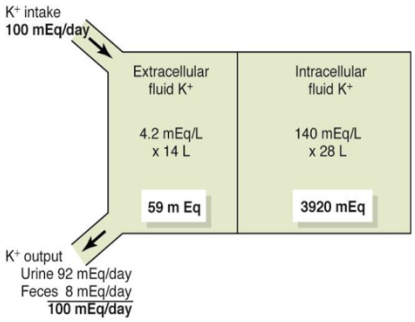
Sereen Draghmeh

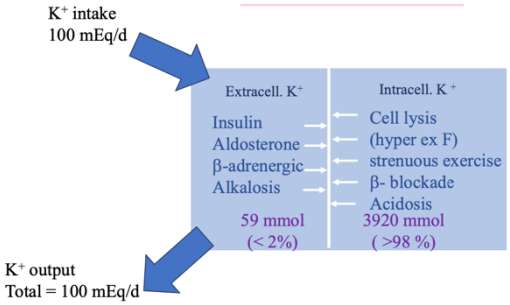
Renal Physiology L1 Final

- **Normal potassium intake, distribution, and output from the body.**
  - The human body fluids is composed of an extracellular and an intracellular compartment
  - Lets make a few things clear:
    - When I say intracellular I mean the components INSIDE the cell
    - While when I say extracellular I mean the components OUTSIDE the cell
      - This includes the blood and plasma as well as the interstitium
    - Plus we took in first year that if someone weighs 70 Kg, 28L of fluid will be found intracellularly and about half of it will be found extracellularly – 14 L
  - Look at the picture and follow along:
    - you can see that the potassium is mainly found intracellular (so the majority of them reside in the cells)
    - Intracellularly we have 140 mEq/L of potassium compared to 4.2mEq/L extracellularly (reflecting the blood or plasma)
  - So any small change in the potassium level in the extracellular will cause a big change, since its very important to control the potassium levels, since many organs like the heart are affected by the potassium concentration in the blood/plasma (extracellularly)
    - So the fluctuations that are allowed is only +/- 0.3 mEq
      - which means the concentration of potassium extracellularly is allowed to increase or decrease by 0.3 mEq
  - From the picture you can see that the daily intake of potassium for any person is around 100mEq/day (so a single meal may contain 20-50 mEq of potassium, and this single meal can cause double the concentration of potassium in the plasma(extracellularly)), and as we said before, we cant have that big of a fluctuation of potassium extracellularly so we have 2 systems to help control this huge fluctuation of potassium extracellularly
    - Fist line is the redistribution between extracellular and intracellular compartments
      - Once we consume our daily intake of potassium, this potassium will be found and absorbed in the blood/plasma (in the extracellular compartment)
        - And remember we said that we cant have big fluctuations of potassium in the extracellular compartment
      - So once we take in potassium there is going to be fast redistribution of potassium from the extracellular compartment to the intracellular compartment
        - so the intracellular compartment will act as a reservoir to prevent sudden big changes in the concentration of potassium in the plasma
    - the second line is the excretion of potassium via the kidneys



- the redistribution of potassium between the extracellular and intracellular compartments occurs until the kidneys are able to excrete the excess potassium
- The kidney is the organ which balances the input and the output of the potassium
  - Form the picture you can see that from the 100 mEq of potassium that was took in the kidneys excreted 92 mEq of it via the urine
    - You can also see that 8 mEq was excreted in the feces via the digestive system BUT it doesn't play an important role
      - The main responsibility is on the kidneys – its responsible for the final correction

