Renal Physiology - Lectures

- ✓ Physiology of Body Fluids – PROBLEM SET, RESEARCH ARTICLE
- ✓ Structure & Function of the Kidneys
- ✓ Renal Clearance & Glomerular Filtration – PROBLEM SET
- ✓ Regulation of Renal Blood Flow - REVIEW ARTICLE
- ✓ Transport of Sodium & Chloride – TUTORIAL A & B
- ✓ Transport of Urea, Glucose, Phosphate, Calcium & Organic Solutes
7. Regulation of Potassium Balance
8. Regulation of Water Balance
9. Transport of Acids & Bases
10. Integration of Salt & Water Balance
11. Clinical Correlation – Dr. Credo
12. **PROBLEM SET REVIEW – May 9, 2011 at 9 am**
13. **EXAM REVIEW – May 9, 2011 at 10 am**
14. **EXAM IV – May 12, 2011**

Renal Physiology Lecture 7

Regulation of Potassium Balance

Chapter 7 Koeppen & Stanton Renal Physiology

1. K^+ Distribution ECF ↔ ICF
2. K^+ Handling by Nephron
3. Control of K^+ Transport
   - DT + CD
4. ↑ P $[K^+]$ = ↑ Aldosterone = ↑ K^+ Secretion

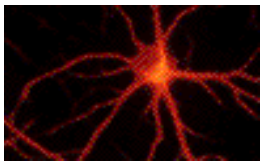
** Renal Failure Patient **

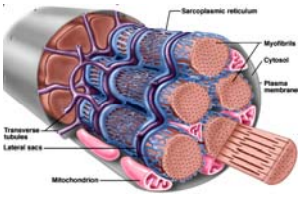
Patient Data	Δ Normal
$Plasma_{K+}$	⇑
P_{Urea}	⇑
BP	⇑
P_{PO4-}	⇑
Hematocrit	⇓
P_{HCO3-}	⇓
P_{pH}	⇓
P_{Ca2+}	⇓

REVIEW - Filtration & Reabsorption

	Amount FILTER/d	Amount EXCRETE/d	% REABSORB
√ Water (L)	**180**	**1.8**	**99.0**
** K^+ (mEq)	**720**	**100**	**86.1**
√ Ca^{2+} (mEq)	**540**	**10**	**98.2**
HCO_3^- (mEq)	**4,320**	**2**	**99.9+**
√ Cl^- (mEq)	**18,000**	**150**	**99.2**
√ Na^+ (g)	**25,500**	**150**	**99.5**
√ Glucose (mmol)	**800**	**0**	***100***
√ Urea (g)	**56**	**28**	**50**

K^+ Critical for Cell Function





- $[K^+]_{ICF}$ / $[K^+]_{ECF}$ – determines resting membrane potential
- Excitable tissues - nerve & muscle
- Cell volume regulation
- Intracellular pH regulation
- DNA and protein synthesis
- Growth
- Enzyme function

K^+ Critical for Cell Function

Sensitive Δ $[K^+]_e$

- $\Uparrow$ P$[K^+]$ of 4 mEq/L
  - Cardiac arrhythmias
  - Cardiac arrest
- Severe $\Downarrow$ $[K^+]_e$
  - Paralysis
  - Cardiac arrhythmias
  - Death

250 mg K^+/ ½ cup serving

- Meats
- Poultry
- Fish
- Apricots
- Cantaloupe



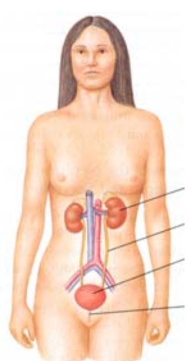
- Honeydew
- Lima beans
- Kiwi
- Prunes
- Squash



KIDNEYS, of course!!!

Primary organ responsible K^+ balance?

