Parathyroids Glands Calcitonin

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The soft osteoid, which does not calcify, may be deformed by gravity and produced bowing, knock knee or other bizarre deformations of the limbs

Introduction

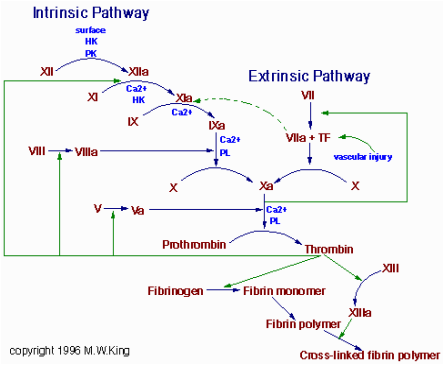
- Minerals (Calcium and Phosphate)
- Parathyroid hormones (PTH), Calcitonin (CT), and Vitamin D (Vit D)
- Bone, Intestine, and Kidney
- Sex steroids, Adrenal steroids, and growth hormone

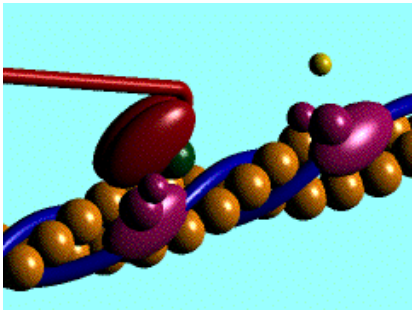
Calcium Ion Metabolism

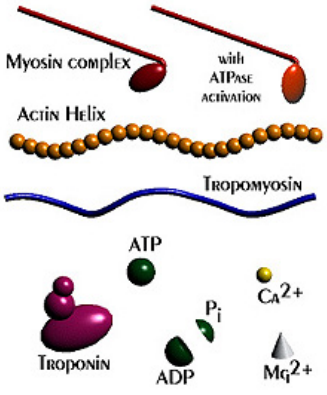
- CALCIUM
  - cation
  - fifth most common inorganic element
  - 99% is in the skeleton
  - Normal range 9-11mg% (2.35-2.75mM/L)

Calcium Ion Metabolism

- CALCIUM
  - bound to proteins (albumin)
  - free ionized calcium
    - blood coagulation
    - normal cardiac contraction
    - skeletal and muscle contraction
    - nerve function
    - bone formation







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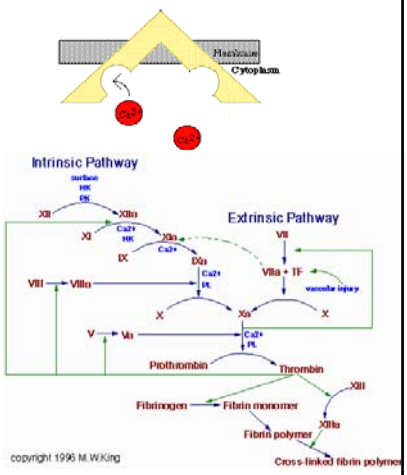


Calcium Ion Metabolism

- CALCIUM
  - IN BONE
    1. readily exchangeable
       - plasma calcium
    2. slowly exchangeable

    - IMPORTANCE
      - provides a rapid buffering mechanism to keep calcium conc. in ECF from rising or falling

Calcium Ion Metabolism

- CALCIUM
  - 1 gram/day
  - upper small intestine
  - HCl, Vitamin D, PTH, lactose and protein
  - excessive fats, excessive quantities of phosphate and oxalate, alkali, chelating agents

Calcium Ion Metabolism

- CALCIUM
  - Physiological Factors that affect Absorption
    - increased
      - pregnancy
      - growth
      - lactation
  - Body needs that affect Absorption
    - increased
      - calcium deficiency
    - decreased
      - calcium excess
  - FECES

Calcium Ion Metabolism

- CALCIUM
  - filtered in the kidneys
  - 98-99% reabsorbed
    - 60% proximal tubules
    - 40% ascending limb of the loop of Henle and the distal tubule
  - Distal Tubular reabsorption is regulated by PTH

Phosphate Ion Metabolism

- ROLE
  - transfer of energy in the intermediary metabolism of foodstuff
  - aid in maintenance of the pH of body fluids
  - important constituent of bone
- In adults 3-4mg% (0.97-1.29)
- not finely regulated
- changes cause serious clinical effects

Phosphate Ion Metabolism

- 1 gram/day
- absorption
  - duodenum
  - linearly proportionate to dietary intake
  - facilitated by Vit. D, PTH, acids, excess fat
  - decrease by high Calcium, Alkaline salts
- URINE
- PTH increase clearance by decreasing reabsorption in the proximal tubules.

