

# Major intra and extra cellular electrolytes

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# Electrolytes

Substances whose molecules dissociate into ions when they are placed in water.

***CATIONS (+)    ANIONS (-)***

Medically significant / routinely ordered electrolytes include:

Cation: Positively Charged particles    Anion: Negatively charged particles.

Sodium (Na<sup>+</sup>)

Potassium (K<sup>+</sup>)

Calcium (Ca<sup>++</sup>)

Magnesium (Mg<sup>++</sup>)

Chloride (Cl<sup>-</sup>)

Bicarbonate (HCO<sub>3</sub><sup>-</sup>)

Phosphate (HPO<sub>4</sub><sup>-</sup>)

# Electrochemical Equivalence

**Equivalent ( $Eq/L$ ) = moles x valence** ▶

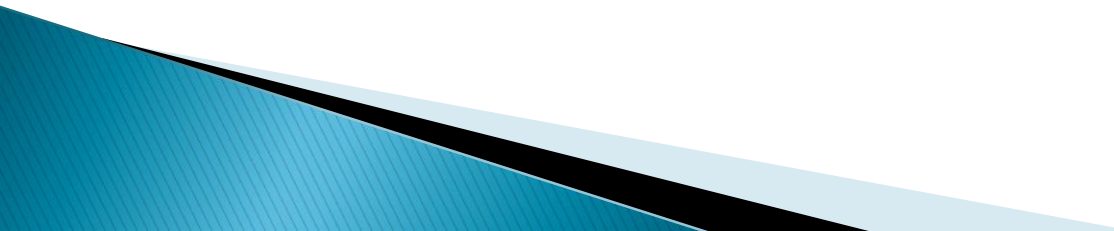
**Monovalent Ions ( $Na^+$ ,  $K^+$ ,  $Cl^-$ ):** ▶

1 milliequivalent ( $mEq/L$ ) = 1 millimole ◦

**Divalent Ions ( $Ca^{++}$ ,  $Mg^{++}$ , and  $HPO_4^{2-}$ )** ▶

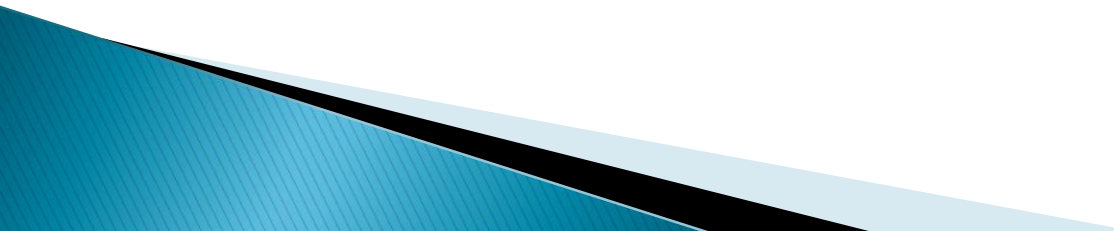
1 milliequivalent = 0.5 millimole ◦

# Electrolyte Functions

- Volume and osmotic regulation
  - Myocardial rhythm and contractility
  - Cofactors in enzyme activation
  - Regulation of ATPase ion pumps
  - Acid-base balance
  - Blood coagulation
  - Neuromuscular excitability
  - Production of ATP from glucose
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# Sodium

## Functions

- Most abundant extracellular cation.
  - Regulates body water distribution.
  - Aids nerve impulse transmission.
  - Aids transfer of calcium into cells.
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## Regulation of Sodium

- Concentration depends on:
  - intake of water in response to thirst
  - excretion of water due to blood volume or -osmolality changes
- Regulation of sodium
  - Kidneys can conserve or excrete  $\text{Na}^+$  depending on ECF and blood volume
    - by aldosterone
    - and the renin-angiotensin system  
this system will stimulate the adrenal cortex to secrete aldosterone.

