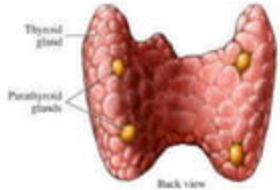
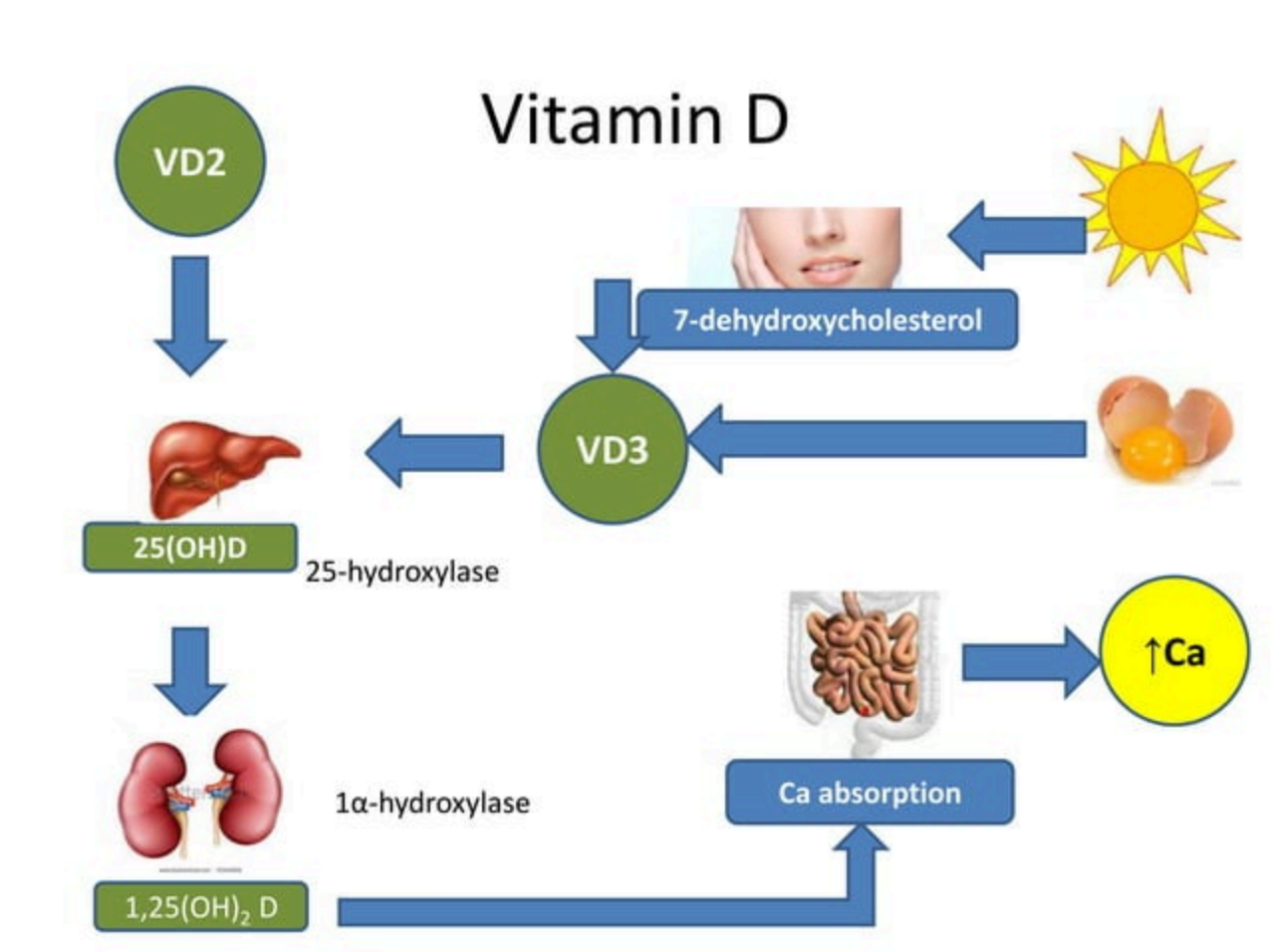


