Physiology Team

# ENDOCRINE BLOCK

## LECTURE 8

Calcium Homeostasis


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# OBJECTIVES

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Not Given :|

# MIND MAP

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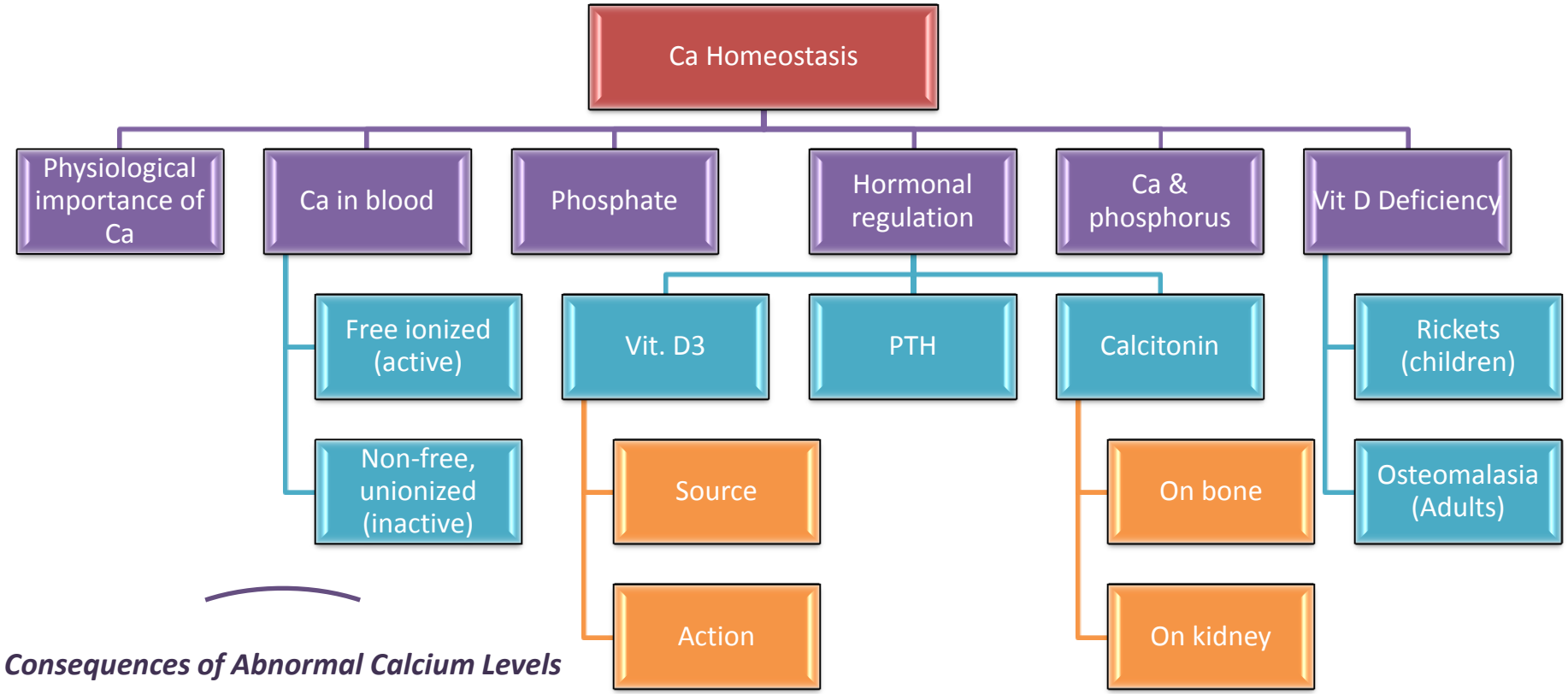


***Consequences of Abnormal Calcium Levels***

hypocalcaemia

Hypercalcaemia

Useful video

# Physiological Importance of Calcium

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- Calcium salts in bone provide structural integrity of the skeleton.
- Calcium ions in **extracellular*** & **cellular fluids** is essential to n**ormal function of biochemical processes:**
  - Neuoromuscular excitability.
  - Blood coagulation.
  - Hormonal secretion.
  - Enzymatic regulation.

