Overview of Fluid and Electrolyte Maintenance

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Disclosure

- I have no relevant financial relationships to disclose.

Pharmacist Objectives

- Discuss the distribution of total body fluid, and apply this concept towards the management of a patient's fluid replacement.
- Recommend an appropriate intravenous fluid regimen based on a patient's clinical characteristics.
- Develop an effective electrolyte replacement plan based on a patient's clinical status and electrolyte abnormalities.
- Identify appropriate clinical situations for the use of hypertonic and hypotonic saline, and recommend monitoring parameters to ensure the safe use of these intravenous fluids.

Technician Objectives

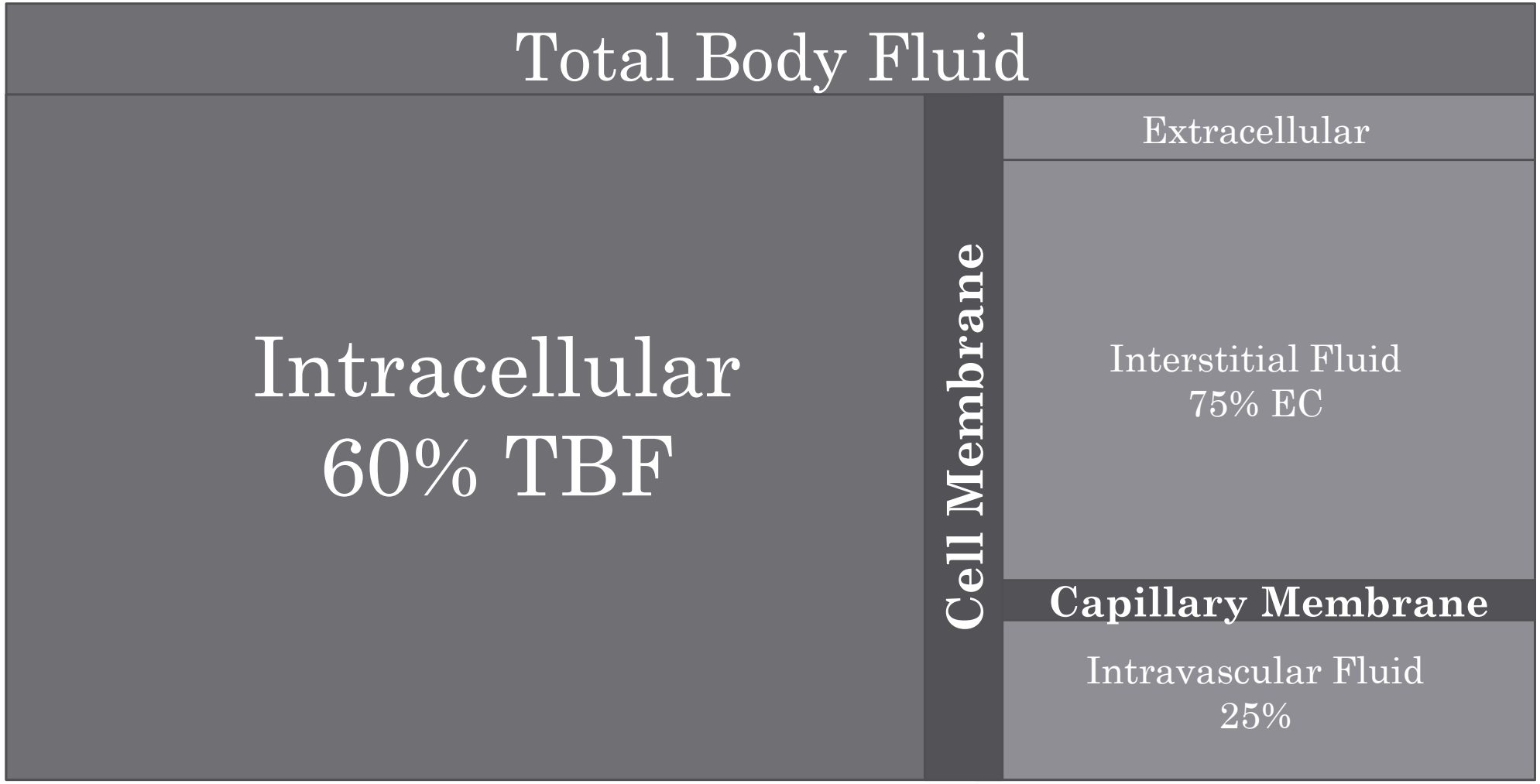
- Recognize appropriate precautions to be taken while compounding intravenous electrolyte replacement products, including hypotonic and hypertonic saline.
- Delineate the differences between colloid and crystalloid fluids, and recall appropriate instances for their use.
- Identify common intravenous fluid regimens and describe appropriate dosages and concentrations for electrolyte additives.
- Identify common units and calculations involved in compounding electrolyte replacement products.

