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Acid-Base, Electrolyte, and Metabolic Abnormalities

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Metabolic Acidosis

Definition and Classification

A metabolic acidosis is a process that, if unopposed, would cause Acidemia:

- a high hydrogen ion concentration
- low pH, of the blood by reducing the extracellular bicarbonate concentration.

Metabolic acidosis can be caused :

- excessive production of fixed acid
- decreased renal secretion of fixed acid
- loss of bicarbonate, either through the kidney or through the intestine

Diagnosis of Acid-Base Disorders

- If the bicarbonate is low, and if the anion gap is clearly elevated on that sample, a diagnosis of high anion gap metabolic acidosis

- If the pH is low, the bicarbonate is low, and the Pco2 is above 40 torr, there is clearly a mixed metabolic and respiratory acidosis.

- *If the bicarbonate is low and the anion gap normal, two possibilities exist: either a hyperchloremic metabolic acidosis or a respiratory alkalosis with metabolic compensation*

anion gap

anion gap :Na- Hco3+Cl

- *Propylene glycol* is a solvent for medications, many of which

(such as lorazepam, nitroglycerine, etomidate, and phenytoin) are commonly infused intravenously in critically ill patients

• BOX 54.2 Causes of High Anion-Gap Metabolic Acidosis

Ketoacidoses
- Diabetic
- Alcoholic
- Starvation

Intoxications
- Methanol
- Ethylene glycol
- Propylene glycol
- Salicylate

Pyroglutamic acidosis
- Congenital
- Acquired

Lactic acidosis (see Box 54.3)

Uremic acidosis

• BOX 54.1 Causes of Hyperchloremic Metabolic Acidosis

Extrarenal Loss of Base
Diarrhea
Pancreatic fistula
Ureteral diversion

Extrarenal Gain of Acid
Ammonium chloride
Hydrochloric acid
Sodium chloride
Toluene inhalation (glue sniffing)

Renal Loss of Base
Type II renal tubular acidosis
Posthypocapnic state
Excretion of organic anions (bicarbonate precursors)

Renal Acid Excretory Defect
Type IV renal tubular acidosis
- Chronic kidney disease
- Hypoaldosteronism
- Urinary tract obstruction

Type I renal tubular acidosis
- Sickle cell nephropathy
- Lupus nephritis
- Renal transplant

The SID offers a quantitative approach to measuring the degree of acidosis in hyperchloremic metabolic
Acidosis

(strong ion difference)SID=Na+K+Mg+Ca-CL

BOX 54.3 Causes of Lactic Acidosis

Type A (Tissue Oxygen Supply: Demand Mismatch)

Decreased tissue oxygen delivery
- Shock
- Hypoxemia
- Severe anemia
- Carbon monoxide poisoning

Increased tissue oxygen demand
- Grand mal seizure
- Extreme exercise

Type B

Impaired oxygen utilization
- Cyanide poisoning
- Linezolid
- Metformin
- Antiretroviral agents (nucleosides and nucleoside reverse transcriptase inhibitors [NRTIs])
- Acetaminophen

Excessive lactate production
- Sepsis
- HIV infection
- Alcohols (EtOH, MeOH, ethylene glycol, propylene glycol, sorbitol)
- Propofol
- Diabetes mellitus
- Alkalemia
- Malignancy
- Pheochromocytoma
- Sorbitol/fructose
- Thiamine deficiency
- Congenital enzyme defects (tricarboxylic acid cycle, pyruvate transport)

Decreased lactate metabolism
- Liver failure

D-lactic acidosis

EtOH, *Ethanol;* MeOH, *methanol;* HIV, *human immunodeficiency virus.*

Treatment of Metabolic Acidosis

- Therefore most clinicians favor treating metabolic acidosis with blood pH ≤ 7.10
- Treatment of hyperchloremic metabolic acidosis is straightforward.In cases of acute metabolic acidosis, treatment depends on successful therapy of the underlying cause (e.g., diarrhea) and reduction of the bicarbonate deficit
- Sodium bicarbonate is the alkalinizing agent of choice for most patients with severe academia. Bicarbonate dosing must be empirical because the bicarbonate deficit is not calculable in practice .Rapid infusion of undiluted ampoules of sodium bicarbonate (1000 mmol/L) is recommended for patients withsevere acidemia. The goal is to raise the blood pH no higher than 7.20

Sodium bicarbonate:

- Hyperosmolality
- volume Overload
- Hypocalcemia
- increased generation of CO_2

<u>Plasma electrolytes and blood gases must be monitored frequently</u>

Treatment of Metabolic Acidosis

- Tris-hydroxymethyl aminomethane, or THAM, is an amino alcohol that buffers without generating CO_2. It has the advantage, therefore, of avoiding a superimposed respiratory acidosis. It has been used successfully in animals and humans with various metabolic Acidoses. It is eliminated by the kidney, and thus should be used with caution in the setting of renal insufficiency. Risks include hyperkalemia, hypoglycemia, and hepatic necrosis (in neonates).
- Continuous hemodialysis (e.g., continuous venovenous hemodialysis) may be a promising tool for treating lactic acidosis, because it provides large amounts of bicarbonate without the risks of volume overload or hypocalcemia

Metabolic Alkalosis

Definition and Classification

Metabolic alkalosis is a process leading to accumulation of extracellular bicarbonate which, if unopposed, will result in an increase in the plasma pH (alkalemia). In its pure form, it is accompanied by compensatory hypoventilation (CO_2 retention)

Metabolic alkalosis often is accompanied by hypokalemia and hypomagnesemia.