Disorders of the parathyroid glands

Pratap Sagar Tiwari , MBBS MD

Lecturer NMC

Vitamin D


VD2
7-dehydroxycholesterol
VD3
25(OH)D
25-hydroxylase
↑Ca
Ca absorption
1α-hydroxylase
1,25(OH)2 D

PTH Effects on Bone

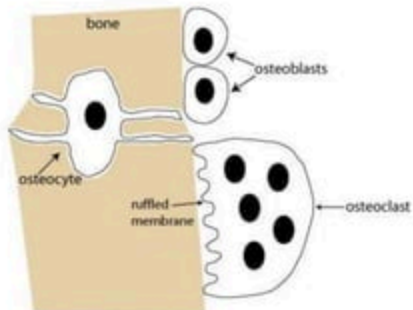
PTH

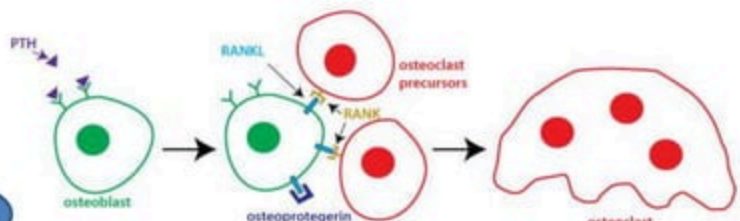
Stimulates

Bone resorption

↑Ca into ECF

↑ Ca



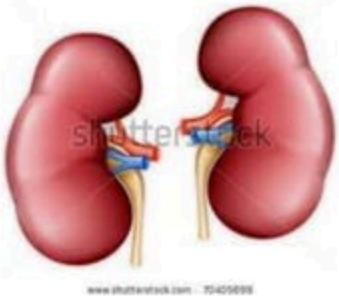


http://courses.washington.edu/conj/bess/bone/bone2.html

PTH Effects on Kidney

1

- ↓the loss of Ca++ ions in the urine by **stimulating Ca++ reabsorption**
- **inhibits phosphate reabsorption**



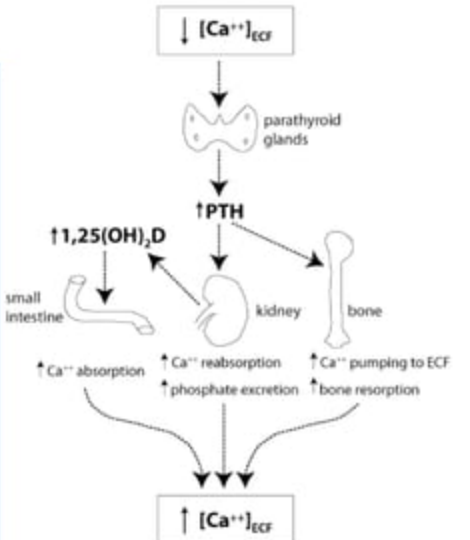
↑Ca
↓ PO4

2

- **stimulate production of 1,25(OH)2D**

Endocrine Regulation of $[Ca^{++}]_{ECF}$

1. PTH stimulates the release of Ca++ from bone, in part by stimulating bone resorption.
2. PTH decreases urinary loss of Ca++ by stimulating Ca++ reabsorption.
3. PTH indirectly stimulates Ca++ absorption in the small intestine by stimulating synthesis of 1,25(OH)2D in the kidney.



http://courses.washington.edu/conj/bess/calcium/calcium.html

Parathyroid hormone

- Parathyroid hormone (PTH) plays a key role in the **regulation of calcium and phosphate homeostasis and vitamin D metabolism.**
- **The four parathyroid glands** lie behind the lobes of the thyroid. The parathyroid chief cells respond directly to changes in calcium concentrations *When serum ionised calcium levels fall, PTH secretion rises.*

Hypercalcemia: causes

With normal or elevated (i.e. inappropriate) PTH levels

- Primary or tertiary hyperparathyroidism
- Lithium-induced hyperparathyroidism
- Familial hypocalciuric hypercalcaemia , MEN

