Hypokalemia (<3.5mEq/L)
- 98% intracellular (150mEq/L) vs 2% extracellular w/ 0.4% in plasma (~4mEq/L) this is maintained by the 3Na/2K ATP pump
- 90% of potassium is absorbed by GI (daily intake is 100mEq/d with 90mEq/d absorbed and 10mEq/d excreted in stool) typically absorption does not change much
- When potassium is filtered (900mEq/d) a fixed amount (~90%) is always reabsorbed by PCT and LOH/DCT while the remaining 10% is variably reabsorbed / secreted at CD depending on aldosterone levels (which reflect plasma potassium levels) and direct plasma potassium concentration, in addition distal sodium delivery, and distal non-reabsorbable anion delivery (in general 90mEq/d is excreted)

Redistribution Transcellular Shift Into Cells

- Stimulates Na/K Pump
  - Insulin
  - Osmotic Diuresis
  - Catecholamines (↑ Epi/β2 tone during exercise, bronchodilators, stress, infection, MI, etc. shift the K+ that leaks out of depolarized muscle cells back into liver and muscle cells by stimulating Na/K pump but after exercise NEP/β1 prevents potential hypokalemia from Epi by inhibiting Na/K)
  - HyperTH (esp in Asian Males who for some reason have higher proportion of Na-K ATPase pumps, thyroid hormone stimulates this pump, so when these specific pts go into thyrotoxicosis they can precipitate an event that is similar to Hypok PP)
  - Intoxication w/ Chloroquine, Risperidone, Seroquel, Barium, Cesium
- Alkalosis (H+ enters cells as a buffer and in turn K+ exits cells to maintain electroneutrality (↑0.1pH → ↓0.5mEq))
- Hypo Periodic Paralysis (partial penetrance AD mutation of CACNA1S/SCN4A genes resulting in a dysfunctional calcium/sodium channel in skeletal muscle which somehow leads to hypokalemia leading to muscle weakness to overt paralysis, manifests during adolescence, triggered by strenuous activity, high carb meals, stress, sudden changes in temp, excitement, noise, light, etc. (events associated w/ release of epi and insulin) lasts for hrs to days, dx w/ CMAP (Compound Muscle Amplitude Potential) which is an exercise EMG (NB genetic dx is unreliable), prognosis varies with full recovery to chronic weakness to permanent muscle damage, interestingly migraines are also common, Tx: no DS b/c stimulates insulin, beta-blockers, azetazolamide, magnesium, potassium (highly variable response) NB confirm pt does not have hyperKPP
- Nonoral or Highly Metabolic States like (1) anemias treated w/ VitB12/Folate (2) rapidly proliferating cancers esp Acute Leukemia, non-Hodgkins Lymphomas, Myeloma (more cells means more K stored in cells) (3) neutropenic pts getting G-CSF (3) refeeding syndrome

Decreased Intake
- Low Diet (rarely a cause b/c the kidneys can effectively reabsorb almost 100% of potassium that is filtered)

<table>
<thead>
<tr>
<th>Extra Renal Loss (usually more acute)</th>
<th>Renal Loss (usually more chronic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spot Urine K &lt;15mEq/L</td>
<td>Spot Urine K &gt;15mEq/L</td>
</tr>
<tr>
<td>24 Hour Urine K &lt;30mEq/D</td>
<td>24 Hour Urine K &gt;30mEq/D</td>
</tr>
<tr>
<td>TTG &lt;3</td>
<td>Trans Tubular Potassium Gradient (UjP,Ren/KJ,Ur) &gt;3</td>
</tr>
<tr>
<td>Alkalosis (Upper GI)</td>
<td>Alkalosis (Lower GI)</td>
</tr>
<tr>
<td>Acidosis (PCT Problem)</td>
<td>Acidosis (PCT Problem)</td>
</tr>
<tr>
<td>LOH/DCT Problem</td>
<td>LOH/DCT Problem</td>
</tr>
<tr>
<td>CD Problem</td>
<td>CD Problem</td>
</tr>
</tbody>
</table>

