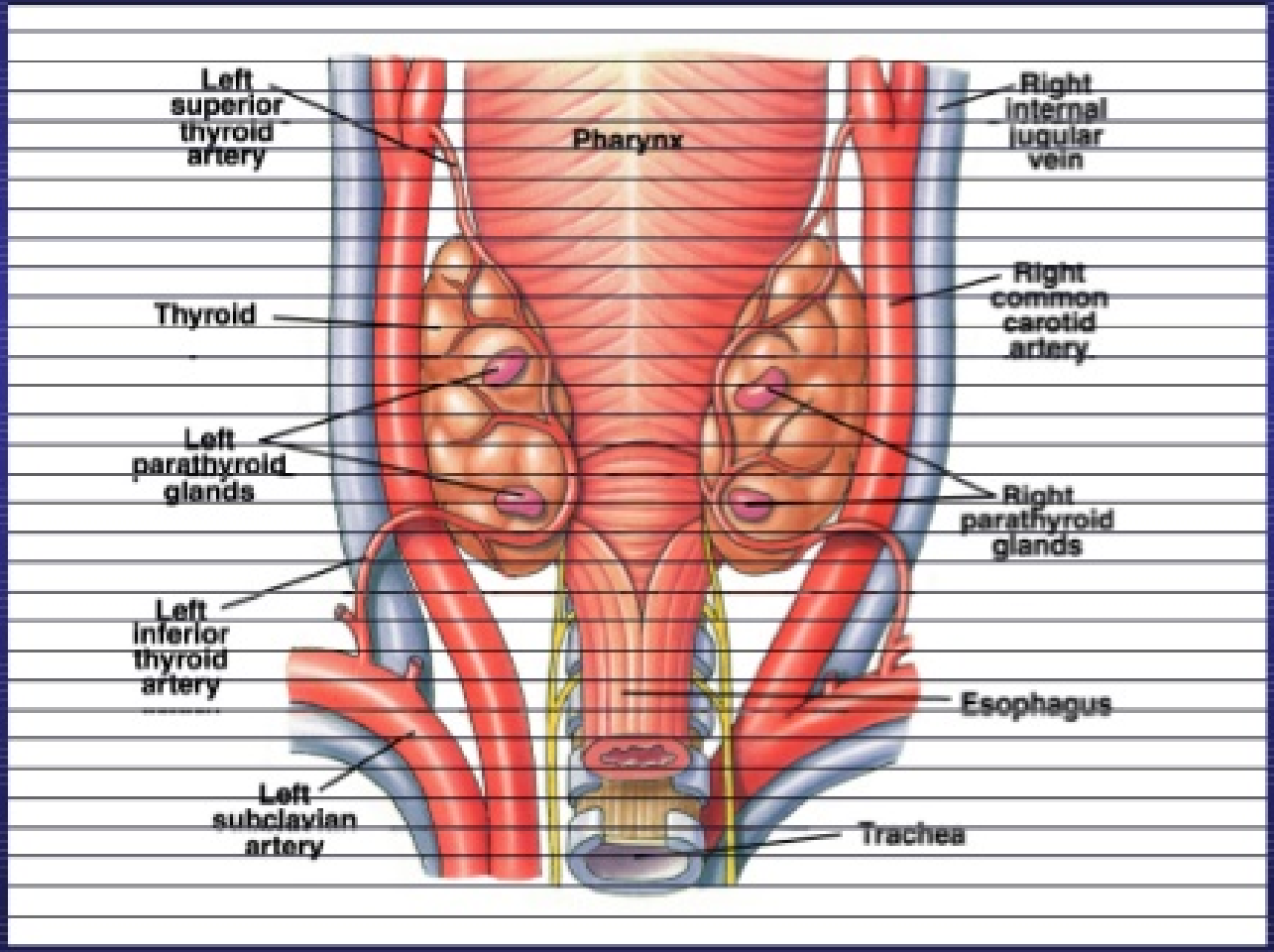
DISORDERS OF THE PARATHYROID GLANDS

