Minerals

University Of Fallujah
College Of Medicine

Lecture : (2)

Stage : 2th Stage

Lecturer : Dr. Mohammed amer

Department: Chemistry and Biochemistry

Date:

MINERALS

PART 2

PHOSPHATE AND MAGNESIUM

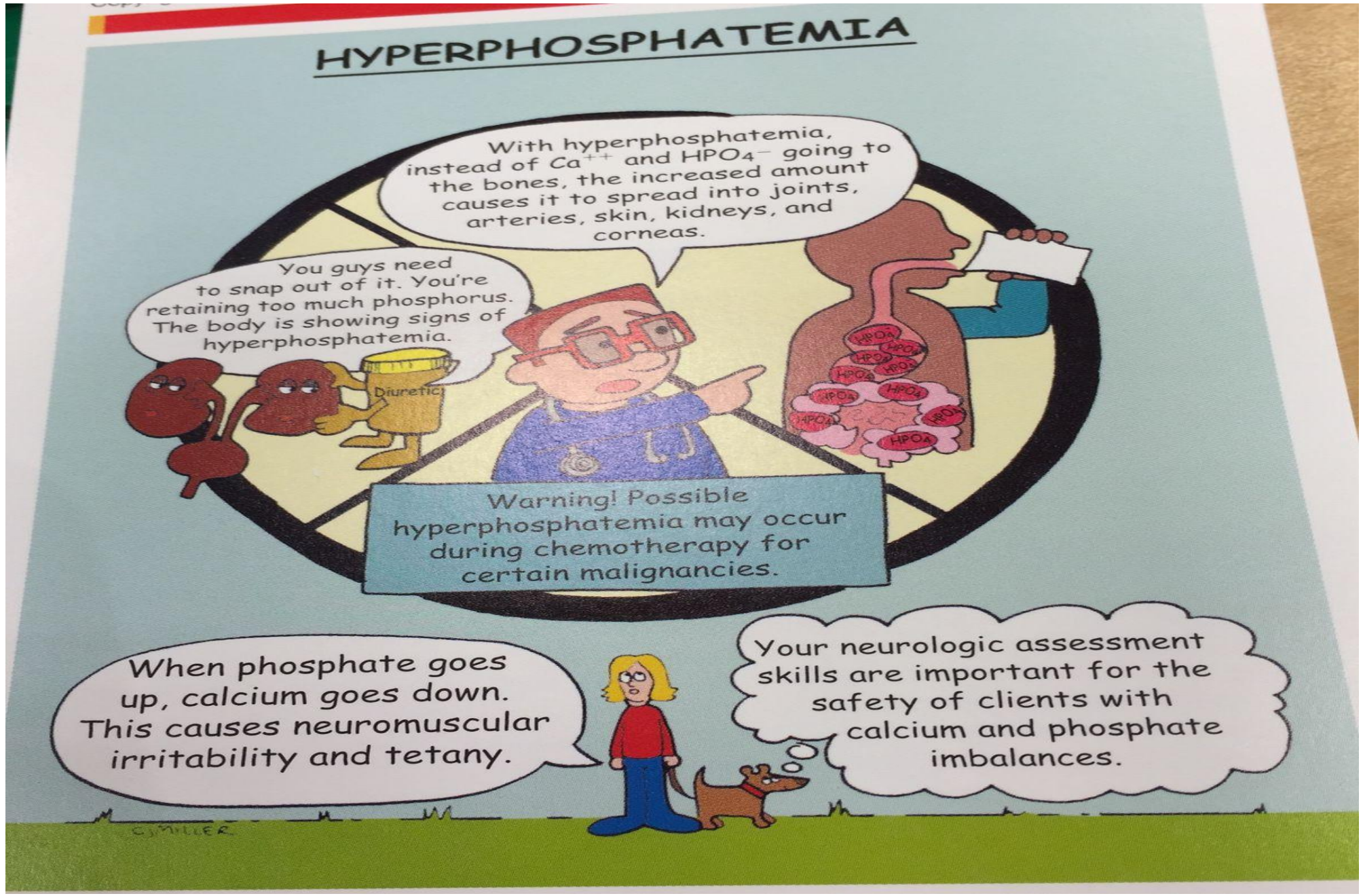
Learning Objectives

1. Describe the biological importance of phosphorus and magnesium.
2. Discuss phosphorus and magnesium distribution , homeostasis.
3. Explain the metabolism and regulation of phosphorus and magnesium .
4. Recognize the clinical importance of phosphorus and Mg imbalances .
5. Explain hormonal and renal regulation of phosphorus and magnesium
6. Interpret laboratory evaluation of serum phosphorus and magnesium.

❑ Phosphorus :

- Phosphorus is the most abundant **intracellular anion** in the human body. Approximately **85% of total body phosphorus** exists as **inorganic hydroxyapatite** in bones and teeth, providing structural rigidity.
- The remaining phosphorus is primarily found within cells, incorporated into **organic compounds** such as **phospholipids**, **nucleic acids (DNA and RNA)**, **ATP**, and **creatine phosphate**, where it plays essential roles in energy storage and transfer.
- Functionally, phosphate acts as a **source of high-energy bonds** in the form of **ATP**, serving kinases during phosphorylation reactions, and provides **inorganic phosphate (Pi)** for phosphorylase-mediated processes.
- These reactions are fundamental to **cellular metabolism, energy balance, and signal transduction**.

HYPERPHOSPHATEMIA



❑ PHOSPHATE HOMEOSTASIS

- Three main regulators of phosphate metabolism in the gut:

1)Dietary phosphate intake: absorption by passive diffusion and load-dependent process across the intercellular spaces in the intestine.

2)Vitamin D (calcitriol): which increases phosphate absorption from the gut and bone, then transported into the epithelial cells by cotransport with sodium active sodium-dependent process.

3)Parathyroid hormone (PTH): regulates Ph excretion, directly causes phosphate resorption from bone and decreases its reabsorption in the proximal tubule, and indirectly by stimulating production of calcitriol .