Aldosterone

*From the (adrenal cortex)*

*Functions*

*promote excretion of K  
in exchange for  
reabsorption of Na*

Sodium normal values

Serum – 135–148 mEq/L

## Clinical Features: Sodium

**Hyponatremia:  $< 135$  mmol/L**

Increased  $\text{Na}^+$  loss

Aldosterone deficiency

*Addison's disease (hypo-adrenalism, result in ↓ aldosterone)*

Diabetes mellitus

*In acidosis of diabetes, Na is excreted with ketones*

Potassium depletion

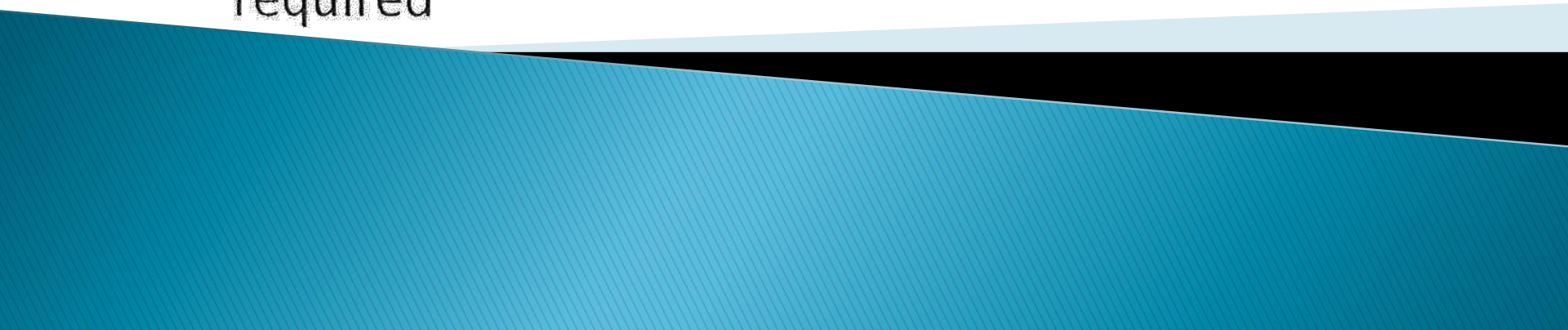
*K normally excreted, if none, then Na*

Loss of gastric contents



# **Electrolyte replacement therapy**

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- Identify when electrolyte replacement is needed and underlying cause
    - Potassium, Magnesium, Calcium, Phosphorous
  - Understand different formulations, route, dosage and adverse effects of replacement
  - Identify when goal replacement has been achieved
  - Identify when maintenance therapy may be required
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# Hypokalemia

- Usually secondary to:
  - GI loss (vomiting, diarrhea)
  - Urinary losses (diuretics)

Also think about : co-existing electrolyte abnormality (hypomagnesemia), hyperaldosteronism, insulin therapy, alkalosis)

- Indications for replacement:
  - Evidence of potassium loss
  - Significant deficit in body potassium
  - Acute therapy in redistributive disorders (periodic paralysis, thyrotoxicosis)



- Symptoms: usually manifest when serum K <3.0
  - Muscle weakness (K <2.5), cramps
  - Respiratory muscle weakness
  - GI symptoms: anorexia, nausea, vomiting
  - Cardiac arrhythmias: atrial tachycardia, junctional tachycardia, AV block, ventricular tachycardia or fibrillation
  - sinus bradycardia, ST segment depression, decreased amplitude of T-wave, increased amplitude of U-wave.
  - If prolonged hypokalemia: functional changes in the kidney and glucose intolerance

# Therapy

- Calculate potassium deficit (if normal distribution is present)
  - Acute: 0.27meq/L decrease in serum K<sup>+</sup> for every 100meq reduction in total potassium stores
  - Chronic: 1meq/L decrease in serum K<sup>+</sup> for every 200-400meq reduction in total potassium stores

## Simplified:

$$\frac{\text{Goal K} - \text{Serum K}}{\text{serum Cr}} \times 100 = \text{total meq K required}$$

10meq of KCL will raise the serum K by ~.1meq/L

# Formulations

- **Potassium Chloride : PREFERRED AGENT**
  - Most patients with hypokalemia and alkalosis are also chloride depleted
  - Raises serum potassium at a faster rate
  - Available as liquid, slow release tablet or capsule, and IV
  - **Oral: 40meq tid-qid; IV 10meq/hr- 20meq/hr**
- **Potassium Bicarbonate/Citrate/Acetate:**
  - can be used in patients with hypokalemia and metabolic acidosis
- **Potassium Phosphate:**
  - Rarely used (Fanconi syndrome with phosphate wasting)



# Ongoing Losses

- In general, use oral therapy
- KCL with normal or elevated serum bicarb
- Potassium citrate/acetate/bicarbonate in presence of acidosis (diarrhea)
- no need for continued supplementation with chronic renal potassium wasting (potassium sparing diuretic is more effective):
  - Chronic diuretic therapy
  - Primary aldosteronism

# Adverse Effects

- Hyperkalemia
- Potassium is osmotically active- can increase tonicity of IV fluids
- Oral therapy- pills are large, can be difficult to swallow
- Peripheral IV therapy:
  - Pain
  - Phlebitis

Make sure to recheck serum potassium 2-4 hours later to assess response to therapy



# Goal of Therapy

- Prevent life threatening complications
- Urgency of replacement depends on severity, rate of decline and co-morbid conditions
  - Elderly
  - underlying heart disease
  - on digoxin or anti-arrhythmic drugs

# Example

- 72 year old female admitted for weakness and dehydration due to acute gastroenteritis. She is having up to 6 BM/day. Her serum K on admission is 2.5 meq and serum Cr is 2.0. ECG reveals u-waves.

