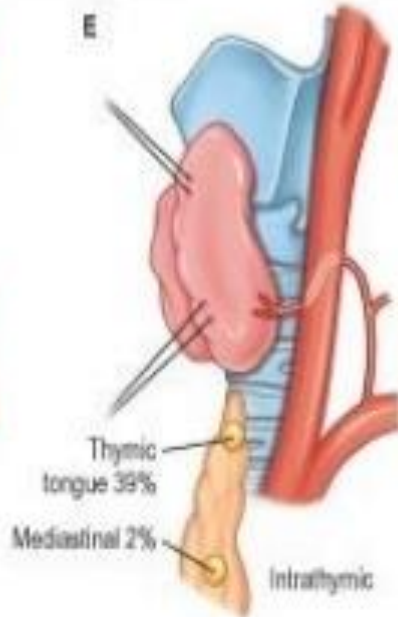
Behind upper pole of thyroid 22%



Retropharyngeal and retroesophageal 1%



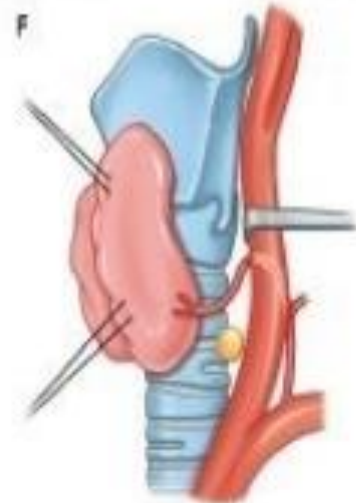
Lower thyroid 42%



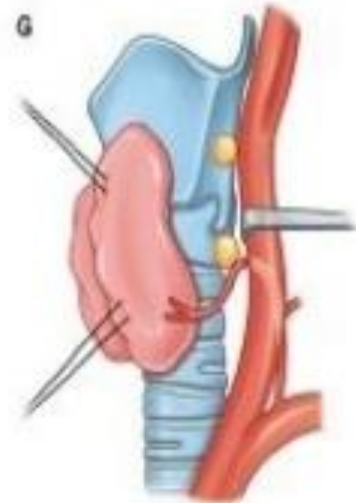
Thymic tongue 39%

Mediastinal 2%

Intrathyroid

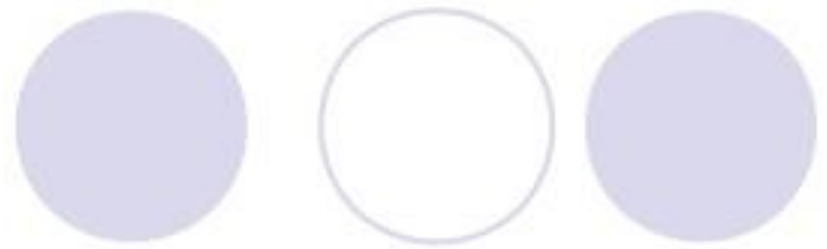


Juxtathyroidal 15%

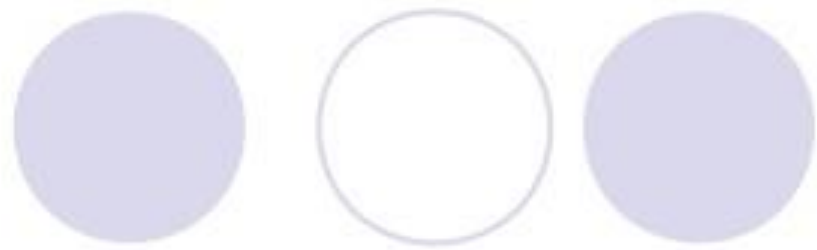


Ectopic 2%

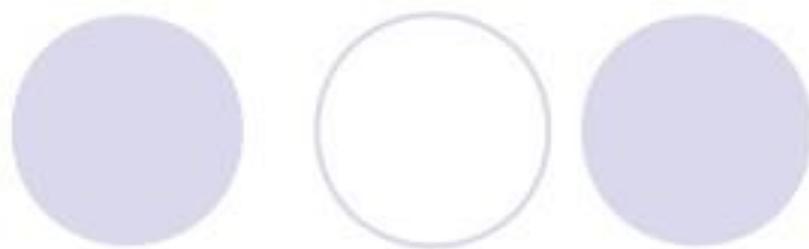




- ARTERIAL SUPPLY
- The inferior parathyroid gland is supplied by the inferior thyroid artery
- approximately 10% of patients, the inferior thyroid artery is absent, most commonly on the left side. In these cases, a branch from the superior thyroid artery supplies the inferior parathyroid gland

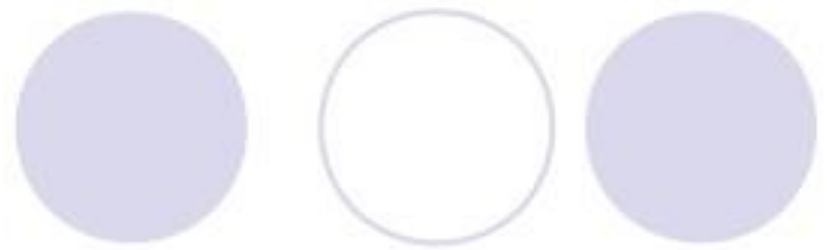


- The superior parathyroid gland is also usually supplied by the inferior thyroid artery
- By an anastomotic branch between the inferior thyroid and the superior thyroid artery
- 20-45% of cases, the superior parathyroid glands receive significant vascularity from the superior thyroid artery

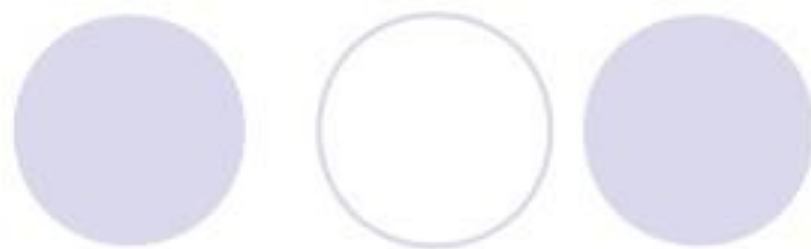


- in the form of a posterior branch of the superior thyroid artery given off at the level of the superior pole of the thyroid
- Venous drainage occurs into superior and middle thyroid veins

