Electrolytes

**Calcium:**

**WHERE:** 99% in bones/teeth, 1% in blood and rapidly exchangeable with ECF
- ~1/2 is bound to proteins, mainly albumin
- Biologically active form is ionized form (unbound)

**ROLES:** bone metabolism, platelet adhesion, contraction of cardiac, skeletal and smooth muscles, neuromuscular activity, endocrine and exocrine secretions, blood coagulation

**HOMEOSTASIS:**
1. PTH: released when low serum [Ca$^{2+}$]:
   - Stimulates Ca$^{2+}$ release from bones
   - ↑ Ca$^{2+}$ uptake in kidneys
   - ↑ hydroxylation of inactive Vit D to Calcitriol
   - Calcitriol (hormonally active form of Vit D) ↑ Ca$^{2+}$ uptake in intestines
2. Thyroid gland: releases calcitonin when Ca↓
   - Calcitonin: inhibits bone resorption of calcium and renal absorption of Ca$^{2+}$ (and phosphate)

**HYPERCALCEMIA:**

Mild: Total 2-6.3, Ionized: 1.4-2; Mod: Total 3-3.5, Ionized: 2.25-2.75; Severe: Total > 3.5, Ionized > 2.5

Symptoms: Stones, Bones, Abdominal Moans, Psychic Groans

<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>↓ concentration, fatigue, confusion, coma</td>
</tr>
<tr>
<td>CV</td>
<td>Bradycardia, Hypertension, QT interval shortening</td>
</tr>
<tr>
<td>GI</td>
<td>N/V, anorexia, constipation, pancreateitis, PUD</td>
</tr>
<tr>
<td>Renal</td>
<td>Polyuria, nephrolithiasis, acute/chronic renal insufficiency</td>
</tr>
<tr>
<td>MSK</td>
<td>Muscle weakness, bone pain, osteopenia/osteoporosis</td>
</tr>
</tbody>
</table>

**Causes:** Hyperparathyroidism, Malignancy, Milk alkali syndrome (excessive CaCO$_3$)
$\rightarrow$ metabolic alkalosis $\rightarrow$ excretion; **Drug Causes:** Thiazides, Lithium, Calcium Carbonate, Tamoxifen, Vitamin D, Calcitriol, Topical calcipotriol

**GoTs:** Resolve symptoms, Correct underlying cause, Restore calcium balance, Prevent complications (renal failure, nephrolithiasis, metastatic calcification)

**Tx:**
- Remove underlying causes
- Adequate oral or IV hydration (to prevent nephrolithiasis)
- If symptomatic:
  - saline infusion, bisphosphonates
  - If aggressive therapy needed: for severe cases, may consider hemodialysis
  - saline infusion for volume expansion (correct intravascular volume depletion) + furosemide
  - salmon calcitonin (rapid onset, efficacy limited to 1-2 48 hours d/t tachyphylaxis)
  - zoledronic acid or pamidronate IV (takes 2-4 days for maximum effect)
  - denosumab (not cleared by kidney, may be preferred in severe renal impairment)

**HYPOCALCEMIA:**

Total < 2.2, Ionized < 1.1

To correct for low albumin levels: for every 10 below 40g/L albumin, add 0.2 to your Ca$^{2+}$
also affected by acidemia + alkalaemia

**Symptoms:**

<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Irritability, depression, confusion, fatigue, seizures, syncope</td>
</tr>
<tr>
<td>HEENT</td>
<td>Dysesthesia</td>
</tr>
<tr>
<td>CV</td>
<td>Hypotension, QT prolongation $\rightarrow$ ventricular arrhythmias, CHF, angina</td>
</tr>
</tbody>
</table>
| MSK    | Tetany (paresthesias of hands/feet, cramps, weakness)
|        | Chvostek Sign: Facial muscle spasm elicited by tapping facial nerve just anterior to earlobe (ranges from twitching of lip to spasm of all facial muscles)
|        | Trousseau Sign: Adduction of thumb, flexion of MCP joints, extension of interphalangeal joints, flexion of wrists (as Ca$^{2+}$ is important for NM activity and muscular contraction)

**Causes:** PTH deficiency, Hypomagnesemia, Vitamin D deficiency or resistance (e.g. CKD), Hyperphosphatemia (binds to Ca$^{2+}$), Massive blood transfusions (citrate binds to Ca$^{2+}$)

**Hungry Bone Syndrome:** Severe and prolonged hypocalcemia despite normal or elevated PTH levels occurs after parathyroidectomy or thyroidectomy

**Drug Causes:** bisphosphonates, denosumab, calcium chelators (foscarin, chemotherapy, aminoglycosides, loop diuretics, calcimimetics (cinacalcet), Anti-convulsants (PHT, phenobarbital)