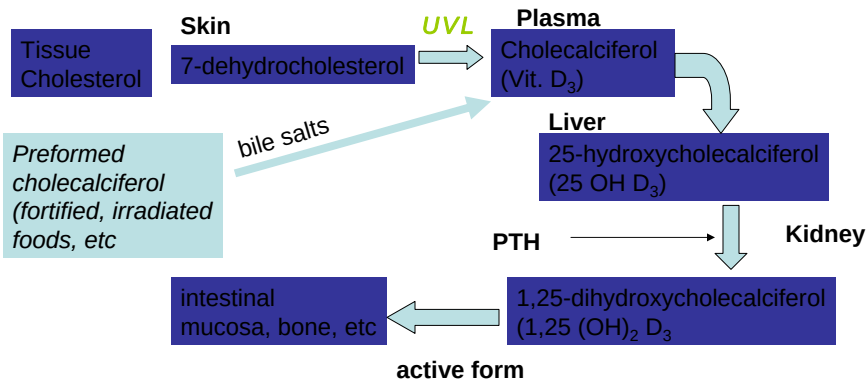
Bone Physiology

- living tissue with collagenous protein matrix
- impregnated with mineral salts (hydroxyapatites)
- Osteoblast, Osteoclasts, Osteocytes

Bone Physiology

- **Osteoblast**
  - bone-forming cells
  - secrete collagen forming a matrix then calcifies
- **Osteocytes**
  - surrounded by calcified matrix
- **Osteoclasts**
  - multinuclear cells
  - erode and resorb previously formed bone
    - release of Ca and PO4 into the ECF
    - breakdown of Collagen into its contituent amino acids

Vitamin D



Vitamin D

- Two Sources
  1. Dietary form (Vitamin D_2 or ergocalciferol)
     - plant
  2. Endogenous form (Vitamin D_3)
     - animal and fish products

Vitamin D

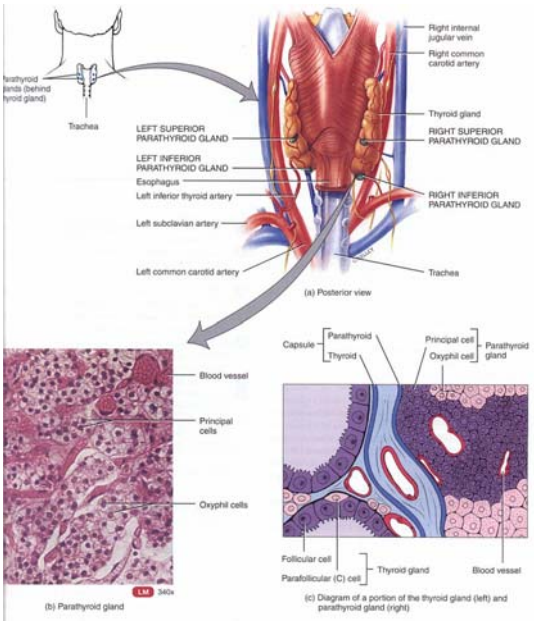
- Primary Sites of Action
  - bone
    - deposition
      - deficiency (rickets, osteomalacia)
    - reabsorption
  - intestine
    - absorption of Ca
      - it acts on the nuclei of the intestinal epithelial cells to initiate the formation of mRNA
      - formation of a calcium-stimulated ATPase in the brush border of the epithelial cells
      - formation of an alkaline phosphatase in the epithelial cells