Vomiting and Nausea
- Diarrhea, Fistula, Villous Adenoma, VIPoma, Laxative Abuse (Severe Direct K Loss > Acidosis 2/2 HCO3 Loss) Lower GI [K] 20-50

Direct K Loss +
- Gastric Acid Loss
- Hyperaldosteronemia

Alkalosis 2/2
- Gastric Acid Loss and b/c of the increased filtered bicarb more sodium is delivered distally therefore these pt also have a component of renal loss
- Upper GI [K] 5-10

Acidosis
- Normotensive
  - Impaired PCT Reabsorption: any type of tubulointerstitial dz, certain drugs damage PCT (aminoglycosides, amphotericin B, cisplatin, cyclosporine, etc), Type II RTA

- Normotensive
  - Impaired LOH/DCT Reabsorption: hypoMg, any type of tubulointerstitial dz, Loop Diuretics / Bartter’s and Thiazide Diuretics / Gittleman’s (this effect also increases distal sodium delivery)


diuretics
- Bartter’s
- Thiazide
- Diuretics
- Gittleman’s

Alkalosis/Hypertension
- High Mineralocorticoid (stimulated by ↓ EAV via AI and directly by ↑ K+) absorbs sodium and in turn secretes potassium (remember some potassium is reabsorbed distally exchanging for H+ hence alkalosis but the net effect is a potassium secretion) (refer to hypphrenal notes)

Alkalosis/Nonresponsive
- Increased Distal Sodium (eg. PCT problems, LOH/DCT problems) allowing for more sodium for aldosterone uptake and thus allows for more potassium to be secreted
- Nonreabsorable Anions Delivery (eg. Bicarb from vomiting and acetazolamide, ketones in DKA, toluene) increased electrical gradient driving potassium into lumen

Acidosis/Nonresponsive
- Type I RTA

Signs & Symptoms

Paradigm: hypok → more negative resting membrane potential (hyperpolarization) hence harder to depolarize to threshold potential (sympt when K<2.5 or when decreases are acute) NB removing calcium lowers the threshold potential so in theory the difference (K+ RMP and TP is “normal”
- Cardiac: QT Prolongation + ST Depression + T Flattening/Inversion + U wave
  - Ventricle Ectopy (PVCs→VT→VF) occurs only when other conditions exists such that hypokalemia is proarrhythmic but does not cause arrhythmia by itself
  - NB no correlation b/t EKG changes and K levels unlike in hyperkalemia
- Skeletal: extremity muscle weakness, fatigue, myalgia, cramps, etc (from legs up) → flaccid paralysis w/ hypok → respiratory failure
- Smooth: constipation → paralytic ileus w/ V and distension
- Neurop: paresthesia, hyporeflexia
- Other
  - Dioxin Toxicity b/c hypokalemia prevents Na/K pump from working as well and thus acts kind of like dig
  - Hepatic/Renal Encephalopathy b/c hypokalemia causes increased renal ammonia production
- Nephrogenic DI b/c hypokalemia causes decreased tubular responsiveness to ADH

Treatment

Asymptomatic and b/t 2.5-3.5 (if 2/2 a redistribution etiology then treat underlying cause first before giving potassium):
- PO KCl 20-40, 25-50mEq Q4-6hrs or just one dose if slightly low
- Two Types of KCl: K-Dur (big horse pill) 20mEq vs K-Lyte (horrible tasting powder dissolved in water) 25mEq
- Foods: dried fruit, nuts, bananas, oranges, tomatoes, spinach, potatoes, meat, etc are often not effective

