Parathyroid Disorders

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Objectives:

- **Understand the calcium and related hormones physiology**
- **Understand hyperparathyroidism**
- **Understand the hypoparathyroidism**

References:
Slides - Black
Doctor's notes - Red
Master the board - Blue
Extra explanation - Grey

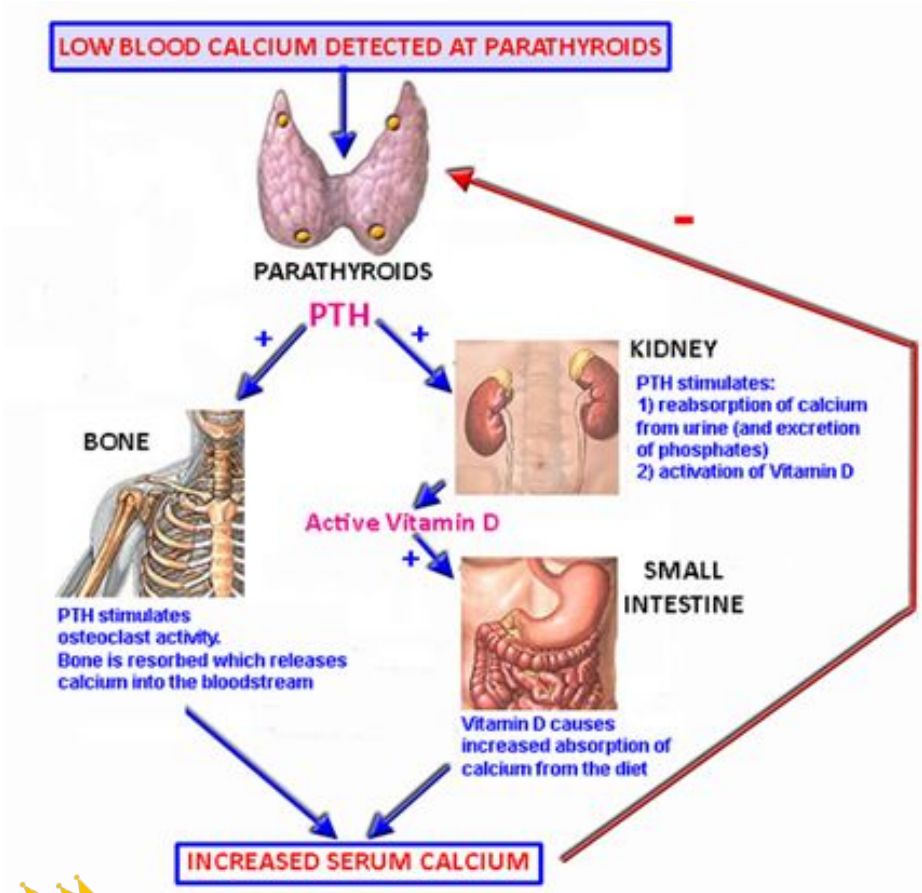
Optional:

Chapter 4 - p180 & p181

Editing file

❖ Normal physiology:

- **Parathyroid hormone (PTH) plays a key role in the regulation of calcium and phosphate homeostasis and vitamin D metabolism**
- **The PTH acts directly on the bones and kidneys and indirectly on the intestine through its effect on the synthesis of 1,25 (OH)2D3. PTH increase the kidney production of active vitamin D**
- **Its production is regulated by the concentration of serum ionized calcium. Lowering of the serum calcium levels will induce an increased rate of parathyroid hormone secretion.**
- **Calcitonin is released by the "C" cells (Para-follicular cells in the thyroid gland) in response to small increases in plasma ionic calcium.**
- **Calcitonin acts on the kidney and bones to restore the level of calcium to just below a normal set point which in turn inhibits secretion of the hormone.**
- **Calcitonin is therefore the physiological antagonist of PTH. The two hormones act in concert to maintain normal concentration of calcium ion in the extracellular fluid.**
- **1,25 (OH)2D3: Calcitriol also called 1,25-dihydroxycholecalciferol or 1,25-dihydroxyvitamin D3**



Vit D - 6:18 min

Nutshell

Calcium metabolism gets controlled in the body by 3 players AND 3 hormones (bone,Kidney,intestine) VS (PTH, Vitamin D, Calcitonin):

PTH:

- **↑ Bone resorption.**
- **↑ Calcium reabsorption from kidney**
- **↓ Phosphate reabsorption**

Vitamin D:

- **↑ Calcium absorption from intestine**
- **↑ Calcium reabsorption from kidney**
- **↑ Phosphate reabsorption**

Calcitonin:

- **↓ Bone resorption.**
- **↑ Calcium reabsorption from kidney**
- **↑ Phosphate reabsorption**

❖ Hypoparathyroidism:

Deficient secretion of PTH which manifests itself biochemically by ↓ hypocalcemia, ↑hyperphosphatemia diminished or absent circulating iPTH (immunoreactive parathyroid hormone) and clinically the symptoms of neuromuscular hyperactivity.

❖ Causes:

1. **Surgical hypoparathyroidism:**
   (the commonest cause):
   a. thyroidectomy.
   b. parathyroidectomy
   c. Radical surgery for head and neck malignancies.
   (Surgeons always be aware of 2 things parathyroids and recurrent laryngeal nerves).

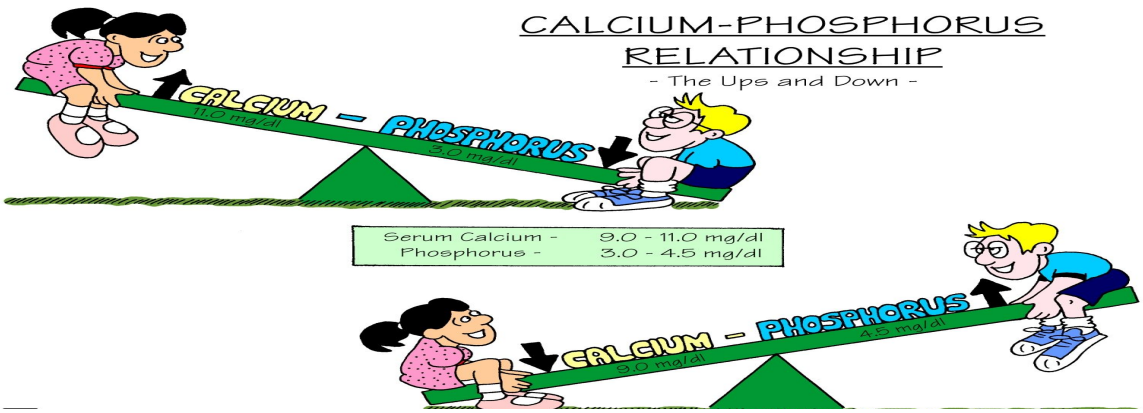
2. **Idiopathic hypoparathyroidism:**
   an early age (genetic origin) with autosomal recessive mode of transmission .
   a. Multiple endocrine deficiency, Autoimmune-candidiasis (MEDAC) syndrome.
   b. Juvenile familial endocrinopathy,
   c. Hypoparathyroidism , Addison's disease, mucocutaneous candidiasis(HAM)syndrome.

- **Circulating antibodies for the parathyroid glands and the adrenals are frequently present.**
- **Other associated disease:**
  - **•Pernicious anemia**
  - **•Ovarian failure**
  - **•Autoimmune thyroiditis**
  - **•Diabetes mellitus**
- **The late onset form occurs sporadically without circulating grandular autoantibodies**

hungry bone syndrome

Hypocalcemia that develops in hyperparathyroid patients treated with parathyroidectomy or in patients with end-stage renal disease treated with calcimimetic drugs.

3. **Functional hypoparathyroidism :**
   Hypomagnesemia: Magnesium is necessary for PTH to be released from the gland. Low magnesium levels also lead to increased urinary loss of calcium.



❖ Hypocalcemia with Non-Hypothyroidism causes:

- **Renal failure**:

Leads to hypocalcemia.
The kidney converts 25 hydroxy-D to the more active 1,25 hydroxy-D.
(Renal failure = Loss of vitamin D)

Other causes include **vitamin D deficiency**, genetic disorders, fat malabsorption, and low albumin states. **Decreased intestinal absorption of vitamin D or calcium due to primary small bowel disease, short bowel syndrome, and post-gastrectomy syndrome.** Drugs that cause rickets or osteomalacia such as **phenytoin, phenobarbital, cholestyramine, and laxative .**

