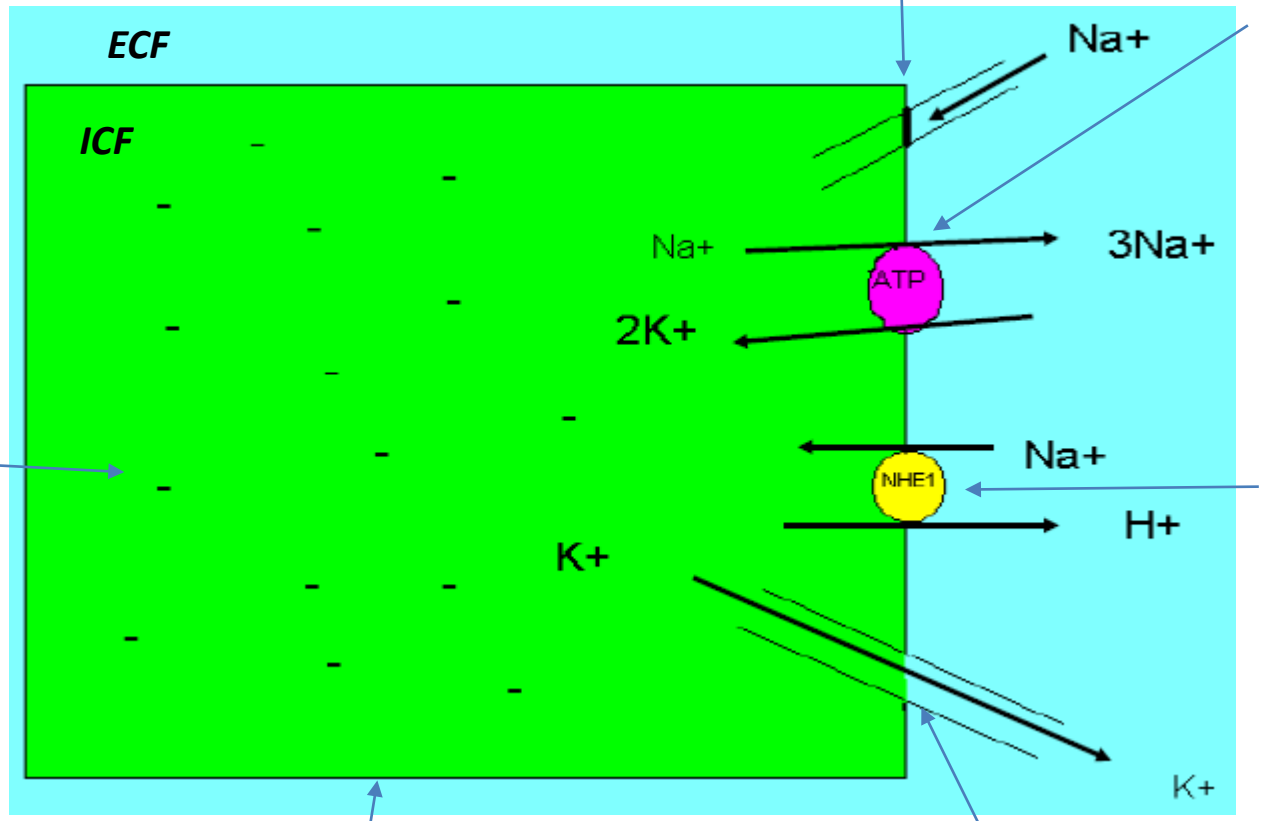
Factors that regulate the [K+] gradient across all cell membranes (and thereby regulate/maintain the cell's Resting Membrane Potential, RMP)

(Image taken from Dr. McLaughlin May 1st 2012 lecture)

3. Na+ channels in the membrane, which tend to be shut when cell is at rest (so Na+ does not regulate the RMP, leaving the job up to K+)



5. Na/K-ATPase: Keeps the ICF side more *negative* than the ECF side; also pumps K+ into the cell

\+ \+ -

Beta-2 stimulation (upregulates Na/K ATPase *directly*)

Alpha-1 stimulation, Digoxin (Inhibits Na/K ATPase *directly*)

Aldosterone (↑ Na/K ATPase *effect* by inserting more of them into the cell membrane – *Thus, slower*) **(Only in the Nephron!)**

4. Negative charges within the cell, I.e. proteins, DNA fixed to the ICF: helps regulate the movement of K+ across the cell membrane

6. Na/H-Exchanger: Imports Na+ into the cell while exporting H+.

→H+ export helps maintain ICF acid-base balance.

→Na+ import helps drive activity of Na/K-ATPase by maintaining a source of intracellular Na+

\+

Insulin

(Stimulates Na/H-exchanger, ↑ Na/K-activity, driving K+ into cells)

→Post-parandial insulin secretion sequesters ingested K+ into the cell, maintaining tight blood [K+] .

→Insulin induced intracellular metabolic activity generates excess H+, this mechanism helps remove H+ from inside the cell.