- **Effects of severe hyperkalemia**
  - Partial depolarization of cell membranes
  - Cardiac toxicity
    - ventricular fibrillation or asystole
- **Effects of severe hypokalemia**
  - Hyperpolarization of cell membranes
  - Fatigue, muscle weakness
  - Hypoventilation
  - delayed ventricular repolarization
- **Potassium Regulation: Internal and External**
  - These are the factors that affect the redistribution of potassium from the intracellular to the extracellular or vice versa
    - Extracellular to Intracellular
      - Insulin
        - Insulin increases the uptake of potassium by the cells
        - Mechanism
          - Via the glucose and sodium
            - The excretion of sodium will cause the intake of potassium
          - Let me explain to make it more clear:
            - Basically when we have excess glucose (like for example after eating a meal) insulin will be released to reuptake the glucose by the cells
            - This insulin also activates the sodium potassium pump , which as we said before would pump sodium out and intake potassium (so it will move the potassium from the outside which is the



extracellular compartment to the inside which is the intracellular compartment)

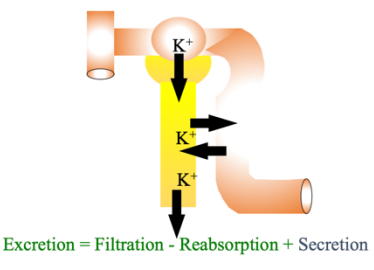
- Aldosterone
  - Its effect is not only on the kidney cells (on the late distal convoluted tubule and the collecting tubules)
  - Even the cells in our body are affected in which it increases the uptake of potassium into our cells
    - This decreases the hyperkalemia by shifting the potassium towards the intracellular compartment
  - People with aldosterone disorders
    - Conns Syndrome
      - People with excessive aldosterone
      - they will have hypokalemia
      - Since there is excess shifting of potassium from the extracellular to the intracellular compartment
    - Addison's Disease
      - People with low aldosterone
      - They will have hyperkalemia
      - Since there is little shifting of potassium from the extracellular to the intracellular compartment
- B-adrenergic
  - They're stimulated especially by epinephrine
  - They increase uptake of potassium , reducing the potassium level in the extracellular compartment
- Alkalosis
  - More uptake of potassium into the cells due to an increase of activity of sodium potassium ATPases

- Intracellular to Extracellular
  - Cell lysis
    - For example in hemolysis
    - The potassium that was found in the cell will now be in the extracellular compartment
  - Hyper extracellular fluid – increase of osmolarity in the extracellular fluid
    - Remember an increase in osmolarity means there is an increase in solutes
    - So an increase the concentration of solutes (like potassium) in the intracellular compartment will cause the solutes (like potassium) to move to the extracellular compartment (shifting)
  - Strenuous exercise – high intensity exercise

- It normally only increases the potassium in the extracellularly compartment mildly
- But if combined with a diuretic or beta adrenergic blockers, it will cause hyperkaliemia that can be very severe to the point the person may enter the ER
- Mechanism isn't very known

- Beta blockers
  - This is the opposite of what we said above
  - Here we are blocking the beta adrenergic receptors so it will increase the outflow of potassium from the intracellular to the extracellular compartments
- Acidosis
  - Opposite to the alkalosis
  - Shifting of potassium outside the cell
  - We will talk about it more briefly in a bit, but in general it is because of the activity of Na+/K+ ATPase which is inhibited by acidosis

- **Control of Potassium Excretion + Renal tubular sites of potassium reabsorption and secretion.**
  - Potassium is filtered, and the filtered load of potassium is dependent on the concentration of it in the blood and the GFR
    - remember filtered load = GFR x Plasma concentration of solute
  - Now we are seeing where the potassium is adjusted in the kidney to control the amount of potassium in the extracellular compartment (remember we said it's the main line of defense)
  - Which part is adjusted in the kidney to control the potassium levels:
    - Filtration:
      - On the level of filtration the GFR isn't changed a lot since we said its autoregulated by many mechanisms so the concertation of potassium is what will determine how much filtration of potassium will occur
      - So its not really adjusted here
    - Reabsorption:
      - Reabsorption of potassium occurs normally in the proximal convoluted tubule and the thick ascending loop of Henle
      - The percentages of reabsorption is relatively constant
        - in the proximal tubule
          - 65%



- In the thick ascending loop of Henle
  - 30%
- So since the reabsorption doesn't change a lot, the body doesn't adjust it a lot