Symptomatic or <2.5 regardless if it is a redistribution or not:
- Tele, Neuro/Resp Checks Q2hrs, Monitor Mg and Replete
- IV KCl ≤10mEq/hr (peripheral IV) ≤20mEq/hr (central IV) in 100mL sterile water, over 1hr, add 1% lidocaine b/c K burns, actually better to give via two peripheral veins vs central line b/c of the theoretical c/o of transient hyperkalemia in the R heart from a central line predisposing to arrhythmias
- X = Cl can be used for any type of hypokalemia but certain conditions might benefit from other forms noted below
- X = HCO3 or any precursor like Citrate/Gluconate/Acetate should be used when a metabolic acidosis is present or Phosphate if a deficiency is likely especially in DKA
  - PO is better b/c larger doses can be given when compared to IV
  - NB 1mEq/L serum decrease = 300mEq total body loss therefore calculate how much potassium the pt will need by this equation (this is not the case for rises in potassium in which a 1mEq/L serum increase = 150mEq total body gain) remember to also factor redistribution in which case
- It is hard to manage hypok b/c both extra and intra cellular K+ levels are low b/c before initial hypok, K+ was leaving cell to maintain extra levels therefore normal labs BUT actually hypok and then after awhile labs show that you are hypok. When you replete the lab value stays low b/c 1st intra levels are repleted but then once repleted extra levels rise but b/c levels are usually low when treating the next day there is a big jump (3.1→3.1→3.1→3.2→3.5)
Hyperkalemia (>5.0 mEq/mL)

**Psuedohyperkalemia**
- tight/prolonged tourniquet or delayed processing of blood specimen b/c the decreased O2 results in local lactic acidosis
- severe thrombocytosis (>1,000,000) or leukocytosis (>10,000) b/c when the blood is allowed to clot, aggregation releases K+, repeat in an unclotted tube
- many times (20%) when blood is drawn it randomly hemolyzes esp if smaller gauge needles are used

- Inhibits Na/K Pump
  - DM (refer above)
  - BB (refer above)
  - Massive Blood Transfusions (stored blood in bank lacks ATP therefore after awhile Na/K pump can’t work as well and when you transfuse this blood you are giving a lot of extracellular K)
  - Intoxication: Digoxin (inhibits Na/K pump)

- Redistribution Transcellular Shift Out of Cells
  - Inhibits Na/K Pump
  - Acidosis (refer above, especially inorganic acids like HCl, effect is not as pronounced in organic acids like lactate b/c lactate can also move into cells, also respiratory acid-base causes typically do not cause much potassium changes)
  - HyperK Periodic Paralysis (refer above)
  - Catabolic or Cell Damage (refer above, trauma esp burn/crush/surgery, rhabdo, infarction esp of bowel, hemolysis, tumor lysis syndrome, profound hypothermia resulting in dead tissue, extreme exercise)
  - Hypertonicity (DKA, hyperglycemia, mannitol, glycerol, radiocontrast, sorbitol, urea) pulls water out of cells creating a gradient for potassium exit from cells
  - Increased Intake
    - High Diet (rarely a cause b/c the kidneys can effectively secrete potassium)

<table>
<thead>
<tr>
<th>Extra-Renal Gain</th>
<th>Renal Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased GFR</td>
<td>Normal GFR</td>
</tr>
<tr>
<td>PCT Problem</td>
<td>LOH/DCT Problem</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>None</td>
</tr>
<tr>
<td>Low Mineralocorticoid</td>
<td>Addison’s</td>
</tr>
<tr>
<td>TR-A (1° HypoAldo)</td>
<td>ACE-I</td>
</tr>
<tr>
<td>Heparin/Ketoconazole</td>
<td>(decreases aldo production)</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>(decreases aldo secretion)</td>
</tr>
<tr>
<td>RTA (2° HypoAldo)</td>
<td>damage to JGA and thus decreased renin production</td>
</tr>
<tr>
<td>DRI</td>
<td>DM/Lead/HIV Nephropathy</td>
</tr>
<tr>
<td>NSAID use</td>
<td>Chronic Outlet Obstruction</td>
</tr>
<tr>
<td>TRA but the CD is Unresponsive to Aldo</td>
<td>ARB</td>
</tr>
<tr>
<td>ARB</td>
<td>Congenital Psuedohypoaldosteronism Syndrome aka Gordon’s Syndrome (similar to Barter’s and Giteleman’s)</td>
</tr>
<tr>
<td>POTassium Sparing Diuretics: Aldo Blockers (spironolactone and eplerenone)</td>
<td>CD Na Channel Blockers (amiloride and triamterene BUT also trimethoprim and pentamidine)</td>
</tr>
<tr>
<td>Chronic Interstitial Nephritis</td>
<td></td>
</tr>
</tbody>
</table>