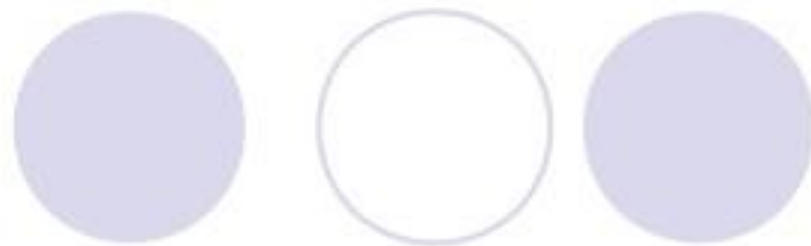




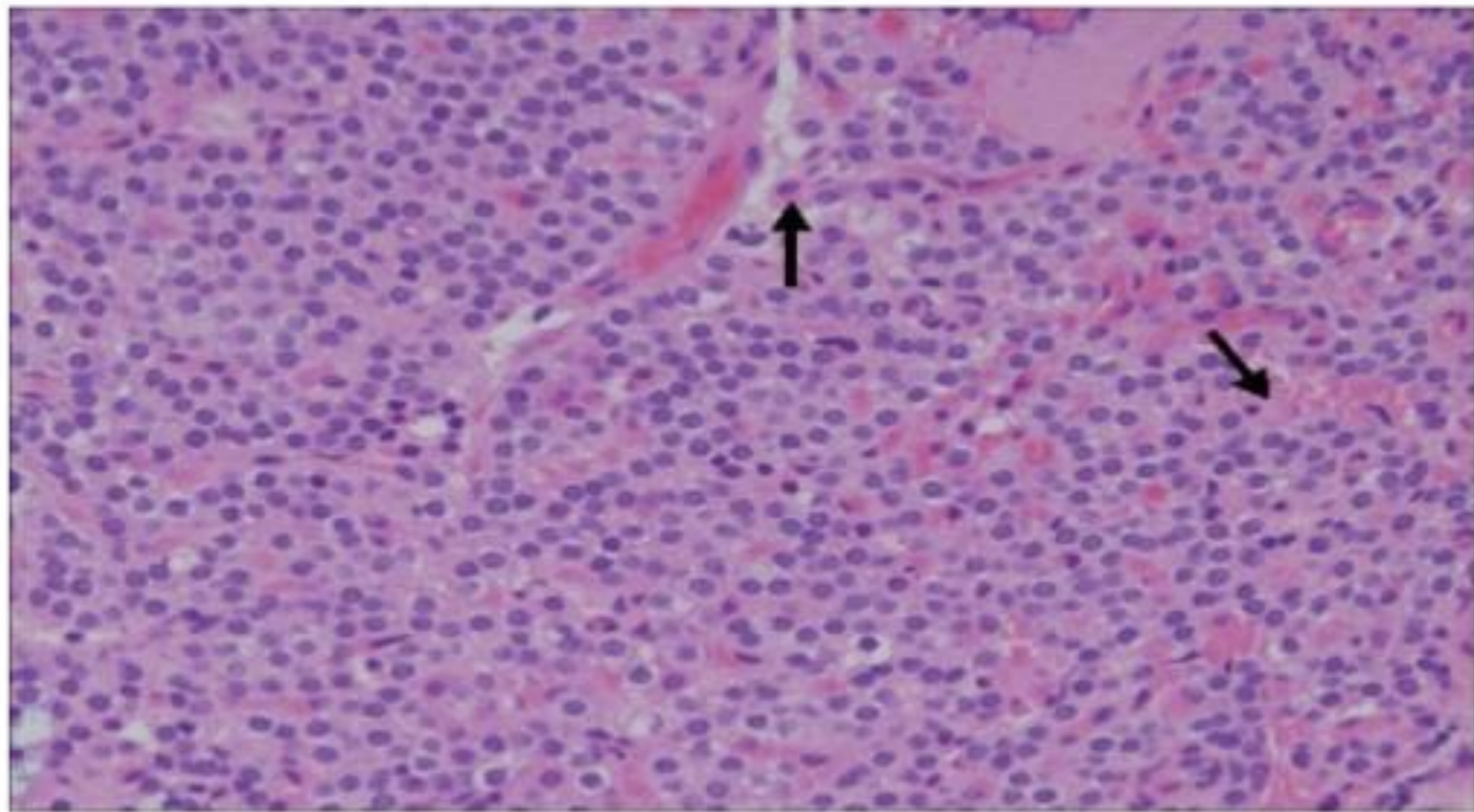
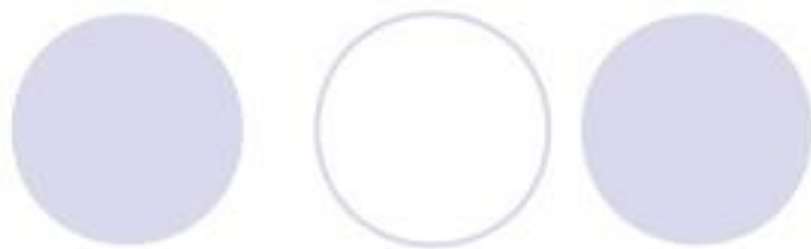
- Nerve supply is by the adrenergic sympathetic system
- Superior and middle cervical sympathetic ganglia
- Perivascular plexus of thyroid gland
- Vasomotor but not secretomotor

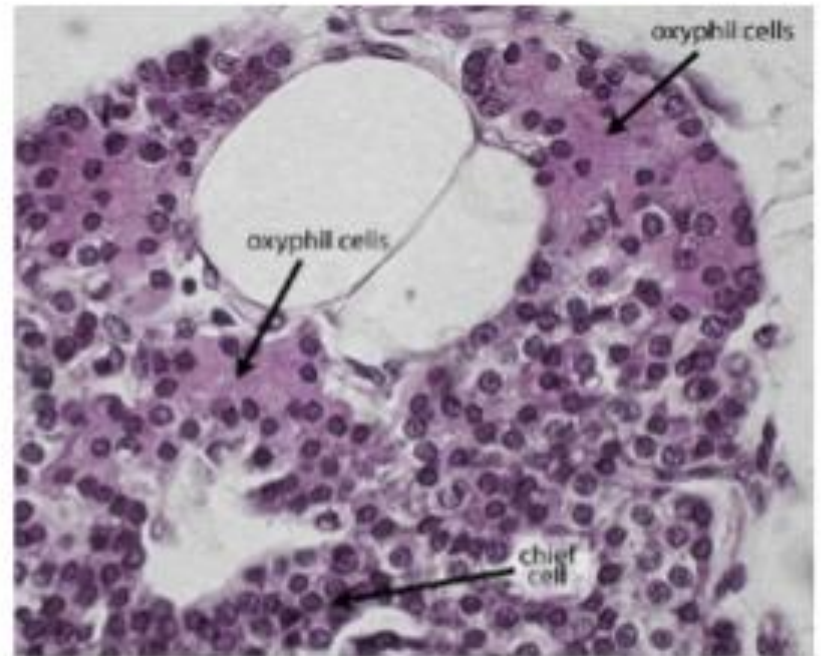
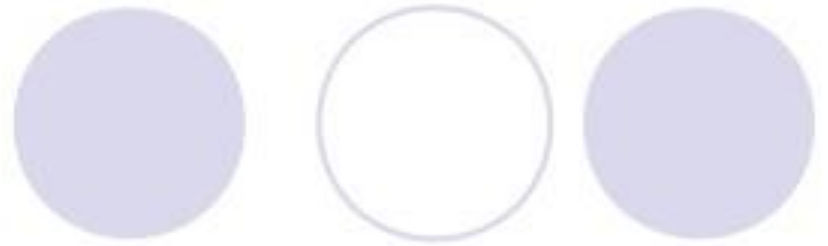


- MICROSCOPY
- Thin connective tissue capsule with intraglandular septa
- Chief cells – principle cells,
- Light, dark or clear cells
- Active chief cells hav large golgi complexes with numerous vesicles



- Clear cells are inactive cells with numerous glycogen granules
- Oxyphil cells – eosinophilic cell
- Rich in mitochondria







# PHYSIOLOGY



- Major function of the parathyroid gland is homeostasis of calcium via Parathyroid hormone (PTH)
- PTH is synthesized in the parathyroid gland as a precursor hormone preproparathyroid hormone 115aa
- which is cleaved first to proparathyroid hormone 90 and then to the final 84-amino-acid PTH

