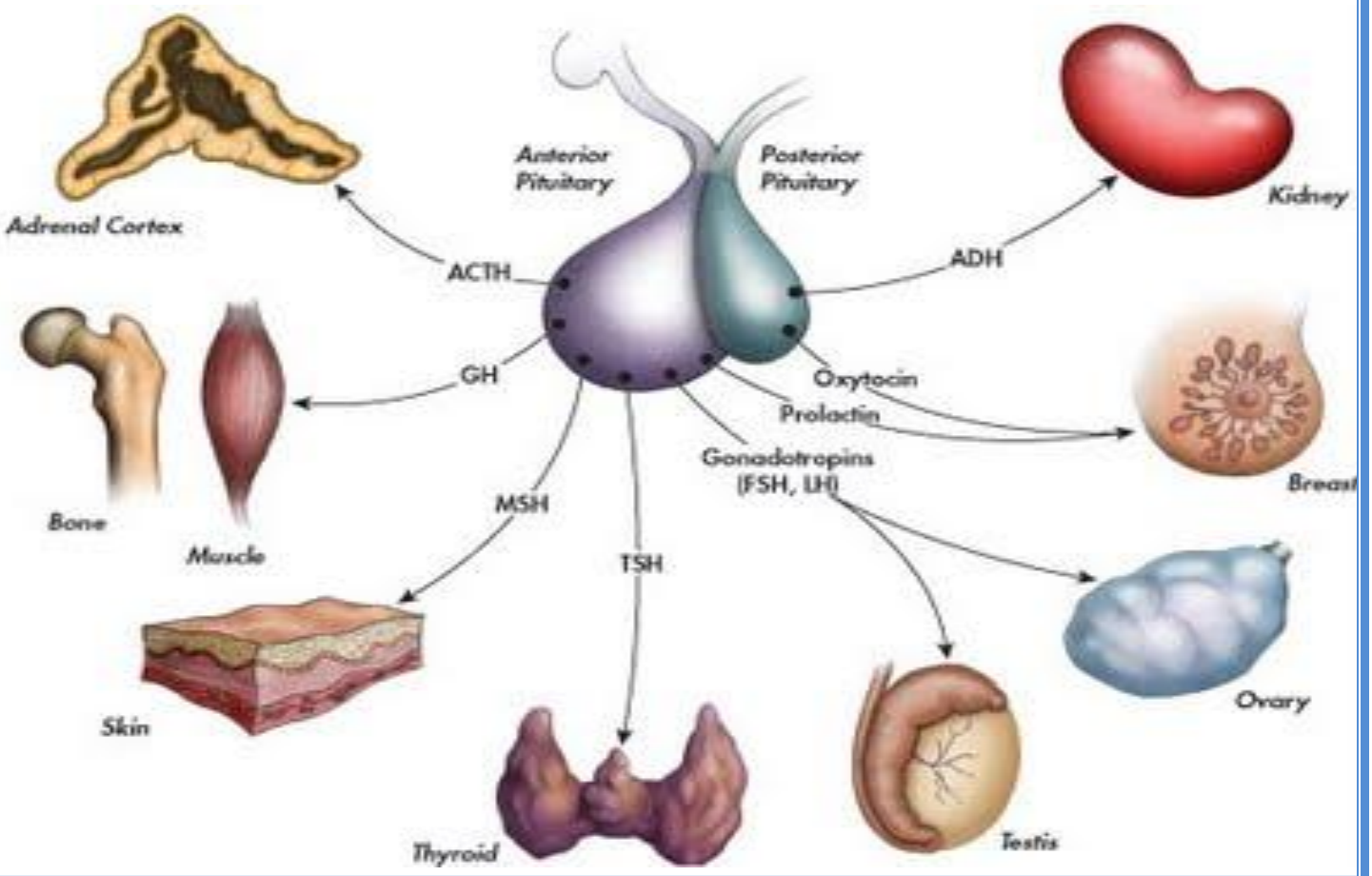
Endocrine Block

8th Lecture

Calcium Homeostasis



PHYSIOLOGY TEAM – 430

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Calcium Homeostasis

- **Introduction:**

– Calcium salts in bone provide structural integrity of the skeleton
– There are three major pools of calcium in the body:

✓ **Intracellular calcium:** Majority of calcium within cells is located in mitochondria and endoplasmic reticulum.
✓ **Calcium in blood and extracellular fluid:** almost half of the calcium in blood is bound to proteins.
✓ **Bone calcium:** A vast majority of body calcium is in bone.

