Physiology for Medical Students

Calcium Homeostasis
Endocrine 8

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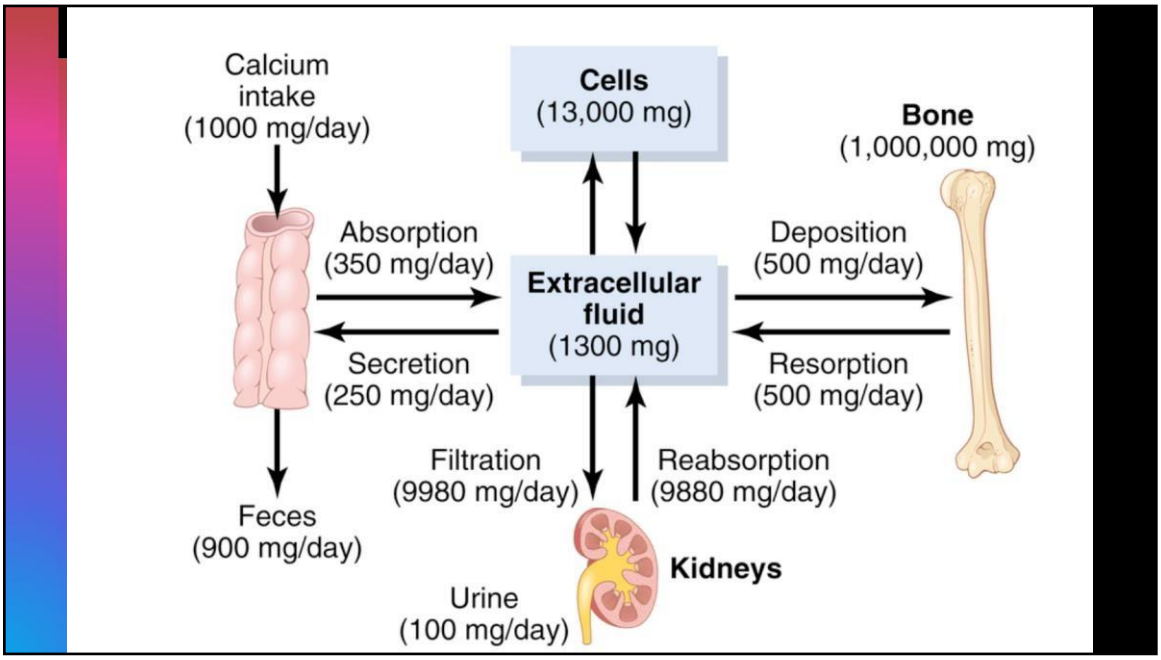
Parathyroid Hormone, Calcitonin, Calcium and Phosphate Metabolism, Vitamin D, Bone

CHAPTER 79


Calcium intake (1000 mg/day)
Cells (13,000 mg)
Bone (1,000,000 mg)
Absorption (350 mg/day)
Extracellular fluid (1300 mg)
Deposition (500 mg/day)
Secretion (250 mg/day)
Resorption (500 mg/day)
Filtration (9980 mg/day)
Reabsorption (9880 mg/day)
Feces (900 mg/day)
Kidneys
Urine (100 mg/day)

Calcium Homeostasis

99% : crystalline form within the **skeleton and teeth.**
0.9% : intracellularly within the soft tissues
less than **0.1%**: is present in the **ECF**.

Approximately **half of the ECF** Ca is **bound to plasma proteins or is complexed with phosphate**

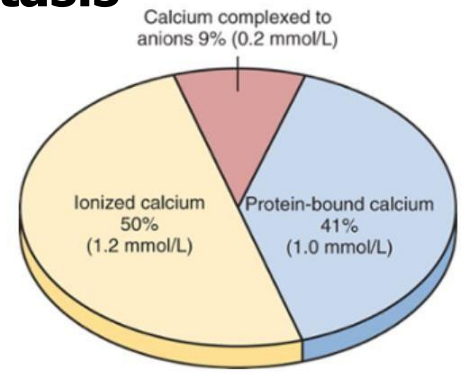


Figure 79-1 Distribution of ionized calcium (Ca^{++}), diffusible but un-ionized calcium complexed to anions, and…

The other half of the ECF Ca is freely diffusible and can readily pass from the plasma into the interstitial fluid and interact with the cells. Only this free ECF Ca **is biologically active and subject to regulation;** it constitutes less than one thousandth of the total Ca in the body

Calcium Homeostasis

- The ionic calcium is the form that is important for most body functions of calcium.