**Signs & Symptoms**

Paradigm: hyperK → less negative resting membrane potential (hypopolarization) hence easier to depolarize to threshold potential (symp when K++7 or more acute onset) NB giving calcium increases the threshold potential so in theory the difference b/t RMP and TP is “normal”

- Cardiac: T peaking (>5) → ↑QRS+↑PR+↓QT (>6) → P wave disappears + QRS/T fusion (“sine wave”) (>7) → Vtach/fib (>8) → asystole (“pull T wave up”)
- Skeletal: extremity muscle weakness, fatigue, myalgia, cramps, etc (from legs up) → paralysis w/ rhabdo→ respiratory failure
- Smooth: constipation → paralytic ileus w/ V and distension
- Neuron: paresthesia, hyporeflexia
- Other
  - decreased renal acid secretion (metabolic academia) 2/2 decreased renal ammonia production

**Treatment**

- recheck K to r/o pseudo causes
- Monitor w/ EKG
- Follow Serial K+ levels
- DC all medications that can cause hyperkalemia
- If digitalis cardiotoxicity then MgSO4 and Digitek

**Step I** If +EKG Changes then Stabilize Membranes then move onto **Step II** (TRANSIENT)

- 10mL of 10% CaGluconate/Cl = 1 amp slow IVp over 2-3min QSmin until nl EKG up to x3 then continuous infusion 0.3-0.7mEq/hr
  - CaCl has 3x more calcium than CaGluconate but causes more tissue necrosis and for some reason the presence of Cl makes it less effective
  - Check and make sure pt does not have Serum Ca >10.8mg/dL
Ca stabilizes the resting membrane potential of myocardial membrane by increasing AP threshold thereby decreasing membrane excitability and depolarization by K therefore prevents pts from dyeing but does not treat hyperK

Use cautiously in digoxin pts b/c can cause toxicity

Step II If –EKG Changes then Shift Potassium Into Cells if you suspect the cause is redistribution (TRANSIENT)

- Insulin: Regular Insulin 10U IVP x1 (not SC)+ 50mL of D50W = 1amp IVP x1 (not necessary if pt is already hyperglycemic) check DFS now and 1hr after
- Beta-2-Agonist: albuterol via MedNebs or 0.5mg IV P x1
- Bicarb: 10mL of 7.5% Sodium Bicarbonate = 1amp slow IVP over 2-3min x1

Problem: bicarbonate binds calcium therefore decreasing membrane stabilization effect therefore not really used any more

Step III Remove Potassium From Body if you suspect the cause is truly decreased renal excretion (PERMANENT)

- Loop Diuretics: furosemide Lasix 40mg IV x1 but also give fluids (the combo of thiazide and loop works even better)
- Resins: sodium polystyrene sulfonate (Kayexalate)
  - 15g(mild) – 30g(severe) mixed w/ 50mL of Sorbitol or Water PO x1
  - 30g(mild) – 60g(severe) mixed w/ 50mL of Sorbitol or Water PR x1 (acts faster)
- Two Functions:
  - (1) binds K in GI lumen preventing absorption
  - (2) stimulates Na/K pump that pumps K into lumen and Na into enterocytes
- SEs: intestinal necrosis
- NB also just inducing diarrhea works

Step IV Address Underlying Cause: dialysis for renal failure, fludicortisone for hypoaldosteronism, etc