Chronic hypocalcemia other than parathyroprival hypoparathyroidism:

- **States of tissue resistance to vitamin D**
- **Excessive intake of inorganic phosphate compounds**
- **Psudohypoparathyroidism**
- **Severe hypomagnesemia**
- **Chronic renal failure**

❖ Clinical Presentations:

1. **Basal Ganglia Calcifications (Fahr's disease) :** genetically dominant, inherited neurological disorder characterized by abnormal deposits of calcium in areas of the brain that control movement. **(Similar to Parkinson's disease symptoms).**

2. **Prolonged QT : Severe ↓ Ca > Prolonged QT > torsades de pointes, a specific type of ventricular tachycardia (Death).**

3. **Malabsorption syndrome :** Presumably secondary to decreased calcium level and may lead to steatorrhoea with long standing untreated disease.

4. **Dental Manifestation :** Abnormal enamel formation with delayed or absent dental eruption and defective dental root formation.

5. **Rickets ,osteomalacia and Posterior lenticular cataract**

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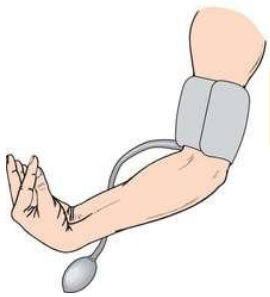
- **Neuromuscular irritability: When nerves are exposed to low levels of calcium they show abnormal neuronal function which may include decrease threshold of excitation, repetitive response to a single stimulus and rarely continuous activity.**
  - **Paresthesia**
  - **Latent Titany:**

A. Hyperactive deep tendon reflexes.
B. Chvostek's sign :Tapping the facial nerve causes contraction of facial muscles.
C. Trousseau's sign : Inflating the BP cuff to a pressure higher than the patient's systolic BP for 3 minutes elicits carpal spasms.

- **Convulsions :** More common in young people and it can take the form of either generalized tetany followed by prolonged tonic spasms or the typical epileptiform seizures.

6. **Grand Mal seizures, Hyperventilation and Adrenergic symptoms** .

Chvostek's sign



Trousseau's sign

❖ Diagnosis:

1. **Low serum calcium.**
2. **High serum phosphate.**
3. **Serum PTH inappropriately low.**
4. **Low urine cAMP.** (The parathyroid hormone works on Gs G protein which then leads to decreased levels of cAMP (as second messenger).

❖ Treatment:

- **Mainstay of treatment:**

Combination of oral calcium with pharmacological doses of vitamin D or its potent analogues.Phosphate restriction in diet may also be useful with or without aluminum hydroxide gel to lower serum phosphate level.

- **Emergent treatment:**

only give in case of symptomatic and present of neural irritability: IV calcium gluconate

Remember:

both vitamin D and calcium replacement can increase urinary calcium excretion, precipitating kidney stones. Therefore, administer with caution to avoid hypercalciuria

NOT Important

❖ Pseudohypoparathyroidism and Pseudopseudohypoparathyroidism

- A rare familial disorders with target tissue resistance to PTH. There is hypocalcaemia, hyperphosphataemia, with increased parathyroid gland function.There is also a variety of congenital defects in the growth and development of skeleton including:
- Short stature
- Short metacarpal and metatarsal bones

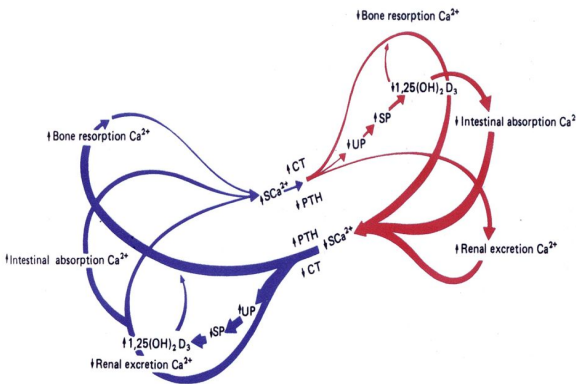
In pseudopseudohypoparathyroidism they have the developmental defects without the biochemical abnormalities

- The diagnosis is established when low serum calcium level with hyperphosphataemia is associated with increased serum iPTH as well as diminished nephrogenous CAMP and phosphaturic response to PTH administration

❖ Hyperparathyroidism: DDx (Causes of Hypercalcemia):