**GoTs:** Resolve symptoms, treat underlying cause, correct Ca$^{2+}$ balance, prevent complications (arrhythmias, seizures, tetany)

**Tx:**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic and/or mild to moderate</td>
<td>Oral supplementation: 1500-2000mg/day elemental calcium in 2-4 divided doses If IV: calcium gluconate 1g over 30-60 min, repeat every 6 hours prn</td>
</tr>
<tr>
<td>Severe acute and/or symptomatic</td>
<td>IV calcium gluconate 1g in 50-100ml NS or DSW over 15-30 mins – may follow with 0.3-0.8% solution (3.5g = 30-50ml) of calcium gluconate in 500-1000ml NS or DSW infused over 3-12 hrs – severe cases (seizures/tetany): calcium chloride (cause more tissue necrosis) push</td>
</tr>
</tbody>
</table>

**Concurrent hypomagnesemia**

| Common cause; correct Mg first |

Calcium carbonate: 40%; Acetate: 25%; Citrate: 21%
**Phosphate:**

**WHERE:** 85% in bone with calcium hydroxyapatite, 14% intracellular, <1% in blood
- charged ion that contains phosphorus

**ROLES:** structural element of bones, phospholipid cell membranes, nucleic acids, phosphoproteins, energy source (ATP), acid/base balance

**HOMEOSTASIS:** closely linked to calcium homeostasis
- usually well-managed...except when there is kidney failure

1. Calcitriol: released when serum phosphate is low
   - ↑ phosphate absorption from GI
   - ↓ renal excretion of phosphate
2. PTH: directly causes phosphate resorption from bone, ↑ renal excretion (but ↓ reabsorption of Ca++)
3. Alkalosis: phosphate shifts intracellularly

**HYPOphosphatemia**
Normal: 0.81-1.45; Mild: 0.65-0.81; Mod: 0.32-0.65; Severe < 0.32

**Symptoms:**
- Metabolic encephalopathy syndrome (irritability, apprehension, numbness, confusion, seizures, coma)
- Respiratory failure
- Myocardial dysfunction, CHF, arrhythmias
- Muscle weakness, rhabdomyolysis
- Chronic: rickets and osteomalacia

**Causes:** ↓ GI absorption (↓ dietary intake, Vit D deficiency/resistance, chronic diarrhea), ↓ renal tubular absorption (hyperparathyroidism, alcoholism, Vit D deficiency), extracellular to intracellular redistribution (resp alkalosis, hungry bone syndrome, tx of DKA)

**Drug Causes:** Phosphate binding drugs (sucralfate, calcium carbonate, aluminum/magnesium antacids, Sevelamer, Lanthanum carbonate), ↑ renal elimination of phosphate (diuretics – acetazolamide and osmotic diuretics)

**GoTs:** Resolve symptoms, treat underlying cause, correct phosphate balance, prevent complications (osteomalacia, arrhythmias, organ failure)

**Tx:** Oral is preferred over IV as it requires less monitoring (QO or Q12hr vs. Q6hr) but PO (esp liquid) can cause quite interactions (osteomalacia, arrhythmias, organ failure)
- PO: Phosphates solution 500mg (16 mmol)/4mL; Phosphate tablets 250mg (8 mmol)
- IV: Na’phosphate (3 mmol/mL;4 Na’mmol/mL); K’phosphate (3 mmol/mL;4.4 K’mmol/mL)

**Recent and uncomplicated:** Phosphate solution 500mg 2-4 times daily or 15mmol PO4³⁻ x 1
**Symptomatic:** 15 mmol PO4³⁻ IV x 1-3 doses Q 8H (levels should be taken no sooner than 4 hrs after infusion or next morning + check serum K⁺ and Ca⁺⁺)

**Potassium:**

**WHERE:** 98% intracellular cation (75% in skeletal muscle), 2% extracellular → 3.5-5mmol/L
- Influx via Na-K ATPase, Efflux via K+ channels
- Maintains resting membrane potential

**HOMEOSTASIS:**
- Excretion of potassium 90% by kidneys (↑ by aldosterone), 10% by stool and sweat
- Mechanisms that alter [K⁺]: K⁺ intake, K⁺ excretion, Trans-cellular shift

**HYPERkalemia:**
Mild: 5-5.9 (ECG: Tall, peaks T waves, Prolonged PR segment); Mod: 6-6.4 (Absent P wave, Prolonged QRS segment, ST-segment elevation), Severe ≥6.5 (Progressive QRS complex widening, sine wave, ventricular fibrillation, asystole)

**Symptoms:**
- Fatigue, malaise, dizziness
- Arrhythmias, bradycardia, palpitations
- N/V/D
- Weakness, cramping paralysis
- Symptoms associated with renal failure + immediate effect