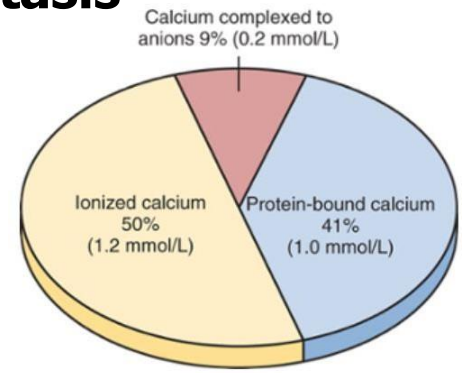


Figure 79-1 Distribution of ionized calcium (Ca^{++}), diffusible but un-ionized calcium complexed to anions, and…

Calcium _ physiological roles

- **Neuromuscular excitability:**
- Hypocalcemia causes the nervous and muscular system to become progressively more excitable.
- By increasing neuronal membrane permeability to sodium ions, allowing easy initiation of action potentials.
- Spontaneous nerve impulses → skeletal muscles (tetany), brain (seizures)
- Conversely, a rise in free Ca depresses neuromuscular excitability.
- Hypercalcemia: cardiac arrhythmias and generalized depression of neuromuscular excitability.

Figure 79-2 Hypocalcemic tetany in the hand, called *carpopedal spasm.*

**Tetany ordinarily occurs when the blood concentration of calcium falls from its normal level of 9.4 mg/dl to about 6 mg/dl, (35%) below the normal, and it is usually lethal at about 4 mg/dl.

Calcium Homeostasis

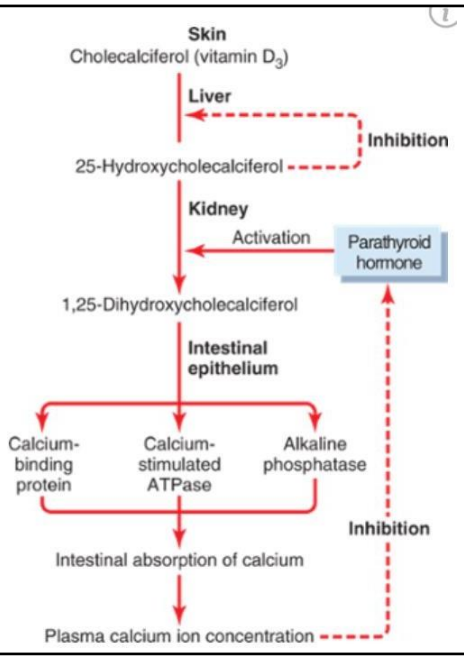
- Regulation of Ca metabolism depends on hormonal control of exchanges between the **ECF** and three other compartments: **bone, kidneys, and intestine.**

- **Three hormones play an integral role in maintaining calcium homeostasis; vitamin D, parathyroid hormone, and calcitonin.**