High blood calcium→ CNS depressed
Low blood calcium→ CNS excited

- ↑ **carbonated beverages** is associated with increased loss of **calcium** from the body.
- Because normal bone function requires **weight-bearing exercise** , increase immobility & total bed-rest cause bones to lose calcium.

- Neurotransmitter release ( e.g. ACh release at the NMJ ).
- Nerve excitability ( normal ECF $Ca^{2+}$ concentration is essential for neuronal membrane stability & RMP )
- Muscle contraction

***ECF= interstitial fluid + plasma**

# Calcium in blood

- total $Ca^{++}$ concentration in blood is ≈ **10 mg/dl** (range 8.5-10 mg/dl )
- **Present in <u>two forms</u>:**

| The free ionized $Ca^{++}$ | non-free , unionized calcium |
|---|---|
| • is about 50% of the total blood Ca++ = 5mg/dl .<br>• It is the only form of Ca++ which is biologically active. | • ***Protein-bound calcium*** → around 40% of total ECF calcium .<br>- "will not diffuse through the capillary membrane"<br>- Most of this calcium is bound to albumin.<br>- Binding of calcium to albumin is pH-dependent.<br>- much smaller fraction is bound to globulin.<br>• ***present as complexed*** **salt**<br>- (mainly bound to serum citrate & phosphate), around 10% of blood calcium . |

**Bone serves as a major reservoir for $Ca^{++}$ storage : 99% of calcium is in the skeleton .**
**However , very little $Ca^{2+}$ can be released from it .**
**Calcium is present in <u>bone</u> as calcium phosphate .**

# Abnormal Calcium in blood

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- Binding of calcium to albumin is pH-dependent.

Acute respiratory alkalosis increases calcium binding to protein, thereby decreases ionized calcium level

↓

When ionized calcium falls below normal, permeability of neuronal cell-membranes to sodium increases

↓

depolarization → hyperexcitability of the nervous system

↓

patients become prone to develop tetanic muscle contractions & seizures .

| Consequences of Abnormal Calcium Levels | |
|---|---|
| Decreased plasma $Ca^{++}$ [hypocalcaemia] | Increased plasma Ca++ conc. [Hypercalcaemia] |
| Increase excitability of nerve and muscle cell membranes → tetany, hyper reflexia, spontaneous twitching, muscle cramps, tingling and numbness. | Cardiac arrhythmias, decrease neuromuscular excitability, lethargy, constipation, polyuria and polydepsia. |

## Phosphorous

- Phosphorous is an essential mineral necessary for ATP, cAMP second messenger systems, and other roles.
- PO4 plasma concentration is ≈ 4 mg/dL.
- Ionized (diffusible) → around 50% of total.
- The remainder ( 50%) is un-ionized (non-diffusible ) and protein- bound.
- Calcium is tightly regulated with Phosphorous in the body

## calcitonin

**On bone [1]↑Ca deposition of bone by:**

**↓osteolysis.**

**↑osteoblastic activity**

**[2] ↓↓ Bone resorption:**

**inhibition of osteoclasts.**

**↓ formation of osteoclasts**

**On kidney**

- **↓↓ Ca reabsorption**
- **↑↑ Ca excretion**

**(in addition to phosphate)**

- 99% of total – body $Ca^{++}$ is contained in bone.
- Bone is not a fixed unchanging tissue, it is constantly being remodeled → it can either withdraws $Ca^{++}$ form ECF or deposit it there.
- Increase in protein concentration → increase in total $ca^{++}$ concentration.
- Decrease in protein concentration → decrease In total $ca^{++}$ concentration.
- The effects on ionized $Ca^{++}$ concentration are in significant.
- Changes in anion concentration Alter the ionized $Ca^{++}$ concentration e.g.
- plasma phosphate concentration → increase The concentration of $Ca^{++}$ complex to phosphate
- Decrease ionized $Ca^{++}$ con

# Hormonal Regulation of Calcium

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- 3 principal hormones regulate serum $Ca^{++}$ level .

