CALCIUM, PHOSPHATE AND VITAMIN D

CALCIUM

- Calcium is the chemical element with symbol Ca and atomic number 20.

- Calcium is essential for living organisms, in particular in cell physiology, where movement of the calcium ion \( \text{Ca}^{2+} \) into and out of the cytoplasm functions as a signal for many cellular processes.

- As a major material used in mineralization of bone and teeth.

- Calcium is an important component of a healthy diet and a mineral necessary for life.

- "Calcium plays an important role in building stronger, denser bones early in life and keeping bones strong and healthy later in life.

- Approximately 99 percent of the body's calcium is stored in the bones and teeth.

- The rest of the calcium in the body has other important uses, such as some exocytosis, especially neurotransmitter release, and muscle contraction.

- In the electrical conduction system of the heart, calcium replaces sodium as the mineral that depolarizes the cell, proliferating the action potential.

- In cardiac muscle, sodium influx commences an action potential, but during potassium efflux, the cardiac myocyte experiences calcium influx, prolonging the action potential and creating a plateau phase of dynamic equilibrium.

- Long-term calcium deficiency can lead to rickets and poor blood clotting and in case of a menopausal woman, it can lead to osteoporosis, in which the bone deteriorates and there is an increased risk of fractures.

- Several sources suggest a correlation between high calcium intake 2000 mg per day.

SOURCES OF CALCIUM

Vitamin D is needed to absorb calcium. Dairy products, such as milk and cheese, are a well-known source of calcium. Many good vegetable sources of calcium exist, including nuts and seeds like almonds, hazelnuts, sesame, pistachio, beans (especially soy beans). In addition, for some drinks (like soy milk or orange juice) it is typical to be fortified with calcium.

Numerous vegetables, notably spinach, have a high calcium content, but they may also contain varying amounts of oxalic acid that binds calcium and reduces its absorption.
This process may also be related to the generation of calcium oxalate.

An overlooked source of calcium is eggshell, which can be ground into a powder and mixed into food or a glass of water.

**REGULATION**

- REGULATION: kidneys filters about 250 mmole of calcium every day, some 95% of which is reabsorbed by the tubules.
- The major portion of this filtered calcium is taken up by proximal tubules without hormonal regulation.
- The amount reabsorbed occurs in distal tubules is under the influence of parathyroid hormones.
- Plasma level of calcium concentration is the principle regulator of parathyroid hormone secretion by a simple negative feedback mechanism.
- PTH rapidly stimulates osteoclastic activity, the increase bone resorption causing an increase in plasma calcium and phosphate.
- The process of bone formation and teeth formation is known as calcification which is a continuous process for bones.
- Calcium plays a role in neuromuscular transmission.
- Calcium ions are needed for excitability of nerves.
- Calcium plays a role in muscle contraction.
CHEMICAL CHANGES IN DISEASES

CALCIUM:-
Two conditions namely hypercalcaemia and hypocalcaemia.

Hypercalcaemia:- when the serum calcium level exceeds 11.0mg/dl it is called as hypercalcaemia (normal serum calcium level is 9 to 11mg/dl).

Causes:
1) Primary hyperparathyroidism:- which may be due to familial hyperplasia of gland. Solitary adenoma parathyroid carcinoma.
2) Renal stone formation:-
   Many patients with mild hypercalcaemia have no symptoms and the condition is discovered during routine laboratory screening.
   o Hypercalcaemia due to hyperparathyroidism:-
   o Gastrointestinal symptoms include loss of appetite, nausea, vomiting, constipation and abdominal pain.
   o If the kidneys are involved, the individual will have to urinate frequently during both the day and night and will be very thirsty.
   o As the calcium levels rise, the symptoms become more serious Stones may form in the kidneys and Blood pressure rises.
   o The heart rhythm may change.
   o Muscles become increasingly weak.
   o The individual may experience mood swings, confusion, psychosis, and eventually, coma and death.
   o Levels of calcium and phosphate in the urine should also be measured.
- High levels of calcium in the blood are a good indication of hypercalcaemia, but these levels may fluctuate.

- Higher calcium and lower phosphate levels may suggest primary hyperparathyroidism.
- Too much PTH in the blood may indicate primary hyperparathyroidism.
- Levels of calcium and phosphate in the urine should also be measured.
- Tumors: deposit in bone show:
  - Increased calcium and phosphate.

Hyperparathyroidism:
- Decreased calcium and increased phosphate.

In vitamin D deficiency:
- Decreased calcium and phosphate.

- **HYPOCALCAEMIA:** when serum calcium level is less than 8mg/dl is called hypocalcaemia.

  - **causes:**
    - Hyperparathyroidism which may be due to surgical induced idiopathic.
    - Malnutrition.
    - Malabsorption.
    - Nephrotic syndrome.
    - Renal failure.
    - Vitamin D deficiency

PHOSPHATE

- **PHOSPHATE:** 90% of daily dietary phosphate is absorbed.
- The absorption is stimulated by both PTH and vitamin D₃.
- Phosphate is the constituent of bone and teeth.
- Uptake of phosphate by the kidneys is sodium dependent about 85% of phosphate is reabsorbed by the proximal tubules.
- Phosphate reabsorption is increased when dietary intake is reduced by a PTH mechanism.