1. How much potassium do you order?

$$\frac{4-2.5}{2} \times 100 = 75\text{meq}$$

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2. What formulation do you choose?

KCL; if bicarb is low then consider potassium bicarb or acetate

3. What route should the potassium be administered?

40meq (initial) oral and 40meq IV; (re-assess 2-4 hours later and give more orally if needed and tolerating po)

3. Serum potassium remains low, what else could be contributing?

Low magnesium, ongoing diarrhea

# Hypomagnesemia

- Average daily intake: 360mg
- Presence of low magnesium (nearly 12% of hospitalized patients) suspected in following cases:
  - Chronic diarrhea
  - Hypocalcemia
  - Refractory hypokalemia
  - Ventricular arrhythmias
- Symptoms/Signs :
  - Tetany (seizures in children/neonates)
  - Hypokalemia
  - Hypoparathyroidism → hypocalcemia (<1.2mg/dL)
  - Vitamin D deficiency (due to low calcitriol)
  - ECG changes: widened QRS, peaked T-waves, → diminution, PR interval prolongation,
  - Ventricular arrhythmias (especially during ischemia or bypass)

# Therapy

- IV if symptomatic (magnesium sulfate)
  - 1.5-1.9mg/dL → 2g magnesium sulfate IV
  - 1.2-1.4mg/dL → 4g
  - .8-1.1mg/dL → 6g
  - <.8mg/dL → 8g
  - **Low K/Ca w/ tetany/arrhythmia: 50meq (~6g) of IV Mg given slowly over 8-24 hrs**
- Oral if asymptomatic: each tablet contains 60-84mg, give 2-4 tabs/day in mild cases, 6-8 tabs for severe depletion
  - Slow Mag (magnesium chloride)
  - Mag-Tab SR (magnesium lactate)
  - Magnesium Oxide
- Avoid replacement in patients with reduced GFR
- Treat underlying disease ( diuretics, alcohol, uncontrolled diabetes)



# Therapy

- Goal of therapy:
  - maintain plasma magnesium concentration over 1.0mg/dL acutely in symptomatic patients
  - In cardiac patients, maintain Mg >1.7 (usually goal 2.0mg/dL) to avoid arrhythmias
  - Serum levels are poor reflection of actual body stores (mostly intracellular) so aim for high-normal serum level
- Adverse effects:
  - Abrupt elevation of plasma Mg can remove the stimulus for Mg retention and lead to increased excretion
  - Diarrhea
  - Drug interactions
  - Magnesium intoxication

# Hypocalcemia

- Clinical Manifestations:
  - Acute: serum Ca <7.5mg/dL
    - Neurologic: tetany (from paresthesias to seizures and bronchospasm)
    - Cardiac: prolonged QT, hypotension, heart failure, arrhythmia
    - Papilledema
    - Psychiatric manifestations
  - Chronic:
    - EPS, dementia, cataracts, dry skin
- Etiology:
  - Vitamin D
  - PTH
  - Hypomagnesemia
  - Drugs

# Therapy

- Correct for albumin
  - Ca lower by 0.8mg/dL for every 1g/dL reduction in serum albumin
  - or check ionized calcium
- Level can be altered by acid/base disturbance
- Symptomatic or acute serum Ca <7.5mg/dL:
  - IV Calcium gluconate 1-2g(amp) over 10-20min (temporary rise for 2-3 hrs, must be followed by slower infusion 50mL/hr if Ca remains low)
- Asymptomatic and serum Ca >7.5mg/dL or chronic:
  - Oral therapy: calcium carbonate or citrate 1-2g/day (500mg bid-qid)
- Add Vitamin D in following cases:
  - Hypoparathyroidism: Vitamin D (Calcitriol .25-.5mcg bid)
  - Vitamin D deficiency: 50,000IU/week for 6-8 weeks then 800-1000IU daily
    - Ergocalciferol (D3)
    - Cholecalciferol (D2)

# Therapy

- **Goals of therapy:**
  - Treat and prevent manifestations of hypocalcemia
  - In hypoparathyroidism: to raise serum Ca to low-normal range (8.0-8.5mg/dL)
- **Adverse Effects:**
  - Rapid infusion- bradycardia, hypotension
  - Extravasation- tissue necrosis
  - Hypercalcemia
  - Hypercalciuria
  - Constipation
  - Hypophosphatemia
  - Milk-alkali syndrome



# Example

35 y/o male with hypoparathyroidism , presents with serum Ca of 6.2, albumin of 3.8, ionized Ca .77. Has some mild muscle cramps, otherwise asymptomatic.