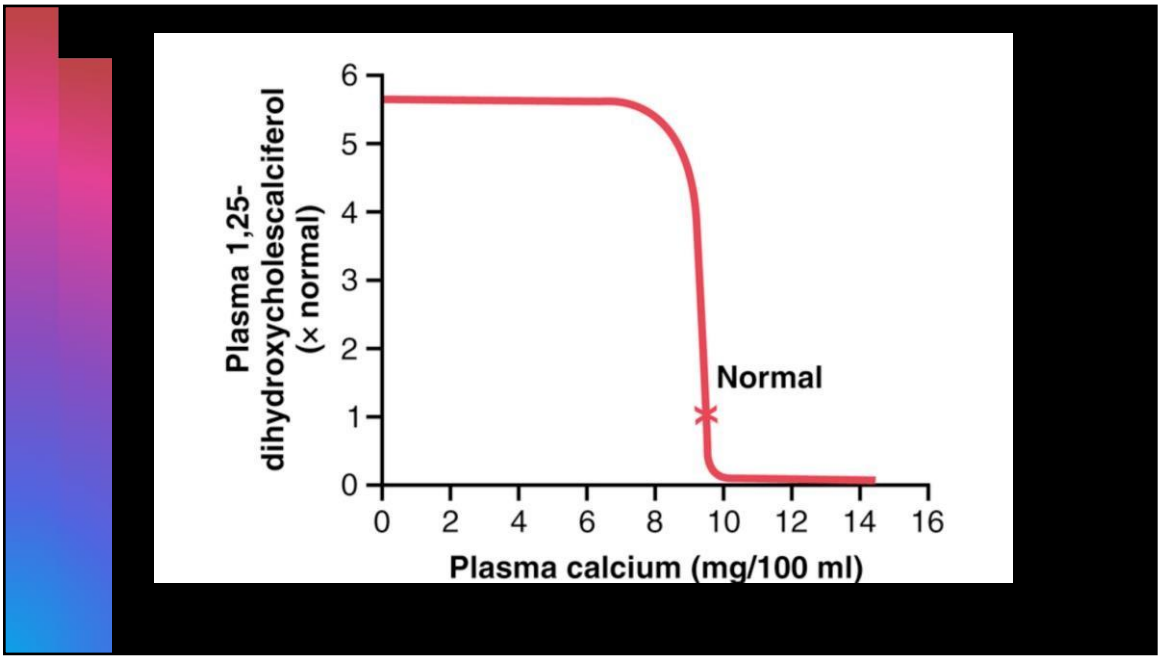
Vitamin D

Vitamin D

- Keratinocytes can produce cholecalciferol from a precursor related to cholesterol (7 - dehydrocholesterol) on exposure to sunlight.
- Activation of vitamin D (addition of two hydroxyl (—OH) groups).
- PTH stimulates the kidney enzymes involved in the second step of vitamin D activation



**it was originally discovered and isolated from a dietary source and tagged as a vitamin.
**the skin would be an adequate source of vitamin D if it were exposed to sufficient sun
** Activation of Vitamin: vitamin D is biologically inactive when it first enters the blood from either the skin or the digestive tract. It must be activated by two sequential biochemical alterations that involve the addition of two hydroxyl (—OH) groups . The first of these reactions occurs in the liver, and the second takes place in the kidneys.
** The end result is production of the active form of vitamin D, 1,25-(OH)2-vitamin D3, also known as **calcitriol**.
** PTH stimulates the kidney enzymes involved in the second step of vitamin D activation in response to a fall in plasma Ca. To a lesser extent, a fall in plasma phosphate also enhances the activation process.
**Vitamin D in its various forms circulates in the blood primarily bound to vitamin D–binding protein.


Plasma 1,25-dihydroxycholescalciferol (× normal)
6
5
4
3
2
1
0
Normal
0
2
4
6
8
10
12
14
16
Plasma calcium (mg/100 ml)

Vitamin D Functions

- **Increase calcium absorption from the intestinal tract.**
- By increasing, over a period of about 2 days, formation of calbindin, a calcium-binding proteins in the intestinal epithelial cells.