• BOX 54.4 Causes of Metabolic Alkalosis

Intravascular Volume Depletion, Absolute or "Effective"

Gastrointestinal acid loss
- Vomiting or nasogastric suction
- Villous adenoma
- Chloride diarrhea

Renal acid loss
- Diuretics (loop, thiazide)
- Bartter syndrome
- Gitelman syndrome
- Magnesium depletion
- Posthypercapnic state
- Congestive heart failure
- Hepatic cirrhosis/ascites

Intravascular Volume Expansion

High renin, high aldosterone
- Renal artery stenosis
- Accelerated hypertension
- Renin-secreting tumor

Low renin, high aldosterone
- Primary aldosteronism

Low renin, low aldosterone
- Cushing syndrome or disease
- Exogenous mineralocorticoid
- Apparent mineralocorticoid excess syndrome
- Liddle syndrome

Renal insufficiency
- Exogenous alkali load
- Milk-alkali syndrome

Modified from Gennari FJ. Pathophysiology of metabolic alkalosis: a new classification based on the centrality of stimulated collecting duct ion transport. Am J Kidney Dis. *2011;58:626–636.*

Treatment Metabolic Alkalosis

- Treatment of metabolic alkalosis entails correcting the factor(s) responsible for its maintenance, and, if possible, correcting the factor that generated the alkalosis
- If the metabolic alkalosis is maintained by chloride depletion and ECF volume contraction, the intravascular volume should be restored to normal, usually with intravenous isotonic saline solution
- Potassium should be given, as potassium chloride (KCl), to replaceany deficits (see “Disorders of Potassium Homeostatis”) because potassium depletion perpetuates the metabolic alkalosis.
- If gastric suction cannot be stopped, acid loss can be reduced by the use of histamine H2 blockers and proton pump inhibitors.
- Treating patients with metabolic alkalosis in the setting of volume overload and diminished effective circulating volume (e.g., congestive heart failure, hepatic cirrhosis) is more challenging, because infusion of saline solution is contraindicated.

Treatment Metabolic Alkalosis

- Acetazolamide (carbonic anhydrase inhibitor) bicarbonat diuresis, worsen the hypokalemia,hypercapnia

- In states of primary mineralocorticoid excess, an aldosterone antagonist such as spironolactone should be used until the underlying abnormality can be corrected.

- If renal function is severely impaired or medical therapy is not possible, hemodialysis against a low-bicarbonate bath may be used

TABLE 54.1 Expected Compensation for Simple Acid-Base Disorders

Disorder	Primary Disturbance	Compensation	Magnitude	Time to Completion
Metabolic acidosis	↓ $[HCO_3^-]$	↓ PCO_2	1.5 • $[HCO_3^-]$ + 8	12–24 h
Metabolic alkalosis	↑ $[HCO_3^-]$	↑ PCO_2	0.9 • $[HCO_3^-]$ +9	12–24 h
Respiratory acidosis, acute	↑ PCO_2	↑ $[HCO_3^-]$	1 mmol/L/10 torr	<6 h
Respiratory acidosis, chronic	↑ PCO_2	↑ $[HCO_3^-]$	3.5 mmol/L per 10 torr	>5 days
Respiratory alkalosis, acute	↓ PCO_2	↓↓ $[HCO_3^-]$	2 mmol/L/10 torr	<6 h
Respiratory alkalosis, chronic	↓ PCO_2	↓ $[HCO_3^-]$	5 mmol/L per 10 torr	>7 days

HCO_3^-, Bicarbonate; *PCO_2*, partial pressure of carbon dioxide.

Disorders of Potassium Homeostasis

Disorders of potassium homeostasis are common in hospitalized patients and may be associated with severe adverse clinical outcomes,including death

The total body potassium content of a 70-kg adult is about 3500 mmol, of which only 2% (about 70 mmol) is extracellular.

Normally, 90% to 95% of dietary potassium is eliminated through the kidney, and only about 5% to 10% through the Intestine.

Magnesium deficiency is associated with renal potassium wasting and may result in severe potassium depletion

• BOX 54.5 Factors Affecting Internal Potassium Balance

Factors Causing Cellular Potassium Influx

Insulin
β_2-Adrenoceptor agonist
(Metabolic alkalosis)[a]

Factors Causing Cellular Potassium Efflux

Cell ischemia/lysis
Exercise
Plasma hypertonicity
α-Adrenoceptor agonist
(Metabolic acidosis)[a]

[a]*Factors shown in parentheses have a minor or variable effect. See text.*

• BOX 54.6 Causes of Acute Hyperkalemia

Excessive Potassium Intake

- Oral
- Intravenous
- Blood transfusion
- Cardioplegic solutions

Transcellular Potassium Shift

- With acute renal failure
  - Rhabdomyolysis
  - Tumor lysis syndrome
- Tissue infarction
  - Mesenteric
  - Limb
- Hypertonicity
  - Hyperglycemia
- Metabolic acidosis
- Drug-induced
  - Digitalis intoxication
  - Succinylcholine
- Hyperkalemic periodic paralysis
- Pseudohyperkalemia
  - Thrombocytosis
  - Leukocytosis
  - In vitro hemolysis
  - Fist clenching with phlebotomy

• BOX 54.7 Causes of Acute Hypokalemia

- Treatment of diabetic ketoacidosis
- Refeeding syndrome
- Rapid cell production
  - Vitamin B_{12} treatment of pernicious anemia
  - GM-CSF treatment of leukopenia
- Pharmacologic agents
  - β_2-Adrenoceptor agonists
  - Epinephrine
  - Soluble barium salts
- Hypokalemic periodic paralysis
  - Familial
  - Sporadic
  - Thyrotoxic
- Pseudohypokalemia

GM-CSF, *Granulocyte-macrophage colony-stimulating factor.*

Chronic Hyperkalemia&Hypokalemia

Chronic Hyperkalemia

Renal Failure

Mineralocorticoid Deficiency

Renal Potassium Secretory Defect

Chronic Hypokalemia

Inadequate Potassium Intake:anorexia nervosa, alcoholism,malignancy.

Excessive Potassium Losses:Gastric

fluid losses (vomiting or gastric suction)

diuretics: thiazides and loop diuretics

Penicillin antibiotics

Mineralocorticoids:(Conn syndrome)

Magnesium deficiency

Hypercalcemia

Clinical Manifestations of Potassium Imbalance Hyperkalemia

❖Cardiac Effects

Hyperkalemia depolarizes the cell membrane, slows ventricular conduction, and decreases the duration of the action potential.