1. How do you initially treat his hypocalcemia?
  - IV Calcium Gluconate 1g IV over 10-20min
2. Repeat serum Ca is 6.6, how do you proceed with treatment?
  - start Calcium gluconate 1mg/mL in D5W 50mL/hr infusion
2. After initial treatment, what maintenance regimen should you initiate?
  - Calcitriol (.5mcg bid, titrated up in this patient)
  - Calcium carbonate (1950mg po tid in this patient)

# Hypophosphatemia

- Due to:
  - Redistribution
  - Decreased intestinal absorption (small bowel)
  - Increased urinary excretion
- Common situations:
  - Chronic alcoholism
  - IV hyperalimentation w/o phosphate supplementation
  - Refeeding syndrome
  - “Hungry Bone” syndrome
  - Respiratory alkalosis (hyperventilation)
  - Chronic ingestion of antacids (containing aluminum or Mg)
  - Hyperparathyroidism (primary or secondary)
  - Vitamin D deficiency
  - Fanconi syndrome (associated with multiple myeloma in adults)

# Hypophosphatemia

- **Signs/Symptoms:** <2.0mg/dL, severe usually when serum PO<sub>4</sub> <1.0mg/dL

## Acute:

- Metabolic encephalopathy- irritability, paresthesias → confusion, seizure, coma
- Respiratory failure due to weakened diaphragm
- Reduction in cardiac output leading to heart failure
- Proximal myopathy, dysphagia, ileus
- Elevated CPK, rhabdomyolysis
- Coagulopathy with thrombocytopenia

## Chronic:

- Hypercalciuria
- Increased bone resorption: Osteomalacia, Ricketts

# Treatment

- Usually aimed at treating the underlying cause (resolution of diarrhea, Vit D therapy, d/c antacid, etc.)
- If tx is needed, oral therapy is preferred
  - Asymptomatic, serum PO<sub>4</sub> <2.0mg/dL or symptomatic with serum PO<sub>4</sub> 1.0-1.9mg/dL
  - Available as tablet and powder/packets (sodium phosphate, potassium phosphate) 250-500mg tid-qid (w/ meals ) over 24 hours
  - Decrease dose by one-half in patients with reduced GFR
  - Increase dose in severely obese patients
  - Recheck after 12 hours to determine if additional/continued supplementation is required



# Treatment

- IV therapy if symptomatic and serum PO<sub>4</sub> <1.0mg/dL
  - sodium phosphate is preferred
  - Weight based
    - PO<sub>4</sub> >1.3mg/dL: .08-.24mmol/kg over 6 hours
    - PO<sub>4</sub> <1.3mg/dL: .25mmol-.05/kg over 8-12 hours
    - Increased dosage for critically ill patients in ICU
    - Frequent monitoring- recheck levels every 6 hours
    - Switch to oral when patient able or serum PO<sub>4</sub> >1.5mg/dL
- Goal of therapy: increase serum PO<sub>4</sub> to 2.0mg/dL
- Side effects of therapy:
  - Oral: Diarrhea, nausea, hyperkalemia (K-phos)
  - IV: Hyperphosphatemia → hypocalcemia, AKI, arrhythmia
- Maintenance therapy is not usually required

	Preferred Route	Preferred Formulation	Dosage	Response
Potassium	Oral	Potassium Chloride	10meq tabs	.1 increase serum K for 10meq given
Magnesium	Oral	Magnesium Oxide	2-4 tabs/day (420mg; 20meq/tab)	.5 increase for 2g (50meq) IV
	IV- arrhythmia	Magnesium Sulfate	2g IVP or slow infusion	
Calcium	IV- acute	Calcium Gluconate	1-2amp (rapid)  1mg/mL in D5W, 50mL/hr Infusion	.5mg/dL increase serum Ca for 1g given
	Oral- maintenance	Calcium Carbonate	1-2g/day	
Phosphate	Oral	Sodium Phosphate (neutra-phos)	1-2 packet tid-qid 1packet=250mg or 8mmol (weight based)	1.2mg/dL increase serum PO4