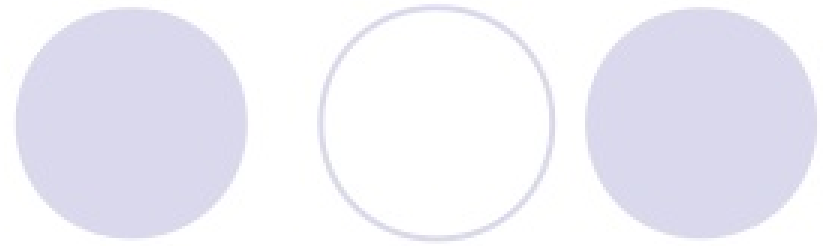
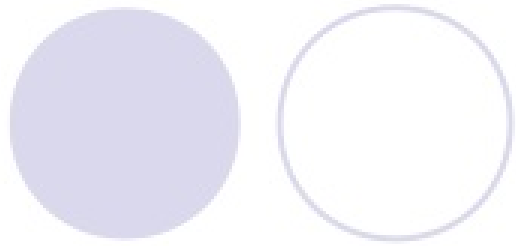


- half-life of 2 to 4 minutes
- Secretion mainly controlled by ionized calcium levels via calcium sensing receptors ( CaSR)
- CaSR G protein coupled receptors present on the chief cells
- is expressed on the surface of the parathyroid cell and senses fluctuations in the concentration of extracellular calcium

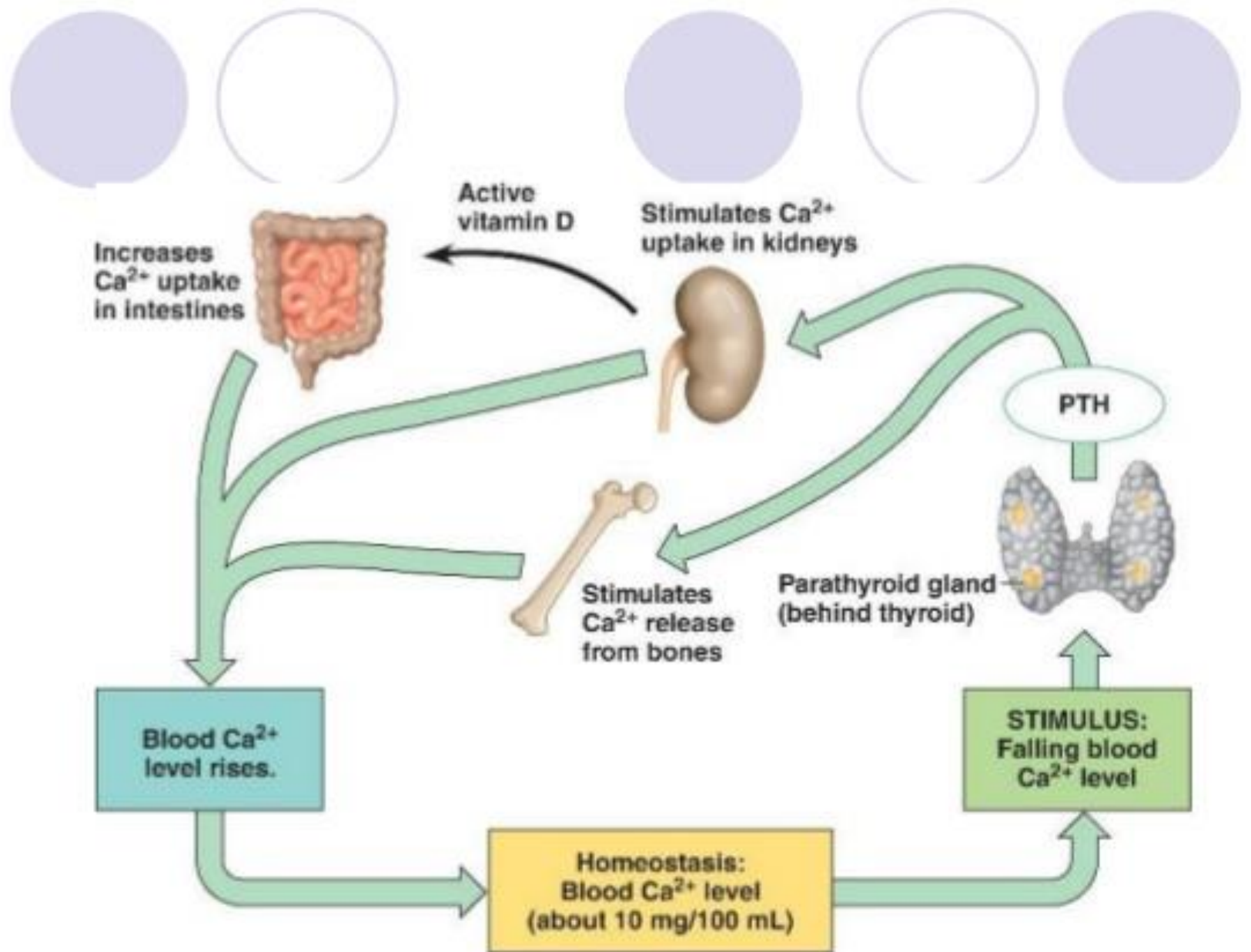


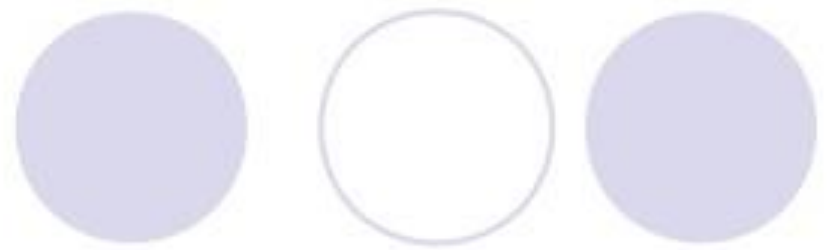
- Calcium binds on CaSR and reduces intracellular cAMP decreases the PTH secretion
- PTH secretion is also controlled by catecholamine levels, magnesium levels





- PTH functions to regulate calcium levels via its actions on three target organs, the bone, kidney, and gut





- Increased PTH secretion leads to an increase in serum calcium levels by increasing bone resorption and enhancing renal calcium reabsorption.
- PTH also enhance 1-hydroxylation of 25-Hydroxyvitamin D, which is responsible for its indirect effect of increasing intestinal calcium absorption.