**NB : While PTH and vitamin D act to increase plasma $Ca^{++}$ → only calcitonin causes a decrease in plasma $Ca^{++}$.**

## (1) Vitamin D3 (1,25-dihydroxy )

( taken in food & synthesized in the skin )

**increases $Ca^{++}$ level by :**

(1) $Ca^{++}$ absorption from the intestine.
(2) $Ca^{++}$ reabsorption from the bone ( by increasing osteoclastic number & activity).
(3) Some believe that it also increases $Ca^{++}$ reabsorption by the kidney.

## (2) Parathyroid hormone (PTH):

- polypeptide hormone secreted by Parathyroid Glands .
- ncreases $Ca^{++}$ levels by→ (1) stimulating $Ca^{++}$ resorption from bone ( by activating, osteoclasts ) → passing $Ca^{++}$ to the ECF
  (2) Stimulating Ca++ reabsorption (and phosphate excretion) by the kidneys

## (3) Calcitonin:

- polypeptide hormone secreted by Parafollicular (C ) cells of Thyroid Gland).
- **High plasma $Ca^{++}$** leads to → increased Calcitonin secretion.
- **The main action of this calcitonin** is to inhibits osteoclasts → inhibition of bone resorption . **So,:**
  (1) increases bone formation .
  (2) decreases blood $Ca^{++}$ level .
- Thus calcitonin plays a central role in bone re-modelling .

# Mechanism of activation of Vitamin D

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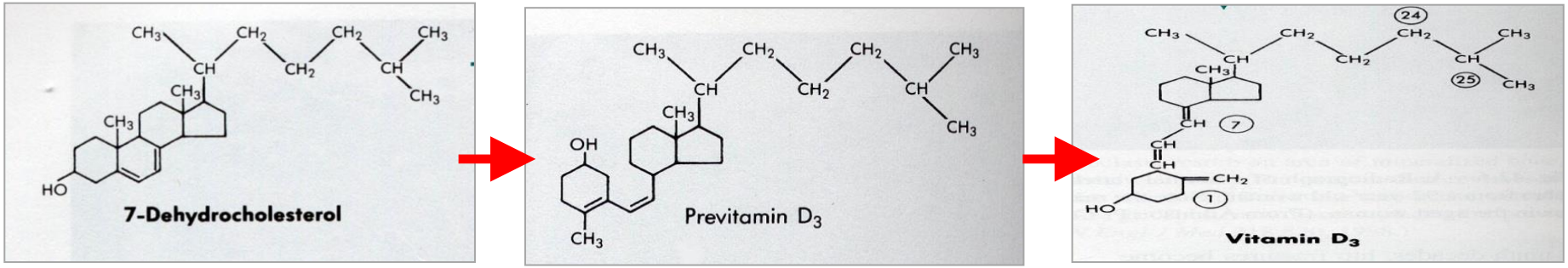
- Keratinocytes in the skin synthesize 7-dehydrocholesterol .
- 7-dehydrocholesterol is photoconverted ( by UV light in skin) to Cholecalciferol (previtamin D3).
- This form of Vitamin D is **inactive**, it requires modification to the active metabolite, 1,25-dihydroxy-D → by two hydroxylation reactions → the **1st** occurs in **liver** and the **2nd** in **kidney**.
- Limited exposure to the sun ,dietary vitamin D is essential . If there is **no sufficient** exposure to the sun , or if there is **dietary deficiency** in vitamin D → Rickets ( in children ) or Osteomalacia ( in adults ) occur .
- PTH stimulates Vit D synthesis.




■ Slides ■ Important ■ Females' Notes ■ Explanation ■ Males' Notes

# Vitamin D deficiency

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Vitamin D deficiency leads to a disease characterized by softening of bone.

| Rickets | Osteomalasia |
|---|---|
| • it occurs in children. | • It occurs in adults.<br>• characterized by a gradual softening and bending of the bones. |

## Most affected areas :

- Metaphyses of long bones subjected to stress.
- Wrists,
- Knees.
- Ankles.