REGULATION OF SERUM PHOSPHATE

PTH reduces the reabsorption of phosphate from the proximal tubule of the kidney, which means more phosphate is excreted through the urine.

However, PTH enhances the uptake of phosphate from the intestine and bones into the blood. In the bone, slightly more calcium than phosphate is released from the breakdown of bone.

In the intestines, absorption of both Calcium and Phosphate is mediated by an increase in activated vitamin D.

The absorption of phosphate is not as dependent on vitamin D as is that of calcium.
PHOSPHATE DEFICIENCY DISORDERS

- PHOSPHATE:
  - Rickets and osteomalacia are important deficiency disorders of calcium phosphorus and vitamin D.
  - Plasma levels in adult is 0.6 to 1.2 mmol.
  - Two condition hyperphosphatemia and hypophosphatemia.
  - HYPERPHOSPHATEMIA: occurs in
    - Increased intake (diet, vitamin D).
    - Increase release from cells (diabetes, acidemia).
    - Increase release from bones (malignancy).
    - Hyperparathyroidism.

- HYPOPHOSPHATEMIA
  - HYPOPHOSPHATEMIA: occurs in
    - Decreased intake.
    - Drug induced such as antacids containing aluminium hydroxide.
    - Increased excretion as in taking diuretics.
    - Hypoparathyroidism.

VITAMIN D

- Vitamin D is a group of fat-soluble steroids responsible for intestinal absorption of calcium and phosphate.
- In humans, vitamin D is unique because it can be ingested as cholecalciferol (vitamin D₃) or ergocalciferol (vitamin D₂) and because the body can also synthesize it (from cholesterol) when sun exposure is adequate (hence its name, the "sunshine vitamin").
- Although vitamin D is commonly called a vitamin, it is not actually an essential dietary vitamin in the strict sense, as it can be synthesized in adequate amounts from sunlight.
In the liver vitamin D is converted to calcidiol, which is also known as 25-hydroxycholecalciferol, or 25-hydroxyvitamin D—abbreviated 25(OH)D; and which is the specific vitamin D metabolite that is measured in serum to determine a person's vitamin D status.

- Part of the calcidiol is converted by the kidneys to calcitriol, the biologically active form of vitamin D.
- Calcitriol circulates as a hormone in the blood, regulating the concentration of calcium and phosphate in the bloodstream and promoting the healthy growth and remodeling of bone.
- Calcidiol is also converted to calcitriol outside of the kidneys for other purposes, such as the proliferation, differentiation and apoptosis of cells; calcitriol also affects neuromuscular function and inflammation.

SYNTHESIS

- In the skin, 7-dehydrocholesterol, a derivative of cholesterol, is photolyzed by ultraviolet light.
- The product is previtamin D₃.
- Previtamin D₃ spontaneously isomerizes to vitamin D₃ (cholecalciferol).
- At room temperature, the transformation of previtamin D₃ to vitamin D₃ takes about 12 days to complete.
- Cholecalciferol is hydroxylated in the liver at position 25 to form 25-hydroxycholecalciferol (calcidiol or 25(OH)D).
- This reaction is catalyzed by the microsomal enzyme vitamin D 25-hydroxylase, which is produced by hepatocytes.
- Once made, the product is released into the plasma, where it is bound to an α-globulin, vitamin D binding protein.
Calcidiol is transported to the proximal tubules of the kidneys, where it is hydroxylated at the 1-α position to form calcitriol (1,25-dihydroxycholecalciferol and abbreviated to 1,25(OH)₂D).

The conversion of calcidiol to calcitriol is catalyzed by the enzyme 25-hydroxyvitamin D₃ 1-alpha-hydroxylase, the levels of which are increased by parathyroid hormone (and additionally by low calcium or phosphate).

DEFICIENCY

- A diet deficient in vitamin D cause rickets in children.
- Low blood calcidiol (25-hydroxy-vitamin D) can result from avoiding the sun.
- Deficiency results in impaired bone mineralization and leads to bone-softening of bones.
- Rickets, leads to impeded growth and deformity of the long bones, can be caused by calcium or phosphorus deficiency as well as a lack of vitamin D.
- Vitamin D deficiency causes osteomalacia beyond that, low serum vitamin D levels have been associated with falls, and low bone mineral density.

supplementation with vitamin D and calcium may improve bone mineral density slightly, decreasing the risk of falls and fractures in certain groups of people, specifically those older than 65 years.

Osteomalacia, a bone-thinning disorder that occurs exclusively in adults, is characterized by proximal muscle weakness and bone fragility.

The effects of osteomalacia are thought to contribute to chronic musculoskeletal pain.