# Primary Hyperparathyroidism

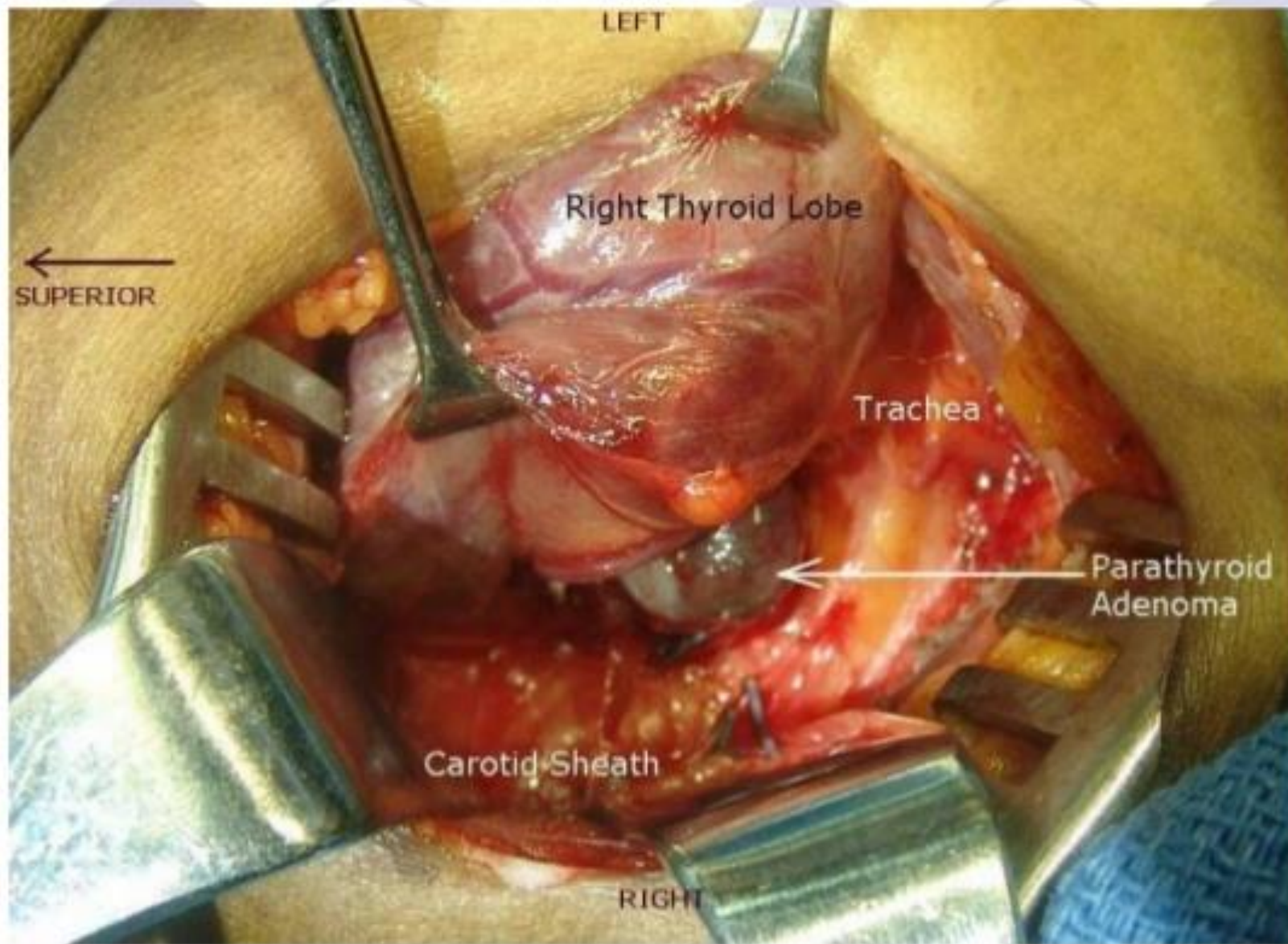
- Occurs in the setting of excessive PTH secretion
- Estimated incidence is 1 case per 1000 men and 2-3 cases per 1000 women
- >80% of cases are caused by a solitary parathyroid adenoma
- 15% multiglandular hyperplasia
- Hereditary syndromes form 5%
- 1% or less Parathyroid carcinoma

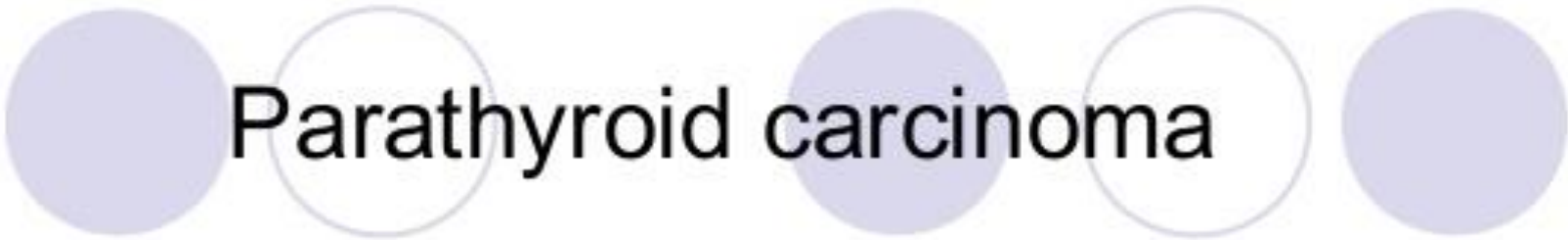


# Parathyroid adenoma

- Usually solitary
- More often affects inferior glands
- Adenomas are ovoid soft reddish brown tumours
- Varying compositions of chief cells, clear and oxyphil cells
- Chief cell adenoma more common

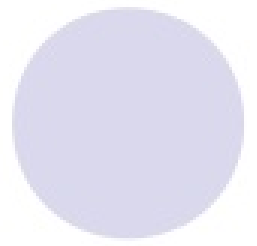
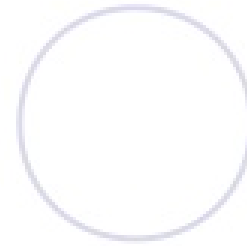
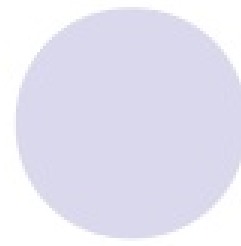
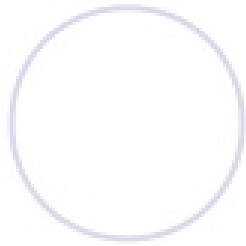
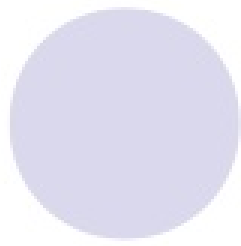






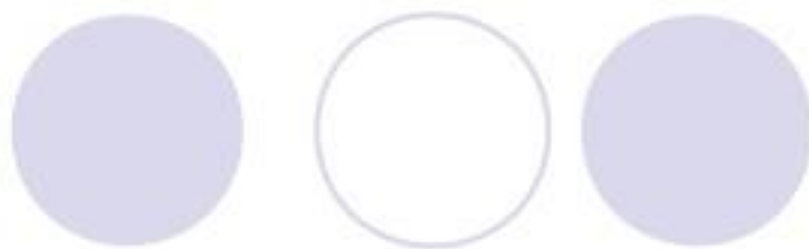
# Parathyroid carcinoma

- Uncommon endocrine malignancy
- 1% of cases of primary hyperparathyroidism
- 40 – 50 yrs of age
- Slow growing but progressive tumour
- Tendancy for spread to local lymph nodes with eventual metastasis to the lung, less commonly to liver and bone

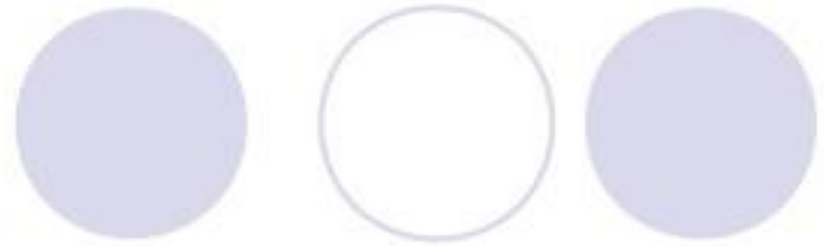


- Majority of tumours are functional with increased PTH and increased calcium levels
- Nonfunctional tumours present as expandable neck mass and usually at an advanced stage





- PRESENTATION
- Palpable neck mass
- Hypercalcemia  $> 14\text{mg/dl}$  ( N – 8.5 – 9.9 )
- Increased PTH 3 to 10 ten times of normal levels
- Increased alkaline phosphatase levels