**Metaphyseal widening in wrists & knees + signs of bone rarfaction**

## Clinical Features:

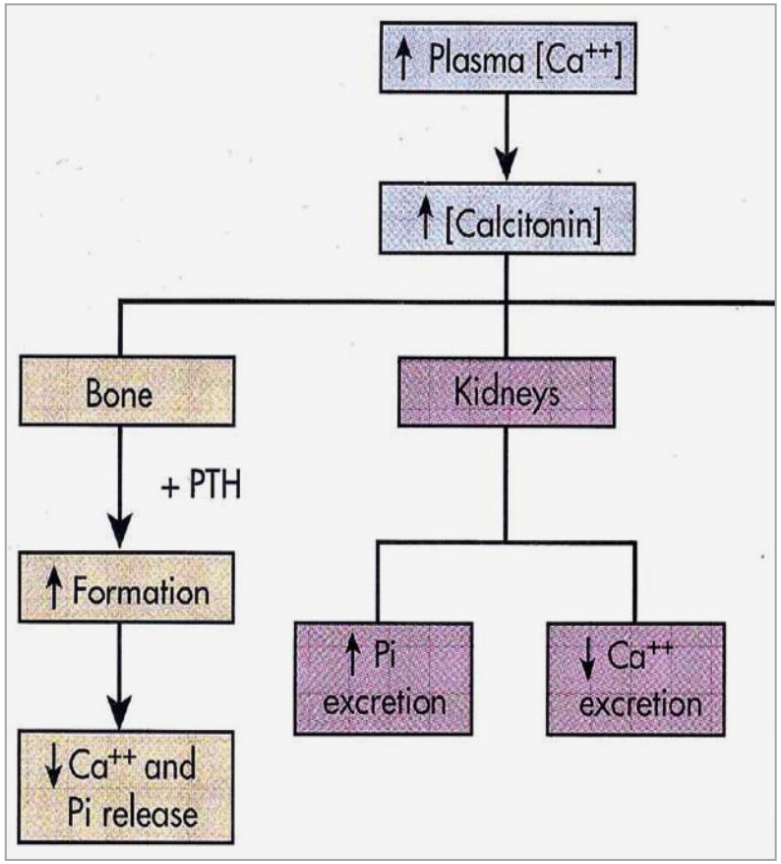
1. Delayed dentition (delayed teething).
2. Bowed legs (Due to the effect of weight bearing on the legs).
3. Swelling of wrists and ankles.
4. Short stature.

**Bowed legs**

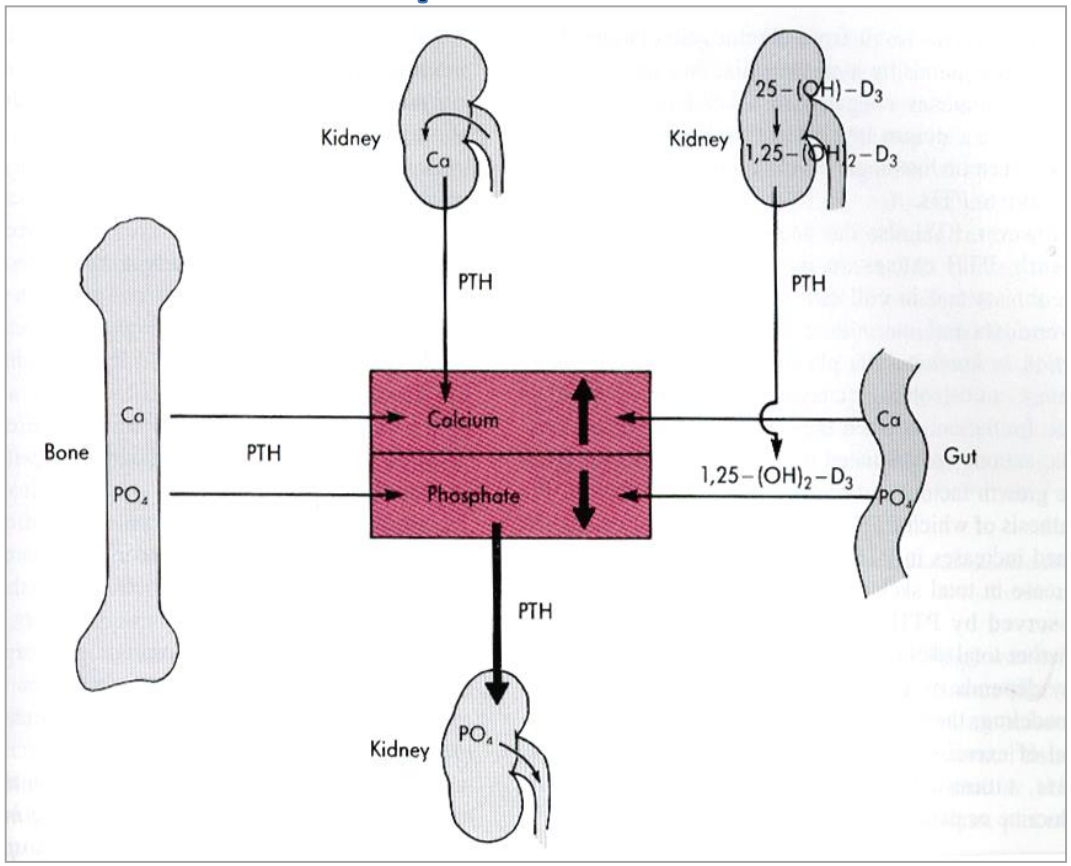
**3 principal hormones regulate serum $Ca^{++}$ level .**