- The end result of the presence of long-standing high PTH concentration in the setting of normal kidney function is a decrease in serum phosphate.

❑ PHOSPHATE HOMEOSTASIS

Bone : The enzymatic activity of alkaline phosphatase is required to generate enough amount of free Ph enters the cell via a sodium-dependent phosphate transporter and is maintained intracellularly.

- In cases of hypophosphatemia, alkaline phosphatase activity rises in order to try to provide more phosphate to the bone cells.

Renal reabsorption:

- Renal handling of phosphate is regulated by a variety of hormonal and non-hormonal factors along the proximal convoluted tubule of the kidney including :

-serum PTH, calcium, $1,25(OH)_2D_3$, bicarbonate concentration, sodium reabsorption, dopamine and serotonin .

PHOSPHATE HOMEOSTASIS

- **Insulin, growth hormone (GH),** and **thyroid hormone** enhance phosphate reabsorption in the **proximal renal tubules**.
- They achieve this by stimulating the **Na^+–phosphate (Na–Pi) cotransporter** located on the **brush border membrane**, thereby increasing phosphate uptake from the tubular lumen.
  - These hormones also **oppose the phosphaturic effect** of parathyroid hormone (**PTH**), helping to conserve phosphate.
- In contrast, **calcitonin**, **PTH**, and **glucocorticoids inhibit phosphate reabsorption** at the proximal tubular brush border, leading to increased urinary phosphate excretion (**phosphaturia**).

❑ PHOSPHATE HOMEOSTASIS

- A **low-phosphate (low-Pi) diet** leads to a **decrease in serum phosphate (Pi) concentration**, which is typically accompanied by a **rise in circulating calcium (Ca^{2+}) levels**.
- The elevation in serum calcium **suppresses parathyroid hormone (PTH) secretion**, thereby **reducing renal phosphate excretion** and conserving phosphate.
- Furthermore, both **low dietary phosphate intake** and **decreased serum phosphate levels** stimulate the **renal synthesis of 1,25-dihydroxyvitamin D [$1,25(OH)_2D$]**.
- This active form of vitamin D enhances **intestinal absorption** and **renal reabsorption of phosphate**, ultimately helping to **restore serum phosphate concentrations to normal physiological levels**.