(ECG) manifestations of hyperkalemia:

- ✓ peaked T waves,
- ✓ prolongation of the PR interval,
- ✓ widening of the QRS complex,
- ✓ loss of the P wave,
- ✓ “sine wave”
- ✓ or ventricular fibrillation and asystole

Consequently, PK greater than6.5 mmol/L, even with a normal ECG, should be treated as an emergency

Clinical Manifestations of Potassium Imbalance Hyperkalemia

❖Neuromuscular Effects

Hyperkalemia may result in **paresthesias** and **weakness progressing** to a **flaccid paralysis**, which typically spares the diaphragm. **Reflexes are depressed or absent.**

❖Metabolic Effects

mild hyperchloremic metabolic acidosis,

Clinical Manifestations of Hypokalemia

❖ Cardiac Effects

Hypokalemia hyperpolarizes the cell membrane and prolongs the cardiac action potential

ECG manifestations:

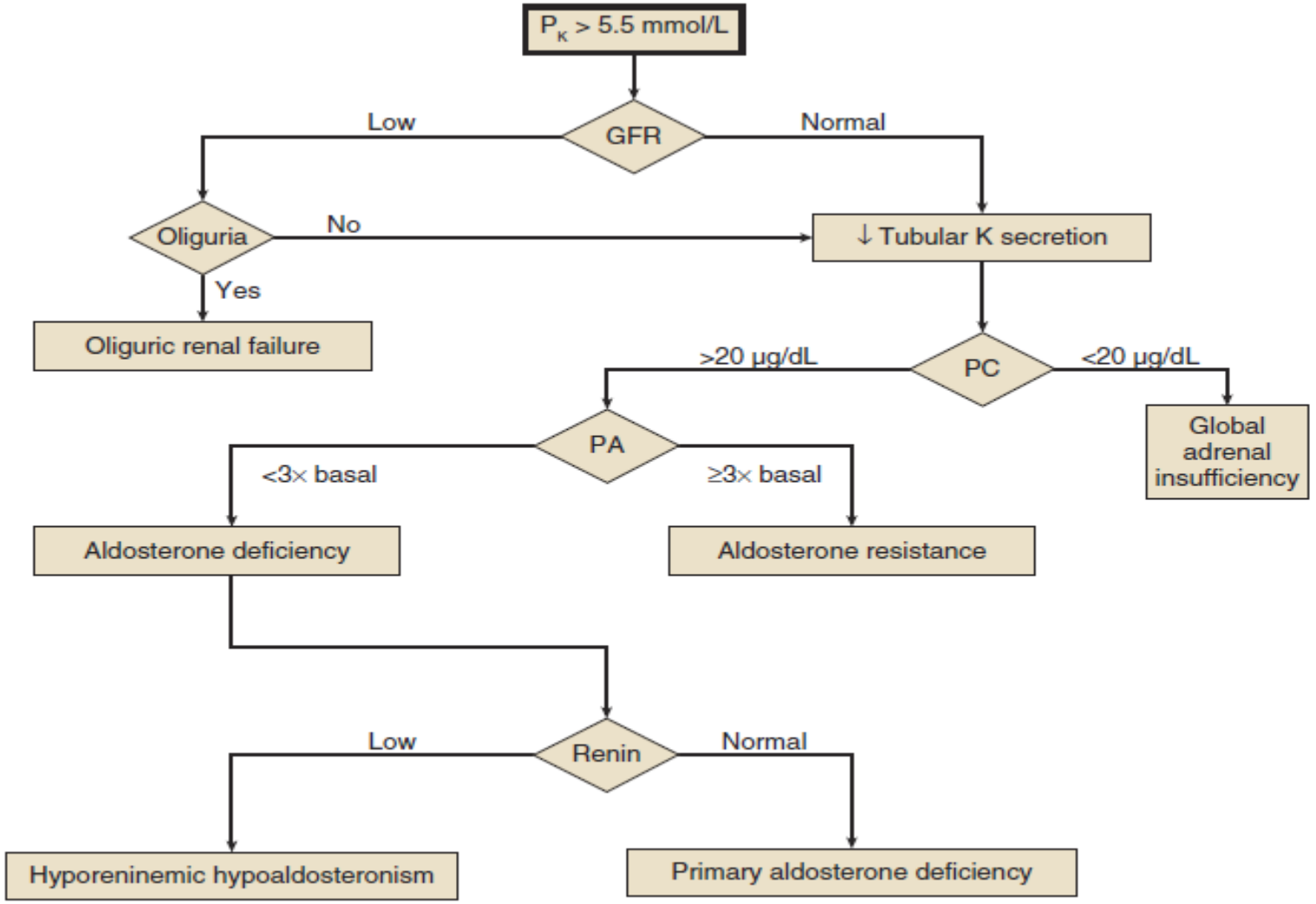
- ✓ STsegment depressiona
- ✓ decrease in T-wave amplitude,
- ✓ increase in U-wave amplitude However

Neuromuscular Effects

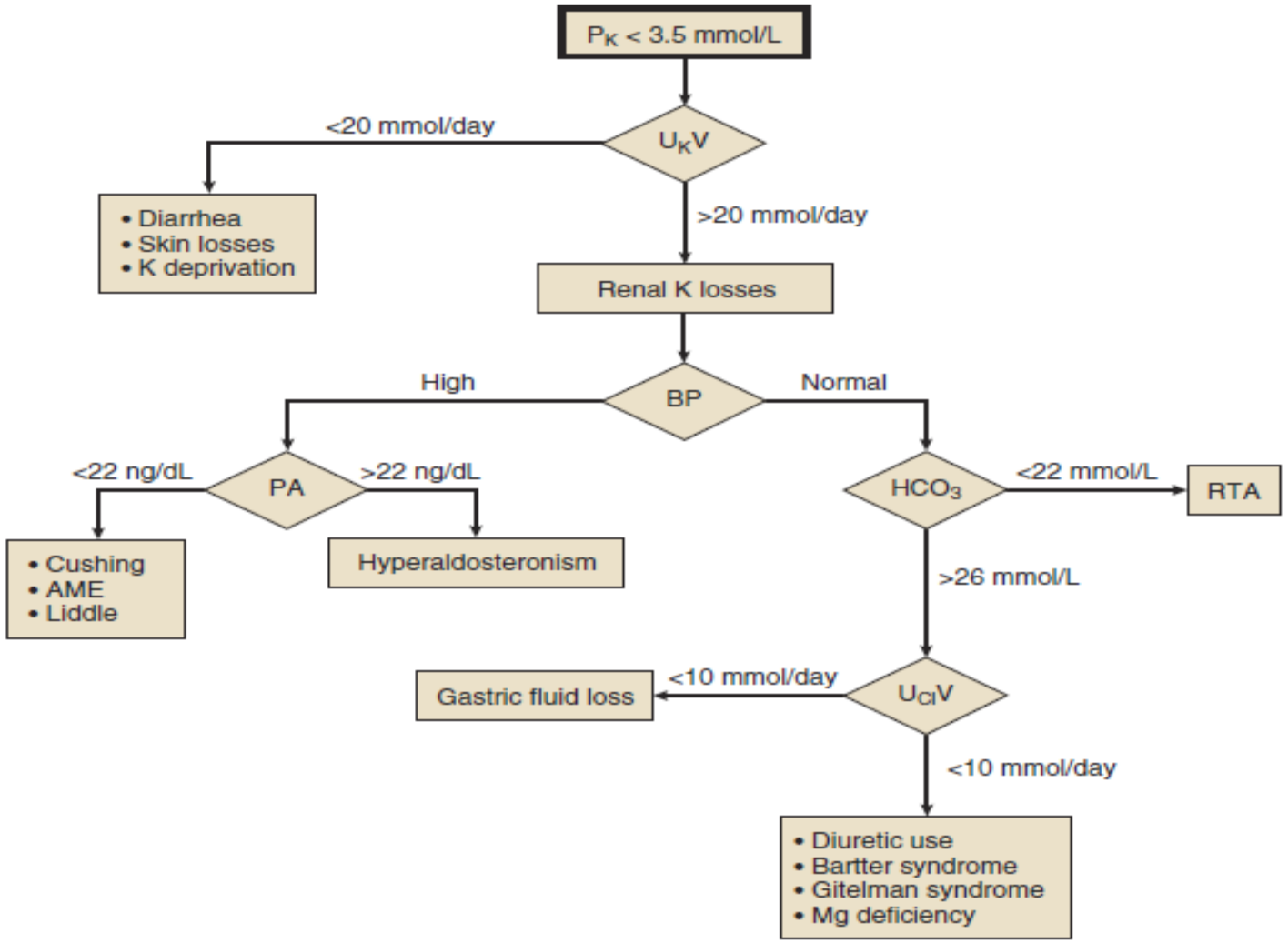
Modest hypokalemia generally presents as weakness, myalgias,muscle fatigue, and “restless” legs. With more severe hypokalemia(<2 mmol/L), paralysis may supervene