Fluid Management

Fluid Distribution

- Total body fluid (TBF)
  - Estimated as ~60% of lean body weight (LBW) in males
  - Estimated as ~50% of LBW in females
- TBF further divided
  - Intracellular (IC) space 60% of TBF
    - Enclosed by the cell membrane
  - Extracelllular (EC) space 40% of TBF
    - Interstitial space 75% of EC fluid
    - Intravascular space 25% of EC fluid
      - Plasma ~3L
      - Red blood cells ~2L fluid
- Distribution in the body determines distribution of intravenous (IV) fluids

Fluid Distribution



Fluid Compartments

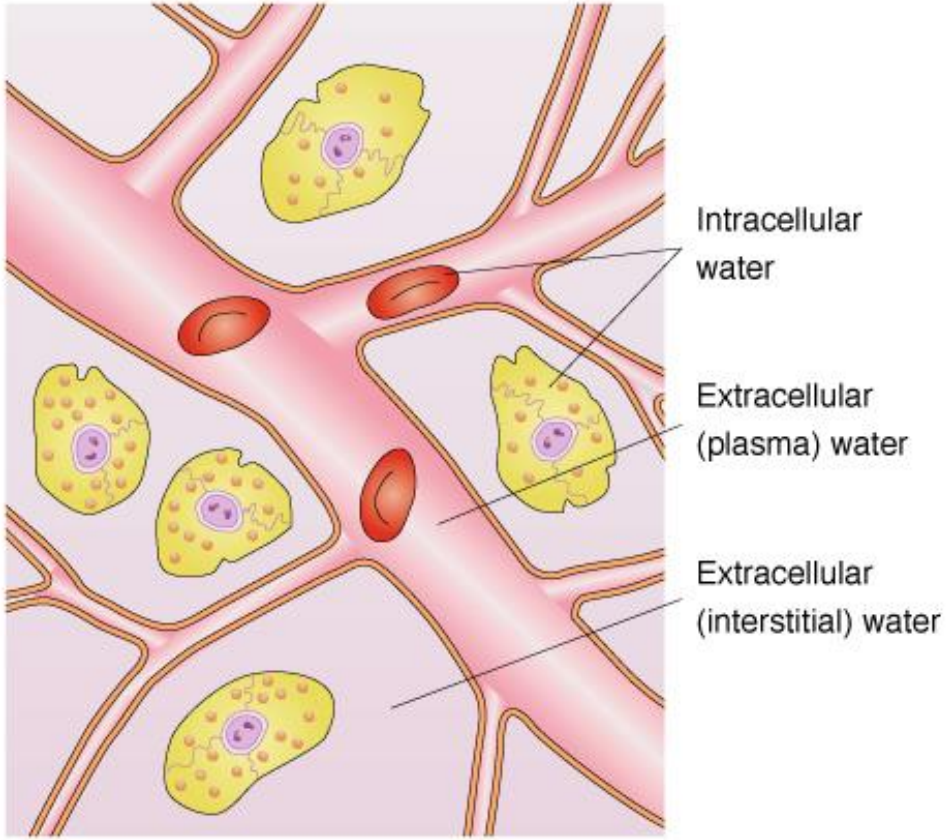


Figure 33-1 Distribution of body water. The extracellular space includes the vascular compartment and the interstitial spaces.

