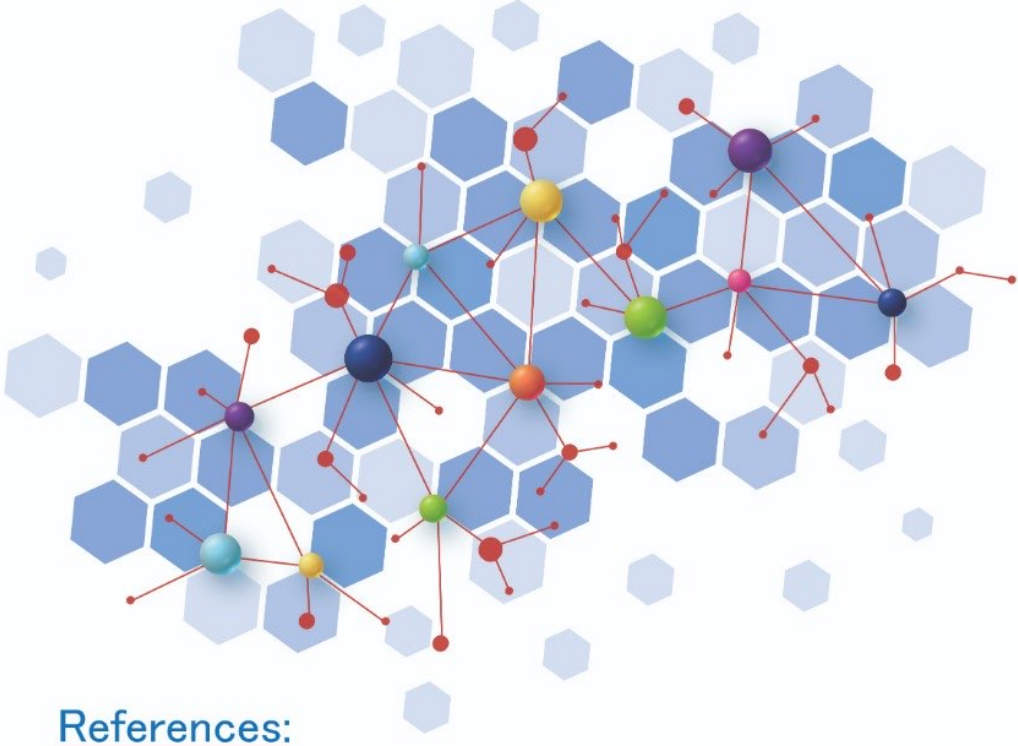
Clinical biochemistry

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References:

- Clinical biochemistry book 13th edition.
- Doctor's slides and records.
- Past years questions.

Version: 1

Lecture #: #10: cont.: calcium, phosphate & magnesium

Hypocalcemia:

- First, we have to exclude if hypocalcemia due to decreased plasma [albumin] or not → do adjusted Ca levels.
- hypocalcemia must be pathological.

❖ **Signs & symptoms**:

1. Muscle cramps & spasms (tetany).
2. Numbness, paraesthesiae.
3. Convulsions & seizures.
4. Behavioral disturbance (personal changes).
5. Prolonged Q-T interval on ECG.
6. Cataracts (especially in chronic hypocalcemia)
7. basal ganglia calcification → occurs in prolonged hypocalcemia.
8. Papilledema (swelling of optic nerve head).
9. **Chvostek sign**: contraction of facial muscles upon tapping the facial nerve
10. **Trousseau sign**: carpal spasm when sphygmomanometer cuff is applied

❖ **Causes of hypocalcemia**

1. **Artifact** → blood collected into EDTA tube.
   - **EDTA** binds with Ca → hypocalcemia
2. **Vitamin D deficiency** → ↓synthesis, ↓dietary supply or malabsorption → ↓ absorption of calcium & phosphate.
3. Impaired vitamin D metabolism (**increased metabolism**):
   - Phenobarbital & Phenytoin (used for epilepsy) → increases the activity of CYT-P450 system of the liver
   - CYT-P450 system is responsible for the metabolism of vitamin D
   - increases the activity of CYT-P450 system→ increase vitamin D metabolism.
4. **End-stage renal disease** → impaired calcitriol synthesis→ **renal osteodystrophy**.
   - Decrease calcitriol → hypocalcemia → hyperparathyroidism → bone resorption (osteodystrophy)
   - So renal failure caused bone resorption
5. inadequate intake of calcium (**malabsorption**).
6. **Hypoparathyroidism**; which may be caused by:
   a. **Autoimmune** disease: results in destruction of parathyroid gland.
   b. **post-surgical**: surgical removal of parathyroid gland especially in those that remove the thyroid gland in cases of thyrotoxicosis (hyperthyroidism)
   c. **Severe Mg^{2+} deficiency**:
      - suppress parathyroid gland because normal Mg^{2+} level is necessary for PTH release & action on target cells.
   d. **infiltrative disease**:
      - parathyroid gland is infiltrated by carcinoma of the thyroid gland.
7. **Pseudohypoparathyroidism**:
   a. target organ resistance to PTH
   b. bone & kidney are not responding to PTH → patients have increased serum PTH levels with low calcium levels.