❖ Miscellaneous Effects

- ✓ glucose intolerance
- ✓ increased protein catabolism
- ✓ polydipsia and polyuria
- ✓ metabolic alkalosis



• **Fig. 54.2** Diagnostic evaluation of chronic hyperkalemia. *GFR,* Glomerular filtration rate; *PA,* stimulated plasma aldosterone (see text); *PC,* stimulated plasma cortisol (see Chapter 56).



• **Fig. 54.3** Diagnostic evaluation of chronic hypokalemia. *AME,* Syndrome of apparent mineralocorticoid excess; *BP,* blood pressure; *HCO_3^-,* bicarbonate; *PA,* stimulated plasma aldosterone (see text); *RTA,* renal tubular acidosis; *$U_{Cl}V$,* urinary chloride excretion; *U_KV,* urinary potassium excretion.

TABLE 54.2 Emergency Treatment of Hyperkalemia

Agent	Dose	Onset	Duration	Complications
Membrane Stabilization				
Calcium gluconate (10%)	10 mL IV over 10 min	Immediate	30–60 min	Hypercalcemia
Hypertonic (3%) sodium chloride	50 mL IV push	Immediate	Unknown	Volume overload Hypertonicity
Redistribution				
Insulin (short-acting)	10 units IV push, with 25–40 g dextrose (50% solution)	20 min	4–6 h	Hypoglycemia
Albuterol	20 mg in 4 mL normal saline solution, nebulized over 10 min	30 min	2 h	Tachycardia Inconsistent response
Elimination				
Loop diuretics				
Furosemide	40–80 mg IV	15 min	2–3 h	Volume depletion
Bumetanide	2–4 mg IV			
Sodium bicarbonate	150 mmol/L IV at variable rate	Hours	Duration of infusion	Metabolic alkalosis Volume overload
Sodium polystyrene sulfonate (Kayexalate, Kionex)	15–30 g in 15–30 mL 70% sorbitol orally)	> 2 h	4–6 h	Variable effect Intestinal necrosis
Hemodialysis		Immediate	3 h	Arrhythmias

Treatment hypokalemia

- nondiabeticpatients with normal renal function should respond well toa 1- to 2-hour infusion of KCl at 0.6 mmol/kg per hour given IV in saline solution.

- In patients with kidney function reduction of any degree, the infusion rate should be halved (0.3 mmol/kgper hour)

- Patients with diabetes mellitus not being treated for DKA or hyperglycemia should receive no more than 0.2 mmol/kgper hour, or about 0.1 mmol/kg per hour in the setting of renalfailure.

- For severe hypokalemia, the ECG should be monitored continuously and the infusion stopped immediately if signs of hyperkalemia develop.

The maximum increase in PK is seen at the end of the infusion, and about 50% of the increase is lost over the next 2 to 3 hours when a new steady state is achieved

Physiology of Water Homeostasis

Plasma osmolality about 285 mOsm/kg
minimum urine osmolality is about 50 mOsm/kg, and the maximum is about 1200 mOsm/kg

$$\text{Estimated } P_{osm} = (2 \times P_{Na}) + \frac{P_{gluc}}{18} + \frac{BUN}{2.8}$$

Hyponatremia

Epidemiology and Clinical Manifestations

very young and very old, females, and alcoholics appear to be at particular risk.

Neurologic symptoms:

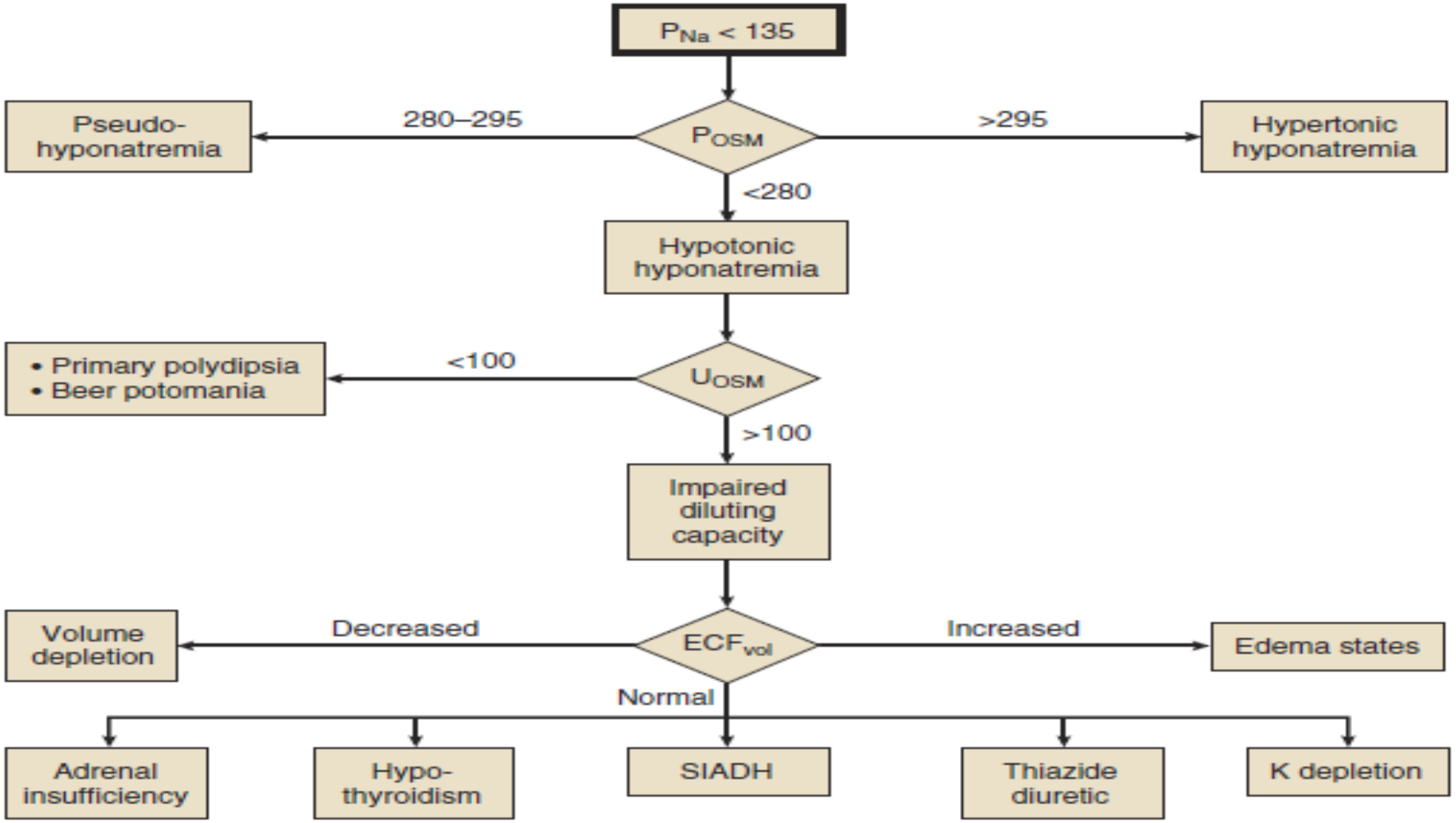
- Na below 125 mmol/L, anorexia, nausea, and malaise

.

- Between 120 and 110 mmol/L, headache, lethargy, confusion, agitation, and obtundation may be seen

.

- below 110 mmol/L: More severe symptoms (seizures, coma) may occur with levels.Focal neurologic, transtentorial cerebral herniation has been described in severe cases, especially in young women following surgery. hypoxemia noncardiogenic pulmonary edema.



• **Fig. 54.5** Diagnostic evaluation of hyponatremia. *ECF_{vol},* Extracellular fluid volume status; *K,* potassium; *P_{Na},* plasma sodium concentration; *P_{osm},* plasma osmolality (mOsm/kg); *SIADH,* syndrome of inappropriate antidiuretic hormone secretion; *U_{osm},* urine osmolality (mOsm/kg).

Hyponatremia

Management and Complications

The therapy of hypotonic hyponatremia must be tailored to
(1) the patient's signs and symptoms and
(2) the duration of the disorder.
Severe hyponatremia (plasma sodium concentration <115 mmol/L) can be life-threatening, especially if it develops rapidly.

Treatment hyponatremia

❖For patients with acute hyponatremia of less than 24 hours' duration severe, symptomatic hyponatremia is treated as an emergency to reduce intracranial pressure and the risk of herniation. An expert panel has recommended treating this condition with an intravenous bolus of 100 mL of 3% saline infused over 10 minutes. If signs or symptoms of increased intracranial pressure persist, the dose may be repeated twice

❖ For patients with severe, symptomatic chronic hyponatremia(>48 hours' duration) or similar hyponatremia of unknown duration,clinicians should aim to raise the plasma sodium concentration by no more than 6 mmol/L in the first 6 hours and then stop the increase

- The treatment of chronic asymptomatic hypotonicity should,be directed at correcting the pathophysiologic mechanisms involved in generating the hypotonic state. Because euvolemic hyponatremia represents pure water excess, treatment depends on restricting water intake to less than the daily water outpu

- SIADH :water restriction, a specific vasopressin (V2) receptor antagonist (VRA) can be used Conivaptan (parenteral) and tolvaptan (oral), demeclocycline (a tetracycline antibiotic that increases electrolyte-free water excretion by inhibiting vasopressin-mediated water reabsorption in the collecting duct)

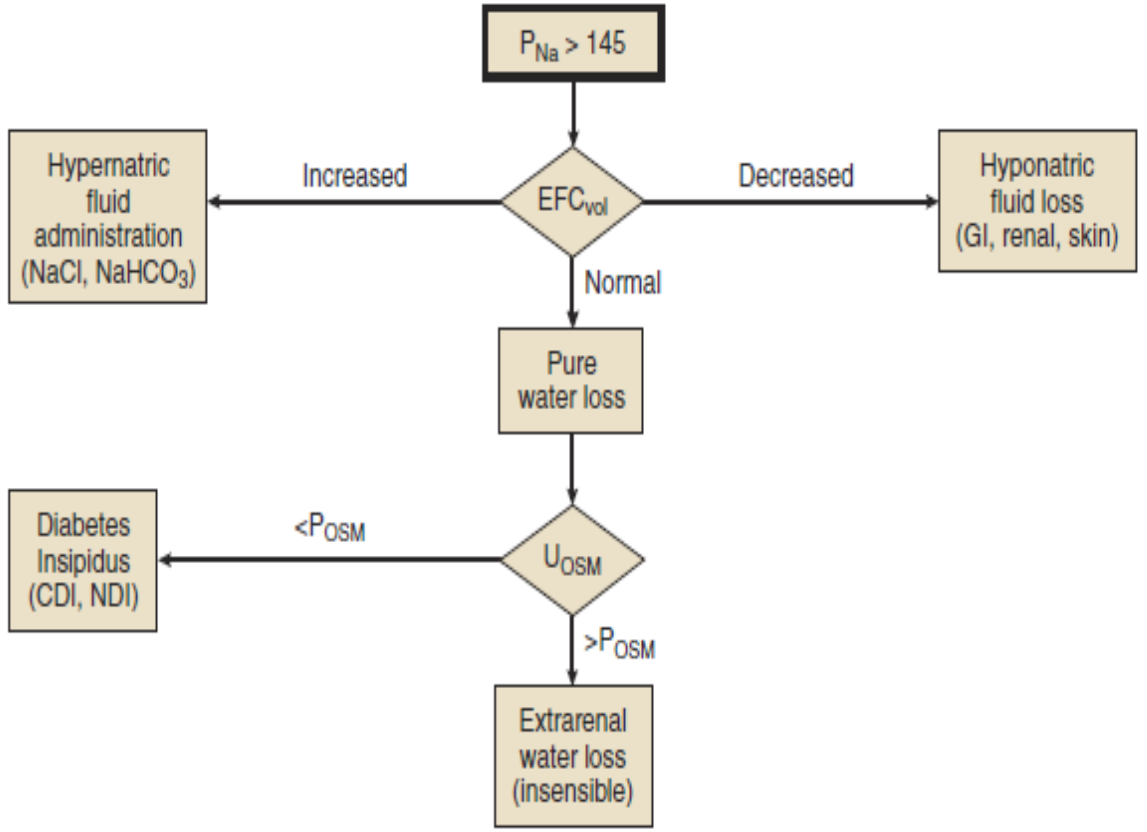
- Therapy of hypovolemic hyponatremia should be directed at restoring intravascular volume with intravenous isotonic saline solution while identifying and correcting the cause of the excessive solute loss