- Management
- En bloc resection with thyroid lobectomy and isthmus
- Paratracheal and central neck nodal dissection  
Intraoperatively, cancer is suggested by the presence of a large, gray-white to gray-brown lobulated mass with fibrous texture that is adherent to or invasive into surrounding tissues
- $^{99}\text{Tc}$  sestamibi helps in localizing the tumour
- USG can also be used
- Close observation of calcium levels for recurrence

## SECONDARY HYPERPARATHYROIDISM

- Occurs secondary to hypocalcemia or vitamin D def which act as a stimulus for PTH production
- Resected glands from secondary HPT show diffuse and nodular hyperplasia on examination
- Decreased expression of CaSR
- Elevated PTH in the setting of low serum calcium levels is diagnostic

# TERTIARY



- **Tertiary hyperparathyroidism develops in patients with long-standing secondary hyperparathyroidism, which stimulates the growth of an autonomous adenoma**

# Familial Syndromes

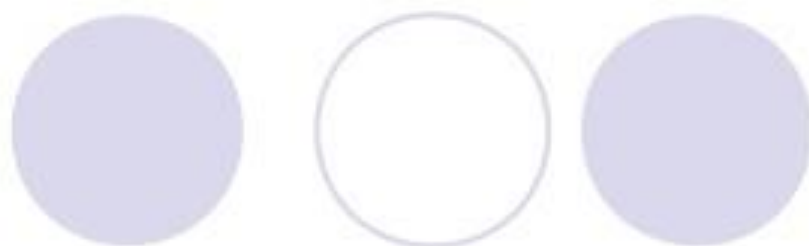
- **MEN I**
- **MEN IIA**
- **Familial Hypocalciuric Hypercalcemia**
- **Hyperparathyroidism-jaw tumor syndrome**
  - Fibro-osseous jaw tumors
  - Renal cysts
  - Solid renal tumors
- **Familial isolated hyperparathyroidism**

# MEN I

- **MEN I**

- 1 in 30,000 persons
- Features:
  - **Parathyroid adenoma(95%)**
    - **Most common and earliest endocrine manifestation**
  - **Gastrinoma (45%)**
  - **Pituitary tumor (25%)**
  - **Insulinoma somatostatinoma**
  - **Facial angiofibroma (85%)**
  - **Collagenoma (70%)**





- **HPT in MEN I**

- Early onset
- Multiple glands affected
- Primary HPT, hypercalcemia
- Surgical intervention is rx of choice
- Subtotal parathyroidectomy B/L neck exploration with excision of three and one half glands
- 20-50mg remnant of vascularized parathyroid tissue is left intact to maintain normocalcemia

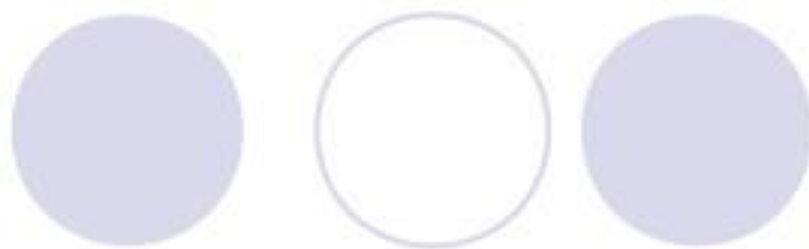


- **Post-op hypoparathyroidism more common (more extensive surgery)**
- **Successful subtotal parathyroidectomy followed by recurrent HPT in 10 years in 50% of cases**



# MEN IIA (Sipple's Syndrome)

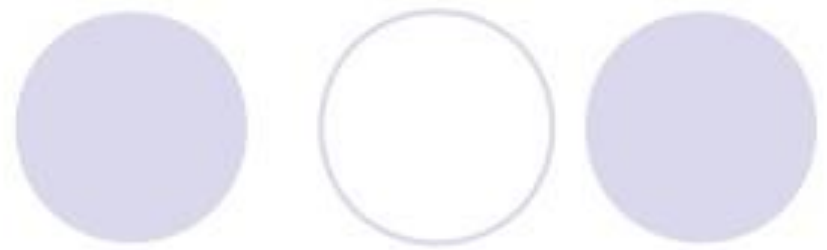
- Features:
  - MTC(95%)
  - Pheochromocytoma(50%)
  - HPT(20%)
  - Cutaneous lichen amyloidosis
  - Hirshsprungs disease



- RET mutation (98%)
- 1 in 30,000-50,000 people
- Usually single adenoma but may have multi-gland hyperplasia
- Symptoms are milder

# HYPERPARATHYROIDISM FEATURES

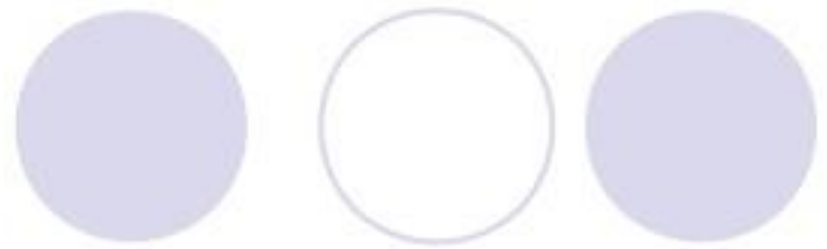
- Symptomatic:
- Musculoskeletal
  - Osteitis fibrosa cystica
  - Bone and joint pain, fatigue lethargy
  - Pathologic fractures
  - Neuromuscular disease



- Renal – ureteric stones
- Gastrointestinal – peptic ulceration, pancreatitis, constipation
- Psychological – anxiety, depression, dementia loss of memory

# Pre-Operative Imaging

- High-resolution ultrasound
  - Sensitivity 65-85% for adenoma; 30-90% for enlarged gland
  - 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
  - Sensitivity of 46-87%
  - Good for ectopic glands in the chest



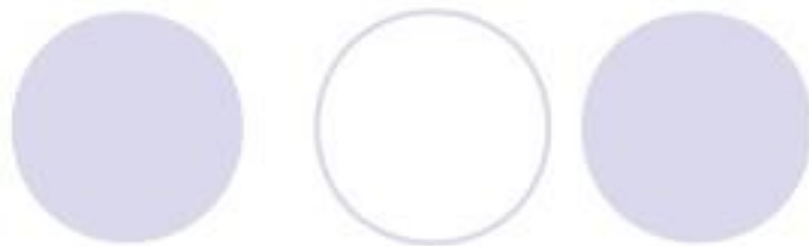
- MRI
  - Sensitivity of 65-80%
  - Good for ectopic glands
- Sestamibi
  - 85-95% accurate in localizing adenoma in primary HPT
- Sestamibi-SPECT
  - Sensitivity 60% for enlarged gland and 98% for solitary adenomas



