Key Points

1. PTH is synthesized in parathyroid gland and increases serum calcium levels, decreases phosphate concentration, and stimulates calcitriol production
2. PTH has negative auto-feedback via calcitriol, and calcitriol has negative auto-feedback on itself
3. Main target organs for calcium regulation are kidneys and bones (PTH) and intestines (calcitriol)
4. Calcitriol is formed in kidney from vitamin D under the influence of PTH

Ionized Calcium function

- Enzymatic reactions
- Membrane transport
- Coagulation
- Nerve conduction
- Neuromuscular transmission
- Muscle contraction
- Vascular smooth muscle tone
- Hormone secretion
- Bone formation
- Control of hepatic glycogen metabolism
- Cell growth and division

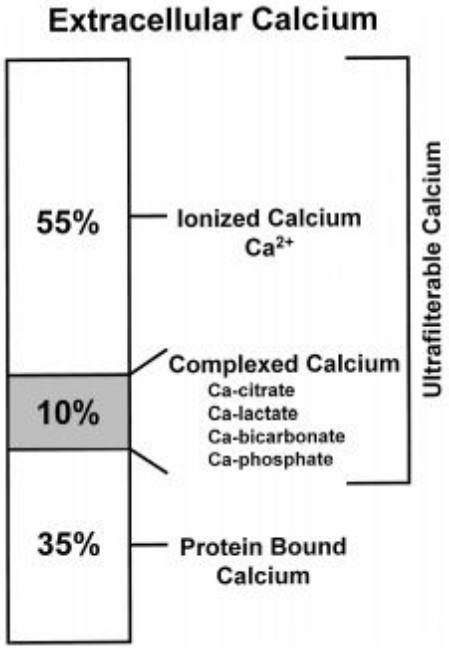
Normal physiology

- Main players
    - PTH
    - Vit D metabolites
        - Calcitriol = 1,25 dihydroxyvitamin D3
    - Calcitonin
- PTH
    - Most responsible for minute-minute control
    - When blood [iCa] decreases, PTH is secreted
    - Acts directly on bone and kidney
        - Increases osteoclast number and activity
        - Increases renal reabsorption (along with calcitriol)
    - Act indirectly on intestine via calcitriol by increasing synthesis which then leads to increased absorption from the intestines
- Calcitriol
    - Most responsible for day-day control
- Target organs
    - Intestines
    - Kidneys

        - Non-protein bound calcium is filtered by the glomerulus and undergoes extensive renal reabsorption (~98%)
    - Bone

Calcium Distribution

- 99% in bone as hydroxyapatite
    - <1% available to rest of body
- ECF calcium is most of the rest
    - Ionized
    - Bound
    - Complexed
        - Phosphate, bicarbonate, lactate, sulfate, citrate