Vitamin D

- Fat soluble vitamins
- dihydroxy derivative 125 $(OH)_2$ D_3

THE PARATHYROIDS

- smallest endocrine glands in the body
- outgrowth of the endoderm 3rd and 4th pharyngeal pouches
- 2 pairs of glands- typical
- 5 or 6 pairs – occasional
- behind thyroid gland
- 6mm long
- 30-35 mg in weight
- superior and inferior thyroid arteries



THE PARATHYROIDS

- Two Types of Cell
  1. Chief cells
     - most numerous
     - seen and identified even at birth
     - secrete the PTH
  2. Oxyphil cells
     - after puberty
     - function not certain

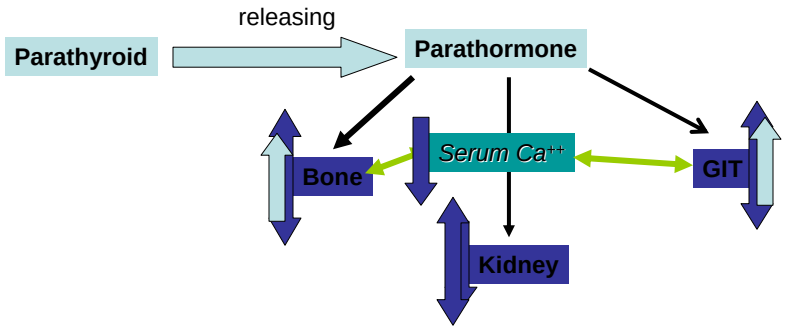
THE PARATHYROIDS

- ROLE
  - regulation of the serum calcium concentration
  - action through its effects on the three tissues
    - bone
    - kidney
    - intestine

THE PARATHYROIDS

- No known pituitary trophic hormone
  - direct action *unlike* (adrenal, gonads, and thyroid)

THE PARATHYROIDS



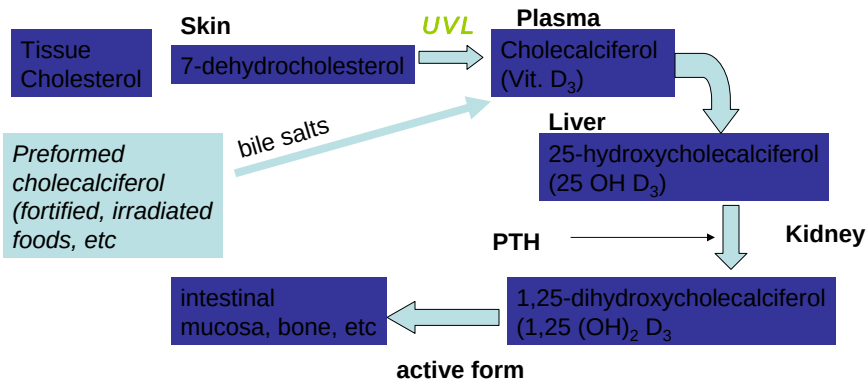
THE PARATHYROIDS

- MECHANISM OF ACTION OF PTH
  - Bone, and Kidney
    - activation of adenyl cyclase→increase formation of cyclic AMP
    - increase permeability of osteoclasts, osteocytes, and osteoblasts to the bone fluid
      - osteoblasts
        - » pump the Ca into the ECF, the pump stimulated by 1,25 – $(OH)_2D_3$
    - On a more long-term basis increase osteoclastic activity

THE PARATHYROIDS

- MECHANISM OF ACTION
  - serve as a trophic hormone for the conversion of 25 $(OH)D_3$ → 1,25- $(OH)_2$ D_3

Vitamin D



CHEMISTRY OF PTH

- linear polypeptide
- 9500 MW
- 84 amino acids
- 34 amino acids
  - active portion
  - has immunological activity
- Half-life > 20 minutes
- secreted polypeptide is rapidly cleared by the Kupfer cells in the liver

CONTROL OF PTH RELEASE

- secretion rate controlled by ionized Ca
- simple inverse linear relationship between plasma Ca and plasma PTH
- Enlarge size (rickets, pregnancy, and lactation)
- Reduced size (excess Ca in the diet, increase Vit. D in the diet