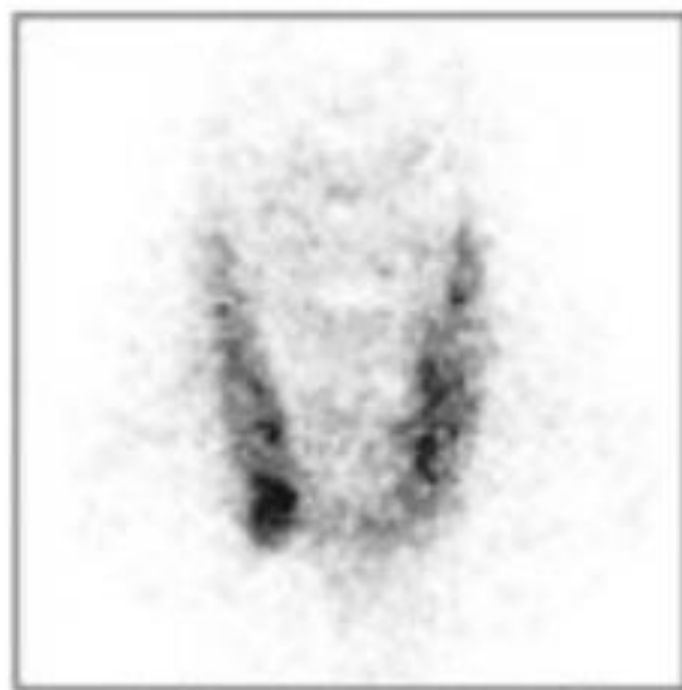
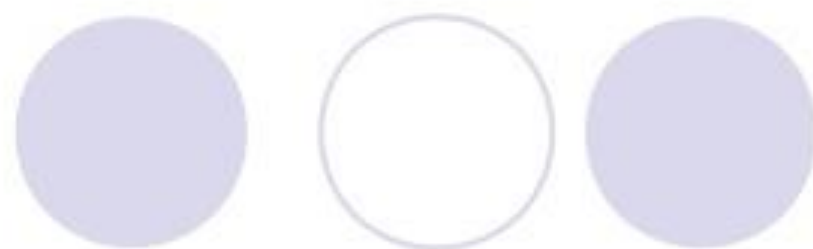
# SESTAMIBI IMAGING



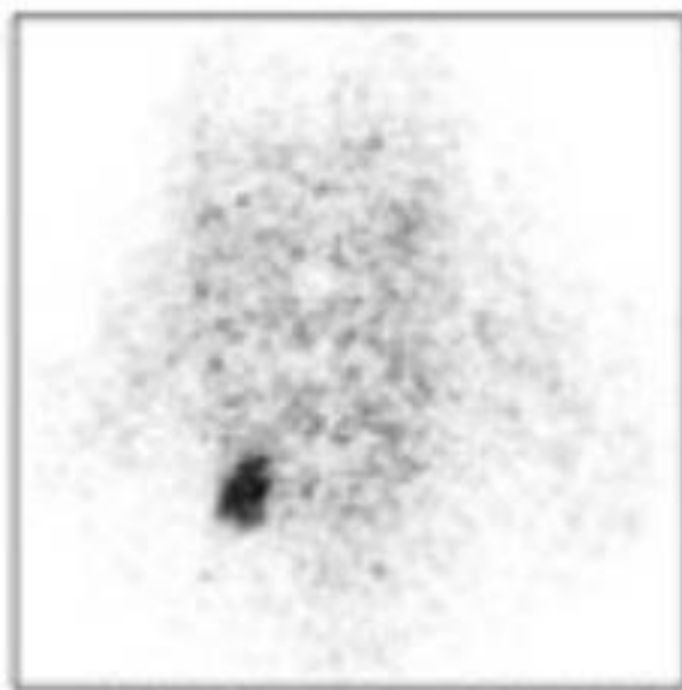
- $^{99}\text{Tc}$  hexakis 2-methoxy isobutyl isonitrile
- First introduced for myocardial perfusion imaging
- Sestamibi localises nonspecifically in mitochondria and cytoplasm
- Parathyroid adenomas concentrate sestamibi because of higher metabolically active mitochondria



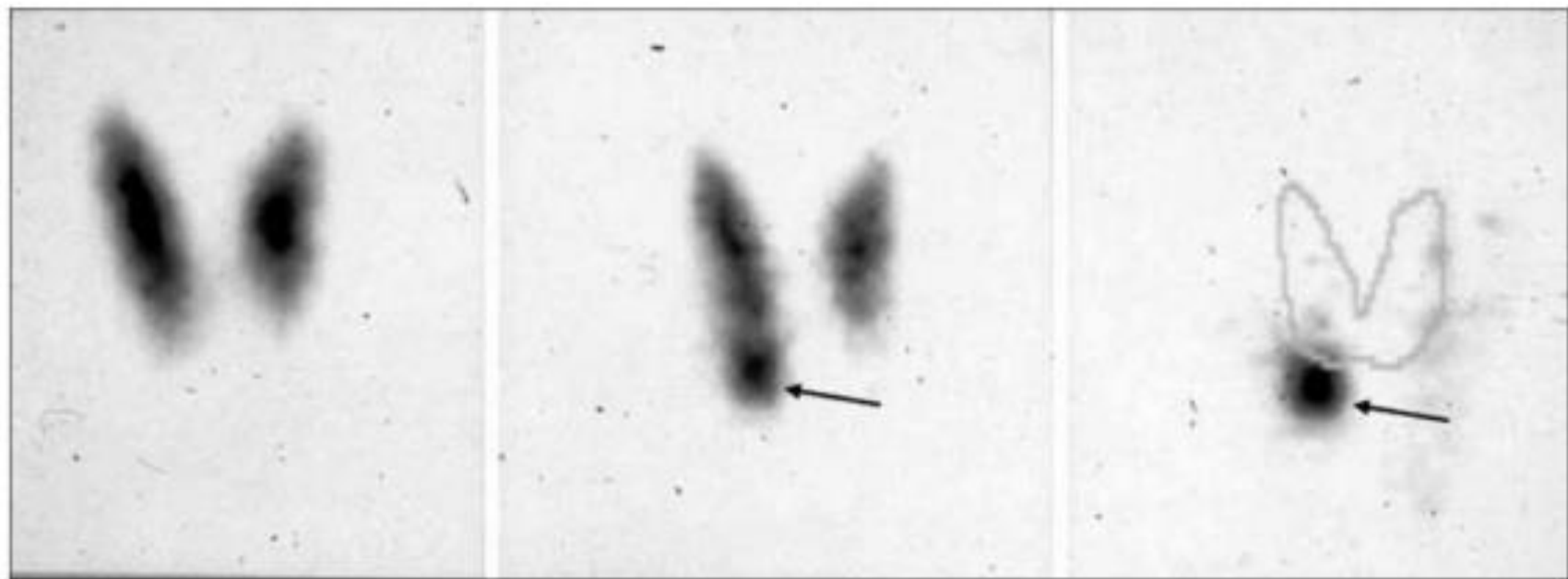
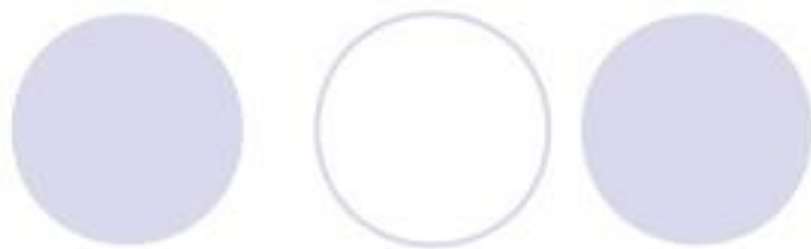
- over time, blood flow causes washout from thyroid and normal parathyroid glands
- delayed images show a discrete “hot spot” in 75-80% patients with primary HPT
- can be used to direct minimally invasive surgical approaches