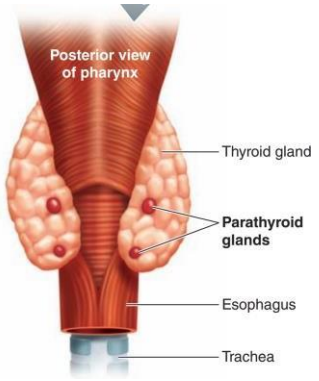
Vitamin D Functions (others)

- Vitamin D promotes phosphate absorption by the intestines.
- Vitamin D decreases renal calcium and phosphate excretion.
- Vitamin D plays important roles in both bone absorption and bone deposition.
- → smaller quantities → promotes bone calcification and mineralization.
- → extreme quantities → resorption

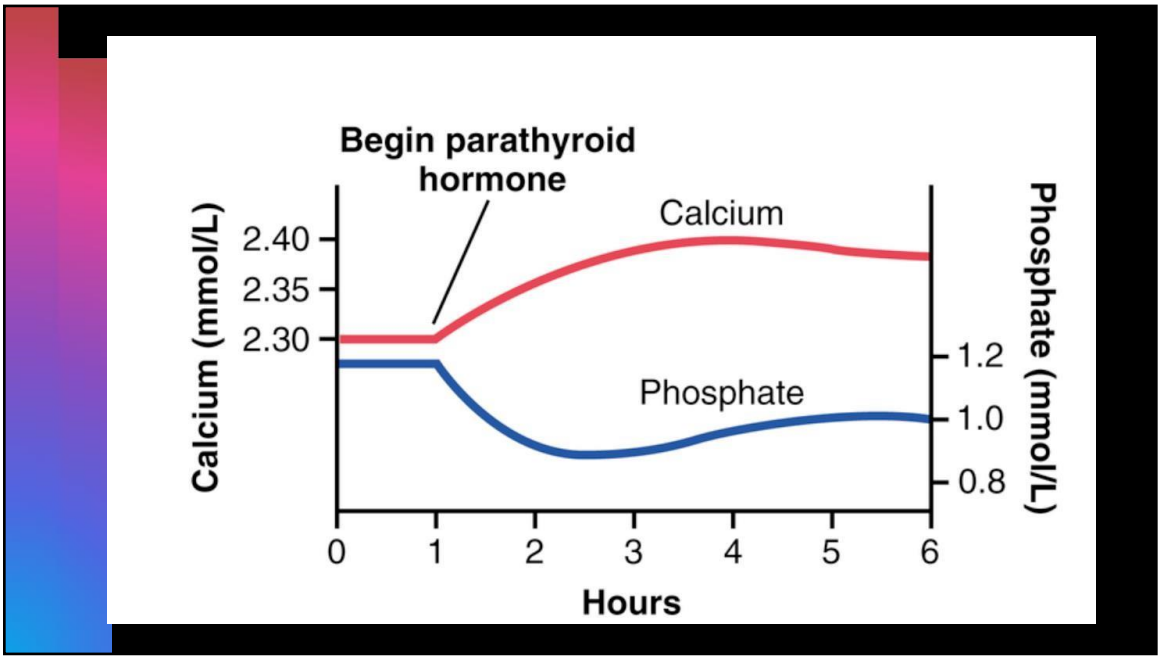
Parathyroid Hormone

Parathyroid hormone raises free plasma Ca, a life-saving effect.

- PTH is a peptide hormone secreted by the parathyroid glands, four rice grain–sized glands located on the back surface of the thyroid gland, one in each corner.
- The overall effect of PTH is to increase the calcium concentration of plasma
- Also lowers plasma phosphate concentration.

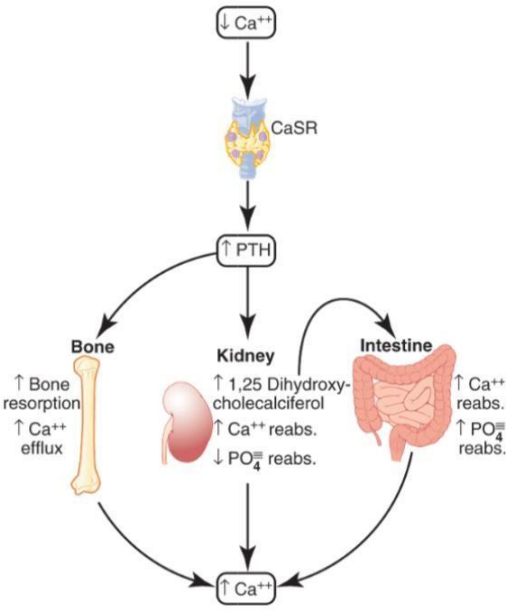


Like aldosterone, PTH is essential for life.


