Phosphate Handling

**A** Handling of Phosphate Along the Nephron

- Classical distal tubule
- 10% reabsorbed
- 90% remaining

**B** Proximal Tubule

- Tubule lumen
- Interstitial space
- Na Pi (Type II)
- Na Pi (Type II)

For individuals on a low-P diet, P excretion is minimal.

Phosphate filtered, excreted, or reabsorbed (mmole/min)

Physiological range of "filterable" plasma [phosphate]

Filtered

Excreted

Reabsorbed

Plasma phosphate concentration (mM)
Calcium Handling

A. HANDLING OF Ca\(^{2+}\) ALONG NEPHRON

1. PCT
   - 100% reabsorbed
   - 55% remaining
   - 45% reabsorbed

2. DCT
   - 25% remaining
   - 25% reabsorbed
   - 75% remaining
   - 0.5% of filtered load remaining

3. PST
   - 15% remaining
   - 15% reabsorbed

B. PROXIMAL TUBULE

Interstitial space
Tubule lumen
H\(_2\)O
Solute
Diffusion
\(\text{Ca}^{2+}\)
\(\text{Ca}^{2+}\)
\(\text{Na}^{+}\)

PTH: parathyroid hormone; PTHrP: parathyroid hormone-related protein.
Calcium Handling

C THICK ASCENDING LIMB (TAL)

D DISTAL CONVOLUTED TUBULE (DCT)

The Ca^{2+}-sensing receptor lowers levels of cAMP, which otherwise stimulates Na/K/Cl cotransporter.

<table>
<thead>
<tr>
<th>FACTORS AFFECTING Ca^{2+} REABSORPTION ALONG THE NEPHRON</th>
</tr>
</thead>
<tbody>
<tr>
<td>SITE</td>
</tr>
<tr>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Proximal tubule</td>
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<tr>
<td>Thick ascending limb</td>
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<tr>
<td>Distal convoluted tubule</td>
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<tr>
<td>Collecting duct</td>
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</tbody>
</table>

AVP, arginine vasopressin; PTH, parathyroid hormone.
Magnesium Handling

FACTORS AFFECTING Mg\(^{2+}\) REABSORPTION ALONG THE NEPHRON

<table>
<thead>
<tr>
<th>SITE</th>
<th>INCREASE REABSORPTION</th>
<th>DECREASE REABSORPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal tubule</td>
<td>Volume contraction</td>
<td>Volume expansion</td>
</tr>
<tr>
<td>Thick ascending limb</td>
<td>PTH, calcitonin, glucagon, AVP</td>
<td>Furosemide and related loop diuretics</td>
</tr>
<tr>
<td>Distal convoluted tubule and collecting tubules/ducts</td>
<td>Low plasma [Mg(^{2+})], Metabolic alkaliuria</td>
<td>Mannitol, High plasma [Mg(^{2+})] or [Ca(^{2+})]</td>
</tr>
<tr>
<td></td>
<td>PTH, calcitonin, glucagon, AVP, aldosterone, PGE(_2), Low plasma [Mg(^{2+})], Amiloride</td>
<td>High plasma [Mg(^{2+})] or [Ca(^{2+})], Metabolic acidosis, K(^+) or phosphate depletion</td>
</tr>
</tbody>
</table>

AVP, arginine vasopressin; PTH, parathyroid hormone.
**Physiological Role of Potassium Ions**

### A. Roles of Intracellular $K^+$

<table>
<thead>
<tr>
<th>Function</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell-voltage Maintenance</td>
<td>Net loss of $K^+$ → Cell shrinkage</td>
</tr>
<tr>
<td></td>
<td>Net gain of $K^+$ → Cell swelling</td>
</tr>
<tr>
<td>Intracellular pH Regulation</td>
<td>Net loss of $K^+$ → Cell acidosis</td>
</tr>
<tr>
<td></td>
<td>Net gain of $K^+$ → Cell alkalosis</td>
</tr>
<tr>
<td>Cell Enzyme Functions</td>
<td>$K^+$ dependence of enzymes: e.g., some ATPases, succinic dehydrogenase</td>
</tr>
<tr>
<td>DNA/Protein Synthesis, Growth</td>
<td>Lack of $K^+$ → reduction of protein synthesis, stunted growth</td>
</tr>
</tbody>
</table>