Osmotic Equilibrium

- Osmotic pressure
  - Created by concentration of ions/electrolytes in each compartment
  - Responsible for containing water in each space, keeps volume constant
- Osmolality
  - Number of particles per kilogram of water
- Osmotic Equilibrium
  - Water moves across the cell membrane from of region of low osmolality to one of higher osmolality
- Plasma osmolality
  - Normal value: 280-300 mOsm/kg

Acute Fluid Resuscitation

- Intravascular fluid depletion can occur as a result of shock
  - Associated with reduced cardiac function and organ hypoperfusion
  - Signs and symptoms usually occur when ~15% (750mL) of blood volume is lost or shifts out of intravascular space
- Signs and Symptoms of intravascular volume depletion
  - Tachycardia
  - Hypotension
  - Orthostatic changes in HR or BP
  - Increased BUN/Scr ration >10:1
  - Dry mucous membranes
  - Decreased skin turgor
  - Reduced urine output
  - Dizziness
  - Improvement after a 500- or 1000-mL fluid bolus
- Fluid resuscitation is indicated in patients exhibiting signs and symptoms

Acute Fluid Resuscitation

- Goal: restore intravascular volume and prevent organ hypoperfusion
- Crystalloids recommended as a rapid infusion
  - NS or LR typically used
  - LR preferred in surgery and trauma patients
  - LR has more physiological amount of Cl than NS
- Crystalloids vs Colloids
  - No difference has been shown in time to resuscitation or outcomes
  - Colloids: higher cost, some adverse effects
- Selective instances to consider colloids (controversial)
  - 4-6L crystalloid fluid resuscitation has failed or caused significant edema
  - Patients with albumin <2.5mg/dL who have required a large volume already
  - Albumin + diuretics for patients with clinically significant edema and low albumin

Maintenance Fluid Replacement

- Indicated in patients unable to tolerate oral fluids
- Goal: prevent dehydration and maintain normal fluid/electrolyte balance
- Administered as continuous infusions through peripheral or central lines
- Example maintenance fluid
  - D_5W with 0.45% NaCl with 20-40mEq of KCl per liter

Maintenance Fluid Replacement

- Calculations to determine daily volume needed in children and adults
  - Administer 100mL/kg for the first 10kg of weight, then 50mL/kg for the next 10-20kg, plus 20mL/kg for every kilogram greater than 20kg

  OR

  - Administer 20-40ml/kg/day (adults only)
- Adjust fluids according to individual patient's input, output, insensible losses

Commonly Used IV Fluids
Crystalloids

- Crystalloids
  - Normal saline, Lactated Ringer's, Normosol-R
  - Contain water, sodium, chloride, and additional electrolytes
  - Hypertonic and hypotonic crystalloid options
- Normal Saline (0.9% sodium chloride)
  - Advantages
    - Low risk for adverse reactions
  - Disadvantages
    - Freely distributes across vascular barrier
    - Risks of hypernatremia and hyperchloremic metabolic acidosis
- Additional Considerations
  - Duration 1-4 hours
  - Isotonic

Commonly Used IV Fluids
Crystalloids

- Lactated Ringers (or Ringers Lactate)
  - Advantages
    - Low risk for adverse reactions
  - Disadvantages
    - Freely distribute across the vascular barrier
    - Risk of respiratory acidosis due to CO_2 accumulation
    - Risk for hyperkalemia (4mEq/L of potassium)
    - Impaired metabolism of lactate to bicarbonate in patients with severe liver disease
- Additional Considerations
  - Duration of action 1-4 hours
  - Considered equally effective as NS
  - Not recommended in hemorrhagic shock or brain trauma
  - Traditionally preferred in surgical patients
  - Contains sodium chloride, sodium lactate, potassium chloride, calcium chloride