**PTH and vitamin D act to increase plasma $Ca^{++}$ → only calcitonin causes a decrease in plasma $Ca^{++}$.**

## Calcitonin




## Calcium & Phosphorus



# SUMMARY

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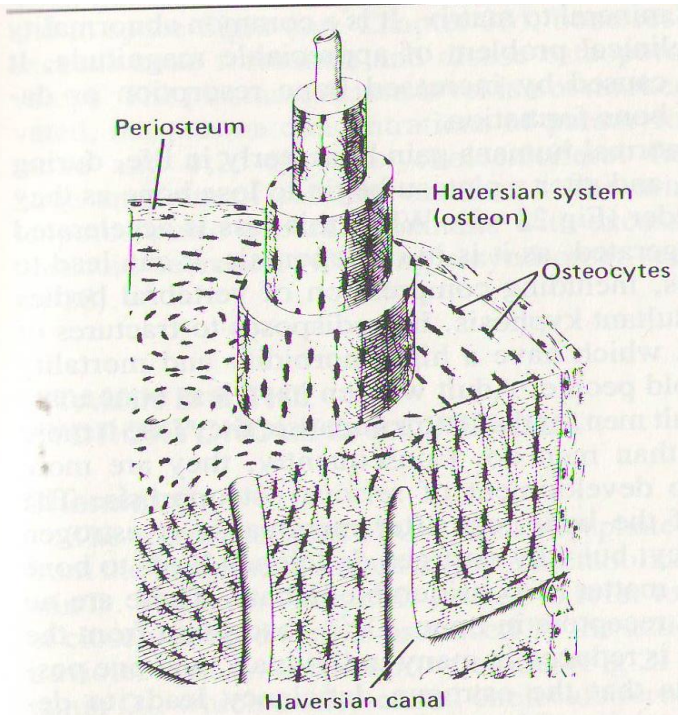
- Secretion of parathyroid hormone is stimulated by low blood calcium levels and inhibited by high blood calcium levels. Therefore, when blood calcium levels are too low, parathyroid hormone is released, which stimulates the breakdown of bone. This frees calcium to enter the blood, restoring the level to normal.
- . Parathyroid hormone can also act on the kidneys to raise blood calcium levels. It does this by stimulating calcium reabsorption by the kidneys, so more calcium stays in the body and less is excreted through urine.
- The antagonist to parathyroid hormone is calcitonin. If blood calcium levels get too high, parathyroid hormone is inhibited and calcitonin is released.
- In adults, the condition is called **osteomalacia**, and in children it's known as **rickets**. Each one is a condition where prolonged and excessive vitamin D deficiency causes bones to soften, weaken, and easily fracture.