With low (i.e. suppressed) PTH levels

- Malignancy (e.g. lung, breast, renal, ovarian, colonic and thyroid carcinoma, lymphoma, multiple myeloma)
- Elevated $1,25(OH)_2$ vitamin D (vitamin D intoxication, sarcoidosis, HIV, other granulomatous disease)
- Thyrotoxicosis , pheochromocytoma
- Paget's disease with immobilisation
- Milk-alkali syndrome
- Thiazide , Lithium, theophylline
- Glucocorticoid deficiency

Signs/Symptoms

- The classic symptoms are described as'**bones, stones and abdominal groans'.**
- Polyuria and polydipsia, renal colic, lethargy, anorexia, nausea, dyspepsia and peptic ulceration, constipation, depression, drowsiness and impaired cognition.
- Patients with malignant hypercalcaemia can have a rapid onset of symptoms.
- A family history of hypercalcaemia raises the possibility of FHH or MEN .

Table

Disease	Ca	PTH
Hyperparathyroidism	High	High
Hypoparathyroidism	low	Low
Hypercalcemia of malignancy	High	Low
Secondary hyperparathyroidism in renal disease	Low	High

Hypercalcemia of malignancy

- one of the most common causes of non-PTH-mediated hypercalcemia.
- DX : confirmed by demonstrating an ↑serum concentration of **PTH-related protein** (PTHrp) .
- Levels of PTH and 1,25-dihydroxyvitamin D (calcitriol) are usually appropriately suppressed in these patients.

Management

- **Mild /mod hypercalcemia** : asymptomatic or mildly symptomatic hypercalcemia (Ca <12 mg/dL do not require immediate Rx. However maintain adequate hydration and avoid factors that aggravate .
- **Severe hypercalcemia** : Patients with Ca >14 mg/dL require more aggressive Rx.

Severe Hypercalcemia

- **Volume expansion** with isotonic saline at an initial rate of 200-300 mL/hr then adjusted to maintain the UO at 100-150 mL/hour.
- **Calcitonin**
- If malignancy: **zoledronic acid or pamidronate**
- Hemodialysis
- Correct hyperparathyroidism if present

Hypocalcemia

- Hypocalcaemia is much less common than hypercalcaemia.
- The most common cause of hypocalcaemia is a **low serum albumin** with normal ionised calcium concentration.

Differential diagnosis of hypocalcaemia

	Total serum calcium	Ionised serum calcium	Serum phosphate	Serum PTH
Hypoalbuminaemia	↓	↔	↔	↔
Alkalosis	↔	↓	↔	↔ or ↑
Respiratory, e.g. hyperventilation				
Metabolic, e.g. Conn's syndrome				
Vitamin D deficiency	↓	↓	↓	↑
Chronic renal failure	↓	↓	↑	↑
Hypoparathyroidism	↓	↓	↑	↓
Pseudohypoparathyroidism	↓	↓	↑	↑
Acute pancreatitis	↓	↓	↔or↓	↑
Hypomagnesaemia	↓	↓	Variable	↓ or ↔

Source: Davidson

Hypocalcemia:Clinical manifestation

- **Hypocalcemic tetany** : This is characterised by muscle spasms due to increased excitability of peripheral nerves.
- Triad of **carpopedal spasm, stridor and convulsions.**
- **Trousseau's sign**; inflation of a bp cuff on the upper arm to >the SBP is f/b carpal spasm within 3 min.
- **Chvostek's sign**: tapping over the branches of the facial nerve produces twitching of the facial muscles.

EXAMINATION TIP

Recognizing carpopedal spasm

In the hand, carpopedal spasm involves adduction of the thumb over the palm, followed by flexion of the metacarpophalangeal joints, extension of the interphalangeal joints (fingers together), adduction of the hyperextended fingers, and flexion of the wrist and elbow joints. Similar effects occur in the joints of the feet.

http://www.fpnotebook.com/legacy/Ortho/Wrist/CrpdlSpsm.htm

Management

- Milder symptoms of neuromuscular irritability (paresthesias) and corrected S. Ca >7.5 mg/dL : initial Rx with **oral Ca** supplementation.
- 1500-2000 mg of elemental Ca given as **calcium carbonate or calcium citrate/d**, in divided doses.
- If symptoms do not improve with oral supplementation, **iv Ca infusion** is required.