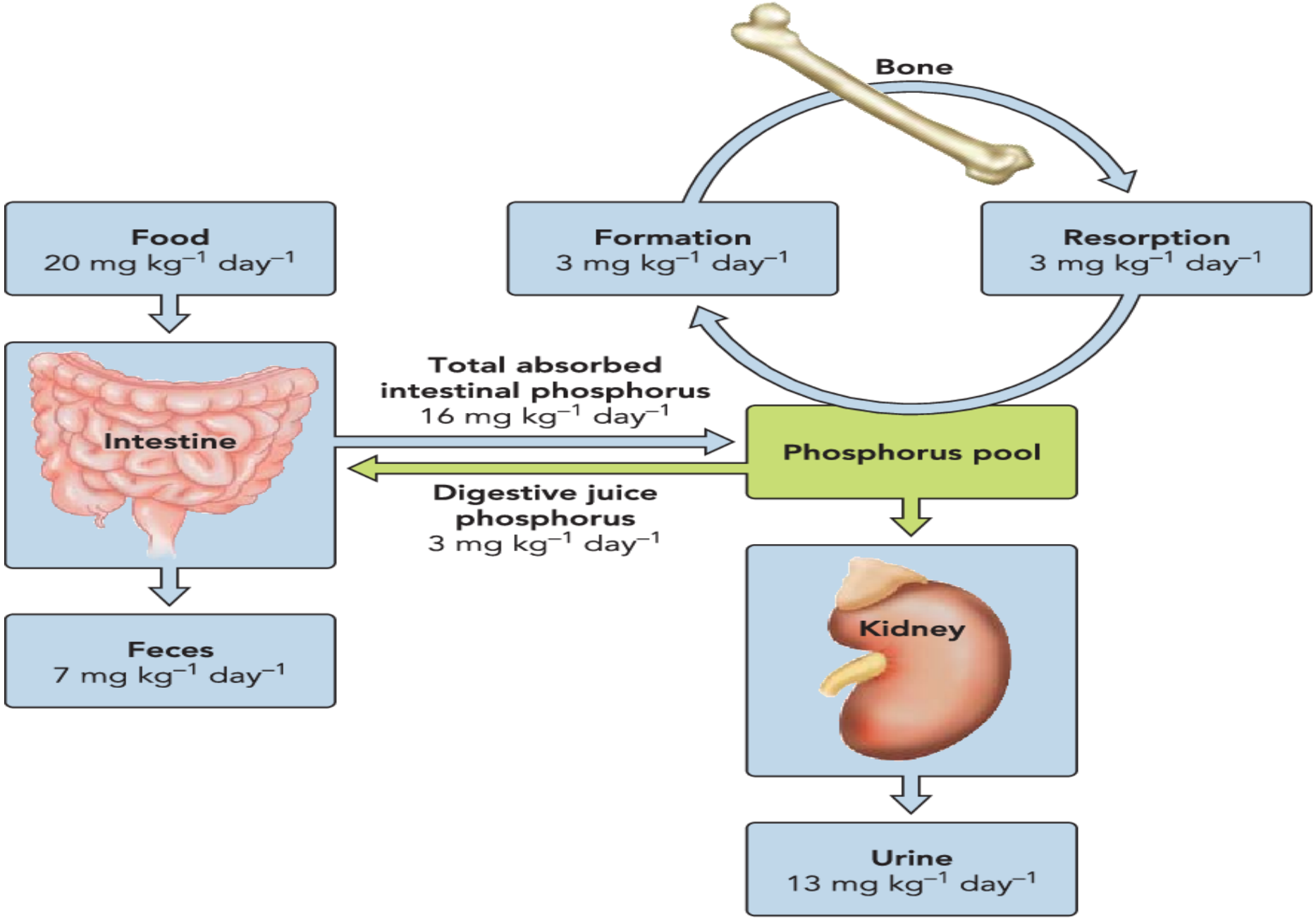


FIGURE 1. **Phosphorus homeostasis in normal humans**

NORMAL RANGE OF PHOSPHATE IN SERUM

Adult: 3.0-4.5 mg/dL or 0.97-1.45 mmol/L

❑ HYPOPHOSPHATAEMIA (low level of ph.)

- **Hypophosphatemia** associated with **calcium metabolism disturbances** is most commonly due to **elevated circulating parathyroid hormone (PTH) levels**.
- Increased PTH enhances **renal phosphate excretion**, leading to significant phosphate loss in the urine.
- Similarly, **renal tubular defects** that impair phosphate reabsorption can also result in excessive urinary phosphate loss and hypophosphatemia.
- In contrast, **severe or prolonged dietary phosphate deficiency** may also lead to hypophosphatemia; however, in such cases, **urinary phosphate excretion is markedly decreased** as the kidneys attempt to conserve phosphate.

Causes of Hypophosphataemia and Phosphate depletion

1. Reduced absorption.
2. Increase cellular uptake.
3. Increased excretion.
4. Dilution due to volume expansion.
5. Chronic alcohol abuse which cause vomiting, diarrhoea.
6. Medical conditions, such as hyperparathyroidism, kidney tubule defects, and diabetic ketoacidosis [reduced renal phosphate reabsorption by the Na-Pi transporters in the renal proximal tubule due to acidosis and hyperglycemia.

❑ Consequences of Hypophosphataemia

- Hemolysis.
- Rhabdomyolysis: muscle breakdown and kidney failure.
- Various CNS features.
- Demineralization of the skeleton.

❑ Causes of Hyperphosphatemia

- Hemolysis during vein puncture.
- Chronic renal failure.
- Untreated acromegaly.
- Excessive Ph administration.