Regulation of K^+ Balance



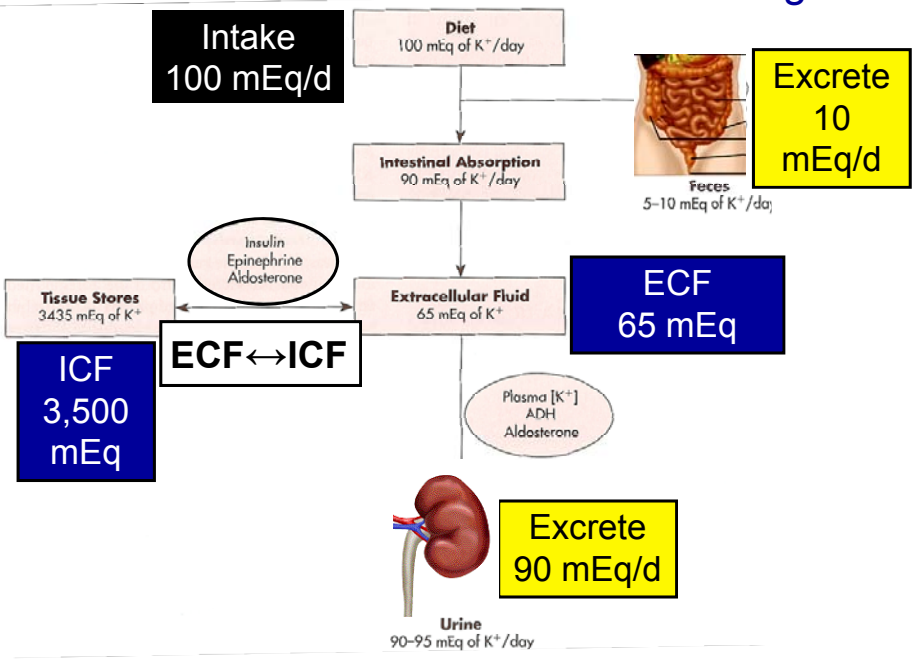
- Potassium (K^+)
  - most abundant intracellular cation – 98% TB K^+ <u>inside</u> cells
    - 150 mEq/L (total body fluid = 42 L)
- Kidneys
  - *regulate* K^+ excretion
  - excrete 90 - 95 % K^+ diet
    - (5 - 10% sweat & feces)