Management of severe hypocalcaemia

- 10-20mL 10% **ca gluconate** i.v. over 10-20 min
- Continuous i.v. infusion may be required for several hrs (equivalent of 10 mL 10% calcium gluconate/hr)
- Cardiac monitoring is recommended .
- If Mg deficiency :50 mmol Mgcl i.v. over 24 hrs

Hyperparathyroidism

Type	Serum Ca	PTH
Primary	**Raised**	**Not suppressed**
Single adenoma (90%) Multiple adenomas (4%) Nodular hyperplasia (5%) Carcinoma (1%)		
Secondary	**Low**	**raised**
Chronic renal failure Malabsorption Osteomalacia and rickets		
Tertiary	**Raised**	**Not suppressed**

Multiple endocrine neoplasia

Features	MEN1	MEN2A	MEN2B
Alias:	Wermer S	Sipple S	
Pancreatic tumors	++		
Pituitary adenoma	++		
Parathyroid hyperplasia	+++	+	
Angiofibroma/Lipoma	+		
Medullary thyroid ca		+++	++
Pheochromocytoma		+	+
Mucosal neuroma			+++
Marfanoid habitus			

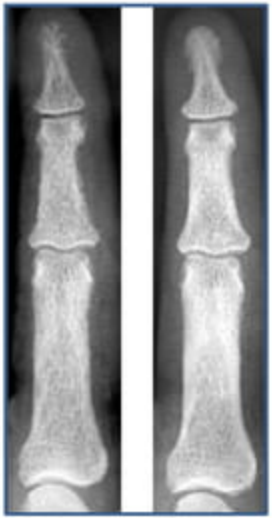
PHPT:Clinical features

- Features of **Hypercalcemia**
- **Osteitis fibrosa**: results from increased bone resorption by osteoclasts with fibrous replacement.
- **Chondrocalcinosis** :due to deposition of Ca pyrophosphate crystals within articular cartilage.

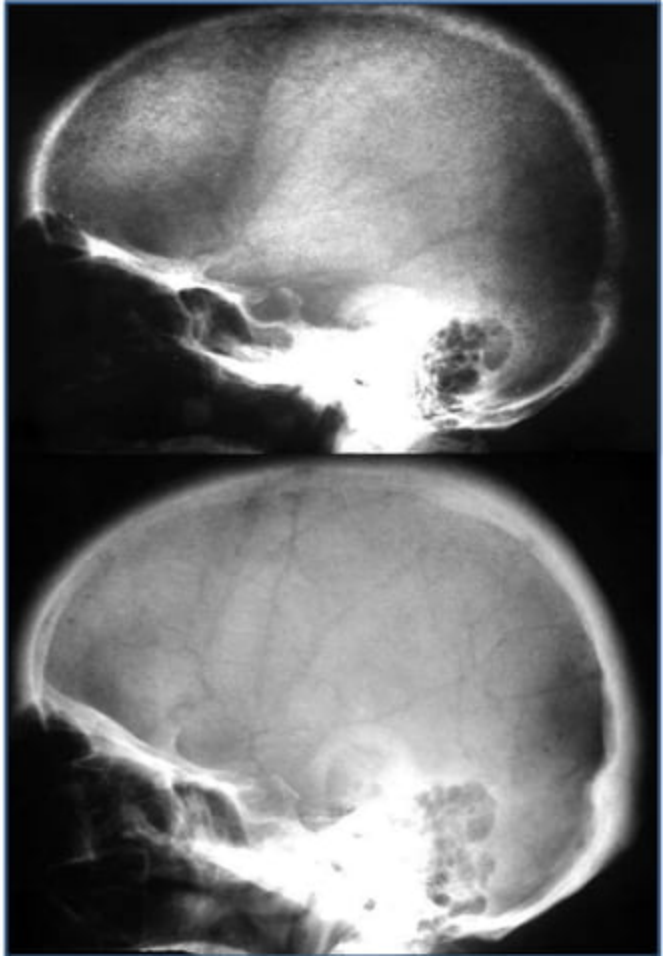
Imaging

- In the early stages there is demineralisation, with subperiosteal erosions and **terminal resorption in the phalanges.**
- **A 'pepper-pot' appearance** :lateral X-rays of the skull.
- Reduced bone mineral density, resulting in either osteopenia or osteoporosis. And is assessed by DEXA
- In nephrocalcinosis, scattered opacities within the renal outline.
- There may be soft tissue calcification in arterial walls, soft tissues of the hands and the cornea.