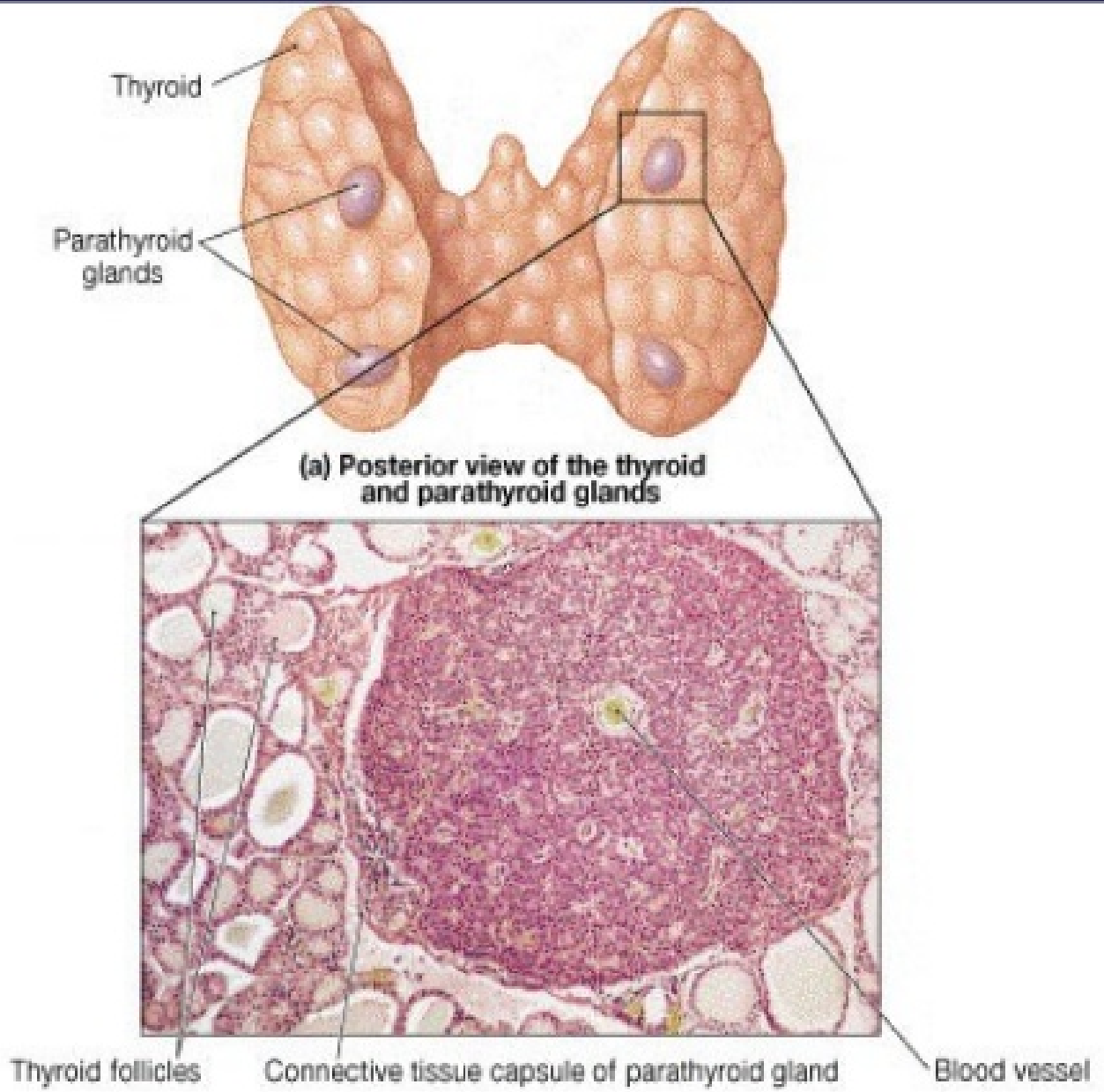
Dr K.Aruldoss
Assistant professor
Periyar Govt Arts Cuddalore