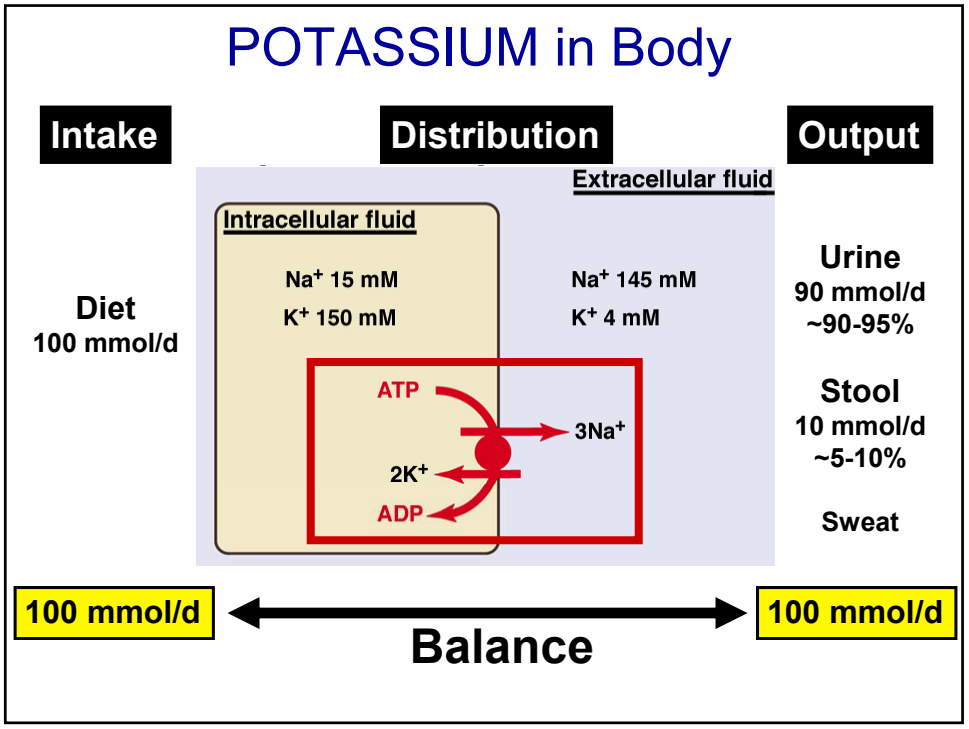
Plasma POTASSIUM

Regulated precisely ~ **4.2 ± 0.3 mEq/L**

- ECF = 2% TB K^+ = 70 mmol
- Normal 3.5 - 5.0 mEq/L
- *Hyper*kalemia
  - ECF [K^+] > 5 mEq/L
- *Hypo*kalemia
  - ECF [K^+] < 3.5 mEq/L
- *Kali*uresis
  - Enhanced K^+ excretion

Distribution & Balance POTASSIUM Fig 7-3



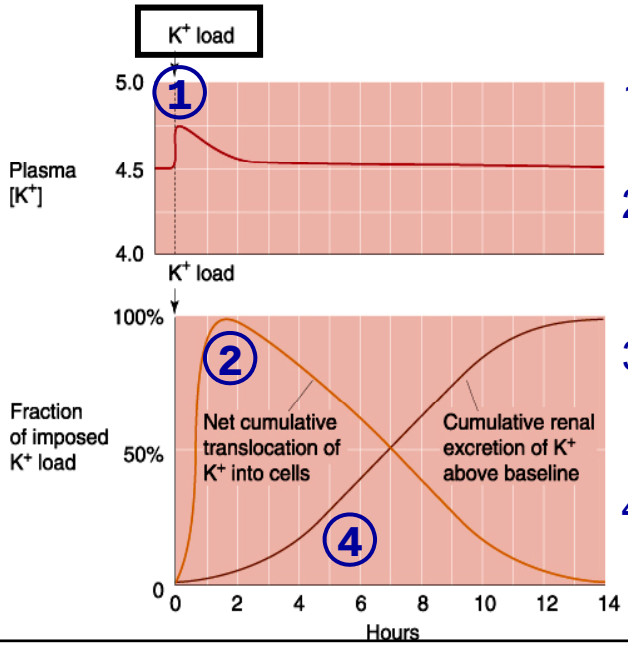


TIME FOR SHOW & TELL

Amount of K^+:

- Contained in entire ICF
  - 3,500 mmoles
- Contained in entire ECF
  - 65 mmoles
- Filtered Load
  - 720 mmole/d
- Excreted in Urine
  - 90 mmol/d

Response to Imposed K^+ Load



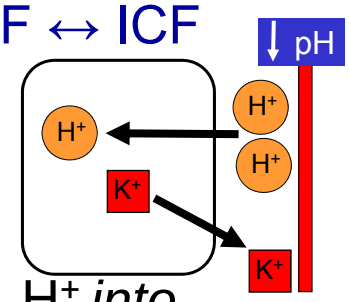
1. Plasma [K+] rises modestly
2. Transfer of 4/5 ingested K+ to ICF w/i 1 hr
3. Due to insulin, epi, aldo via Na/K pump
4. Kidneys begin to excrete K+

K^+ Distribution ECF ↔ ICF

- ⇑ P [K^+] following K^+ absorption by GI stimulates:
- Hormones:
  - Insulin secretion
  - Epinephrine secretion
  - Aldosterone release