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❖ **Management of hypocalcemia:**
- **IV Ca-gluconate** for symptomatic hypocalcemia or severe hypocalcemia (less than 1.9)
- correct Mg^{2+} deficiency
- Vit.D and calcium supplements.

❖ **Case scenario:**
- A 56 years old woman was admitted for cataract extraction. She has a hstory of thyroid gland multinodular goiter that was removed (thyroidectomy) 20 years ago.
- Physical exam: **Chvostek & Trousseau signs were positive**
- **Labs:** adjusted Ca: 1.6 (low) // phosphate: 2.53 (high) // alkaline phosphatase: normal // PTH: low
- **Explanation:** this patient who underwent thyroidectomy removed her thyroid gland → parathyroid glands are found on the posterior aspect of the thyroid gland and may have been removed accidentally during the surgery→ no PTH → hypoparathyroidism causing hypocalcemia → cataracts formation.
- **Note:** patents should be monitored for hypocalcemia for long periods of time.

Phosphate (PO^{2-}):

- Complexes with calcium in the bone.
- Required for energy production (ATP).
- Required for nucleic acid production (DNA)→ when cells die → release phosphate
- Buffering system (in cells & in urine): responsible for H excretion
- in plasma, 85% of phosphate is free & 15% is protein bound.
- Its plasma concentration depends on:
  i. PTH → ↑phosphate excretion.
  ii. Calcitriol → ↑ phosphate absorption from GI tract

Hypophosphatemia:

- Common.
- little consequences when mild.
- **Severe**:
  - plasma [phosphate] < 0.3 mmol/L
  - causes cell dysfunction due to lack of energy (ATP) especially in muscle cell → muscle weakness & rhabdomyolysis
  - RBCs, WBCs & platelets are affected too
- Chronic hypophosphatemia → **rickets & osteomalacia**.

❖ **Causes** of hypophosphatemia:

1) **Decreased intake or absorption:**
   A. Malabsorption
   B. Vomiting
   C. vitamin D deficiency
   D. antacids
   E. alcohol withdrawal (due to decreased intake, alkalosis…etc.)

2) **increase renal loss:**
   A. primary hyperparathyroidism

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B. renal tubular disease
    a. renal tubules can't reabsorb phosphate back to blood
C. diuretics

3) **Redistribution**:
- Cases when cells are deprived from phosphate and then→ insulin is increased → sudden increase in phosphate uptake to tissues→ hypophosphatemia
- **Ex: recovery from diabetic ketoacidosis:**
    - **hyper**phosphatemia is usual in diabetic ketoacidosis
    - respiratory alkalosis occurs because of stimulating phosphofructokinase & the formation of phosphorylated glycolytic intermediates
    - treatment is with insulin, k &glucose.
    - when insulin is administered → increase uptake of phosphate into depleted (starved) tissues → hypophosphatemia

❖ **treatment:**
- phosphate supplementation (orally or IV)

hyperphosphatemia:

❖ **causes of hyperphosphatemia:**
1. **Increased intake**:
    a. IV phosphate therapy during
        i. parenteral feeding
        ii. phosphate enemas.
2. **Decreased excretion:**
    a. renal insufficiency
    b. hypoparathyroidism
    c. pseudo-hypoparathyroidism:
        i. kidneys don't respond to PTH → no excretion of phosphate → hyperphosphatemia
    d. vitamin D toxicity

3. **Redistribution:**
    a. tissue catabolism which occurs in
        i. **tumor lysis** during treatment of malignant disease like hematological malignancy→ large number of cells die → phosphate are released from these cells → hyperphosphatemia
        ii. **rhabdomyolysis**
        iii. **diabetic ketoacidosis**: due to tissue catabolism & renal impairment
4. **artefactual**:
    a. **blood hemolysis** → all intracellular phosphate get outside → hyperphosphatemia