osmotic demyelination syndrome (ODS)

neurologic deficits (dysarthria, dysphagia,
behavioral disturbances, ataxia, quadriplegia, coma), which
typically develop 3 to 10 days after treatment rapid hyponatremia

risk factors osmotic demyelination:hypokalemia,
malnutrition, alcoholism, advanced age, female sex, and the
postoperative state, particularly after orthotopic liver transplantation

Hypernatremia



• **Fig. 54.6** Diagnostic evaluation of hypernatremia. *CDI,* Central diabetes insipidus; *ECF_{vol},* extracellular fluid volume status; *GI,* gastrointestinal; *NaCl,* sodium chloride; *$NaHCO_3$,* sodium bicarbonate; *NDI,* nephrogenic diabetes insipidus; *P_{Na},* plasma sodium concentration; *P_{osm},* plasma osmolality; *U_{osm},* urine osmolality.

Euvolemic Hypernatremia

The loss of large amounts of dilute, electrolyte-free water in the urine is typical of diabetes insipidus (DI).DI may be central (CDI) or nephrogenic (NDI) depending on whether the defect is in vasopressin release from the posterior pituitary or in the renalresponse to circulating vasopressin, respectively. Of special interest to intensivists is a classic triphasic syndrome

• BOX 54.9 Causes of Diabetes Insipidus

Central Diabetes Insipidus

- Posthypophysectomy
- Posttraumatic
- Granulomatous diseases
  - Histiocytosis
  - Sarcoidosis
- Infections
  - Meningitis
  - Encephalitis
- Inflammatory/autoimmune:hypophysitis
- Vascular
  - Hypoxia
  - Thrombotic or embolic stroke
  - Hemorrhagic stroke
- Neoplastic
  - Craniopharyngioma
  - Pituitary adenoma
  - Lymphoma
  - Meningioma
- Drugs or toxins
  - Ethanol
  - Snake venom
- Congenital/hereditary

Nephrogenic Diabetes Insipidus

- Drug-induced
  - Lithium
  - Demeclocycline
  - Cisplatin
  - Ethanol
- Hypokalemia
- Hypercalcemia
- Vascular
  - Sickle cell anemia
- Infiltrating lesions
  - Sarcoidosis
  - Multiple myeloma
  - Amyloidosis
  - Sjögren syndrome
- Congenital
  - Autosomal recessive: aquaporin-2 water channel gene mutations
  - X-linked recessive: arginine vasopressin V_2 receptor gene mutations

Treatment

For patients with pure water losses(euvolemic), therapy has two goals:
(1) reduction and/or replacement of ongoing water losses
(2) replacement of the existing water deficit.

- The rate of water replacement should be proportional to the rapidity with which the hypernatremia developed. Thus if the hypernatremia had developed over only a few hours (such as in salt poisoning, postsurgical or posttraumatic DI), it can be corrected just as quickly.
- On the other hand, hypernatremia of more than a day's duration, or of unknown duration, must be correctly slowly to avoid cerebral edema.

One should aim to lower the plasma sodium concentration by no more than 10 mmol/Lper day.

The water deficit to be corrected over 24 hours can be estimated

Target positive water balance over24 h\ L=TBW(Na p-Current PNa)\Current Pna

where TBW is total body water in liters (estimated as about 0.5 × lean body weight [kg] in women and 0.6 × lean body weight in men).

- ❑ Water is best administered enterally as tap water.
- ❑ If that route is unavailable, 5% dextrose in water (D_5W) may be used, with the understanding that the capacity to metabolize glucose is limited to about 15 g/h in a critically ill adult.

- Half-normal (0.45%)saline solution may be a good alternative, as long as one recognizes that only half the administered volume is electrolyte-free water

and that the sodium load may cause unwanted volume expansion.

- Regardless of the degree of hypernatremia, normal (0.9%) saline solution should be given intravenously to patients who present with obvious volume depletion, manifested by hypotension,tachycardia, and evidence of impaired tissue perfusion

- Patients with hypervolemic hypernatremia need reduction in their extracellular and intravascular volume before their water deficit can be corrected

TABLE 54.3 Pharmacologic Treatment of Central Diabetes Insipidus

Agent	Total Daily Dose	Frequency of Administration	Onset of Action (h)	Duration of Action (h)	Comments
Arginine vasopressin, 20 units/mL	5–10 units subcutaneously	q2–q4 h	1–2	2–6	Intravenous route may cause vasoconstriction and coronary spasm
Desmopressin acetate (DDAVP)					
10 μg/0.1 mL intranasal	10–40 μg intranasal	Daily or bid	1–2	8–12	
4 μg/mL injection	1–2 μg IV or subcutaneously	Daily or bid	1–2	8–12	

bid, Twice daily; *DDAVP*, 1-deamino-8-D-arginine vasopressin; *q*, every.

Modified from Singer I, Oster JR, Fishman LM. The management of diabetes insipidus in adults. *Arch Intern Med*. 1997;157:1293–1301.