Parathyroid Gland

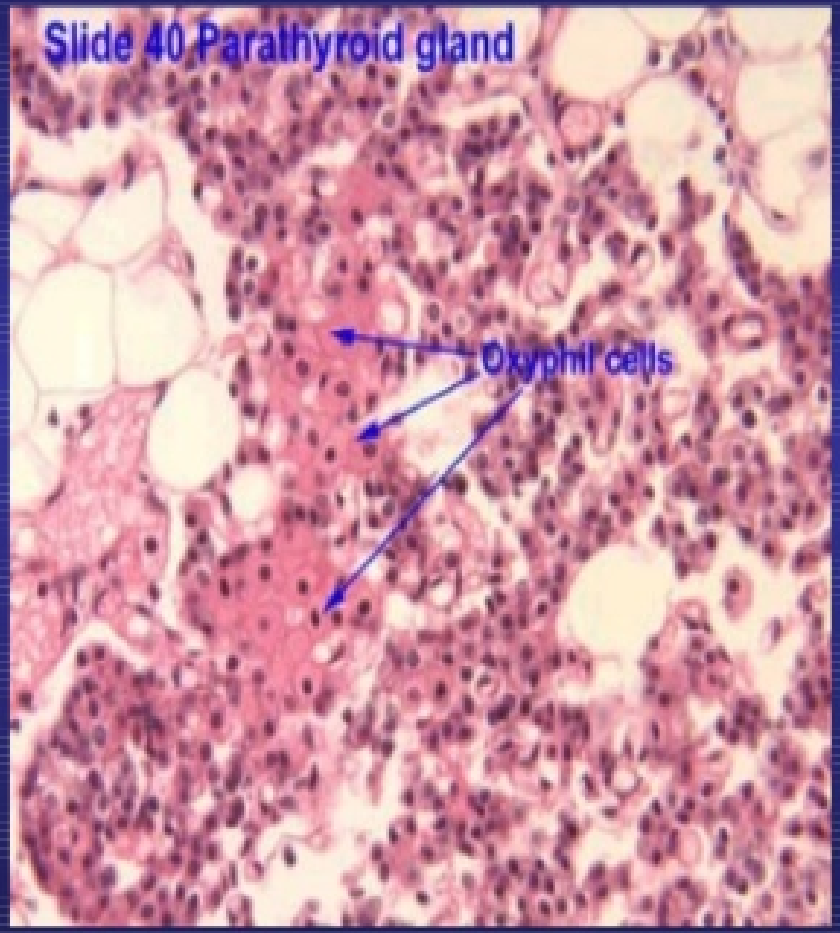
- 4 Small glands located on the dorsal side of the thyroid gland
- Essential for life
- Produces parathyroid hormone
- Responsible for monitoring plasma ca^{2+}

Anatomy & Location of Parathyroid Gland




Thyroid
Parathyroid glands
(a) Posterior view of the thyroid and parathyroid glands
Thyroid follicles
Connective tissue capsule of parathyroid gland
Blood vessel
(b) Thyroid and parathyroid tissues (LM × 116)

Histology



- 50/50 parenchymal cells, stromal fat
- Chief cells – secrete PTH
- Water clear cells
- Oxyphil cells

Parathyroid Gland - Overview

- Calcium & Phosphate Metabolism
- Distribution & Balance of Ca & PO_4
- Hormones involved
  - **Parathyroid Hormone**
  - **Calcitonin**
  - **Vit. D**

)Parathyroid Hormone (PTH

- a peptide hormone that increases plasma Ca^{2+} causes increase in plasma Ca^{2+} by

- Mobilization of Ca^{2+} from bone
- Enhancing renal reabsorption
- Increasing intestinal absorption (indirect)

Parathyroid hormone

Actions (to increase plasma calcium):

- increasing osteoclastic resorption of bone.
- increasing intestinal absorption of calcium.
- increasing synthesis of $1,25\text{-}(OH)_2D_3$.
- increasing renal tubular reabsorption of calcium.
- increasing excretion of phosphate.