❖ **treatment:**
- treat the underlying cause
- give phosphate binders
    - calcium salts → bind phosphate inside the gi system → prevent phosphate absorption
- low phosphate diet

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Magnesium:

- adult body contains 1000 mmol of magnesium.
- Half of the amount is in the bone & the remainder distributed equally between muscle & other soft tissues.
- Only 11-17 mmol is found in the ECF.
- Excess magnesium is excreted through the kidneys.
- Urinary excretion of magnesium is **increased** by ECF expansion (**hypervolemia**), **hypercalcemia** & **hypermagnesemia** and is **decreased** in the opposite of these states.
    - PTH & aldosterone effect on magnesium:
        - **PTH** → directly increases tubular reabsorption of filtered magnesium.
        - **Aldosterone** → causes hypervolemia → more Mg filtration → more excretion (secondary to changes in ECF volume).

❖ Functions of magnesium:

- Cofactor for enzymes involved in protein synthesis, glycolysis & transmembrane transport of ions.
- Magnesium-ATP complex is the substrate for many ATP requiring enzymes.
- Important in the maintenance of the structure of ribosomes, nucleic acids & some proteins.
- interacts with calcium & affects the permeability of excitable membranes & their electrical properties:
    - ECF magnesium **depletion** causes **hyperexcitability** → tetany
    - **Excess** ECF magnesium causes **decrease** in excitation to CVS/CNS systems

Hypermagnesemia:

- Significant hypermagnesemia is uncommon when renal function is normal
- **Cardiac conduction** is affected at concentrations of **2.5-5**
    - Normal level of Mg is 0.8-1.2
- Very high concentrations **(> 7.5** mmol/L) → **respiratory paralysis & cardiac arrest**.
- Such extreme hypermagnesemia may occasionally be seen in **renal failure**.
- **IV calcium gluconate** gives short term protection against the adverse effects of hypermagnesemia on the heart
- in renal failure→ **dialysis** may be necessary especially when Mg levels are very high.

Hypomagnesaemia:

- almost always indicates magnesium deficiency (not related to albumin..etc.)
- more frequent than hypermagnesemia.
- decreased PTH secretion→ **hypocalcemia**
- causes **hypophosphatemia** & **hypokalemia**
- Treatment: magnesium supplementation.
    - Mild deficiency → oral supplementation
    - severe deficiency → slow IV infusion
- Refractory **hypocalcemia** & **hypokalemia** → always check Plasma concentration of magnesium
    - Must correct Mg levels

❖ Causes of hypomagnesaemia:

1. Malabsorption.
2. Malnutrition.
3. Chronic alcoholism & alcohol withdrawal.

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4. Cirrhosis.
5. Diuretic therapy (especially loop diuretics)
6. Renal tubular disorders:
    a. in advanced renal disease, hypomagnesaemia is usual
7. Chronic mineralocorticoid excess.
8. Drug toxicity → e.g. amphotericin, aminoglycosides, cisplatin, cyclosporine.
9. Gitelman's syndrome:
    a. an autosomal recessive kidney disorder where the distal tubules can't reabsorb NaCl
    b. characterized by **hypokalemic metabolic alkalosis** with **hypocalciuria**, and **hypomagnesemia**.

❖ **Clinical features of hypomagnesaemia:**

1. Tetany (with normal or decreased calcium).
2. Agitation, delirium.
3. Ataxia (lack of voluntary coordination of muscle movements)
4. tremor.
5. Muscle weakness.
6. Cardiac arrhythmias.

❖ **Treatment:**

- Mild hypomagnesemia → oral Mg supplements
- Severe deficiency → slow iv infusion

❖ **Case scenario:**

- An elderly woman with weight loss and malabsorption. She has osteolomalacia and hypocalcemia. She was given parental nutritional support but she remains hypocalcemic despite adequate calcium supplements and vitamin D
- Labs: adjusted Ca: low //PTH: low // Mg: low
- Explanation: malabsorption caused hypomagnesemia → resistant hypocalcemia → maybe the cause of osteomalacia.

❖ **Case scenario:**

- A young man with severe diarrhea; abdominal pan; weight loss and rectal bleeding. He has cramps in his legs and arms
- Examination: chvostek and trousseau signs were positive
- Investigation : rectal biopsy → crhon disease
- Labs: low potassium &Mg // normal adjusted Ca &phosphate
- Explanation: severe hypomagnesemia from crhon disease (malabsorption) caused hypokalemia and tetany (cramps)
- **Note: when hypocalcemia signs present with normal adjusted Ca levels → check from hypomagnesemia**

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