- Hypercatabolic state.
- Cardiovascular disease (CVD): increase in serum phosphate associated with higher risk of atrial fibrillation due to calcification and atherosclerosis.

MAGNESIUM

- Magnesium is predominately an intracellular divalent cation and is important for optimal cell function.
- It is an essential cofactor to many enzymes, as well as being important for membrane function.
- Furthermore, it can act as an antagonist to calcium in cellular responses and has a structural role within the cell.
- The body contains about 1 mol (approximately 25 g) of magnesium, mostly in the bone and muscle.

❑Biochemical Functions

- Co-factor role:
  - Magnesium acts as a co-factor for more than 300 enzymes
  - Serves as an allosteric activator for many enzyme systems
  - Essential for peptidases, ribonucleases, glycolytic enzymes, and carboxylation reactions
  - Influences PTH secretion by parathyroid glands; hypomagnesaemia may cause hypoparathyroidism

❑Additional Functions

- Affects neuromuscular irritability similarly to Ca^{2+}
  - High levels depress nerve conduction
  - Low levels may produce tetany (Hypomagnesemic tetany)
- About 70% of body magnesium is present as apatites in bones, dental enamel, and dentin
- Insulin-dependent glucose uptake is reduced in Mg^{2+} deficiency; supplementation improves glucose tolerance

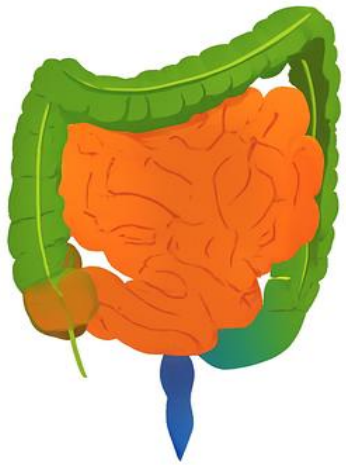
❑Normal Plasma Levels & Absorption

- Normal serum magnesium range: 1 to 3.5 mg/dl
- Distribution in plasma:
  - 70% exists in free state
  - 30% is protein-bound (primarily albumin)
  - Small amount complexed with anions like phosphate and citrate