Commonly Used IV Fluids
Crystalloids

- 5% Dextrose in Water (D_5W)
  - "Free water": metabolized to water and carbon dioxide
  - Water crosses any membrane in the body
    - 60% into the IC space and 40% to the EC space
- Hypotonic
  - Isotonic in bag but becomes hypotonic when metabolized to free water
- Additional Considerations
  - Not preferred for fluid resuscitation
  - 50 grams of dextrose per liter
  - Not recommended in patients with neurologic injury or elevated intracranial pressure

Commonly Used IV Fluids
Colloids

- Colloids
  - PRBCs, albumin, dextran, hetastarch
  - Too large to cross capillary membrane
  - Provide significant volume increase because they remain in intravascular space
- Controversial use
  - Albumin showed no mortality benefit over NS (SAFE trial)
  - Hydroxyethyl starch no longer recommended due to adverse effects
  - Expensive compared to crystalloids
  - Higher risk of adverse and allergic reactions

Commonly Used IV Fluids
Colloids

- Albumin (5% and 25% formulations)
  - Advantages
    - Colloids provide greater volume expansion than equal volumes of crystalloids
  - Disadvantages
    - Potential for allergic reactions
    - Potential for transmission of infection
    - Hyperoncotic albumin may cause kidney damage
    - Expensive
- Additional Considerations
  - Natural colloid (blood product)
  - Duration of action 12-24 hours
  - 5% albumin is iso-oncotic, 25% albumin is hyperoncotic

Commonly Used IV Fluids
Colloids

- Dextran
  - Advantages
    - Provides greater volume expansion than equal volumes of crystalloids
  - Disadvantages
    - High risk for adverse reactions
    - Potential for allergic reactions or anaphylactoid reactions
    - Impairs hemostasis
    - May cause kidney damage
- Additional Considerations
  - Artificial colloid
  - Duration of action 1-2 hours
  - Use for fluid resuscitation has fallen out to favor due to risk of adverse reactions

Commonly Used IV Fluids
Colloids

- Hydroxyethyl starch (HES)
  - Advantages
    - Provides greater volume expansion than equal volumes of crystalloids
    - May modulate inflammation
  - Disadvantages
    - Potential for anaphylactoid reactions
    - May accumulate in tissues and cause prolonged itching
    - May impair platelet function and/or cause kidney damage
    - Expensive
- Additional Considerations
  - Synthetic colloid
  - Duration of action up to 36 hours
  - Hyperoncotic (6%)
  - Larger molecular weight than albumin
  - Not recommended in patients with severe sepsis (increased mortality, bleeding)

Composition of Commonly Used Intravenous Replacement Solutions

Solution	Dextrose	Na (mEq/L)	Cl (mEq/L)	Tonicity	Distribution (% ECF)	Distribution (% ICF)	Free water/L
D_5W	5g/100mL	0	0	Hypotonic	40	60	1000ml
0.45% NaCl	0	77	77	Hypotonic	73	37	500mL
0.9% NaCl	0	154	154	Isotonic	100	0	0mL
3% NaCl	0	513	513	Hypertonic	100	0	-2331mL
LR	0	130	109	Hypotonic (slightly)	100	0	0mL

IV Fluid Distribution

Intravenous Fluid	Infused Volume (mL)	Equivalent Intravascular Volume Expansion (mL)
NS	1000	250
LR	1000	250
Normosol-R	1000	250
D_5W	1000	100
Albumin 5%	500	500
Albumin 25%	100	500
Hetastarch 6%	500	500

Electrolyte Replacement

Electrolyte Composition

Total Body Fluid	
Intracellular Compartment • Potassium • Magnesium • Phosphate	Extracellular Compartment • Sodium • Chloride • Bicarbonate • Calcium

Disorders of Sodium

- Normal range 135 – 145 mEq/L
- Role in the body
  - Sodium in the ECF determines the tonicity of the ECF
  - Directly affects the distribution of water between EC and IC compartments
  - Sodium concentration is the ratio of Na:H_2O (not absolute amount of either)
  - Sodium level does not indicate whether abnormality is due to increase in the total amount of Na, H_2O, or both