**Causes:** ↑ dietary intake, renal disorder, Addison’s disease (low aldosterone), diabetes, cell lysis (e.g. TSL), metabolic acidosis, cell trauma (e.g. post-surgery, lab error)

**Drug Causes:** potassium supplements, ↓ aldosterone (ACEI/ARBs, K+ sparing diuretics, NSAIDs, Heparin, Non-selective BB), block Na⁺ channels (K+ sparing diuretics, TMP-SMX), Transcellular shift (Digoxin, NSAIDs, Non-selective BB, Anesthetics – e.g. succinylcholine)

**GoTs:** Resolve symptoms, correct underlying causes, correct potassium balance, prevent complications (e.g. CV complications, respiratory paralysis)

**Tx:**
- Cardiac membrane stabilization (will not change K+)
  - Calcium gluconate 1-3 g IV over 2-5 mins *preferred as less risk of tissue necrosis and less frequent side effects (2.2mEq/10mL)
  - Calcium chloride 1g IV over 10 mins *greater bioavailability but higher risk of tissue necrosis (6.8mEq/10mL)
- Intracellular K⁺ shift: stimulate Na-K ATPase pump to pull K⁺ into cells, rapid but temporary effects, require other therapies to change total body K⁺ levels
  - Insulin + glucose 5-10 units IV + 50mL of 50% dextrose (25g)
  - β2-agonists (salbutamol) – 10-20mg nebulized/inhaled over 10 min
  - Sodium bicarbonate 50-100 mEq IV over 2-5 min, max ↓ 0.4 mEq/L *not used unless metabolic acidosis present*
- Elimination: reduction of total body K⁺ stores
  - Loop diuretics: Furosemide 20-40mg IV (not useful if patient is anuric)
  - Resins: Sodium polyxerate (Kayexalate), Calcium resonium (delayed onset of 2-6 hrs, efficacy, risk of intestinal necrosis)
  - Dialysis: if above agents fail or hyperK⁺ associated with renal failure + immediate effect
HYPOkalemia
Mild: 3-3.4 (ST-segment depression, T wave flattening), Mod: 2.5-2.9 (Presence of U waves), Severe <2.5 (T wave inversion)

Symptoms:

<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Fatigue, malaise, lethargy</td>
</tr>
<tr>
<td>CVS</td>
<td>Arrhythmias, palpitations</td>
</tr>
<tr>
<td>GI</td>
<td>N/V, constipation</td>
</tr>
<tr>
<td>GU</td>
<td>Polyuria</td>
</tr>
<tr>
<td>MSK</td>
<td>Weakness, spontaneous contraction and spasms, ascending paralysis</td>
</tr>
</tbody>
</table>

Causes: ↓ chronic dietary intake, hypomagnesemia (impairs Na-K ATPase), Diarrhea/Vomiting, Hyperglycemia (↑ urinary flow), Cushing syndrome (high aldosterone), excessive sweating, excessive burns, metabolic acidosis (initially hyperK+ then hypok+ d/t osmotic push), refeeding syndrome (induces insulin release)

Drug Causes: Thiazide diuretics, loop diuretics, mineralocorticoids + high dose glucocorticoids, amphotericin, high dose penicillins, aminoglycosides, cisplatin, laxative abuse – GI loss, Insulin, β-adrenergic agents, levothyroxine, caffeine/theophylline, decongestants, verapamil (high dose)

GoTs: Resolve symptoms (if present), Correct underlying causes, Correct K+ balance, Prevent complications (i.e. CV complications)

Tx: Once K+ is > 3.5-3.7, can stop supplement and monitor afterwards
– Correct magnesium deficiency if present
– Preventative: PO 20-40 mmol/day
– Mild to moderate hypokalemia in asymptomatic patient or on digoxin: PO 40-200mmol/day in divided doses
– Severe or symptomatic hypokalemia: IV 20-40 mmol/day, Max infusion rates: Central line = 40mmol/hr, Peripheral line = 20 mmol/hr (due to risk of phlebitis)

Available options:

<table>
<thead>
<tr>
<th>Salt</th>
<th>Form</th>
<th>Strength</th>
<th>Elemental K+</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chloride</td>
<td>Tablet (Slow-K)</td>
<td>600mg</td>
<td>8 mmol</td>
<td>Most common</td>
</tr>
<tr>
<td></td>
<td>Large orange</td>
<td>1500mg</td>
<td>20 mmol</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tablet (K-Dur)</td>
<td>Liquid</td>
<td>1500mg/15mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Large white +</td>
<td>Injection</td>
<td>2 mmol/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>dissolvable for NG</td>
<td></td>
<td>20 mmol/15mL</td>
<td></td>
</tr>
<tr>
<td>Citrate</td>
<td>Effervescent tablet (K-lyte)</td>
<td>2.5g</td>
<td>25 mmol</td>
<td>Useful for NG</td>
</tr>
<tr>
<td>Acetate</td>
<td>Injection</td>
<td>-</td>
<td>4 mmol/mL</td>
<td>Useful in metabolic acidosis to correct acidemia</td>
</tr>
</tbody>
</table>