❑Absorption:

- About 1/3 of dietary magnesium is absorbed
- Primarily occurs in the small intestine
- Remainder is passively excreted in feces

Regulation of Magnesium Homeostasis



GI Tract

Magnesium

(Passive diffusion)

Blood

Bones

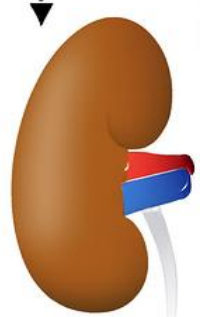
Claudin-16

↓ plasma Ca

↓ plasma Mg

↓ plasma Ph

Mg



Kidneys

There are no known hormo or enzymes that directly reglate magnesium

Electrolytes

Non-Hormone, Non-Enzyme Protein

❑Factors Affecting Absorption

- Size of Mg load: Absorption doubles when dietary requirement doubles
- Dietary calcium: Low calcium increases Mg absorption; excess calcium decreases it
- Vitamin D enhances absorption
- Parathormone and growth hormone increase absorption
- High protein intake increases absorption
- Fatty acids, phytates, and phosphates decrease Mg absorption

❑Excretion

- Magnesium is lost through feces, sweat, and urine
- 60-80% of orally taken Mg is lost in feces
- Urinary excretion:
  - ✓Regulation of Mg balance depends on renal mechanisms
  - ✓Mg is reabsorbed from the loop of Henle, not from proximal tubules
  - ✓Normal daily excretion: 3 to 17 mEq

HYPERMAGNESAEMIA

- **Hypermagnesemia** can lead to significant **neuromuscular and cardiovascular disturbances**.
- Elevated serum magnesium levels may cause **cardiac arrhythmias**, including **heart block** and **inhibition of atrioventricular (AV) conduction**, which in severe cases can progress to **cardiac arrest**.
- Neurological manifestations include **seizures**, **depressed nerve conduction**, and **reduced deep tendon reflexes**.

Other systemic effects include **paralytic ileus**, **nausea**, **vomiting**, and **respiratory depression** due to suppression of the respiratory center.