Calcium

Calcium :
bone mineralization, muscle contraction,nerve conduction, blood coagulation , required for cell division, hormone secretion, phagocytosis, chemotaxis and activation of numerous intracellular second messengers.

The total body calcium content of an average adult is approximately 1 kg, 99% of which is found in bones and teeth, with only 1% in plasma and soft tissues

• BOX 54.10 Causes of Hypocalcemia

Hypoparathyroidism
Acquired
- Parathyroidectomy
- Infiltrative or malignant disease

Congenital
Idiopathic

Vitamin D Deficiency
Malnutrition
Malabsorption
Liver disease
Kidney disease

Redistribution
Tissue sequestration
- Acute pancreatitis
- Rhabdomyolysis

Complexation
- Alkali
- Citrated blood-product transfusions
- Citrate anticoagulation in continuous renal replacement therapy
- Plasmapheresis
- Bicarbonate infusion for metabolic acidosis
- Phosphate
- Tumor lysis syndrome
- Fleet enemas and phosphate-containing laxatives
- Rhabdomyolysis

Ethylenediamine tetraacetic acid (EDTA)

Drugs
Cis-platinum
Bisphosphonates
Plicamycin

Miscellaneous
Sepsis/systemic inflammatory response syndrome
Hypomagnesemia
Acute renal failure

Clinical Manifestations Hypocalcemia

Neuromuscular manifestations:
paresthesias, hyperactive reflexes, tetany (carpopedal spasm and other muscle spasm), seizures. Laryngospasm and bronchospasm ,Tetany may be provoked by tapping over the facial nerve and noting ipsilateral facial muscle twitching (Chvostek sign) and transiently occluding the brachial artery with a tourniquet and noting carpal spasm (Trousseau sign), although neither of these signs is specific for hypocalcemia. Prolonged hypocalcemia polyneuropathy and myopathy.

Psychiatric manifestations :
anxiety, irritability, confusion, and psychosis.

Cardiovascular *manifestations* : prolonged QT interval and, in severe hypocalcemia, bradycardia, hypotension refractory to fluids and vasopressors, heart block, heart failure, and cardiac arrest.

Treatment hypocalcemia

serious cardiovascular or neuromuscular signs should be treated urgently.

- Calcium gluconate (10% in 10 mL containing 90 mg elemental calcium) can be given over 5 to 10 minutes, followed by calcium gluconate infusion (500–1000 mg in 500 mL 5% dextrose over 6 hours).
- Calcium chloride (10% in 10 mL containing 272 mg elemental calcium)
- Patients with renal failure,hyperphosphatemia, and serious hypocalcemia may require dialysis.
- Magnesium deficits, hyperphosphatemia, severe metabolic acidosis should await correction of the hypocalcemia

Hypercalcemia

• BOX 54.11 Causes of Hypercalcemia

Primary Hyperparathyroidism

Malignancy
- Parathyroid hormone–related peptide
- Ectopic parathyroid hormone
- Vitamin D–mediated
- Lytic bone lesions

Vitamin D
- Exogenous
- Endogenous

Hyperthyroidism

Adrenal insufficiency

Rhabdomyolysis, recovery

Immobilization

Drugs
- Thiazide
- Lithium
- Vitamin D/calcium supplements
- Vitamin A

Clinical Manifestations Hypercalcemia

muscle weakness, fatigue, depression, and altered mental
status. At extremely high levels, stupor and coma may ensue. Prolonged
hypercalcemia lasting longer than 36 hours has been associated with the development
of critical illness polyneuropathy
and myopathy.

Cardiac symptoms:
increased rate of cardiac
repolarization and results in shortened QT interval. Conduction
disturbances and malignant arrhythmias

Renal symptoms:renal failure from volume depletion and renal vasoconstriction,
and polyuria and polydipsia owing to NDI.

GI symptoms:anorexia, nausea,vomiting, and constipation. Peptic ulcer disease
and acute pancreatitis

Treatment Hypercalcemia

Mild hypercalcemia
(total calcium ≤12 mg/dL or 3mmol/L)
is usually caused by primary hyperparathyroidism, thiazide diuretics,calcium and vitamin D supplements, lithium, and immobilization.Treatment should begin with withdrawal of the offending agent(if possible). Volume deficits should be replaced orally if possible.Early mobilization should be encouraged. Loop diuretics should be avoided in patients with mild asymptomatic hypercalcemia as they may exacerbate the volume depletion, leading to increased renal calcium reabsorption.

Treatment Hypercalcemia

moderate hypercalcemia (total calcium > 12 mg/dL or 3 mmol/L, and ≤ 14 mg/dL or 3.5 mmol/L) includes the measures discussed earlier, as well as intravenous volume expansion with isotonic saline solution. A loop diuretic will enhance renal excretion of calcium, but care must be taken to avoid volume depletion.

Severe hypercalcemia (total calcium >14 mg/dL or 3.5 mmol/L), even in the absence of signs and symptoms, should be treated as an emergency. Strategies for treatment include

(1) enhanced calcium Elimination(Forced diuresis, Volume expansion normal saline solution rate of 200 to 300 mL/h, patients with congestive heart failure unresponsive to diuretics, or with advanced kidney failure, dialysis)

(2) reduced bone resorption(Bisphosphonates inhibit Pamidronate (60–90 mg IV) reduces the plasma calcium in 48 to 72 hours and the effect may last for a month

(3) decreased gut absorption of calcium,

(4) identification and treatment of the underlying cause.

Magnesium

Magnesium

- plays a vital role in cellular physiology
- Catalyzes more than 300 enzymatic reactions
- integral part of all adenosine triphosphate–dependent reactions
- Involved in synthesis of proteins
- energy-rich compounds, electron, and proton transporters
- DNA and ribonucleic acid transcription;
- translation of messenger RNA and regulation of mitochondrial Function
- regulate intracellular calcium concentration, especially in vascular smooth muscle, and thereby affects vascular tone
- In vitro studies suggest a role for magnesium in inflammation and immunity

• BOX 54.12 Causes of Hypomagnesemia

Deficient Intake
Magnesium-deficient parenteral nutrition
Protein-calorie malnutrition
Alcoholism

Renal Loss
Drug-induced
- Loop diuretics
- Thiazide diuretics
- Aminoglycosides
- Amphotericin b
- Cis-platinum
- Cetuximab
- Foscarnet
- Pentamidine

Volume Expansion
Osmotic diuresis (e.g., hyperglycemia)
Alcohol
Hypercalcemia
Tubular dysfunction
- Recovery from acute tubular necrosis
- Bartter syndrome
- Gitelman syndrome

