Endocrine Regulation of Calcium and Phosphate Metabolism

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Outline

• Hormonal Regulation of $[\text{Ca}^{2+}]$
  – Action of PTH
  – Action of vitamin D(1,25- (OH)$_2$-D$_3$)
  – Action of calcitonin
Importance of Maintaining Extracellular $[\text{Ca}^{2+}]$

- Muscle contraction & relaxation
- Nerve conduction
- Blood clotting
- Bone and teeth formation
- Secretory activity of endocrine & exocrine cells
- Second messenger
Endocrine Regulation of Calcium and Phosphate Metabolism

• Hormonal control:
  – PTH, vitamin D(1,25-(OH)₂-D₃), calcitonin

• Major regulatory organs:
  – intestine, bone, kidneys
Vitamin D

- **Sources of vitamin D:**
  - produced in the skin by UV(290-315 nm) radiation
  - ingested in the diet (D$_3$ rich in fish, liver, milk)

Vitamin D is not a “classic hormone” because it is not produced by an endocrine gland. However, its metabolite acts as a hormone by the mechanism similar to that of thyroid and steroid hormones.
Actions of 1,25-(OH)$_2$-D$_3$

- **plasma [Ca]**

- **Intestine**
  - increases Ca absorption
  - stimulates phosphate absorption

- **Bone**
  - stimulates Ca and Pi resorption
  - provides Ca and Pi from old bone to mineralize new bone

- **kidney**
  - enhances Ca and Pi reabsorption of renal tubule
Rickets

- Caused by deficiency of vitamin D activity (dietary deficiency, insufficient sun exposure, liver/kidney diseases)

- Deficiency of vitamin D causes inadequate mineralization of new bone matrix (lowered ratio of mineral/organic matrix)

- Symptoms: decreased mechanical strength and distortion especially in the long bones of legs.
Parathyroid Glands

- 4 glands located behind the thyroid
- Each gland weighs 30-50 mg
- Main cell type:
  - Chief cells
  - Parathyroid Hormone
Parathyroid Hormone (PTH)

- Polypeptide
- PTH is synthesized as prepro-PTH
- [PTH]=10~50ng/L
- Half life: 20~30 min
- Receptor: PTH/PTHrpR
**PTH Actions**

- **Major target organs**
  - **bone**
  - Bone resorption by stimulating osteoclasts and inhibiting osteoblasts
  - **kidney**
  - Reabsorption of Ca\(^{++}\) and excretion of phosphate
  - **intestinal tract (indirect effect)**
  - Absorption of calcium from the small intestine

- **Overall effect**
  - Increase plasma [Ca\(^{2+}\)]
  - Decrease plasma [P\(_i\)]
Factors Affecting PTH Secretion

- **Ca** and PTH form a negative feedback pair
- **1,25-(OH)2-D** and PTH form a negative feedback loop

![Graph showing Parathyroid hormone release vs. Extracellular Ca++](image)
Hypocalcemia

damage to blood supply during thyroidectomy → a characteristic spasm of the muscles of the upper extremity (Trousseau's sign). Tetany, convulsion muscle cramps

Plasma \([\text{Ca}^{2+}]\) falls below normal

↑ neuronal membrane Na permeability

Initiation of action potentials

↑ Excitability of nerve fiber

Tetanic muscle contraction

brain

seizures
Calcitonin

- Parafollicular or C cells
- Peptide
- Action
  - \( \downarrow \) Plasma \([\text{Ca}^{2+}]\)
    - Bone
      - by inhibiting synthesis and activity of osteoclasts (for bone resorption) & stimulating calcium uptake by bones
    - Kidney
      - It plays no role in normal day-to-day regulation of plasma calcium in humans
- Regulation: \([\text{Ca}^{2+}]\)
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<th>PTH</th>
<th>Vitamin D</th>
<th>Calcitonin</th>
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<tbody>
<tr>
<td><strong>Stimulus for secretion</strong></td>
<td>↓ serum [Ca^{2+}]</td>
<td>↓ serum [Ca^{2+}]</td>
<td>↑ serum [Ca^{2+}]</td>
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<tr>
<td></td>
<td>↑ PTH</td>
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<td>↓ serum [phosphate]</td>
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<td><strong>Action on:</strong></td>
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<tr>
<td>Bone</td>
<td>↑ resorption</td>
<td>↑ resorption</td>
<td>↓ resorption</td>
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<tr>
<td>Kidney</td>
<td>↓ P reabsorption (↑ urinary cAMP)</td>
<td>↑ P reabsorption</td>
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<td>↑ Ca^{2+} reabsorption</td>
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<tr>
<td>Intestine</td>
<td>↑ Ca^{2+} absorption (via activation of vitamin D)</td>
<td>↑ Ca^{2+} absorption (Calbindin D-28K)</td>
<td>↑ P absorption</td>
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<td><strong>Overall effect on:</strong></td>
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<tr>
<td>Serum [Ca^{2+}]</td>
<td>↑</td>
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<tr>
<td>Serum [phosphate]</td>
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Osteoporosis

Change of Bone Mass

Fracture (vertebral, hip, wrist ...) occurs
loss of height & severely rounded upper back
Osteoporosis

- **Risk factors**
  - declining estrogen levels with aging *(major factor!)*
  - endocrine diseases: hyperthyroidism, hyperparathyroidism, Cushing disease
  - others: inadequate Ca intake, alcoholism, cigarette smoking, sedentary lifestyle

- **Prevention begins in the premenopausal years**
  - Ca intake
  - consistent program of weight-bearing exercises

- **Treatment**
  - Estrogen
  - Calcitonin
  - Vitamin D + Ca
Consistent Exercise!

Not just another new year’s resolution!
A patient with parathyroid deficiency 10 days after inadvertent damage to the parathyroid glands during thyroid surgery would probably have

A. low plasma phosphate and Ca\(^{2+}\) levels and tetany
B. low plasma phosphate and Ca\(^{2+}\) levels and tetanus
C. a low plasma Ca\(^{2+}\) level, increased muscular excitability, and a characteristic spasm of the muscles of the upper extremity (Trousseau’s sign)
D. high plasma phosphate and Ca\(^{2+}\) levels and bone demineralization
E. increased muscular excitability, a high plasma Ca\(^{2+}\) level, and bone demineralization
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Which of the following is not involved in regulating plasma Ca$^{2+}$ levels?

A. Kidneys  
B. Skin  
C. Liver  
D. Lungs  
E. Intestine
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A. Kidneys
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C. Liver
D. Lungs
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The End.