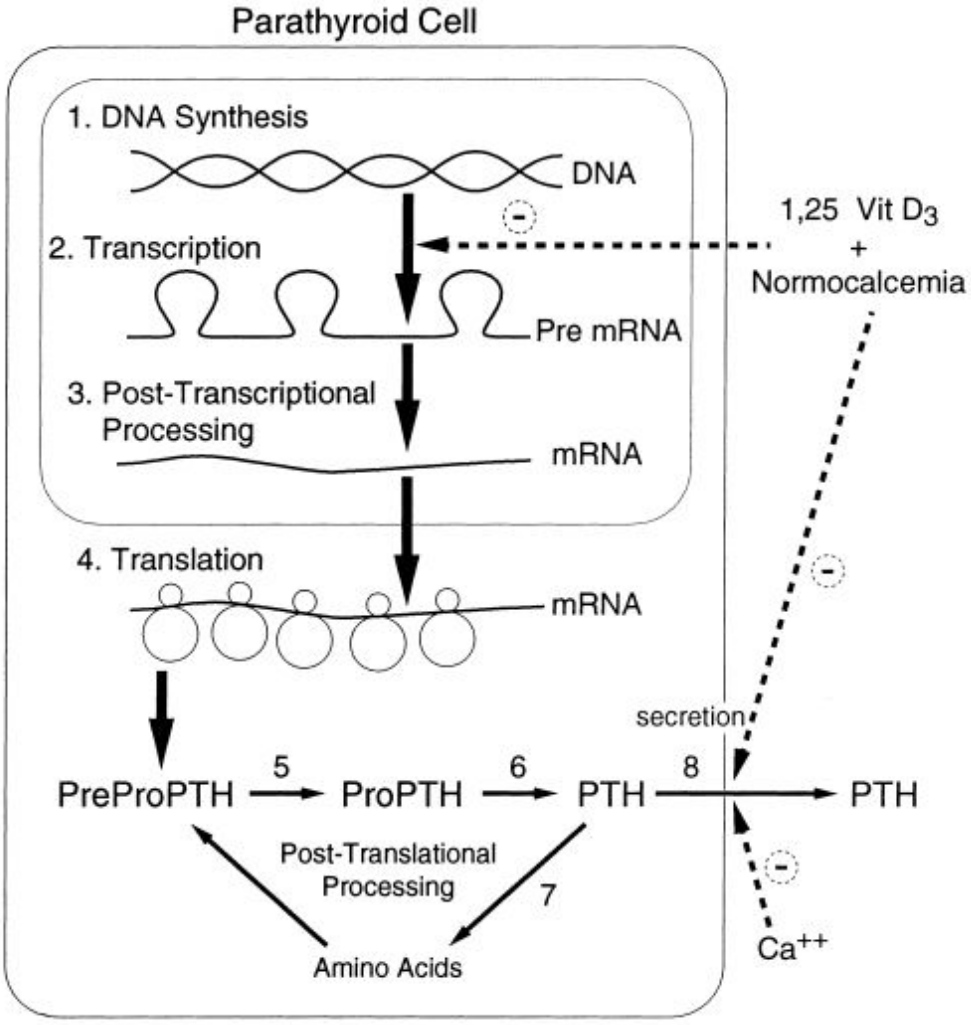


- Intracellular Ca
    - 10,000 fold less than ECF
    - 2nd messenger
    - Sequestered in organelles or bound to membrane proteins

Parathyroid Hormone

- Synthesized by chief cells in parathyroid hormone
- Short serum half-life (3-5 minutes)
- Calcitriol exerts overall control of PTH synthesis and secretion
    - Inhibits PTH mRNA synthesis
    - Uremia and reduced calcitriol (due to high serum phosphorous concentration) results in poorly regulated chief cell function and renal secondary hyperparathyroidism

- Secretion is relatively constant
    - Approx 25% of maximal rate
    - Never turned 100% off
- Hypocalcemia is main stimulator of PTH secretion
- Epinephrine, isoproterenol, dopamine, secretin, postaglandin E2 and nerve stimulation within parathyroid gland all have minor effects
- High serum iCa and calcitriol inhibits PTH secretion
- Rate of PTH secretion is inversely proportional to ECF iCa concentration
    - Sigmoidal curve allows for large changes in PTH concentration for small iCa changes, allowing precise control



- Main roles of PTH
    - Increased tubular reabsorption of calcium
    - Increase bone resorption and osteoclast number and activity
    - Accelerate formation of calcitriol by the kidney
        - Distal convoluted tubule and ascending thick limb of loop

        - Inhibits phosphate reabsorption in distal tubules and collecting ducts reducing serum phosphate concentration