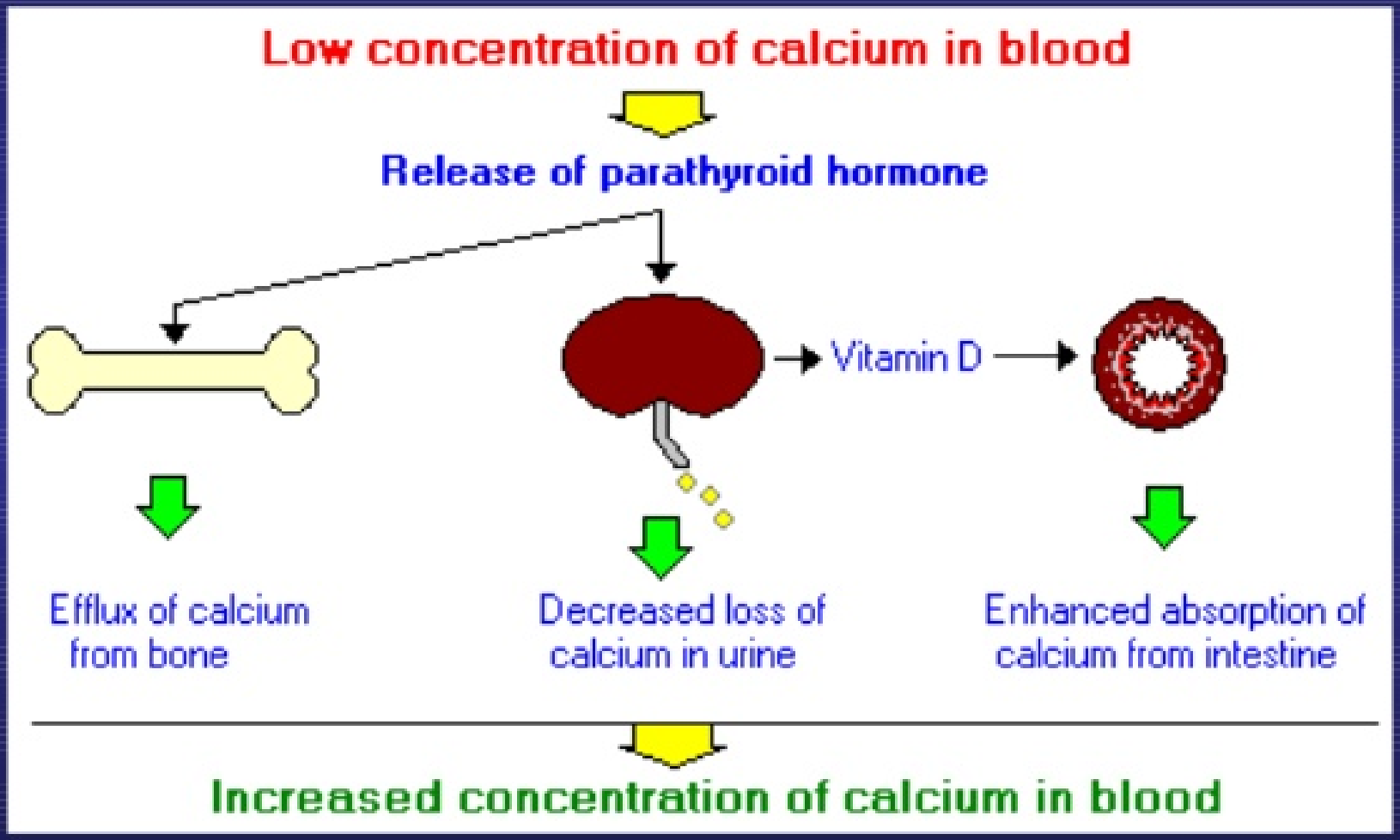
Regulation of PTH release by Plasma Ca^{2+} Levels

- PTH is released by chief cells in the parathyroid gland.
- Chief cells contain receptors for Ca^{2+}
- A decrease in plasma Ca^{2+} levels mediates the release of PTH
- Conversely, hypercalcemia inhibits PTH release