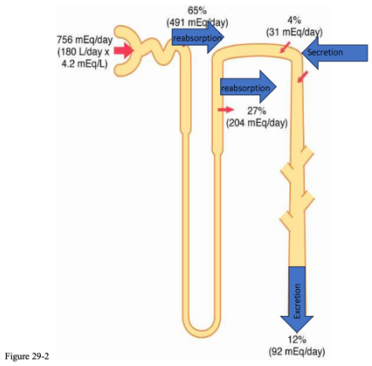
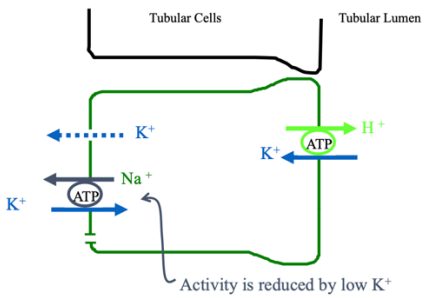


Figure 29-2

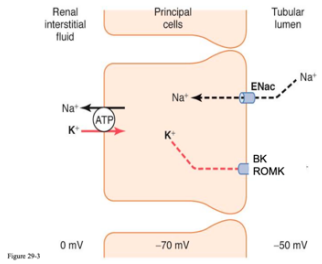
- Excretion:
  - the body focuses mainly on the secretion process of potassium to control the amounts
  - Secretion occurs in the late distal tubules and the collecting ducts in the principal cells mainly but can also be in the intercalated cells
  - So depending on the adjustment of the secretion rate, it controls the final excretion rate of potassium
    - Since excretion = filtration – reabsorption + secretion
  - Percentage of the secretion (summation of 12% together)
    - In the late distal
      - 8% (fix it in the picture, since it only says 4%)
    - In the collecting tubules
      - 4 %
  - Remember these numbers here aren't fixed, since these numbers depend on factors like the intake of potassium and the tendency of the balance of potassium (like is it favored towards the input or output)
  - So here is where the main adjustment of potassium occurs

- **Late Distal and Cortical Collecting Tubules: Intercalated Cells –Reabsorb K+**
  - In the intercalated cells especially type A cells (in the late distal and the cortical collecting tubule cells), there are pumps which are the hydrogen potassium ATPase pump
  - This pump secretes the hydrogen in exchange of the reabsorption of potassium
    - Remember when I say I'm reabsorbing potassium that means I'm taking it back into the blood into the extracellular compartment
  - This process occurs when there hypokalemia
    - Makes sense since I have less potassium in the extracellular compartment so reabsorbing potassium will mean I am taking the potassium back into the blood increasing the potassium concentration extracellularly
  - The sodium potassium ATPase is affected by many factors like
    - The concentration of potassium in the plasma and ECF
      - Remember the sodium potassium pump releases sodium and intakes potassium into the cell
      - So as the ECF concentration of potassium increases, the higher the activity of this pump and vice versa
        - Makes sense since as the ECF concentration of potassium increases that means I need to shift the potassium from the extracellular to the



intracellular compartment (since as we said , we cant have a high fluctuation in potassium extracellularly)

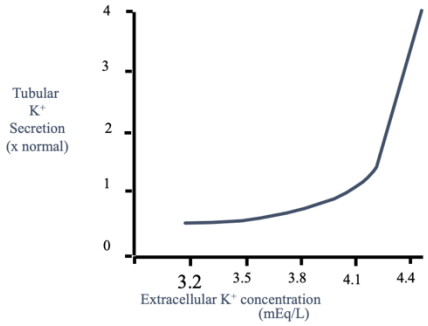
- **Potassium Secretion by Principal Cells**
  - We took in the mid how the principal cells secrete potassium
    - We have sodium potassium ATPase which causes a low gradient of sodium and we have the ENac which reabsorbs sodium
    - The potassium that entered the principal cell to get excreted, in exchange of sodium that is released to the blood, this will cause an increase in potassium intracellular
  - 2 types of potassium channels on the luminal side
    - BK
    - ROMK
      - These two channels, cause the excretion of potassium when there is high intracellular potassium that occurred due to the Na+/K+ pump
  - All these channels increase in their activity in the presence of aldosterone
    - Aldosterone levels increase due to 2 stimuli
      - Hyperkalemia
      - Angiotensin II (in hypertension)