**$^{99m}\text{Tc}$ -Sestamibi**  
**15 min**

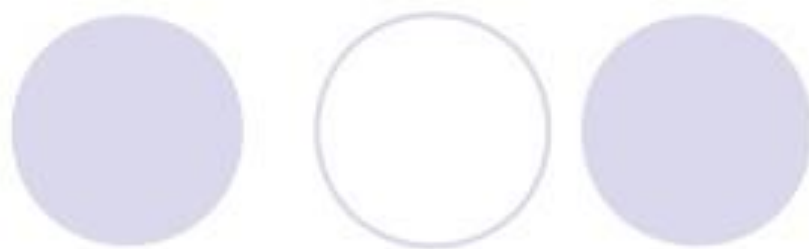


**$^{99m}\text{Tc}$ -Sestamibi**  
**2.5 hr**



# Medical Management

- Asymptomatic patients may elect to be closely followed and managed medically
  - A recent study of pts with asymptomatic primary HPT showed that the majority of pts followed for ten years did not demonstrate an increase in serum calcium or PTH levels—25% of patients had progressive disease including worsening hypercalcemia, hypercalciuria and reduction in bone mass—  
younger patients more likely to have progression of disease



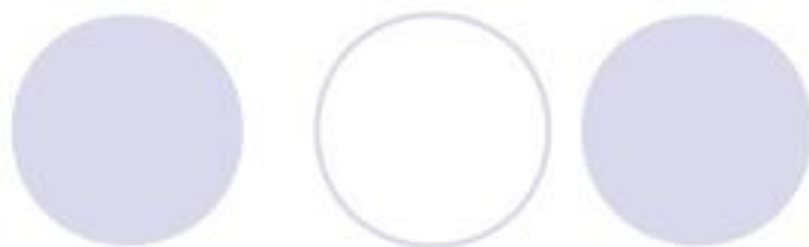
- Patients opting not to have surgery should have a serum calcium level drawn every 6 months and should have annual bone densiometry at all three sites



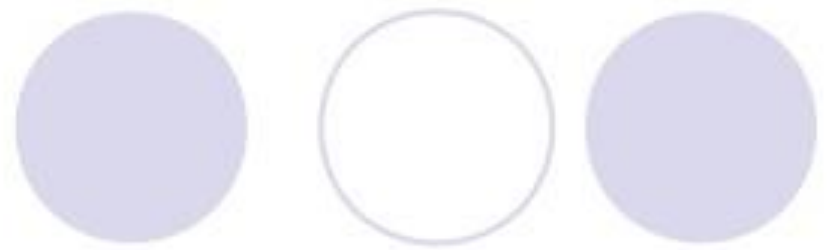


# Medical Management Primary HPT

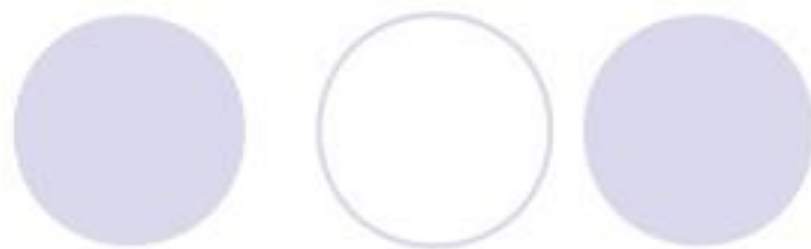
- Estrogen
  - Dose required is high
- Bisphosphonates
  - Studies have shown increase in lumbar spine and femoral neck mineral density
- Calcium/Vitamin D
- Calcimimetic agents (Cinacalcet)
  - Under investigation for primary HPT



- Indications for surgery
- Symptomatic patients
- Asymptomatic patients with calcium levels above 3.00mmol



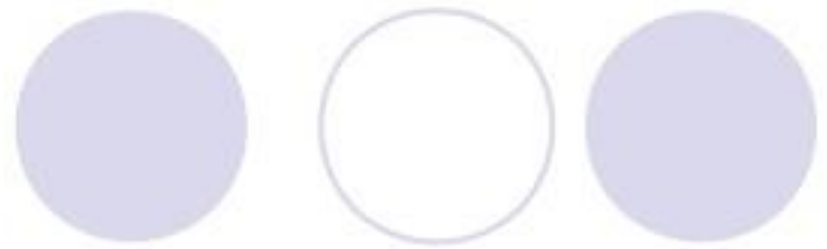
- markedly elevated serum  $\text{Ca}^{++}$
- episode of life-threatening hyper $\text{Ca}^{++}$
- reduced creatinine clearance  $<30\%$
- renal stones
- markedly elevated 24 hr urinary  $\text{Ca}^{++}$
- substantially reduced bone mass (by DEXA scan)
- age  $<50$  (relative indication for surgery)



- Management of primary HPT is mainly surgical
- Conventional parathyroidectomy
- Unilateral or bilateral exploration

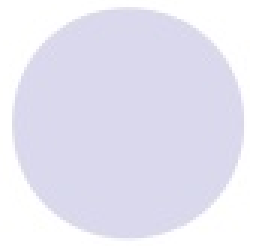
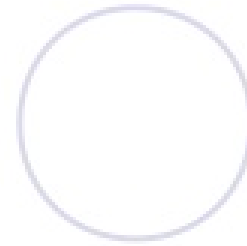
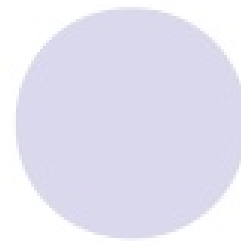
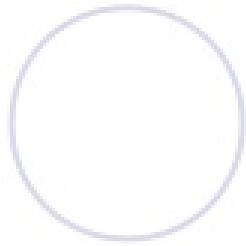
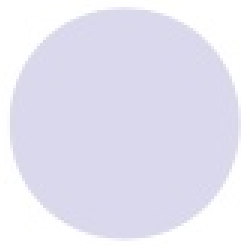


- Unilateral exploration
- Decreased risk of RLN injury
- Decreased incision size
- Decreased early post op hypocalcemia

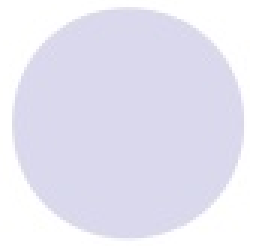
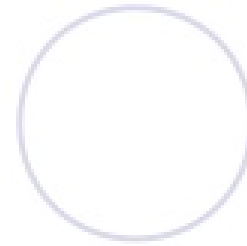
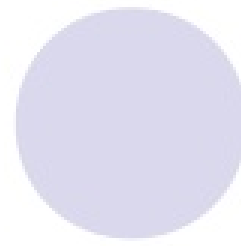
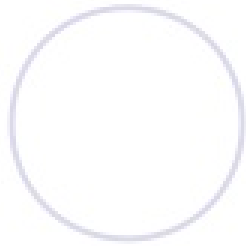
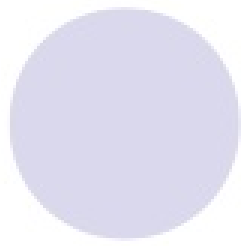


- Bilateral exploration
- Indications MEN, secondary and tertiary HPT where multiple gland pathology suspected
- Access to all 4 glands
- Ability to diagnose hyperplasia, double adenoma that might be missed by minimally invasive technique