• Parathyroid - related	1.Primary hyperparathyroidism • A.Solitary adenomas • B.Multiple endocrine neoplasia 2.Lithium therapy. 3.Familial hypercalciuria hypercalcemia.
• Vitamin D – related	1.Vitamin D intoxication 2. 1,25(OH)2D; sarcoidosis and other granulomatous diseases 3.Idiopathic hypercalcemia of infancy
• Malignancy - related	1.Solid tumor with metastases(breast) 2.Solid tumor with humoral mediation of hypercalcemia (lung kidney) 3.Hematologic malignancies (multiple myeloma, lymphoma, leukemia)
• Associated with high bone turnover	1.Hyperthyroidism 2.Immobilization 3.Thiazides 4.Vitamin A intoxication Associated with Renal Failure: 1.Severe secondary hyperparathyroidism 2.Aluminum intoxication 3.Milk alkali syndrome

	Primary Hyperparathyroidism	Secondary Hyperparathyroidism	Tertiary Hyperparathyroidism
Calcium	↑	↓/N	↑
PTH	↑	↑	↑↑
Phosphate	↓	↑/N	↑



❖ Secondary hyperparathyroidism:

An increase in PTH secretion which is adaptive and unrelated to intrinsic disease of the parathyroid glands is called secondary hyperparathyroidism.This is due to chronic stimulation of the parathyroid glands by a chronic decrease in the ionic calcium level in the blood.

- **In General, Hyperparathyroid patients complaint of:**

"Painful bones, renal stones, abdominal groans, and psychic moans"

Jamie foxx was an actor in Django movie .
He did Surgical removal of parathyroids.
In Django Unchained movie he was that slave who kills anyone (Depressed) treat him like a slave and throw a lot of stones. Dicaprio's crushed some bones on a front of him to makes him realize that he is a slave.
At the end Django excised (Surgery) the the whole slavery from the town

❖ Diagnosis:

Blood test:

- ◇ **high** calcium and PTH levels,
- ◇ **low** phosphate level
- ◇ **high** chloride level
- ◇ EKG with a **short** QT
- ◇ sometimes an **elevated** BUN and creatinine.

The Glucocorticoid suppression test: The hypercalcemic of non-parathyroid origin e.g., vitamin D intoxication, sarcoidosis and lymphoproliferative syndromes generally respond to the administration of prednisolone in a dose of 40-60 mg daily for 10 days by a decrease in serum calcium level.

- **Radiographs:**
  - **Plain X-ray of hands can be diagnostic showing subperiosteal bone resorption usually on the radial surface of the distal phalanx with distal phalangeal tufting as well as cysts formation and generalized osteopenia.**
  - **Ultrasonography**
  - **MRI**
  - **CT**
  - **Thallium 201 – Tehcnichum99m scan (subtraction study)**
  - **Sestamibi scan**

❖ Treatment:

- **Surgical: Surgery is a definitive treatment of hyperparathyroidism. Patients who should have surgical treatment are: Symptomatic patient, and young patients.** Old people >50 and asymptomatic usually would have a medical treatment.
- **Medical:**
- **IV fluid .**
- **Diuretics (eg: furesemide).** For the volume overload due to IV fluid + To flush the calcium
- **Drugs that suppress the osteoclast (PTH increase the activity of the osteoclast):**
  - **Bisphosphonates work by slowing down the osteoclasts.**
  - **Calcitonin(antagonist to the PTH) It inhibits the activity of osteoclasts.**
- **Steroids used in some forms of hypercalcemic states like sarcoidosis or Multiplemyeloma**
- Mithramycin: A toxic antibiotics which inhibit bone resorption and is used in hematological and solid neoplasms causing hypercalcaemia.
- Phosphate: Oral phosphate can be used as an antihypercalcaemic agent and is commonly used as a temporary measure during diagnostic workup.
  Estrogen: It also decrease bone resorption and can be given to postmenopausal women with primary hyperparathyroidism using medical therapy

Osteomalacia: (لِينُ العِظَامِ)

- Failure of organic matrix (osteoid) or bone to mineralize normally.