– Calcium ions in extracellular and cellular fluids is essential to normal function of a host of biochemical processes:

✓ Neuromuscular excitability
✓ Blood coagulation
✓ Hormonal secretion
✓ Enzymatic regulation

– Excessive intake of carbonated beverages (Carbonated water, Cola, Soft drinks) is associated with increased loss of calcium from the body, because normal bone function requires weight-bearing exercise
– prolonged immobility & total bed-rest cause bones to lose calcium

Note:
weight-bearing exercise is essential for building and maintaining healthy bones. Weight-bearing exercise is any activity you do while on your feet and legs that works your muscles and bones against gravity

- **Calcium homeostasis:**

– 3 organs maintain homeostasis: intestine, kidney, bone
– **The small intestine:** is the site where dietary calcium is absorbed.
– **Bone:** serves as a vast reservoir of calcium.
– **The kidney:** is critically important in calcium homeostasis. Under normal blood calcium concentrations, almost all of the calcium that enters glomerular filtrate is reabsorbed from the tubular system back into blood.

- The total Ca^{++} concentration in blood is around 10 mg / dl (range = 8.5-10 mg / dl)
- It exists in ionized , free to react form and in a bound form

✓ **The free ionized Ca^{++}:**

- is about 50% of the total blood Ca^{++} = 5mg/dl.
- It is the only form of Ca^{++} which is biologically active

✓ **The remaining 50% is non-free , unionized calcium:**

1) Protein-bound calcium:

- Around 40% of total ECF calcium
- Most of this calcium is bound to albumin , & much smaller Fraction is bound to globulin

2) Present as complexed salt:

- Mainly bound to serum citrate & phosphate
- Around 10% of blood calcium.

- 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 →hyper excitability of the nervous system → patients become prone to develop tetanic muscle contractions &seizures.

- **Positive calcium balance:**

✓ Is seen in growing children where intestinal absorption exceeds urinary excretion and the difference is deposited in bones.

- **Negative Calcium balance:**

✓ Is seen in women during pregnancy and lactation where intestinal absorption is lesser than urinary excretion and the difference comes from maternal bones.

- **Consequences of Abnormal Calcium Level**

– **Decreased plasma Ca^{++} [hypocalcaemia]:**

✓ Increase excitability of nerve and muscle cell membranes → tetany, hyper reflexia, spontaneous twitching, muscle cramps, tingling and numbness.

– **Increased plasma Ca^{++} [Hypercalcaemia]:**

✓ Cardiac arrhythmias, decrease neuromuscular excitability, lethargy, constipation, polyuria and polydipsia.

- **Phosphate**

– Phosphorous is an essential mineral necessary for ATP, cAMP second messenger systems, and other roles

– Phosphate (PO_4) plasma concentration is around 4 mg/dL.

– Most of it is ionized (diffusible) → around 50% of total

– The remainder (50%) and much less of it is un-ionized (non-diffusible) and protein- bound

– Calcium is tightly regulated with Phosphorous in the body.

- **Hormonal Regulation of Calcium**

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

1) Vitamin D3 (Calcitriol) "Increase":
(1,25-dihydroxy) (taken in food & synthesized in the skin)

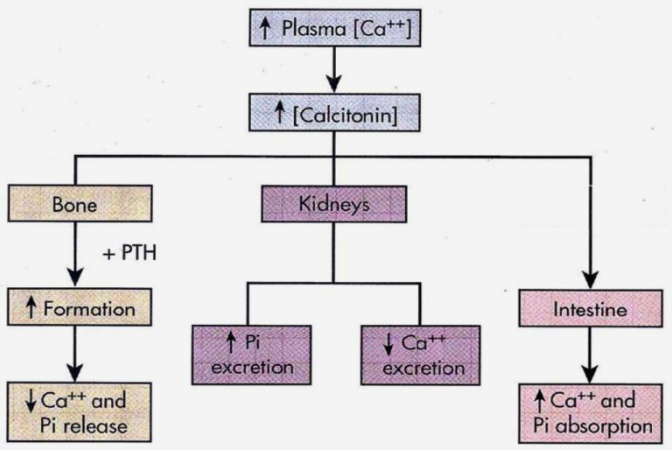
2) Parathyroid hormone (PTH) "Increase":
Polypeptide hormone secreted by Parathyroid Glands .

3) Calcitonin "Decrease":
polypeptide hormone secreted by Parafollicular (C) cells of Thyroid Gland