1. An in-tact cell membrane is essential to maintaining ion concenetration differences across the membrane, creating the RMP

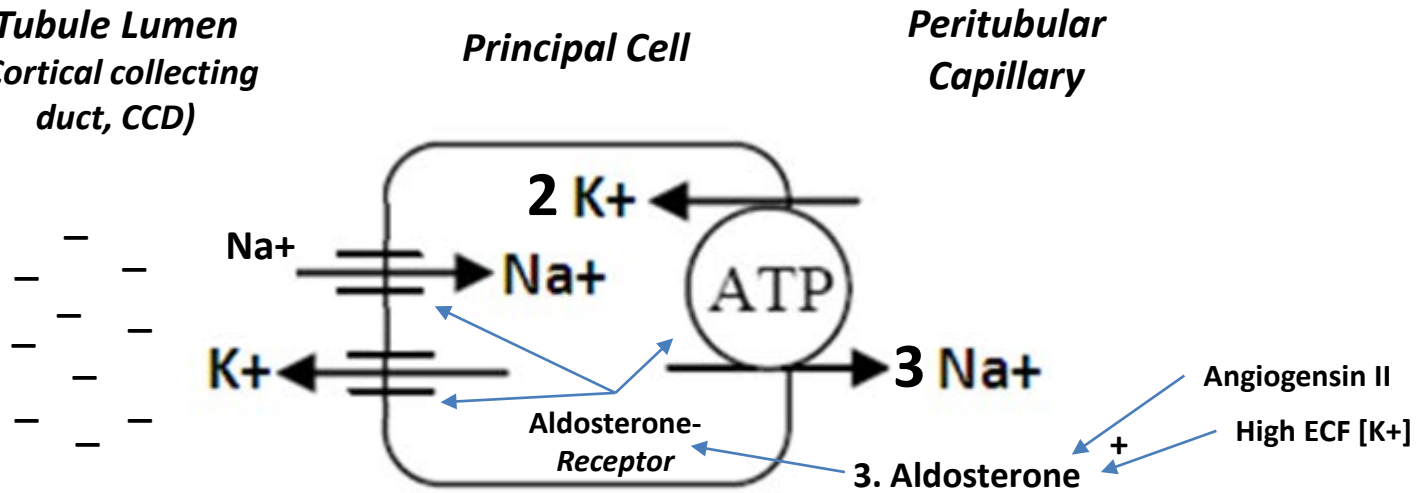
2. K+ channels in the membrane, which are always open in the resting cell (which is why K+ regulates the RMP)

Factors controlling K+ excretion by the Collecting Duct Principal Cell

(the main site of [K+] fine-tuning/regulation in the body)

1. [Na+] flowing past the Principal Cell:

- Na+ in the CCD can diffuse into the Principal cell down its [ ] gradient created by the NaK-ATPase
- Influx of Na+ leaves the tubular lumen more – relative to the inside of the cell, pulling K+ out.
- **↑ tubular [Na+] ↑ K+ excretion**
- Implication: if ↓ Na+ in collecting duct, ↓ Na+ entry into Principal Cell, ↓ trans-epithelial potential difference, ↓ K+ efflux!



2. Negative Charges in the Collecting Duct Lumen

→More –'ve charges (i.e. HCO_3-) in the tubule lumen → ↑ the trans-epithelial protential difference (↑ the charge gradient for K+ to diffuse down) → K+ leaves principal cell and enters the lumen

→**↑ Neg Charges in tubule lumen ↑ K+ excretion**

3. Aldosterone

→Aldosterone activates the Aldo-Receptor, causing insertion of more:

1. Na+ channels on the luminal membrane
2. K+ channels on the luminal membrane
3. Na/K-ATPases on the basolateral membrane

→Anything that ↑ blood [Angiotensin II] and [K+]s will directly stimulate the adrenal cortex to produce more Aldosterone!

→**↑ Aldosterone ↑ K+ excretion**

Implication:

- If EABV is low (during hypovolemia or instances causing underfill-edema) → aldosterone will cause principal cells to retain Na+ and water, at the expense of K+.
- *Maintaining good blood volume trumps electrolyte homeostasis*

→Principal Cell K+ excretion can be quantified by the Trans-Tubular [K+] Gradient (TTKG):

- Compares luminal [K+] to capillary [K+]; reflects how much K+ has been excreted into the lumen by the principal cell.
- **Normally, TTKG should be btw 4-7.**

$$TTKG = \frac{CCD[K^+]}{Serum[K^+]} = \frac{Urine[K^+] \times SerumOsm}{Serum[K^+] \times UrineOsm}$$

- **TTKG > 7** = high Principal cell activity, appropriate when the ECF is hyperkalemic (to excrete more K+)
- **TTKG < 4** = low Principal cell activity, appropriate when ECF is hypokalemic (to preserve more K+ in the ECF)
- If the TTKG is ever inappropriate given the ECF [K+] status, it's a principal-cell defect!

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