Begin parathyroid hormone
Calcium
Phosphate
Calcium (mmol/L)
2.40
2.35
2.30
Phosphate (mmol/L)
1.2
1.0
0.8
0
1
2
3
4
5
6
Hours

PTH functions

- (1) PTH stimulates bone resorption.
- (2) PTH increases reabsorption of calcium and decreases phosphate reabsorption by the renal tubules.
- (3) PTH is necessary for vitamin D activation, so it indirectly increases both calcium and phosphate absorption from the small intestine.



**summarizes the main effects of increased PTH secretion in response to decreased extracellular fluid calcium ion concentration: (1) PTH stimulates bone resorption, causing release of calcium into the extracellular fluid; (2) PTH increases reabsorption of calcium and decreases phosphate reabsorption by the renal tubules, leading to decreased excretion of calcium and increased excretion of phosphate; and (3) PTH is necessary for conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol, which, in turn, increases calcium absorption by the intestines. These actions together provide a powerful means of regulating extracellular fluid calcium concentration.

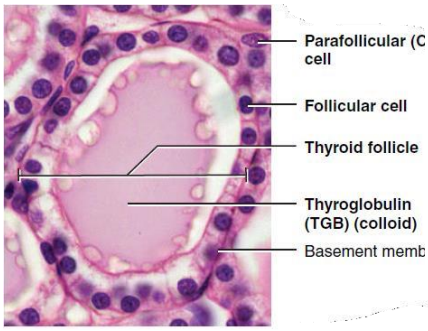
PTH regulation

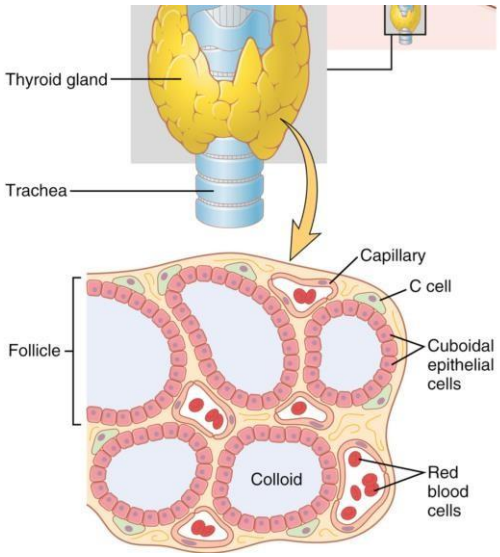
- The primary regulator of PTH secretion is plasma concentration of free calcium.
- Appropriately, PTH secretion increases when plasma calcium falls and decreases when plasma calcium rises

Calcitonin

Thyroid gland

- Thyroid follicles produce thyroid hormones
- Parafollicular cells or C cells produce calcitonin