CONTROL OF PTH RELEASE

- Increase Secretion of PTH
  - decrease in plasma Ca
  - decrease in plasma Mg
  - decrease β- adrenergic discharge
  - decrease cyclic AMP
- HORMONES Indirectly stimulate PTH
  - calcitonin
  - cortisol
  - growth hormones

PHYSIOLOGIC EFFECT OF PTH

- Parathyroidectomy
  - decline in plasma Ca
- Metabolic Changes after Parathyroidectomy
  - hypocalcemia
  - hyperphosphatemia
  - hypocalciuria

PARATHORMONE AND VITAMIN D

- promote intestinal absorption of *Ca* and *P*
- The conversion of Vitamin D (active form) requires PTH
- Excessive doses of Vit. D produces disturbances comparable to Hyperparathyroidism
  - *weakness, nausea, vomiting, abdominal cramps, abnormal calcification of tissues*
- Dihydrotachysterol

PARATHORMONE AND THE KIDNEYS

- ACTION
  1. It induces phosphaturia
  2. Decreases calcium excretion
  3. Enhances 25 (OH) D3-1- α hydroxylase activity

- Decrease in reabsorption of PO_4 in proximal tubules

PARATHORMONE AND THE BONE

- TWO EFFECTS ON BONE CAUSING ABSORPTION OF CALCIUM AND PHOSPHATES
  1. The Rapid Phase
  2. Slow Phase

THE RAPID PHASE OF CALCIUM AND PHOSPHATE ABSORPTION

"The Osteocytic Membrane System"

- Osteoblast and Osteocytes
  - osteoblastic in nature
  - associated with bone deposition and its calcification
  - function to cause bone salt absorption
- PTH activate a calcium pump in the osteocytic membrane that takes place in minutes

THE SLOW PHASE OF BONE ABSORPTION AND CALCIUM PHOSPHATE RELEASE

- Activation of the Osteoclasts
  1. Immediate activation of the osteoclasts
  2. formation of new osteoclasts from osteoprogenitor cell

- Several days of excess PTH cause the osteoclastic system to become well develop

PARATHORMONE AND OTHER TISSUES

- INTESTINES
  - increase absorption of Ca^{++}
    - indirect
- Diminish the Ca^{++} content of the milk of lactating women
  - hormones inhibits possibly the loss of Ca^{++} into the mother's milk
- In hypoparathyroidism
  - deposits are found in soft tissues (lens, CNS)

CALCITONIN

- 32 amino acids
- c- cells of the parafollicular cells of the thyroid gland
- ACTION
  - inhibit bone resorption
  - decrease blood calcium
  - increase intestinal secretion of water and electrolytes
  - increase Na^{+}, Ca^{++} and phosphate excretion in the urine
  - decrease gastric acid secretion
- ANTAGONIST to PTH

CALCITONIN

- regulated by blood Ca^{++}
- secretion is directly proportional to plasma Ca^{++} concentration
- lowers the circulating Ca^{++} and phosphate level

CALCITONIN

- REDUCES PLASMA CALCIUM IN 3 WAYS
  1. decrease the activity of the osteoclast
  2. increase in osteoblastic activity
  3. prevent formation of new osteoclast from osteoprogenitor cells
- Increase both urinary calcium and phosphate clearance

CALCITONIN

- Mechanism of Actions
  - bones
    - inhibits resorption
  - kidneys
    - increase Ca^{++} clearance
    - increase phosphate clearance
  - GIT
    - inhibits multiple functions
  - BLOOD
    - decreases Ca^{++}

HYPOPARATHYROIDISM AND HYPOCALCEMIA

- CAUSES
  1. Idiopathic hypoparathyroidism, hypoplasia or absence of parathyroid tissue
  2. Accidental removal of the glands
  3. Pseudohypoparathyroidism, ineffective in its action because
     - unresponsiveness of end organs or target cells
     - hormone being produced is different from the normal
  4. Temporary hypoparathyroidism

HYPOPARATHYROIDISM AND HYPOCALCEMIA

- TETANY
  - MacCallum and Voetglin 1909 (tetania thyreopriva)
  - determining factor is the conc. of ionized calcium in the plasma and extracellular fluids of the body
  - 9.4mg%→6mg%