– High plasma Ca^{++} leads to → increased Calcitonin secretion

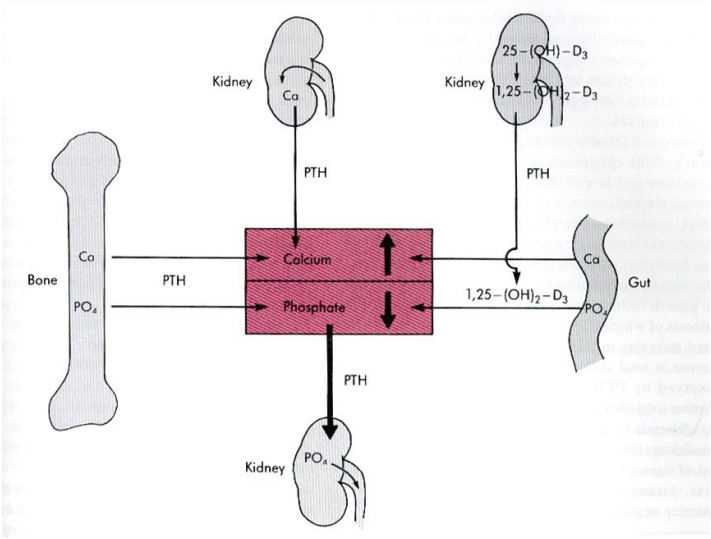
– The main action of this calcitonin is to inhibit osteoclasts → inhibition of bone resorption → (1) increases bone formation + (2) decreases blood Ca^{++} level .

– Thus calcitonin plays a central role in bone re-modeling .



Note:
Osteoclast: is a type of bone cell that removes bone tissue by removing its mineralized matrix and breaking up the organic bone

- **Calcium & Phosphorus**

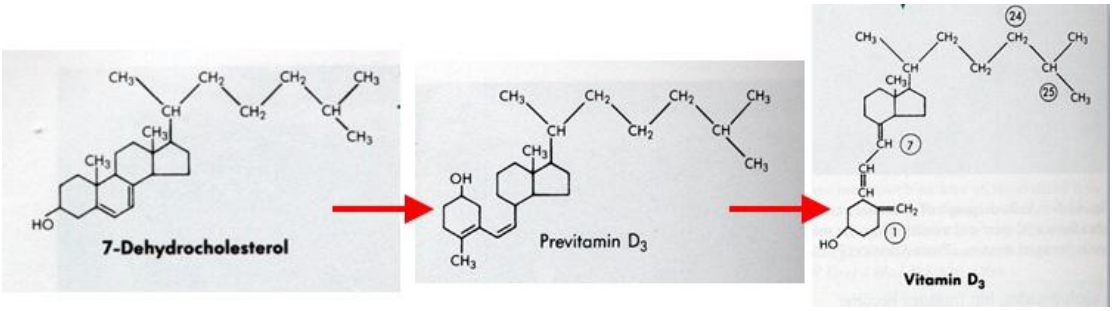


– Vitamin D3 increases Ca^{++} level by :

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

– Humans acquire vitamin D from two sources →

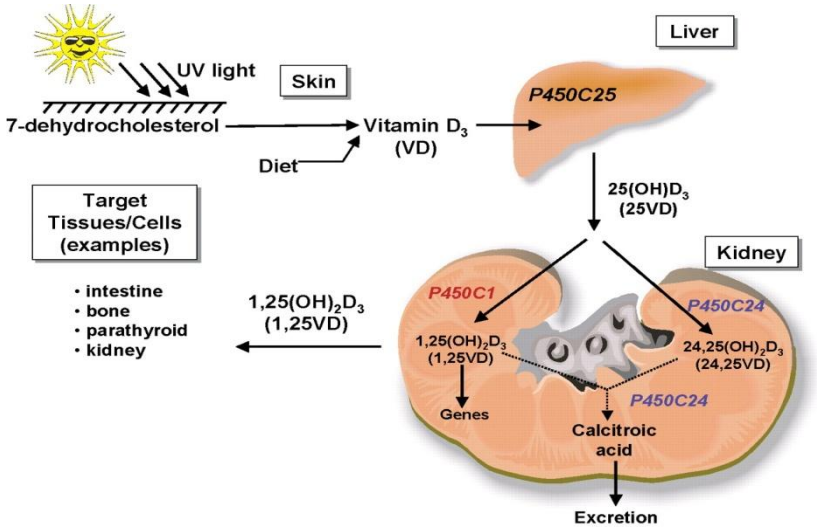
1) Ingestion in diet (food)
2) Skin : Vitamin D is produced in the skin by ultraviolet light (Sun Exposure)



- **Mechanism:**

– 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 first one occurs in the liver and the second one in the kidney

Keratinocytes: is the predominant cell type in the epidermis, the outermost layer of the skin



- When there is 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) occurs
- ✓ PTH stimulates Vit. D synthesis
- Most affected areas in Rickets and Osteomalacia → Metaphysis of long bones subjected to stress → Wrists, Knees and Ankles
- Osteomalacia: an adult disease characterized by a gradual softening and bending of the bones

- **Clinical Features:**

- Delayed dentition (delayed teething)
- Bowed legs (Due to the effect of weight bearing on the legs)
- Swelling of wrists and ankles
- Short stature

Metaphyseal widening in wrists & knees + signs of bone rarfaction

Bowed legs (Bowing of legs)