Magnesium:
WHERE: Found in bone >50%, muscle and soft tissues, 2nd most prevalent intracellular cation (>95% bound to other molecules, mostly ATP)

ROLES: Extracellular Mg – neuromuscular excitability and nerve conduction

HOMEOSTASIS: Regulated by intestines, bone and kidneys; Degree of absorption and reabsorption in small intestines and kidneys is determined by serum [ ] and minimally by PTH

HYPERmagnesemia:
Mild: 1.1-1.6, Mod: 1.6-5.1, Severe >5.1 (ECG changes: similar to hyperK+, ↑ T-wave amplitude, QRS widening, PR prolongation)

Symptoms:

<table>
<thead>
<tr>
<th>System</th>
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</tr>
</thead>
<tbody>
<tr>
<td>CVS</td>
<td>Hypotension, bradycardia, cardiac arrest</td>
</tr>
<tr>
<td>GI</td>
<td>N/V</td>
</tr>
<tr>
<td>Derm</td>
<td>Cutaneous flushing</td>
</tr>
<tr>
<td>MSK</td>
<td>Hyporeflexia, muscle paralysis (particularly facial)</td>
</tr>
</tbody>
</table>

Causes: Renal failure, hypothyroidism, Addison’s Disease, Tissue breakdown (sepsis, large burns) Drug causes: Lithium, excessive antacid/laxative use

GoTs: Relieve symptoms, correct magnesium balance, correct underlying causes, prevent complications

Tx:
♦ Cardiac membrane stabilization – IV calcium gluconate
♦ Restrict intake of Mg containing foods/products
♦ Enhance elimination
– Diuresis (saline or loop diuretics)
– Dialysis if severe

HYPOmagnesemia:
Mild/mod: 0.5-0.65; Severe <0.5 (nonspecific, potential ST segment depression, possible U waves, QT prolongation and Torsades de Pointes)

Symptoms: often asymptomatic

<table>
<thead>
<tr>
<th>System</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>Confusion, weakness, seizures</td>
</tr>
<tr>
<td>HEENT</td>
<td>Nystagmus</td>
</tr>
<tr>
<td>CVS</td>
<td>Arrhythmias</td>
</tr>
<tr>
<td>MSK</td>
<td>Parasthesias, tremors, twitches, twitches, spasms</td>
</tr>
</tbody>
</table>

Causes: malnutrition, alcoholism, pancreatitis, GI abnormalities, Renal tubular defects, Hyperthyroidism, Hyperaldosteronism/Cushing, DM, Refeeding, Hungry bone syndrome Drug Causes: High dose catecholamines, insulin, loop diuretics, antimicrobials (AMG, AmB), chemotherapy (cisplastin, cyclosporin), Antivirals, PPIs (chronic), digoxin, tacrolimus, theophylline
**GotTs**: Relieve symptoms, correct underlying causes, correct magnesium imbalance, correct associated electrolyte abnormalities

**Tx:**
♦ Mild to mod: PO 12.5-17.5 mmol/day
  – Magnesium gluconheptonate 60-90mL/day in 3-4 divided doses
  – Magnesium complex 300-400mg/day in 2-3 divided doses
  – IV Magnesium sulphate 5g (20 mmol) in 100mL D5W or NS over 3-4 hrs q12-24h x 3-4 doses
♦ Severe:
  – IV Magnesium sulphate 5g (20 mmol) in 100mL D5W or NS over 3-4 hrs q12-24h x 3-4 doses
♦ Renal insufficiency and Cardiac arrhythmia
  – IV Magnesium sulphate 2g (8 mmol) in 50mL D5W or NS over 30-60 min x 1 dose
  – IV Magnesium sulphate 5g (20 mmol) in 100mL D5W or NS over 3-4 hrs x 1 dose

**Options:**

<table>
<thead>
<tr>
<th>Salt</th>
<th>Form</th>
<th>Strength</th>
<th>Elemental Mg⁺⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucoheptonate (Rougier)</td>
<td>Liquid</td>
<td>100mg/mL</td>
<td>5mg/mL (0.4mEq/mL, 0.2 mmol/mL)</td>
</tr>
<tr>
<td>Complex</td>
<td>Tablet</td>
<td>50</td>
<td>2 mmol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100mg</td>
<td>4 mmol</td>
</tr>
<tr>
<td>Sulphate</td>
<td>Injection</td>
<td>500mg/mL</td>
<td>2 mmol/mL</td>
</tr>
</tbody>
</table>