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

**Extracellular Calcium**

- 55% Ionized Calcium
  - Ca^2+
- 35% Protein Bound Calcium
- 10% Complexed Calcium
  - Ca-citrate
  - Ca-lactate
  - Ca-bicarbonate
  - Ca-phosphate

**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, prostaglandin 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
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.

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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.