Parathyroid hormone raises blood Ca :by acting on 3 organs

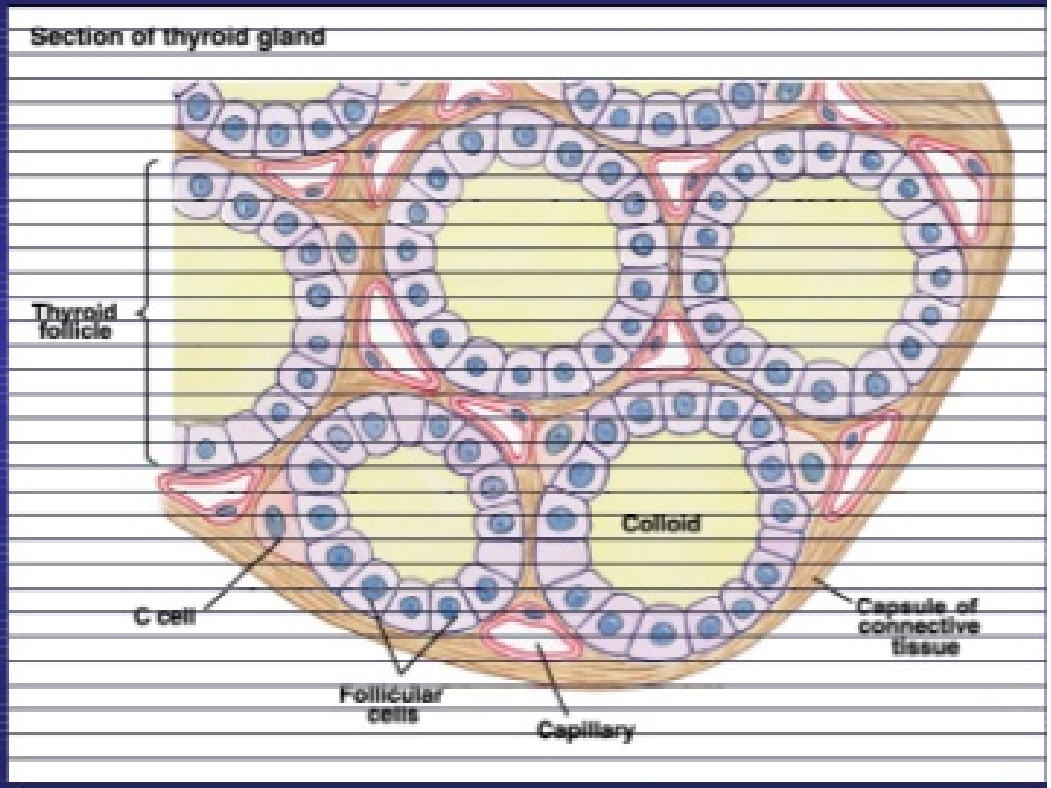
- Bone: main effect- stimulates osteoclasts -> bone breaks down -> Ca released
- Intestines: increases uptake of Ca from intestine
- Kidney: stimulates reabsorption of Ca from the Ca in kidney tubules

PTH function



Calcitonin

- a thyroid hormone
- produced by C-cells
- physiological effects are **antagonist** to those of PTH
- rapid acting, short term regulator of plasma Ca levels



Calcitonin Lowers Blood Ca

- Calcitonin is made by the C cells of the thyroid gland
- A large peptide "prohormone" is made and then cut down to the 32 amino acid calcitonin
- Stimulates osteoblasts, inhibits osteoclasts
- Causes removal of Ca from plasma to calcify new bone
- Lowers plasma Ca (opposes PTH)
- Minor role in adult due to PTH feedback
- Major role in children due to the rapid nature of bone remodeling and its effect on osteoclastic activity

Vit. D

- Vit. D family comprises of several diferent compounds, all having similar functions.
- Most important is Vit. D_3 (cholecalciferol)
- Derived from irradiation of 7-dehydrocholesterol in skin by UV rays
- Causes Ca absorption fron intestinal tract
- Active form of this hormone is 1,25-dihydroxycholecalciferol (calcitriol)

Active Vitamin D (Calcitrol) is Made in 3 Steps by Different Organs

- The skin uses ultraviolet sunlight to make vitamin D3 (cholecalciferol) from cholesterol
- The vitamin D3 is converted to 25-Hydroxycholecalciferol in the liver
- Stimulated by PTH
- The 25-Hydroxycholecalciferol is made into calcitriol (1, 25-Dihydroxycholecalciferol) in the kidney
- Stimulated by PTH
- The main effect of calcitriol is to increase intestinal absorption of Ca

Disorders of the Parathyroid Function

Hyperparathyroidism

- Primary hyperparathyroidismis due to excessive production of PTH by one or more of hyperfunctioning parathyroid glands.
- This leads to hyprcalcemia which fails to inhibit the gland activity in the normal manner.

Hyperparathyroidism

- Primary Hyperparathyroidism
  - Normal feedback of Ca disturbed, causing increased production of PTH
- Secondary Hyperparathyroidism
  - Defect in mineral homeostasis leading to a compensatory increase in parathyroid gland function
- Tertiary Hyperparathyroidism
  - After prolonged compensatory stimulation, hyperplastic gland develops autonomous function

Disorders of the Parathyroid Function

Hyperparathyroidism

- The cause of primary hyperparathyroidism is unknown.
- A genetic factor may be involved.
- The clonal origin of most parathyroid adenomas suggests a defect at the level of the gene controlling the regulation and/or expression of parathyroid hormone.