PTHrP

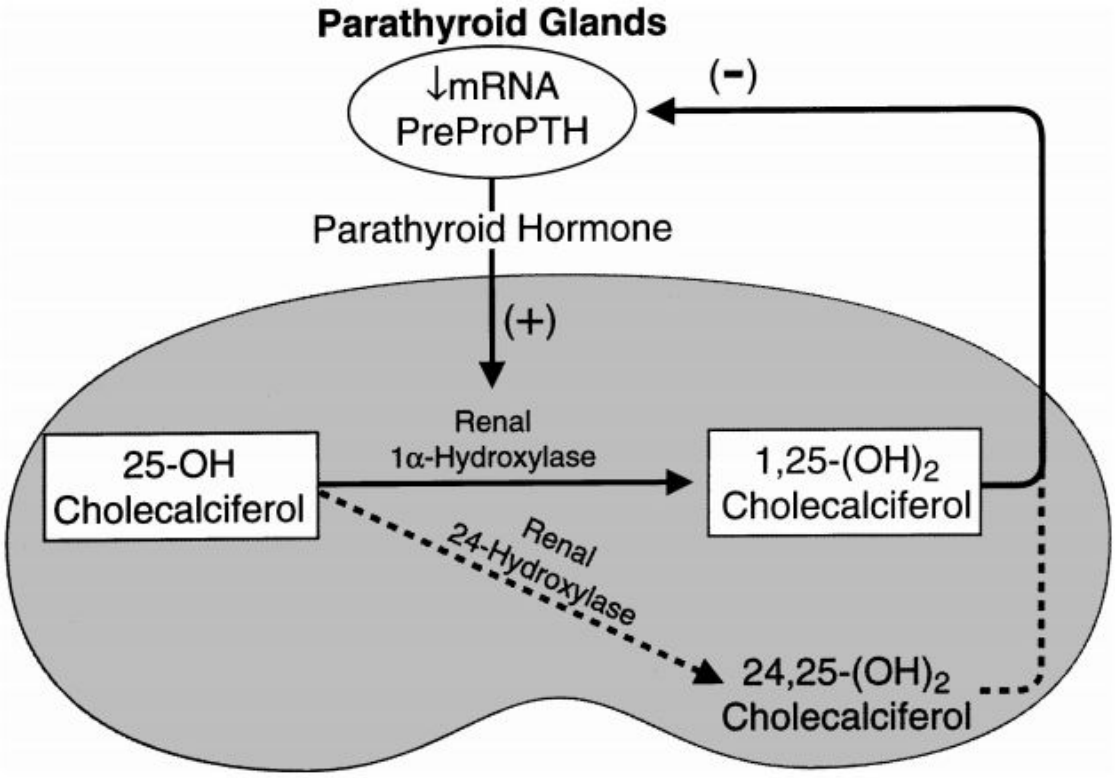
- Has multiple actions including calcium regulation
- Produced in larger amounts in the fetus than adults

Vitamin D (calciferol)

- Metabolites include calcidiol and calcitriol
- Obtained via consumption or from skin (not in ithaca)
- Dogs/cats cannot form it in the skin efficiently, so are more dependant on consumption
- Calcitriol is synthesized from vit D in proximal tubules of kidney
    - Synthesis stimulation
        - Decreased calcium, phosphorus or calcitriol lead to increased PTH levels, which will stimulate further calcitriol production
    - Inhibition
        - Calcitriol, hypercalcemia, and phosphate loading decrease calcitriol synthesis
    - Actions
        - Increase serum calcium and phosphorus concentrations
        - Major target organ is intestines
        - Enhances intestinal absorption of calcium and phosphate, (ATP dependant pumps)
        - Negatively feedbacks on calcitriol formation in kidney
        - Negatively feedbacks on PTH formation (in the presence of normal serum calcium levels)

Calcitonin

- Limits postprandial hypercalcemia
- Effects on normal calcium homeostasis is minor


Parathyroid Glands
↓mRNA
PreProPTH
(-)
Parathyroid Hormone
(+)
Renal
1α-Hydroxylase
25-OH
Cholecalciferol
1,25-(OH)2
Cholecalciferol
Renal
24-Hydroxylase
24,25-(OH)2
Cholecalciferol

Questions

1. PTH causes an increase/decrease in serum calcium and an increase/decrease in serum phosphate, while calcitriol causes an increase/decrease in serum calcium and increase/decrease in serum phosphate

2. True/false: Injecting a hypocalcemic patient with physiologic doses of calcitriol will cause a reduction in PTH secretion from the parathyroid gland

3. The main target organ for PTH are _____ and _____ and to a lesser extent, the _____.

4. True/false: Relatively minor changes in PTH will cause relatively large changes in serum iCa

5. Approximately _____% of total body calcium is located in the bones, with approximately _____% 'available' for use.

Answers

1. PTH causes an **increase**/decrease in serum calcium and an increase/**decrease** in serum phosphate, while calcitriol causes an **increase**/decrease in serum calcium and **increase**/decrease in serum phosphate

2. True/**false**: Injecting a hypocalcemic patient with physiologic doses of calcitriol will cause a reduction in PTH secretion from the parathyroid gland

3. The main target organ for PTH are **kidneys** and **bone** and to a lesser extent, the **intestines**.

4. True/**false**: Relatively minor changes in PTH will cause relatively large changes in serum iCa

5. Approximately **99**% of total body calcium is located in the bones, with approximately **1**% of this store 'available' for use.