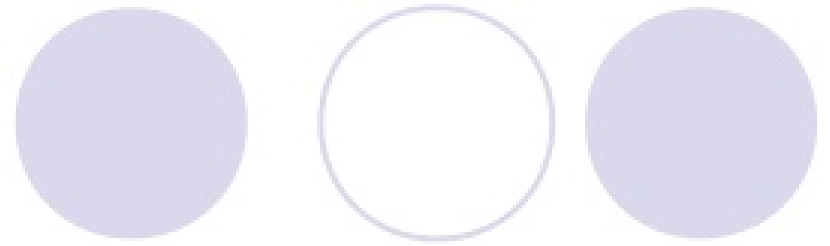
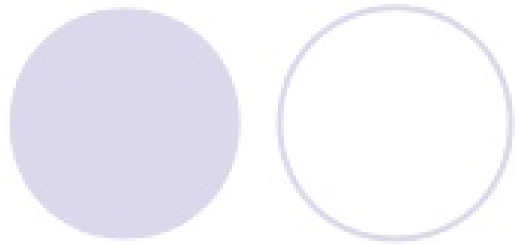
- A bloodless field is important to identify the parathyroids
- Middle thyroid veins are ligated and divided this enables medial and anterior retraction of thyroid lobe
- Space between carotid sheath and thyroid is gently dissected from the cricoid cartilage to the thymus



- Aprox 85% of the glands are found within 1cm of junction of RLN and ITH
- Parathyroids are partly surrounded by fat
- Are soft, yellowish to reddish brown, distinct capsule can b seen

# AUTOTRANSPLANTATION

- For pts with hyperplasia, titanium clip is placed across the most normal gland, leaving a 50mg remnant taking care to avoid disturbing the vascular pedicle and the gland is resected
- Resected parathyroid can be confirmed with frozen section
- Transplanted into nondominant forearm
- Horizontal incision made over the brachioradialis, few cms below the cubital fossa



- Pockets are made in the belly of the muscle and one to two pieces of the gland measuring about 1mm each is placed into the pocket



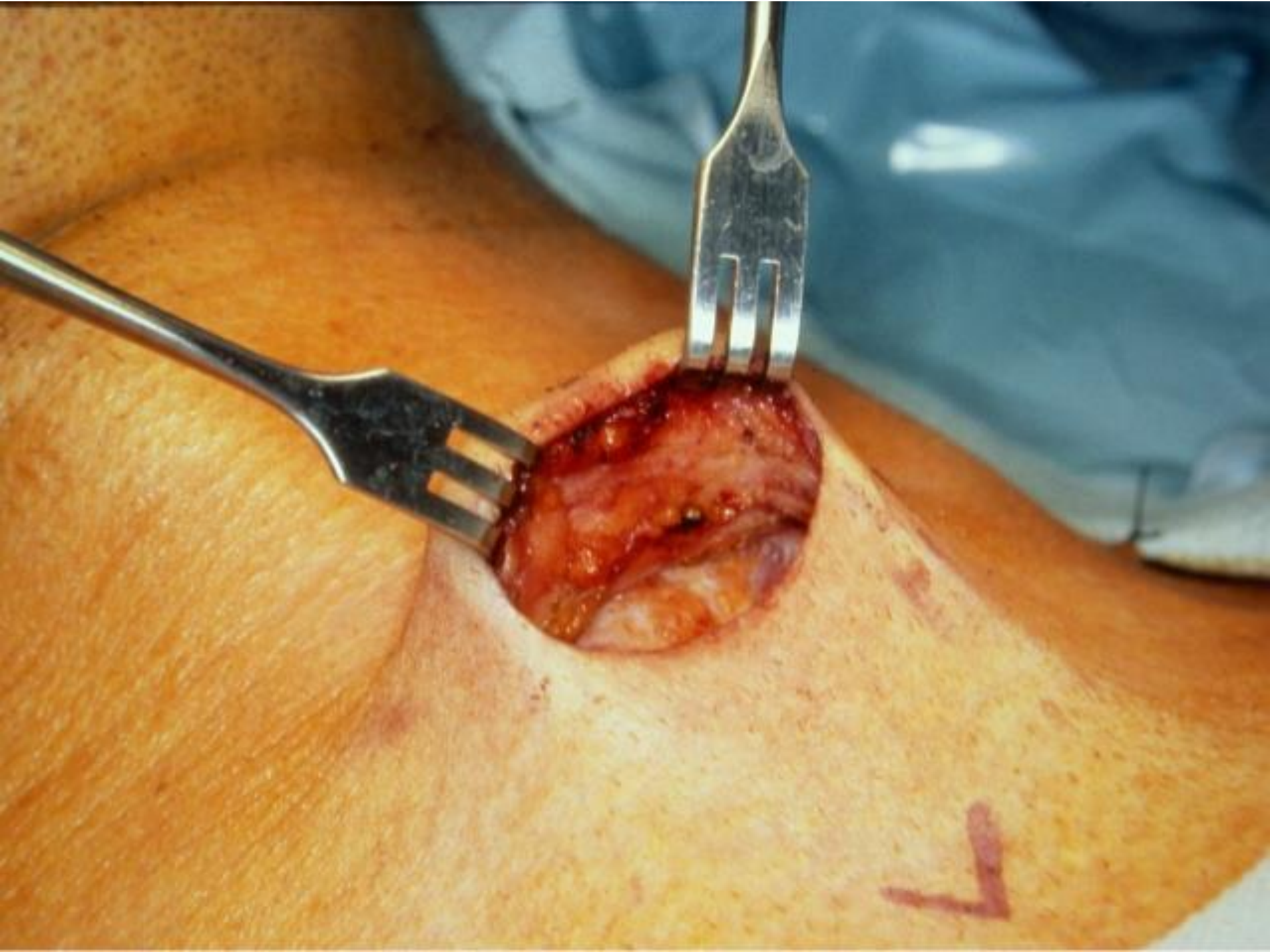
## Minimally Invasive Radioguided Parathyroidectomy (MIRP)

- only in patients who localize by pre-op sestamibi scan (75% with primary HPT)
- sestamibi scan performed 2-3 hours before exploration - timing crucial
- gamma probe used to find the “hottest” spot

3 cm

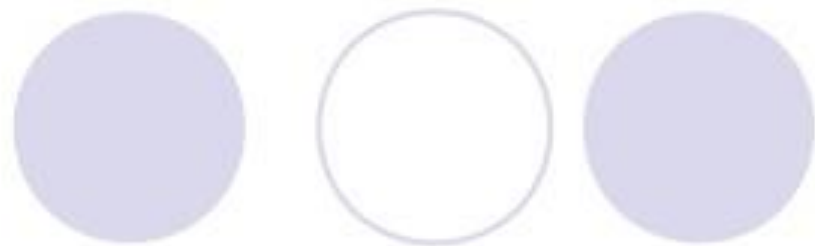








# MIRP - results



- 2 cm incision
- local w/ sedation, out-patient procedure
- 100% cure rate
- no complications
- mean operating time = 25 minutes
- re-operative cure rate = 100%

-Norman J, 1997



# Complications of Parathyroid Surgery

- persistent HPT - 1-20% (experience dependent)
- temporary or permanent hypocalcemia - 1-20%
- nerve injury - recurrent or superior laryngeal - 1-10%
- bleeding - <5%

# Pseudohypoparathyroidism



A rare familial disorder with target tissue resistance to PTH. There is hypocalcaemia, hyperphosphataemia, with increased parathyroid gland function. There is also a variety of congenital defects in the growth and development of skeleton including:

- Short stature

- Short metacarpal and metatarsal bones



# Pseudopseudohypoparathyroidism

In pseudopseudohypoparathyroidism they have the developmental defects without the biochemical abnormalities

The diagnosis is established when low serum calcium level with hyperphosphataemia is associated with increased serum iPTH as well as diminished nephrogenous CAMP and phosphaturic response to PTH administration