CAUSES OF TETANY

1. Inadequate or insufficient functioning of the parathyroid glands
   - experimental
   - accidental removal
   - infantile or idiopathic change
2. Renal Failure
   - impaired reabsorption of Ca by the renal tubules
   - decreased excetion of phosphates by renal tubules
   - increased phosphates in serum

CAUSES OF TETANY

3. Alkalosis
   - hyperventilation tetany
     - excessive CO2 elimination
   - Gastric tetany
     - persistent vomiting and loss of chlorides
   - Alkali tetany
     - excessive administration of alkalies
4. Malabsorption
   - Celiac disease and sprue
   - Other syndromes (due to Vit D deficiency)
     - rickets osteomalcia

HYPERPARATHYROIDISM AND HYPERCALCEMIA

A. Primary hyperparathyroidism
   - inappropriate secretion of PTH which may be due to
     - adenoma
     - hyperplasia
     - carcinoma
- extreme osteoclastic activity occurs
- hypercalcemia, hypophosphatemia, demineralization, and hypercalciuria
- formation of renal calculi (calcium phosphate, or calcium oxalate

HYPERPARATHYROIDISM AND HYPERCALCEMIA

- Osteitis fibrosa cystica
  - multiple bone cyst when the osteoclastic absorption of bone soon far outstrips osteoblastic deposition, and the bone may be eaten away almost entirely.

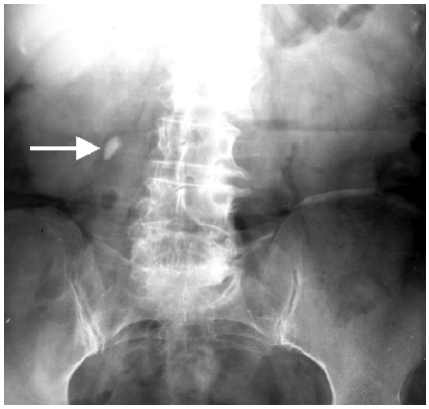
Osteitis Fibrosa Cystica

R femur with long-standing severe osteopenia and bony cystic formation secondary to primary Hyperparathyroidism.

R. Cotran Robbins Pathologic Basis of Disease , 4th ed. 1989

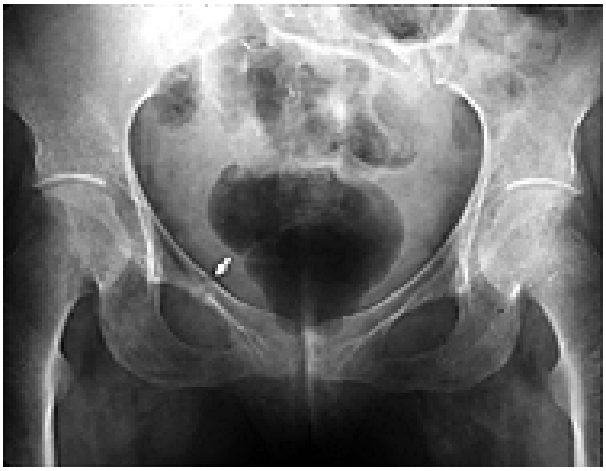
HYPERPARATHYROIDISM AND HYPERCALCEMIA

- Renal Lesions in Hyperparathyroidism
  - precipitation of calcium phosphate
    - dehydration
    - alkaline urine
    - high intake of milk
  - Two types of Calcium PO4 deposition
    - Nephrocalcinosis
    - Nephrolithiasis
  - Rare Type Renal Failure
    - Calcium levels 18-22mg%



HYPERPARATHYROIDISM AND HYPERCALCEMIA

B. SECONDARY HYPERPARATHYROIDISM
- Chronic azotemic bright's disease
- Rickets
- Osteomalacia
- Pregnancy and Lactation



HYPERPARATHYROIDISM AND HYPERCALCEMIA

C. Tertiary Hyperparathyroidism

- tissue becomes very large
- adenomatous development occurs

THANK YOU
FOR LISTENING!

GOOD LUCK!