Box 6.5 Some causes of hypermagnesaemia

Increased intake of magnesium

Antacids, milk–alkali syndrome
Purgatives
Parenteral nutrition

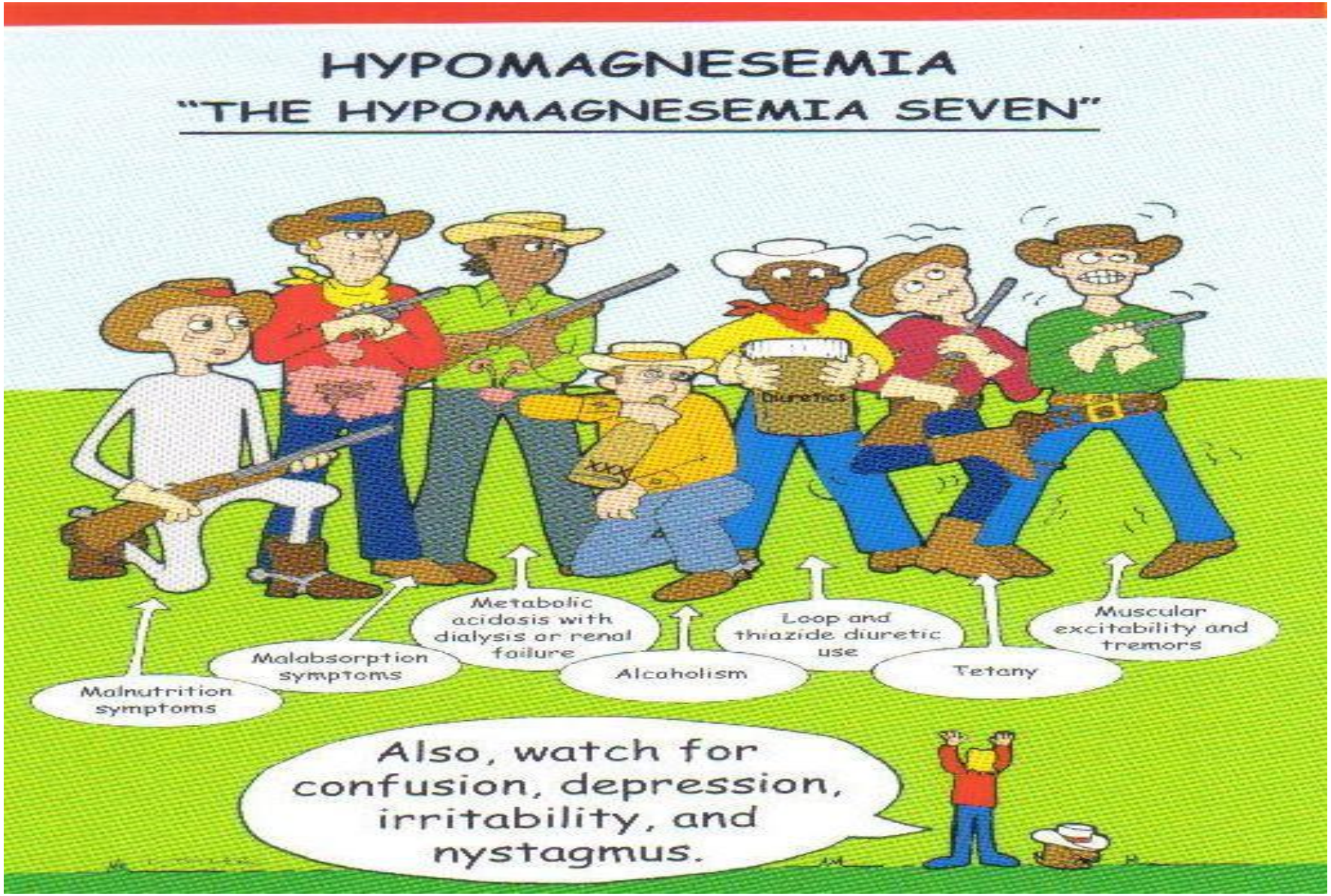
Impaired renal excretion of magnesium

Acute kidney injury and chronic kidney disease
Familial hypocalciuric hypercalcaemia
Lithium treatment

Miscellaneous causes

Hypothyroidism
Adrenal insufficiency

HYPOMAGNESAEMIA



HYPOMAGNESAEMIA

- Some causes of hypomagnesaemia are shown in Box
- The symptoms of hypomagnesaemia are very similar to those of hypocalcaemia.
- If the plasma calcium concentrations (allowing for that of albumin) and blood pH are normal in a patient with tetany, the plasma magnesium concentration should be assayed. Hypomagnesaemia can result in cardiac arrhythmias

Box 6.6 Some causes of hypomagnesaemia

Redistribution of magnesium between cells
Excess of catecholamines
Refeeding syndrome
Hungry bone syndrome

Reduced intake of magnesium
Parenteral nutrition
Starvation/undernutrition

Poor magnesium absorption
Intestinal resection
Gastrointestinal fistulae
Malabsorption states

Increased renal loss of magnesium
Post-renal transplantation
Dialysis
Bartter's and Gitelman's syndromes

Drugs
Diuretics
Proton pump inhibitors, e.g. omeprazole
Cytotoxics
Aminoglycosides
β_2-Adrenergic agonists
Ciclosporin and tacrolimus
Pamidronate, pentamidine, amphotericin B, foscarnet

Miscellaneous causes
Alcoholism
Hypercalcaemia
Hyperthyroidism
Hyperaldosteronism
Diabetes mellitus