Disorders of the Parathyroid Function

Hyperparathyroidism

- The incidence of the disease increases dramatically after the age of 50 and it is 2-4 folds more common in women.
- A single adenoma occurs in about 80% of patients with primary hyperparathyroidism.
- Four **glands hyprplasia** account for 15-20% of cases.
- A parathyroid carcinoma could be the etiology in a rare incidence of less then 1%.

Disorders of the Parathyroid Function

:Clinical Features

- The two major sites of potential complications are the **bones and the kidneys.**
- The kidneys may have renal stones (nephrolithiasis) or diffuse deposition of calcium-phosphate complexes in the parachyma **(nephrocalcinosis).**
- Now a days such complications are seen less commonly and around 20% of patients or less show such complications.

Disorders of the Parathyroid Function

:Clinical Features

- In skeleton a condition called **osteitis fibrosa** cystica could occur with subperiosteal resorption of the distal phalanges, distal tappering of the clavicles,
- a "salt and pepper" appearance of the skull as well as bone cysts and brown tumors of the long bones.
- Such overt bone disease even though typical of primary hyperparathyroidism is very rarely encountered.

Disorders of the Parathyroid Function

:Clinical Features

- Other symptoms include **muscle weakness,** easy fatigability, **peptic ulcer** disease, pancreatitis, hypertension, gout and pseudogout
- as well as anemia and **depression** have been associated with primary hyperparathyroidism.

Emotional Disturbances

- Hypercalcemia of any cause – assoc w/ neurologic or psychiatric disturbances
  - Depression, anxiety, psychosis, coma
- Severe disturbances not usually correctable by parathyroidectomy

Differential Diagnosis

Causes of Hypercalcemia

Parathyroid - related

1. Primary hyperparathyroidism
   A. Solitary adenomas
   B. Multiple endocrine neoplasia
2. Lithium therapy
3. Familial hypocalciuric hypercalcemia

Vitamin D – related

1. Vitamin D intoxication
2. ↑ 1,25(OH)2D; sarcoidosis and other granulomatous diseases
3. Idiopathic hypercalcemia or infancy

Differential Diagnosis

Causes of Hypercalcemia

Malignancy - related

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

Associated with high bone turnover

1. Hyperthyroidism
2. Immobilization
3. Thiazides
4. Vitamin A intoxication

Assocated with Renal Failure:

1. Severe secondary hyperparathyroidism
2. Aluminum intoxication
3. Milk alkali syndrome

Diagnosis

- The presence of established hypercalcaemia in more than one serum measurement accompanied by elevated immunoreactive PTH
- Serum phosphate is usually low but may be normal.
- Hypercalcaemia is common and blood alkaline phosphatase (of bone origin) .
- Urinary hydroxyproline concentrations are commonly elevated when the bones are involved.

Other Diagnostic tests

:The Glucocortisoid suppression test

- The heypercalcaemic of non-parathyroid origin e.g., vitamin D intoxication, sarcoidosis and lymphoproliferative syndromes
- generally respond to the administration of prednisolone in a dose of 40-60 mg daily for 10 days by a decrease in serum calcium level.
- A positive test result i.e. significant decrease in serum calcium is a contraindication to neck exploration and signals the need for investigation for a non-parathyroid cause of the hypercalcaemia.

Other Diagnostic tests

:Radiograph

- Plain X-ray of hands can be diagnostic showing subperiosteal bone resorption usually on the radial surfacy of the distal phalanx with distal phalangeal tufting as well as cysts formation and generalzed osteopenia.
- Ultrasonography
- MRI
- CT

Treatment

- A large proportion of patients have "biochemical" hyperparathyroidism but with prolonged follow up they progress to overt clinical presentation.
- In acute severe forms the main stay of therapy is adequate hydration with saline .
- Forced diuresis by diuretics to increase the urinary excretion of calcium rapidly along with sodium and prevent its reabsorption by the renal tubules.

Other agents

- Glucocostiroids
  - In hypercalcaemia associated the hematological malignant neoplasms
- Mythramycin
  - A toxic antibiotics which inhibit bone resorption and is used in hematological and solid neoplasms causing hypercalcaemia.
- Calcitonin
  - Also inhibit osteoclast activity and prevent bone resorption
- Bisphosphonates
  - They are given intravenously or orally to prevent bone resorption.