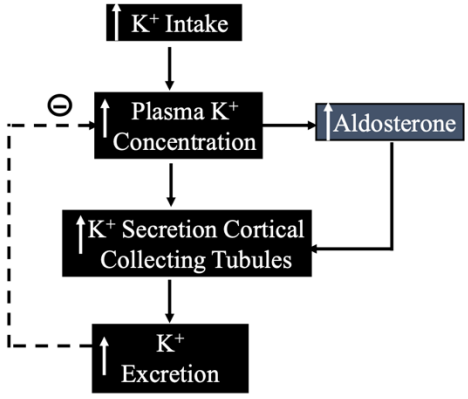
- **Control of Cortical Collecting Tubule : (Principal Cells) K+ Secretion**
  - Increase in extracellular K+ concentration : increases K+ secretion
    - There is more than one reason
      - Na+/K+ Pump
        - One of the reasons is because the activity of the sodium potassium pump increases in activity when there is hyperkalemia
      - Gradient
        - As the extracellular K+ concentration increases the greater gradient so the more excretion will occur
  - Aldosterone : increases K+ secretion
    - We know that aldosterone is released when there is hyperkalemia
    - And as we said above, this aldosterone increases the activity of many channels including the ENac, Na+/K+ pump and the BK and ROMK potassium channels
      - All these favor excretion of potassium

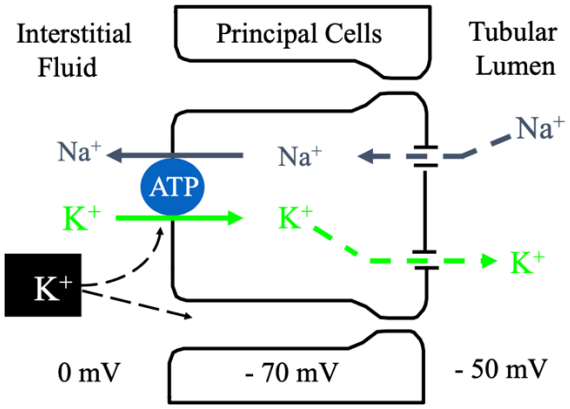
- Sodium (volume) delivery : increases K+ secretion
  - When a person has a high salt intake, this will cause volume expansion due to water expansion in tubules due to more GFR, this increases the tubular flow rate , which increases the flushing/washing out of potassium especially in the distal tubules and collecting duct , this also will also increase the gradient, favoring the secretion of potassium
- Acid - base status:
  - acidosis : decreases K+ secretion
    - as we said above, in acidosis the Na+/K+ pump is less active, decreasing the secretion of potassium
    - so in acidosis, hyperkalemia occurs
  - alkalosis : increases K+ secretion
    - in alkalosis the Na+/K+ pump is more active, increasing the secretion of potassium
    - so in alkalosis there is more tendency for hypokalemia

- **Effect of Extracellular K+ on Excretion of K+**
  - From the graph you can see that
    - The normal extracellular K+ concentration is 4.2 as we mentioned above
      - At 4.2 potassium concentration extracellularly the tubular secretion of potassium is around 1
    - When the extracellular K+ concentration is less than 4.2, there is still tubular secretion of K+ its just less than normal (less than 1)
      - In which the closer the extracellular potassium concentration approached the normal, the greater the tubular K+ secretion
    - When the extracellular concentration of K+ was more than normal (more than 4.2), the tubular secretion of K+ increased drastically