⇑ K^+ uptake into cells

K^+ Distribution ECF ↔ ICF

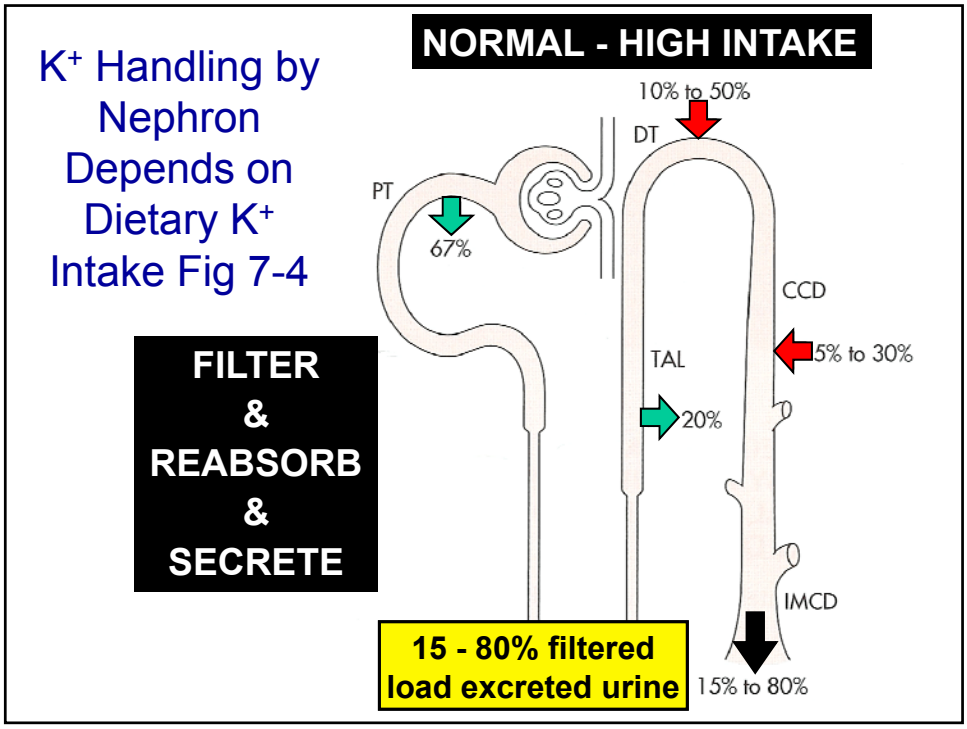


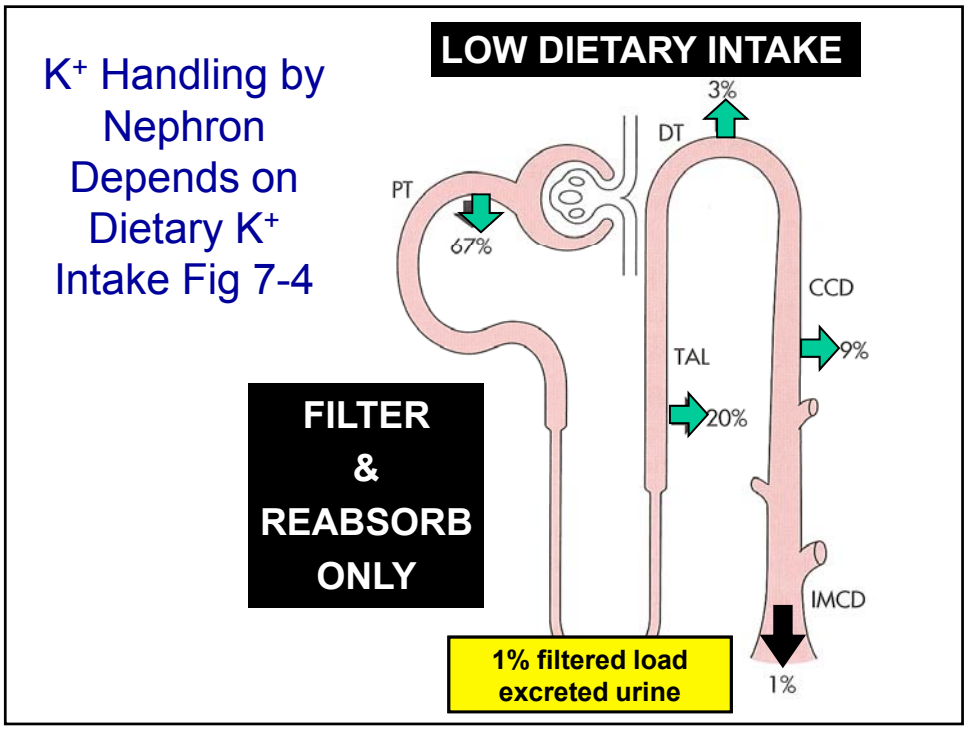
Metabolic acid-base disturbances

- Acidemia - ⇓ pH ⇑ H^+ *into* cells ⇑ K^+ *out* of cells - ⇓ K^+ uptake = *hyperkalemia*
- Alkalemia - ⇑ pH ⇓ H^+ *into* cells ⇑ K^+ *into* cells - ⇑ K+ uptake = *hypokalemia*

Renal Physiology Lecture 7

1. K^+ Distribution ECF ↔ ICF
2. K^+ Handling by Nephron
3. Control of K^+ Transport DT + CD
4. ↑ P [K+] ↑ Aldosterone ↑K+ Secretion


K+ Handling by Nephron Depends on Dietary K+ Intake Fig 7-4
NORMAL - HIGH INTAKE