Other agents

- Phosphate
  - Oral phosphate can be used as an antihypercalcaemic agent and is commonly used as a temporary measure during diagnostic workup.
- Estrogen
  - It also decrease bone resorption and can be given to postmenopausal women with primary hyperparathyroidism using medical therapy

Surgery

- Surgical treatment should be considered in all cases with established diagnosis of primary hyperparthyroidism.
- During surgery the surgeon identifies all four parathyroid glands (using biopsy if necessary) followed by the removal of enlarged parathyroid or 3 ½ glands in multiple glandular disease.

Other Complications

- Deterioration of renal function
- Metabolic disturbance e.g. hypomagnesia, pancreatitis, gout or pseudogout

Hypoparathyroidism

- Deficient secretion of PTH which manifests itself biochemically by hypocalcemia, hyperphospatemia 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 occuring at an early age (genetic origin) with autosomal recessive mode of transmission "multiple endocrine deficiency –autoimmune-candidiasis (MEDAC) syndrome"
  - "Juvenile familial endocrinopathy"
  - "Hypoparathyroidism – Addisson's disease – mucocutaneous candidiasis (HAM) syndrome"

Hypoparathyroidism

:Causes

- **Idiopathic hypoparathyroidism**
  - Circulating antibodies for the parathyroid glands and the adrenals are frequently present.
  - Other associated disease:
    - Pernicious anemia
    - Ovarian failure
    - Autoimmune thyroiditis
    - Diabetes mellitus

Hypoparathyroidism

:Causes

- 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.

Major causes of chronic hypocalcemia other than hypoparathyroidism

- Dietary deficiency of vitamin D or calcium
- Decreased intestinal absorption of vitamin D or calcium due to primary small bowel disease, short bowel syndrome, and post-gastrectomy syndrome.
- Drugs that cause rickets or osteomalacia such as phenytoin, phenobarbital, cholestyramine, and laxative.

Major causes of chronic hypocalcemia other than parathyroprival hypoparathyroidism

- States of tissue resistance to vitamin D
- Excessive intake of inorganic phosphate compunds
- Psudohypoparathyroidism
- Severe hypomagnesemia
- Chronic renal failure

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

A. Neuromuscular

- Parathesia (sensation of numbness or tingling on the skin)
- Tetany
- Hyperventilation
- Adrenergic symptoms
- Convulsion (More common in young people and it can take the form of either generalized tetany followed by prolonged tonic spasms or the typical epileptiform seizures.
- Signs of latent tetany
  - Chvostek sign (nilateral spasm of the oris muscle is initiated by a slight tap over the facial)
  - Trousseau sign
  - Extrapyramidal signs (due to basal ganglia calcification) Involuntary movements, Tremors and rigidity

Trousseau sign

Ask the patient to relax his facial nerves. Next, stand directly in front of him and tap the facial nerve either just anterior to the earlobe or below the zygomatic arch and the corner of the mouth. A positive response varies from twitching of the lip at the corner of the mouth to spasm of all facial muscles, depending on the severity of hypocalcaemia.

Hypoparathyroidism

:Clinical Features

B. Other clinical manifestation

1. Posterio lenticular cataract
2. Cardiac manifestation:
3. Prolonged QT interval in the ECG
4. Resistance to digitalis
5. Hypotension
6. Refractory heart failure with cardiomegally can occur.

Hypoparathyroidism

:Clinical Features

B. Other clinical manifestation

3. **Dental Manifestation**

   Abnormal enamel formation with delayed or absent dental eruption and defective dental root formation.

4. **Malabsorption syndrome**

   Presumably secondary to decreased calcium level and may lead to steatorrhoea with long standing untreated disease.

Hypoparathyroidism

:Diagnosis

- In the absence of renal failure the presence of hypocalcaemia with hyperphosphataemia is virtually diagnostic of hypoparathyroidism.
- Undetectable serum iPTH confirms the diagnosis or it can be detectable if the assay is very sensitive.

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.

Emergency Treatment for Hypocalcaemic

:Hungry bone syndrome

In patients with hypoparathyroidism and severe bone disease who undergo successful parathyroidectomy hypocalcaemia may be severe and parenteral calcium infusion with later supplementation with oral calcium and vitamin D.