Hyponatremia

- Sodium concentration <135 mEq/L
- Most common electrolyte abnormality
- Significant morbidity and mortality
- Signs and symptoms
  - Clinically do not appear until sodium <125 mEq/L
  - Acute: cerebral edema, seizures, increased mortality risk
  - Chronic: N/V, confusion, personality changes, neurologic dysfunction, gait disturbances, seizures

Serum sodium (mEq/L)	Clinical manifestations
120-125	Nausea, malaise
115-120	HA, lethargy, obtundation, unsteadiness, confusion
<115	Delirium, seizure, coma, respiratory arrest, death

Types of Hyponatremia

	Hypovolemic Hypotonic Hyponatremia	**Euvolemic Hypotonic Hyponatremia**	**Hypervolemic Hypotonic Hyponatremia**
Description	Deficit of both Na and fluid, but total Na is decreased more than TBW	Normal total body Na with excess fluid volume (dilutional)	Caused by excess Na and fluid, but fluid excess predominates
Example	Fluid loss, third spacing, renal loss	SIADH, medications	HF, cirrhosis, nephrotic syndrome
Treatment	Fluid resuscitation	Treat cause Fluid restriction Vasopressin receptor antagonists	Na and water restriction Treat underlying cause Vasopressin receptor antagonists

Principles of Hyponatremia Correction

- AVOID overly rapid increases in serum sodium (>10-12 mEq/L in 24 hours)
- Treat underlying cause
- Chronicity of hyponatremia impacts the rate at which correction should be undertaken
- Transient or permanent brain dysfunction may result from overly rapid correction of hyponatremia
  - Osmotic demyelination syndrome

3% Sodium Chloride Infusion

- High alert medication
- Administration
  - Symptomatic hyponatremia: infusion rate 1-2ml/kg/hour
  - Central IV access (osmolarity >900mOsm/L)
  - If peripheral IV must be used (emergency), monitor for phlebitis
  - Monitor serum sodium changes every 1-4 hours depending on symptom severity
- Complications
  - Osmotic demyelination syndrome
  - Hypokalemia
  - Hyperchloremic acidosis
  - Hypernatremia
  - Heart failure
  - Coagulopathy
  - Hypotension

Hypernatremia

- Sodium level >145mEq/dL
- Hypertonic state resulting in cellular dehydration
- Commonly observed in patients without thirst response
- High mortality rates if serum sodium >160mEq/dL (~60-75%)
- Signs and symptoms
  - Thirst, dry mucous membranes, decreased skin turgor, acute weight loss, weakness, lethargy, restlessness, irritability, confusion, hallucinations, ICH, coma, seizures, death

Types of Hypernatremia

	Hypovolemic Hypernatremia	Euvolemic Hypernatremia	Hypervolemic Hypernatremia
Description	Water loss exceeds sodium loss	Water loss only	Sodium gain exceeds water gain
Example	Insensible losses exceed intake	DI	Sodium overload, mineralicorticoid excess
Treatment	0.9%NS until VS stable, then free water	Free water replacement, vasopressin	Free water replacement with loop diuretic, HD

Hypernatremia

- Treatment
  - Depends on cause: too little water or too much sodium
- Rapid correction is NOT indicated
  - Results in cerebral edema, seizures, neurologic damage, death
  - Do not exceed a change of greater than 10mEq/day
- Hypovolemic Hypernatremia
  - NS adminstered to correct ECF volume
  - Then hypotonic solution to correct H_2O deficit
- Euvolemic hypernatremia
  - Hypotonic solution
  - Treatment for DI if indicated
- Hypervolemic hypernatremia
  - Goal: to remove sodium from the body
  - Diuretics (loops) and hypotonic solution (D_5W)

Disorders of Potassium

- Normal range: 3.5 – 5 mEq/L
- Intracellular ion
  - Most abundant cation in the body
  - 98% in intracellular compartment, 2% in extracellular space
- Role in the body
  - Cellular synthesis and metabolism, action potential across cell membrane, neuromuscular activity, cardiac conduction