Gastrointestinal
Small intestine resection
Inflammatory bowel disease
Jejunoileal bypass surgery
Diarrhea
Steatorrhea
Malabsorption syndromes
Proton pump inhibitors

Redistribution
Acute pancreatitis
Hungry bone syndrome

• BOX 54.13 Clinical Manifestations of Hypomagnesemia

Cardiovascular

Ventricular arrhythmias
- Torsades de pointes
- Ventricular fibrillation; premature ventricular contractions
- Increased digitalis toxicity

Conduction disturbances
- Prolonged QT interval
- Prolonged QRS duration
- ST depression
- Peaked T wave

Neuromuscular

- Muscle weakness
- Tetany
- Horizontal and vertical nystagmus
- Choreoathetoid movements
- Seizures

Metabolic

Hypokalemia, refractory
Hypocalcemia, refractory

Treatment Hypomagnesemia

✓ In patients who have malignant cardiac arrhythmias (ventricular fibrillation or torsades de pointes) or seizure attributed to hypomagnesemia, intravenous magnesium must be given immediately (2 g of magnesium sulfate over minutes).Less urgent cases, but those in which signs and symptoms are present, may be treated with magnesium sulfate 6 g IV in the first 24 hours followed by 3 to 4 g daily for the next 2 to 6 days, For patients with impaired renal function, the dose should be reduced by 50% to 75%

✓ For mild asymptomatic hypomagnesemia, patients who can tolerate oral medication should receive oral magnesium salts (e.g., magnesium chloride, 500 mg slow-release tablets, 10–12 per day in divided doses). High doses of oral magnesium salts may cause diarrhea.

Hypermagnesemia

• BOX 54.14 Causes of Hypermagnesemia

Patients With Renal Insufficiency

Magnesium-containing antacids (e.g., magnesium aluminum hydroxide)
Magnesium-containing laxatives or enemas (e.g., magnesium citrate)

Patients With Normal Renal Function

Treatment of preeclampsia or eclampsia
Treatment of hypomagnesemia

Miscellaneous

Hypothyroidism
Hyperparathyroidism
Addison disease
Lithium treatment

• BOX 54.15 Clinical Manifestations of Hypermagnesemia

Cardiovascular
- Hypotension
- Facial flushing
- Bradycardia
- Sinoatrial or atrioventricular heart block
- Asystole

Gastrointestinal
- Nausea and vomiting
- Ileus

Neuromuscular
- Hyporeflexia
- Flaccid skeletal muscle paralysis
- Respiratory muscle weakness and paralysis
- Lethargy
- Coma

Urinary retention

Treatment Hypermagnesemia

- ✓ Patients with adequate renal function and mild asymptomatic hypermagnesemia require no treatment except to remove all sources of exogenous magnesium.Magnesium excretion may be enhanced by saline solution infusion and the use of loop diuretics

- ✓ Patients with symptomatic hypermagnesemia, especially those with cardiovascular manifestations,require urgent treatment. The recommended therapy is calcium gluconate 1 g IV over 5 minutes.

- ✓ Patients with acute or chronic renal failure and symptomatic hypermagnesemia require dialysis to remove excess magnesium. Hemodialysis removes magnesium efficiently

Phosphorus

• BOX 54.16 Causes of Hypophosphatemia

Redistribution

Acute respiratory alkalosis
Refeeding syndrome
Treatment of diabetic ketoacidosis
Hungry bone syndrome—postparathyroidectomy
Leukemia

Increased Renal Excretion

Hyperparathyroidism
Vitamin D deficiency or resistance
Volume expansion
Postobstructive diuresis
Recovery from acute tubular necrosis
Fanconi syndrome
Postrenal transplantation
Drugs
- Acetazolamide
- Corticosteroids

Inherited disorders
Tumor-induced osteomalacia

Decreased Intestinal Absorption

Malnutrition
Phosphate-binding medications
Chronic diarrhea
Chronic alcoholism

• BOX 54.17 Clinical Manifestations of Hypophosphatemia

Skeletal muscle
- Weakness
- Rhabdomyolysis

Decreased cardiac output
Hematologic
- Erythrocytes
- Decreased 2,3-diphosphoglycerate
- Decreased tissue oxygen delivery
- Spherocytosis
- Hemolysis
- Impaired leukocyte function
- Impaired platelet function

Neurologic
- Anorexia
- Irritability
- Confusion
- Paresthesias
- Ataxia
- Seizure
- Coma

Skeletal
- Bone pain
- Pseudofractures
- Osteomalacia

Insulin resistance

Treatment Hypophosphatemia

- In mild to moderate hypophosphatemia(>1.5 mg/dL or about 0.5 mmol/L) oral replacement is usually sufficient. Skim milk is an excellent source of phosphorus and provides 900 mg/L of inorganic phosphate. In patients who cannot tolerate milk, oral sodium phosphate, formulated to provide 250 mg of phosphate in each tablet
- Patients with severe hypophosphatemia (<1.5 mg/dL), or those for whom the enteral route is not an option, require intravenous phosphorus repletion. In such patients, the recommended dose is 2.5 to 5.0 mg (0.08–0.16 mmol)/kg body weight over 6 hours

Hyperphosphatemia

• BOX 54.18 Causes of Hyperphosphatemia

Redistribution
- Tumor lysis syndrome
- Rhabdomyolysis
- Pancreatitis
- Respiratory acidosis
- Lactic acidosis
- Diabetic ketoacidosis

Increased Intake
- Phosphate-containing enemas and laxatives
- Intravenous phosphate
- Hypervitaminosis D

Decreased renal excretion
- Acute renal failure
- Chronic kidney disease
- Hypoparathyroidism

Pseudohyperphosphatemia

Treatment Hyperephosphatemia

Treatment of hyperphosphatemia:

- ✓ reducing the phosphate intake and enhancing the removal of excess phosphate. If the patient is taking an oral diet, dietary phosphate should be restricted to less than 800 mg/day.
- ✓ Oral phosphate binders can be added with meals to decrease intestinal phosphate absorption.
- ✓ Patients with normal renal function can be treated with saline solution diuresis to increase renal phosphate excretion.
- ✓ Acetazolamide can be added to enhance phosphaturia, taking care to avoid a metabolic acidosis.
- ✓ Patients with severe hyperphosphatemia with coexisting renal failure may require renal replacement therapy in the form of intermittent or continuous hemodialysis.


سپاس از همکاری شما