FILTER & REABSORB & SECRETE
10% to 50%
DT
PT
67%
CCD
5% to 30%
TAL
20%
IMCD
15 - 80% filtered load excreted urine
15% to 80%

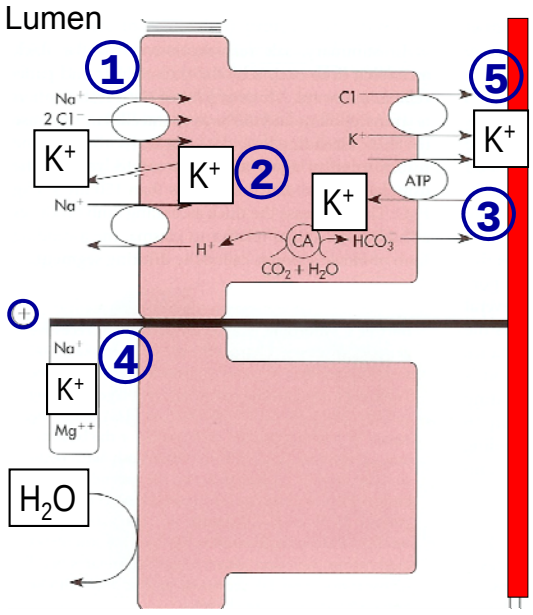

K+ Handling by Nephron Depends on Dietary K+ Intake Fig 7-4
LOW DIETARY INTAKE
FILTER & REABSORB ONLY
3%
DT
PT
67%
CCD
9%
TAL
20%
IMCD
1% filtered load excreted urine
1%

% Filtered K^+ Reabsorbed

- PT reabsorb 67% *(paracellular)*
- TAL reabsorb 20% (*NKCC2*)
- DT reabsorbs 3% *(H^+/K^+ ATPase) or* *secretes* 10 - 50% *(K^+ channel)*
- CD reabsorbs *9% or* *secretes* *5 - 30% (K^+ channel)*
- Excreted 1 - 80%