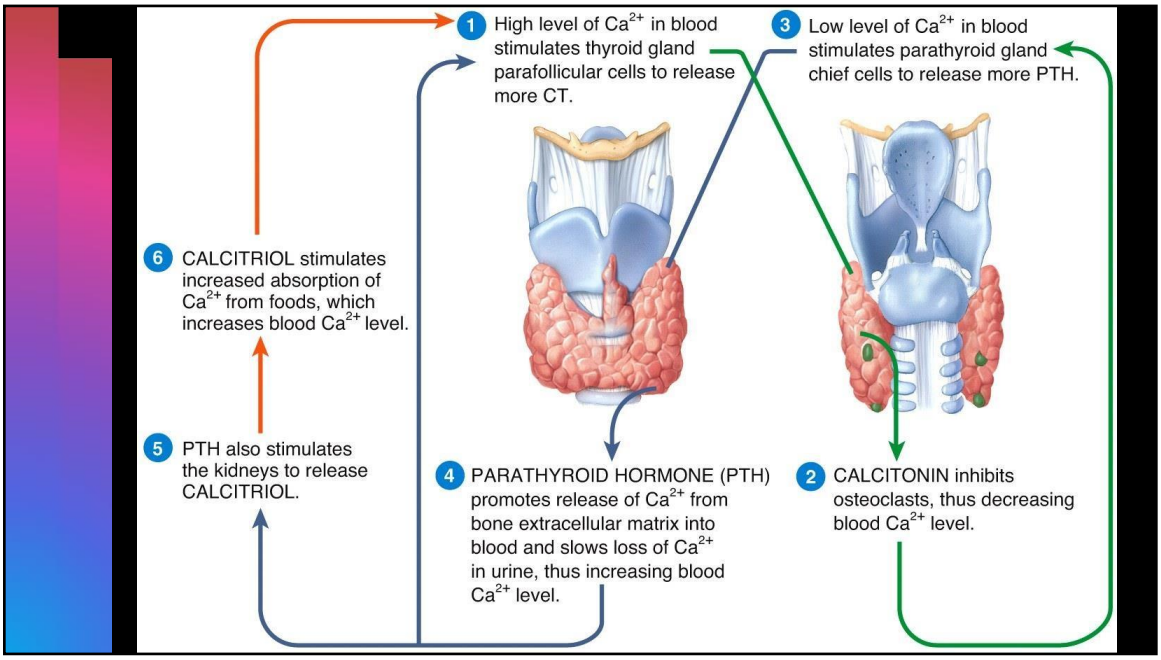




Calcitonin

- A peptide hormone secreted from parafollicular cells, or C cells in the thyroid gland.
- Decrease plasma calcium concentration.
- Two effects on bone:
- Short term, calcitonin decreases calcium movement from the bone fluid into the plasma.
- Long term, calcitonin decreases bone resorption.
- Inhibits calcium and phosphate reabsorption from the kidney tubules.

- Calcitonin has no effect on the intestine or on vitamin D
- However, the quantitative role of calcitonin in humans is far less than that of PTH in regulating calcium ion concentration.
- The primary stimulus for calcitonin secretion is increased extracellular fluid calcium ion concentration.



PTH is principally responsible for controlling Ca homeostasis because the actions of vitamin D are too sluggish for it to contribute substantially to the minute-to-minute regulation of plasma Ca21 concentration. However, both **PTH and vitamin D are essential** to Ca balance, the process ensuring that, over the long term, dietary Ca input into the body is equivalent to Ca output in the urine. When dietary Ca21 intake is reduced, the resultant transient fall in plasma Ca level stimulates PTH secretion. The increased PTH has two effects important for maintaining Ca balance: (1) It stimulates **Ca reabsorption by the kidneys**, thereby decreasing Ca output; and (2) it **activates vitamin D**, which increases the efficiency of uptake of ingested Ca. Because **PTH also promotes bone resorption**, a substantial loss of bone minerals occurs if Ca intake is reduced for a prolonged period, even though bone is not directly involved in maintaining Ca input and output in balance.

Vitamin D Deficiency

- The major consequence of vitamin D deficiency is impaired intestinal absorption of calcium.
- PTH maintains the plasma calcium level at the expense of the bones.
- As a result, the bone matrix is not properly mineralized. The demineralized bones become soft and deformed, bowing under the pressures of weight bearing, especially in children.
- This condition is known as rickets in children and osteomalacia in adults.

****The plasma calcium concentration in rickets is only slightly depressed, but the level of phosphate is greatly depressed.**
This is because the parathyroid glands prevent the calcium level from falling by promoting bone absorption every time the calcium level begins to fall. However, there is no good regulatory system for preventing a falling level of phosphate, and the increased parathyroid activity actually increases the excretion of phosphates in the urine.

V2: Doctor`s notes added to these pages: 14, 16, 20, and 22