❖ Causes:

- **Vitamin D deficiency:** - (commonest cause)
  - Inadequate sunlight exposure without dietary supplementation.
  - Gastrointestinal diseases that interrupts the normal enterohepatic recycling of vit. D & its metabolites, resulting in their fecal loss.
    - Chronic steatorrhea (pancreatic)
    - Malabsorption (gluten-sensitive enteropathy)
    - Surgical resection of large parts of intestine.
    - Formation of biliary fistulas
  - Impaired synthesis of 1,25(OH)2D3 by the kidney.
  - Target cell resistance to 1,25(OH)2D3 e.g. absent, or diminished number of 1,25(OH)2D3 receptors, as in vit.D-dependency rickets type II.
  - .
- **Phosphate deficiency:**
  - Dietary:
    - Low intake of phosphate.
    - Excessive ingestion of aluminum hydroxide.
  - Impaired renal tubular reabsorption of phosphate:
    - X-linked hypophosphataemia.
    - Adult-onset hypophosphataemia.
  - Other acquired & hereditary renal tubular disorders associated with renal phosphate loss(Fanconi's sydnrome, Wilson's disease).
  - Tumor-associated hypophosphataemia.

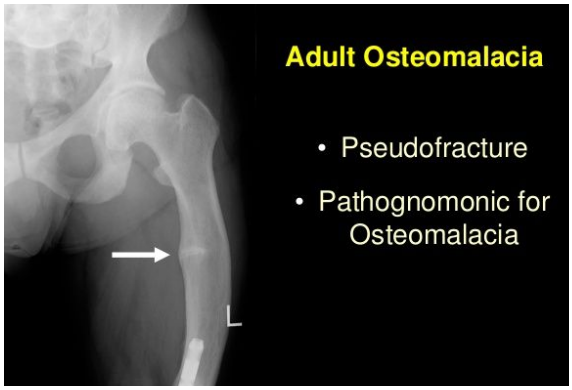
- **Drugs**: anti epileptic drugs. interfere with hydroxylation of vitamin D in the liver → ↓ vit.D
- **Systemic Acidosis:**
  - Chronic renal failure
  - Distal renal tubular acidosis
  - Ureterosigmoidoscopy
  - Chronic acetazolamide & ammonium chloride administration

❖ Findings:

• **First stage:**	• Mild hypocalcaemia, increased serum PTH, normal or slightly decreased serum phosphate and decreased serum 25OHD3.
• **Second stage:**	• Serum 25OHD3 decreases slightly or not at all, the serum calcium concentration is restored to normal, but paradoxically there is only a small decrease in serum PTH.
• **Third stage:**	• When florid osteomalacia manifests, serum 25OHD3 decreases to almost undetectable levels, Hypocalcaemia is again apparent and is more severe than in stage I

The underlying defect leading to these changes is the decrease in the production of 1,25(OH)2D3 which is due to diminished availability of the major circulating metabolites of vit D 25OHD3.
The decreased 1,25(OH)2D3 results in decreased intestinal calcium absorption, decreased bone resorption, hypocalcaemia, increased PTH secretion and hypophosphatemia

❖ Findings: Cont'd



- **Radiology: they will have pseudofracture (see the pic)**
- **The resulting decreased CaxPho. Product in serum is insufficient for the normal mineralization of bone and the osteomalacic process is initiated.**
  The increased PTH secretion and hypophosphatemia occur at the expense of osseous demineralization caused by hyperparathyroidism.
- **Clinically patients with osteomalacia have a characteristic waddling gait, that is due to the proximal muscle weakness and to the pain and discomfort during movements of the limbs. Some patients have severe muscular hypotonia and paradoxically brisk deep tendon reflexes.**

❖ Treatment:

- **sun exposure.**
- **high vit D dosage.**
- **calcium supplement.**
- **1,25(OH)2D3 (calcitriol): for simple osteomalacia.**
- **correct the underlying cause.**
- **Serum ALP and PTH decrease slowly over several weeks but improvement in radiological appearances may take several months.**
- **osteomalacia secondary to malabsorption may require huge doses of vit D (200,000 IU orally) because of the poor absorption of the drug or even I.V./I.M. vit D (40,000-80,000 IU).**

Osteoporosis

Decrease in bone mass and strength associated with an increased tendency to fractures and It is usually an asymptomatic disease until fractures occur on the following: Common sites

- **Hip fractures.**
- **Vertebral fractures.(chronic back pain)**
- **Forearm fractures.**

with loss of height and dorsal Kyphosis.