Hypokalemia

- Potassium level < 3.5 mEq/L
  - Mild: 3 – 3.5 mEq/L
  - Moderate : 2.5 – 3 mEq/dL
  - Severe: < 2.5 mEq/L
- Causes
  - GI loss
  - Medications
  - Metabolic acidosis
  - Hypomagnesemia
- Signs and Symptoms
  - Mild: asymptomatic
  - Moderate to severe: muscle weakness, cramping, ileus, EKG changes, cardiac arrhythmias

Hypokalemia Treatment

- Potassium level 3.5 – 4 mEq/L
  - Increase dietary intake of potassium rich foods
- Potassium level 3 – 3.5 mEq/L
  - PO potassium supplementation in patients with cardiac conditions or on digoxin
- Potassium level <3 mEq/L
  - IV infusion recommended
- Correct hypomagnesemia first
  - Low magnesium impairs the function of the Na-K-ATPase pump
  - Impairment results in increased renal excretion of potassium

Hypokalemia Treatment

Plasma K^+ (mEq/L)	Treatment	Comments
3-3.5	Oral KCl 60-80 mEq/day if no signs or symptoms	Doses >60mEq should be divided to avoid GI effects Recheck K^+ daily
2.5-3	Oral KCl 120 mEq/day or IV 60-80 mEq administered at 10-20mEq/hour if signs or symptoms	Monitor K^+ (i.e. 2 hours post-infusion)
2-2.5	IV KCl at 10-20mEq/hour	Consider continuous ECG monitoring
<2	IV KCl at 20-40mEq/hour	Consider continuous ECG monitoring

Potassium IV Administration

	General Med-Surg Areas	ICU/Telemetry Beds
Rate	Not to exceed 10mEq/hour	Recommended: 10mEq/hour Max rate: 20mEq/hour
Concentration	Not to exceed 10mEq/50mL	20mEq/50mL (central line)
Notes		Rates >10mEq/hour must be monitored
KCl: Never to be administered IV Push!		

Hyperkalemia

- Potassium level >5.5 mEq/L
  - Mild: potassium level 5.5 – 6 mEq/L
  - Moderate: potassium level 6.1 – 6.9 mEq/L
  - Severe: potassium level > 7 mEq/L
- Causes
  - Renal failure, acidosis, red cell hemolysis, overcorrection, medications, salt substitutes, traumatic injury (MVC), adrenal insufficiency
- Signs and Symptoms
  - EKG changes
    - Peaked T waves, depressed ST segment, disappearance of P wave, widened QRS complex
  - Additional
    - Muscle weakness, paresthesias, GI hypermotility, paralysis

Hyperkalemia Treatment

- Treatment Goals
  - Reverse cardiac effects immediately
  - Redistribute potassium from extracellular space into the cell
  - Eliminate potassium from the body
  - Additionally: treat underlying cause and stop excess intake or medications
- Treatment
  - Calcium gluconate
  - Insulin and glucose
  - B_2-agonists
  - Sodium bicarbonate
  - Sodium polystyrene sulfonate
  - Loop diuretics
  - Dialysis

Disorders of Magnesium

- Normal Range: 1.5 – 2.2 mEq/L
- Role in the body
  - Intracellular ion predominantly
  - Found in bone and muscle

Hypomagnesemia

- Magnesium level <1.4 mEq/L
- Causes
  - Reduced intake, reduced absorption, increased loss, drug-induced
  - Often due to other electrolyte abnormalities
- Signs and Symptoms
  - Neuromuscular: tremor, hyperactive reflexes, seizures
  - Cardiac: arrhythmias (ventricular fibrillation, Torsades de Pointes)

Hypomagnesemia Treatment

- PO, IV infusion, or IM
- PO
  - Magnesium containing antacids or laxatives
  - Magnesium oxide
  - SE: diarrhea
- IV infusion
  - Magnesium sulfate
  - Dose depends on the depletion 8-12 g (1 gram = 4 mEq)
  - Standard infusion rate: 1-2 grams/hour