### B. Roles of Transmembrane $[K^+]_r$ Ratio

- **Resting Cell Membrane Potential**
  - Reduced $[K^+]_r/[K^+]_o$ → membrane depolarization
  - Increased $[K^+]_r/[K^+]_o$ → membrane hyperpolarization
- **Neuromuscular Activity**
  - Low plasma $K^+$: muscle weakness, muscle paralysis, intestinal distention, peripheral vasodilation, respiratory failure
  - High plasma $K^+$: increased muscle excitability; later, muscle weakness (paralytic)
- **Cardiac Activity**
  - Low plasma $K^+$: slowed conduction of pacemaker activity, arrhythmias
  - High plasma $K^+$: conduction disturbances, ventricular arrhythmias and ventricular fibrillation
- **Vascular Resistance**
  - Low plasma $K^+$: vasoconstriction
  - High plasma $K^+$: vasodilatation

ATP, adenosine triphosphate.

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**Potassium Flux**

- GI intake 100 mmole/day
- Gut 90 mmole/day
- Feces 10 mmole/day
- Reabsorbed 770 mmole/day
- Secreted 50 mmole/day
- Kidneys Filtered 810 mmole/day
- ECF 65 mmole
  - [K] = 4.5 mM
- Muscle 2600 mmoles
- Liver 250 mmoles
- Bone 300 mmoles
- RBC 250 mmoles

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The handling of an acute K+ load is first accomplished by cellular loading, then by renal excretion.

When dietary K+ is very low:
- The PCT reabsorbs 80% of filtered K+
- The Loop of Henle reabsorbs 10% of filtered K+
- The DCT reabsorbs up to 2% of filtered K+
- The IMCD reabsorbs up to 6% of the filtered K+ load.
When dietary $K^+$ is very high:

- The PCT reabsorbs 80% of filtered $K^+$
- The Loop of Henle reabsorbs 10% of filtered $K^+$
- The DCT can secrete up to 180% of filtered $K^+$
- The IMCD reabsorbs up to 20-40% of the filtered $K^+$ load.

Juxtamedullary nephron handling of $K^+$ when dietary $K^+$ is very high:

- The tDLH can secrete up to 100% filtered $K^+$
- This secreted $K^+$ (and more) is reabsorbed by the tALH, the TALH, and the medullar collecting ducts
- The net effect is the trapping of $K^+$ in the medullar interstitium.
- The DCT can raise fluid [K+] to 200 mosm or higher, and the elevated medullary interstitial [K+] lowers the $K^+$ diffusion gradient across the collecting duct epithelium, which minimizes passive $K^+$ reabsorption at this site and maximizes $K^+$ excretion.
Cellular $\text{K}^+$ transport along the nephron.

Reabsorption (all paracellular)

Reabsorption (½ paracellular and ½ transcellular)

Reabsorption (all transcellular)

Active transcellular excretion

Hypokalemic alkalosis

Luminal flow increases $\text{K}^+$ secretion.

This is because of the high apical $\text{K}^+$ permeability of the principle cells of the CCD.
Aldosterone induces $K^+$ secretion by the cortical collecting duct.

Stimulates Na-K pumps on basolateral membrane of principle cells.

Increases area of basolateral membrane and number of Na-K pumps.

Stimulates apical Na channels, which depolarizes the apical membrane and increases the driving force for $K^+$ diffusion from the cell to lumen.

Increases $K^+$ conductance of the apical membrane.
Acidosis decreases K⁺ secretion.

Affects are largely on principle cells:

Decreased pH inhibits Na-K pumping and thus K⁺ secretion. Decreased pH reduced conductance of apical K⁺ channels.
Renal pH Regulation

Rids body of phosphate, urate, lactate, ketone bodies. Also reabsorsbs, synthesizes or excretes $HCO_3^-$.  

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

Losing a $HCO_3^-$ is the same as gaining a $H^+$. 

Generating or reabsorbing a $HCO_3^-$ is the same as losing a $H^+$. 

Hence to reabsorb $HCO_3^-$, $H^+$ has to be secreted. Alternatively, $HCO_3^-$ secretion requires that $H^+$ be retained.

Reabsorption of filtered $HCO_3^-$ is coupled to $H^+$ secretion. Alternatively, $HCO_3^-$ excretion is coupled to $H^+$ retention.
Regeneration of $\text{HCO}_3^-$

Buffering of excreted $\text{H}^+$ by $\text{HPO}_4^{2-}$

Glutamine metabolism and $\text{NH}_4^+$ secretion