Images



Source: http://uwmsk.org/residentprojects/hpth.html



Investigations

- The diagnosis can be confirmed by finding a **raised PTH level** in the presence of **hypercalcaemia**, provided that FHH is excluded.
- Parathyroid scanning by **99mTc-sestamibi** scintigraphy or **ultrasound examination** to **localise an adenoma** and allow a targeted resection.

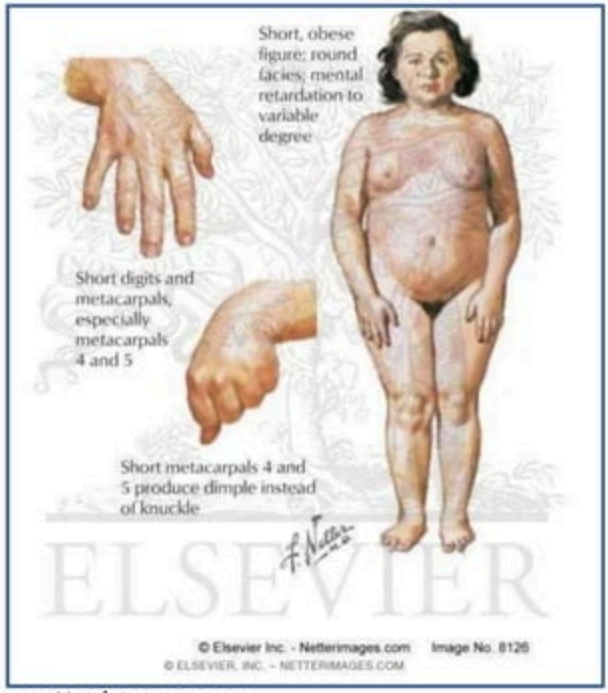
Management

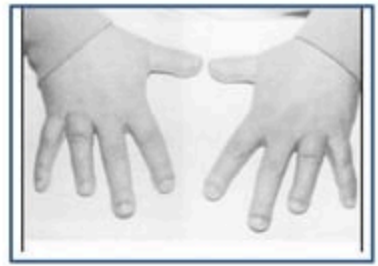
- Surgery
- Post op vit D and Calcium supplements according to lab values.
- Treatment of Hypercalcemia

Hypoparathyroidism

- The MC cause is **damage to the parathyroid glands** (or their bld supply) **during thyroid Sx**.
- Rarely, hypoparathyroidism can occur as a result of **infiltration of the glands**, e.g. in **haemochromatosis and Wilson's disease.**

Albright's hereditary osteodystrophy





Source:www.netterimages.com

Pseudohypoparathyroidism

- The disorder is characterized by a lack of responsiveness to PTH, resulting in **↓ Ca, ↑Po4, and appropriately ↑ PTH.**
- Individuals with **Albright's hereditary osteodystrophy** have short stature, shortened 4th & 5th metacarpals, rounded facies, and often mild mental retardation.
- The kidney responds as if PTH were absent. The PTH receptor itself is normal, but there are **defective post-receptor mechanisms due to mutations**.

Management of hypoparathyroidism

- Persistent hypoparathyroidism and pseudohypoparathyroidism are Rx with **oral calcium salts and vitamin D analogues**, either 1α-hydroxycholecalciferol (alfacalcidol) or 1,25-dihydroxycholecalciferol (calcitriol).
- **Recombinant PTH** is available as SC injection therapy for osteoporosis.

End of slides

References:

- Davidson's Principles & practice of Medicine. 21st ed.
- Harrison's
- Uptodate 20.3
- Medscape