Hypermagnesemia

- Magnesium level: > 2.2 mEq/L
- Causes
  - Renal failure (acute vs chronic), elderly, adrenal insufficiency, hypothyroidism, lithium
- Signs and Symptoms
  - Asymptomatic < 4 mEq/L
  - Weakness, N/V, hypotension, respiratory depression, muscle paralysis, coma, cardiac arrhythmias

Hypermagnesemia Treatment

- Reduce magnesium intake
- Enhance magnesium excretion
  - Loop diuretics
- Antagonize physiologic effects of magnesium
  - IV calcium – antagonizes neurological and cardiovascular effects of magnesium

Disorders of Phosphorous

- Normal range: 2.5 – 4.5 mg/dL
- Role in the body
  - Intracellular ion
  - Cell membrane function, DNA/RNA/proteins, part of energy molecule (ATP), RBC function, bone mineral

Hypophosphatemia

- Phosphate < 2.6 mg/dL
- Causes
  - Decreased GI absorption, increased urinary excretion, redistribution
- Signs and Symptoms
  - Neurological: irritability, neuropathy, seizures, coma
  - Musculoskeletal: weakness, atrophy, rickets, osteomalacia
  - Cardiopulmonary: CHF, respiratory failure
  - Hematologic: hemolysis, anemia

Hypophosphatemia Treatment

- Mild to moderate hypophosphatemia
  - Usually asymptomatic
  - PO phosphorous replacement
- Severe hypophosphatemia
  - IV phosphorous 15-30mmol (0.5 – 0.75 mmol/kg of IBW)
  - Max IV rate 7.5 mmol/hour
  - Monitor q6hours for up to 72 hours

Hyperphosphatemia

- Phosphate > 4.5 mg/dL
- Causes
  - Chronic kidney disease or hypoparathyroidism
- Signs and Symptoms
  - Generally asymptomatic
  - Hypocalcemia, ECG changes, and paresthesias can occur
- Treatment
  - Limit intake of phosphorous
  - Phosphate binding agents
  - Dialysis
  - Replace calcium if patient is also hypocalcemic

Disorders of Calcium

- Normal range: 8.5 – 10.5 mEq/dL (ionized calcium 1.1 – 1.3 mmol/L)
- Distribution
  - Extracellular fluid contains <1% of calcium, 99% of total body stores is in skeletal bone
    - Half of calcium in EC fluid is bound to albumin and other plasma proteins
    - Ionized calcium (unbound) is the active form
  - Ionized calcium is regulated by parathyroid hormone, phosphorous, vitamin D and calcitonin
- Role in the body
  - Bone mineral, blood coagulation, membrane excitability, muscle contraction, neuron activation

Hypocalcemia

- Total serum calcium level <8.5 mg/dL
- Ionized calcium level <1.1 mmol/L
- Causes
  - Post-operative hypoparathyroidism, vitamin D deficiency, renal failure, malnutrition, medications, hyperphosphatemia
- Signs and Symptoms
  - Neuromuscular: paresthesias, muscle cramps, tetany, laryngeal spasm
  - Cardiovascular: prolonged QT interval, arrhythmias, bradycardia, hypotension
  - Dermatologic: hair loss, brittle nails, eczema
  - CNS: depression, anxiety, memory loss, confusion, hallucinations, seizures

Hypocalcemia Treatment

- Acute hypocalcemia
  - IV calcium (calcium chloride or calcium gluconate)
  - 200-300mg of elemental calcium
  - Monitor calcium q4-6 hours during IV therapy
  - Treat underlying disorder
- Chronic hypocalcemia
  - Oral calcium supplementation
  - Oral vitamin D supplementation

Hypercalcemia

- Serum calcium >10.5mg/dL
- Ionized calcium >1.3 mmol/L
- Causes
  - Usually due to malignancy, hyperparathyroidism
- Signs and Symptoms
  - Muscle weakness, anorexia, N/V, constipation, ventricular arrhythmias, lethargy, depression, psychosis, coma
- Treatment
  - Beyond the scope of this discussion
  - ECG changes: volume expansion, loop diuretics, HD
  - Treat underlying disorder

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