❖ Eitology:

Osteoporosis occurs because of a defect in attaining peak bone mass and/or because of accelerated bone loss

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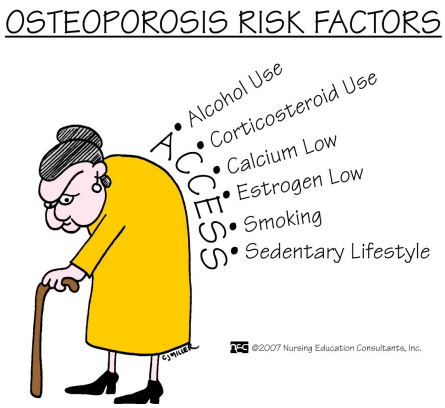
- **Menopause**
- **Old age**
- **Calcium and vitamin D deficiency**
- **Estrogen deficiency in women and androgen deficiency in men**
- **Use of steroids : Renal Ca loss, Inhibition of intestinal Ca absorption increase osteoclast and inhibition of osteoblast activity Suppression of gonadotropin secretion (high dose).**



❖ Diagnosis:

- **The most accurate test is bone densitometry (DEXA) scanning.**
- **X-rays of skeleton not very sensitive because it doesn't show a decrease in osseous density until at least 30% of bone mass has been lost**

TABLE 1

World Health Organization criteria for diagnosing osteoporosis using bone density measurements

CATEGORY	T SCORE
Normal	Not more than 1.0 standard deviations (SD) below the young adult mean
Osteopenia	Between 1.0 and 2.5 SD below the young adult mean
Osteoporosis	More than 2.5 SD below the young adult mean
Severe or established osteoporosis	More than 2.5 SD below the young adult mean with a fracture

❖ Treatment:

- **Prevention: To prevent from fractures .**
- **Public awareness.**
- **Vitamin D and calcium are the best initial therapy.**
- **Bisphosphonates (alendronate, risedronate, ibandronate) reducing bone breakdown.**
- **Intermittent parathyroid hormone will give paradoxical effect which means the opposite of the real parathyroid hormone function .**
- **If a hypocalcemic patient with no improvement after management check directly to magnesium levels .**

MCQ's

Q1: An otherwise healthy 60-year-old man undergoes a health maintenance examination. Physical examination and medical history are unremarkable. A blood chemistry panel is normal except for a serum calcium level of 11 mg/dL when corrected for serum albumin. The measurement is repeated two times, giving values of 10.5 mg/dL and 11.2 mg/dL, respectively. Serum phosphorus is 2.5 mg/dL, and alkaline phosphatase is 50 U/L. Immunoradiometric assay (IRMA) reveals higher than normal serum levels of parathyroid hormone. Urine calcium excretion is within normal limits. The patient denies previous renal colic or urinary tract infections. Which of the following is the most appropriate next step in management?

(A) Bone x-ray films
(B) Extensive cancer screening
(C) Generous fluid intake
(D) Treatment with bisphosphonates (e.g., alendronate)
(E) Surgical exploration of the neck

Q2: A 55-year-old man with a history of recurrent calcium containing renal stones presents to the emergency department with excruciating flank pain and bloo.d in the urine.
This patient is likely to have which of the following underlying disorders?

(A) Anemia of chronic disease
(B) Chronic proteus infection
(C) Factor VIII deficiency
(D) Hyperaldosteronism
(E) Hyperparathyroidism

Q3:A 45-year-old woman with chronic alcohol abuse admitted 3 days ago for nausea and severe diarrhea now complains of perioral and fingers tingling. She was admitted for rehydration after 1 week of severe watery diarrhea. She has been receiving intravenous hydration and dextrose but has not been able to take oral nutrition secondary to continued nausea. Her blood pressure is 130/74 mm Hg, pulse is 68/min, and respiratory rate is 16/min. She is afebrile. Physical examination is significant for facial twitching on percussion of her facial nerve just anterior to the ear, as well as the induction of carpal spasm after the inflation of a blood pressure cuff on her arm. Which of the following is most likely to have caused these findings?

(A) Azotemia
(B) Hypernatremia
(C) Hypomagnesemia
(D) Hypophosphatemia
(E) Hyperuricemia

Answers: 1.C, 2.E, 3.C

Thank you

If you have any question please contact with us at:
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