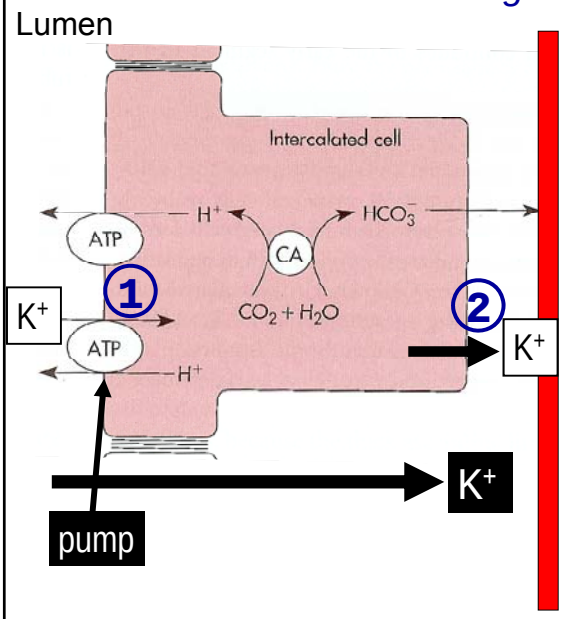
K^+ handling critically dependent on dietary K^+ regulated *distal* segments

K^+ Transport - *Thick Ascending Limb (TAL)* Fig 4-8



1. *Reabsorb* $Na^+/K^+/2Cl^-$ (**NKCC2**) - K^+ moves against conc gradient
2. Secrete (recycle) K^+ channel (ROMK)
3. K^+ pumped into cell Na^+-K^+-ATPase
4. *Reabsorb* K^+ paracellular
5. *Reabsorb* K^+ with conc gradient

K^+ Reabsorption *Cortical Collecting Tubule – Intercalated Cell Fig 4-10 & pg 120*



α-Intercalated cells

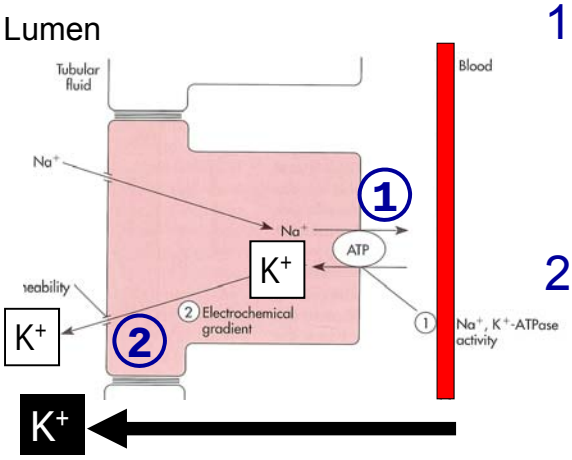
active reabsorption during <u>low</u> dietary K^+ intake

1. Apical uptake via H^+-K^+-ATPase (ATP driven pump)

   ↑ $[K^+]i$

2. Exits via basolateral K^+ channel

K^+ Secretion *DT CD – Principal Cell* Fig 7-5



1. K^+ uptake interstitium via basolateral Na^+K^+-ATPase

   ↑ intracellular $[K^+]$

2. Passive (*electrochemical driving force*) flux K^+ across apical membrane (K^+ channel)

Active movement K^+ from blood to cell
Passive movement K^+ from cell to lumen

Renal Physiology Lecture 7

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What causes hypokalemia?

Causes Hypokalemia

⇓ ECFV
⇑ Aldo

- Certain diuretics
- Chronic or severe vomiting or diarrhea
- Nasogastric suction
- *Gitelman's syndrome* – genetic defect NCC symporter
- Hyperaldosteronism
- Abuse laxatives
- Bulimia

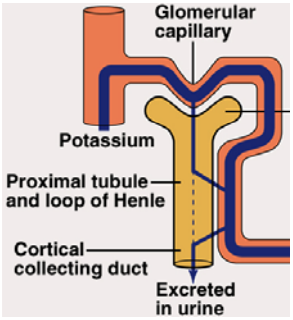
Regulation of K+ Balance

K^+ excretion depends on rates:

- filtration (GFR X P $[K^+]$)
- reabsorption
- *secretion*

Major physiological regulators:

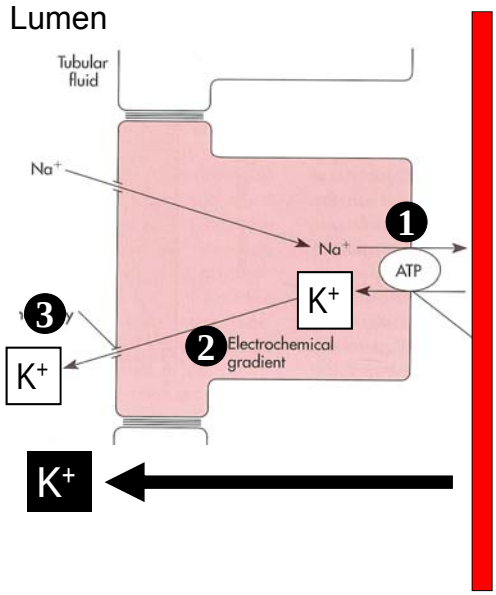
- Plasma $[K^+]$
- Aldosterone



Control of K^+ Balance

- Under most conditions - normal or high dietary K^+ intake
- K^+ excretion controlled by varying rate K^+ *secretion by principal cells distal nephron*
- Occurs ***entirely*** by altering *electrochemical* gradient favoring K^+ movement into tubular fluid

Control Rate of K^+ Secretion



1. activity Na^+/K^+-ATPase pump
2. electrochemical gradient
3. permeability apical membrane

Effects of Diuretics on K^+ Excretion

K^+-Wasting Diuretics (mannitol, furosemide)

- Inhibit Na^+ (and H_2O) reabsorption PT or LOH
- Mechanism: increased tubular fluid flow in DT & CD promotes K^+ secretion

K^+-Sparing Diuretics (amiloride, spironolactone)

- Inhibit Na^+ (and H_2O) reabsorption CNT & CD by acting on same cells that secrete K^+
- Mechanism: increased tubular fluid flow on K^+ secretion minimized by effect of decreased Na^+ reabsorption to decrease lumen negativity

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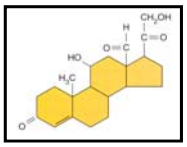
Regulation of K^+ Secretion

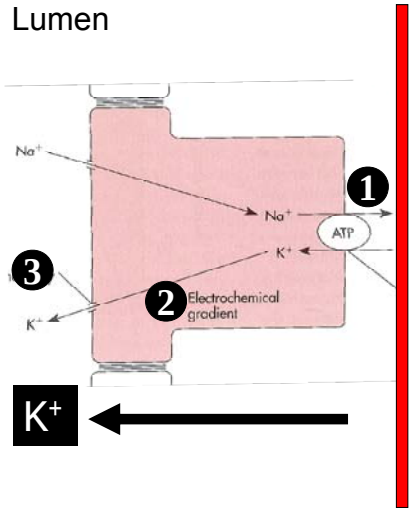
⇑ P_{K+} = ⇑ Aldosterone

1. adrenal cortex sensitive to ECF [K^+]
2. ⇑ ***amount*** of Na^+/K^+ ATPase basolateral membrane distal nephron
3. ⇑ ***expression and activation*** ENaC channels enhances Na^+ entry into cell = ⇑ lumen negative = ⇑ K^+ secretion
4. ⇑ ***permeability*** apical membrane to K^+ by ⇑ # K^+ channels
5. ⇑ ***activation*** K^+ channels



⇑ secretion K^+ ⇑ excretion K^+

Hyperkalemia = K^+ Secretion by DT & CD



1. ⇑ Na^+K^+-ATPase activity → ⇑ $[K^+]i$ → ⇑ electrochemical driving force → ⇑ K^+ secretion
2. ⇑ permeability apical membrane to K^+
3. Stimulate aldosterone
4. ⇑ tubular flow → secreted K^+ flushed downstream → ⇓ $[K^+]$ lumen → ⇑ K^+ secretion

Summary

1. ⇑ K^+ intake
2. ⇑ **P** [K^+]
3. ⇑ **ECF** [K^+]
4. Stimulate <u>aldosterone</u> release

   Distal nephron ⇑ K^+ ***<u>secretion</u>***