## Sources of Vit D:

1. Ingestion in diet (food)
2. skin: Vit D is produced in the skin by Ultraviolet light

# Extra from ganon



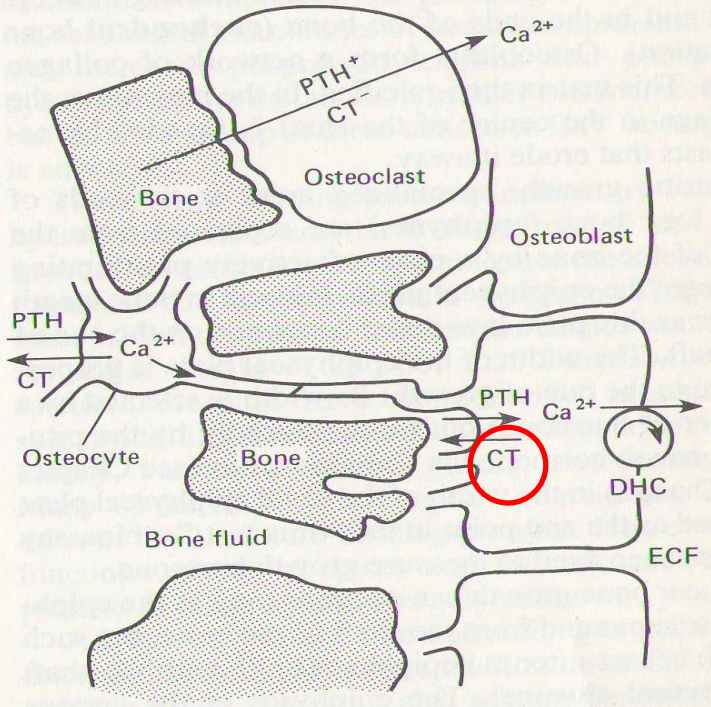




**Figure 21–2.** ***Left:*** Schematic drawing of compact bone. (Modified and reproduced, with permission, from Junqueira LC, Carneiro J: *Basic Histology*, 4th ed. Lange, 1983.) ***Right:*** Proposed organization of bone cells. Note that the osteoblasts form a partial membrane which separates bone fluid from ECF and that their cytoplasmic processes connect via tight junctions to the cytoplasmic processes of osteocytes deep in the bone. According to this view, parathyroid hormone (PTH) increases and calcitonin (CT) decreases the permeability of bone cells to $Ca^{2+}$, whereas 1,25-dihydroxycholecalciferol (DHC) facilitates the active transport of $Ca^{2+}$ from osteoblasts into ECF. (Courtesy of H Heath III and CD Arnaud.)

# QUESTIONS

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**1. Which one of the following will happen when blood calcium levels are high?**

A. The bones will lose calcium
B. Calcitonin will be secreted
C. Parathyroid hormone will be secreted
D. Osteoclasts will break down bone

**2. What effect can Parathyroid Hormone (PTH) have on the kidneys?**

A. PTH can stimulate calcium reabsorption in the kidneys.
B. PTH can stimulate calcium excretion in the kidneys.
C. PTH can stimulate the production of osteoblasts in the kidneys.
D. PTH has no effect on the kidneys.

**3. Which of the following will happen when blood calcium levels are low?**

A. PTH will stimulate osteoblasts to store calcium in bone
B. PTH will stimulate osteoblasts to break down bone
C. PTH will stimulate osteoclasts to break down bone
D. PTH will stimulate osteoclasts to store calcium in bone

**4. Choose the correct statement regarding the formation of the biologically active form of vitamin D in the body in the proper order from beginning to end:**

A. Cholecalciferol (sun or supplementation)-Calcidiol (liver)-Calcitriol (kidneys)
B. Cholecalciferol (sun or supplementation)-Calcidiol (kidneys)-Calcitriol (liver)
C. Cholecalciferol (sun or supplementation)-Calcitriol (kidneys)-Calcidiol (liver)

**5. Which one of the following is a normal level of plasma calcium ?**

A. 6 mg/dl
B. 8 mg/dl
C. 10 mg/dl
D. 12 mg/dl

**6. Which of the following occur in case of decreased plasma Ca++ conc. [hypocalcaemia]?**

A. Decrease excitability of nerve and muscle cell membranes
B. Cardiac arrhythmia
C. Increase excitability of nerve and muscle cell membranes
D. constipation

| | |
|---|---|
| 1 | B |
| 2 | A |
| 3 | C |
| 4 | A |
| 5 | C |
| 6 | C |

# THE END

Physiology Team

If there are any Problems or Suggestions,
Feel free to contact us:


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## THANK YOU

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