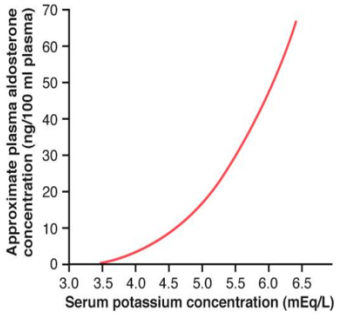


- These pictures show the different factors that affect the potassium secretion in the principal cells
  - Na+/K+ pump activity
    - Affected by the extracellular potassium concentration
      - As it increases, it will increase the activity of this pump (secreting more K+)
  - Gradient of K+ between the interstitial fluid and the tubular fluid
    - As the the potassium concentration extracellularly increases the greater the gradient between the interstitial fluid and the tubular fluid, so the more paracellular diffusion (passive) from the interstitial fluid to the tubular lumen (so more secretion)
  - Aldosterone
    - Increases activity of Na+/K+ pump
      - This increases the secretion of K+
  - Tubular flow rate
    - The greater the flow rate, the more flushing/washing of potassium so more secretion of potassium since the concertation of potassium in the tubular fluid will remain low, favoring secretion



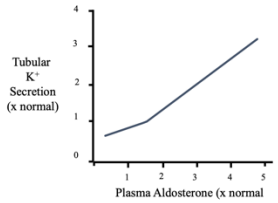


- **Increased serum K+ stimulates aldosterone secretion**
  - Here we are seeing the effect of the serum potassium concentration with the aldosterone concentration
    - At the normal serum level of potassium concentration (4.2), the aldosterone level was about 8 ng/100ml
      - Which shows that even at normal levels of serum potassium we still had aldosterone
    - As the serum potassium concentration increases the aldosterone level also increased
    - You can also see that there is also inhibition of aldosterone when there is little serum potassium concentration (below 3.5)

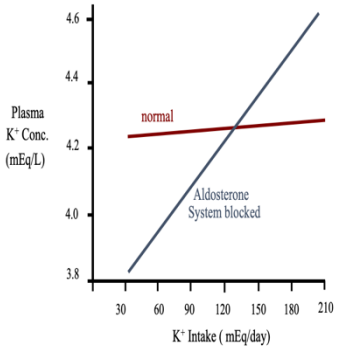


gure 29-5

- **Effect of Aldosterone on K+ Excretion**
  - You can see from this figure you can see that as the plasma aldosterone increased (x times normal) the tubular excretion of potassium also increased



- **K+ After Blocking Aldosterone System**
  - Here we are seeing if there are any other mechanisms that can replace aldosterone if we blocked it
    - What they did is that they brought an animal with an intact adrenal cortex, and another animal without an adrenal cortex and they infused aldosterone at a constant level
      - In the normal animal (with the adrenal cortex):
        - they noticed that as the K+ intake increases, the plasma concentration stayed relatively constant but it did increase a little
      - In the animal where they removed its adrenal cortex but they infused the animal with a constant level of aldosterone:
        - they noticed that as the K+ intake increased, the plasma K+ concentration also increased



  - This experiment showed us that there is nothing that can replace aldosterone, so its the major regulator for potassium in our whole body

- **Effect of collecting tubule flow rate on K+ secretion**
  - As the potassium diet increased, the tubular flow rate also increased, which caused an increase in potassium secretion
  - people who consume a low potassium diet if they took a diuretic, their secretion of potassium wont be affected a lot due to the tubular flow rate compared to people who consume a high potassium diet, then a diuretic would affect the tubular flow rate increasing secretion of potassium

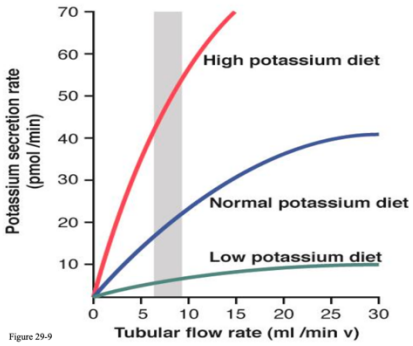


Figure 29-9