PHYSIO

MODIFIED NO.10 P1&2

الكُتّاب: عبدالله الخوالدة وليان العودات وصهيب زعيتر

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Urinary System: Renal Physiology for Medical Students, L10

Chapter 29 : Renal Regulation of Potassium, Calcium, Phosphate,
and Magnesium; Integration of Renal Mechanisms for Control of Blood Volume and Extracellular Fluid Volume

Reference: Guyton & Hall, Jordanian first edition
Chapter29

Color code

- Slides
- Doctor
- Additional info
- Important

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2023

بسم الله وصلى الله على رسول الله نبينا محمد المجاهد الشهيد، الضَّحوك القتّال
اللهم علمنا ما ينفعنا وانفعنا بما تعلمنا وزدنا بفضلك وكرمك علما وعملا صالحا متقبلا ترضاه يا أرحم الراحمين

Objectives

- Identify the mechanisms by which the kidney regulates Potassium, Calcium, Phosphate homeostasis
- Identify renal tubular mechanisms of potassium reabsorption and secretion
- Understand factors affecting homeostasis of potassium
- Understand examples of integration of renal mechanisms for control of blood volume and extracellular fluid volume

Question

- A 26-year-old woman recently adopted a healthier diet to eat more fruits and vegetables. As a result, her potassium intake increased from 80 to 160 mmol/day. Which of the following conditions would you expect to find 2 weeks after she increased her potassium intake, compared with before the increase?

	Potassium Excretion Rate	Sodium Excretion Rate	Plasma Aldosterone Concentration	Plasma Potassium Concentration
A)	↔	↔	↑	Large increase (>1 mmol/l)
B)	↔	↓	↑	Small increase (<1 mmol/l)
C)	↑ 2×	↔	↑	Small increase (<1 mmol/l)
D)	↑ 2×	↑	↓	Large increase (>1 mmol/l)
E)	↑ 2×	↑	↔	Large increase (>1 mmol/l)

K+ excretion will increase to get rid of the excess k+
Na+ wont be effected (will be discussed later)
Aldosterone > increases the excretion of the K+ and it's stimulated by hyperkalemia
Plasma potassium > Small increase

Normal potassium intake, distribution, and output from the body.

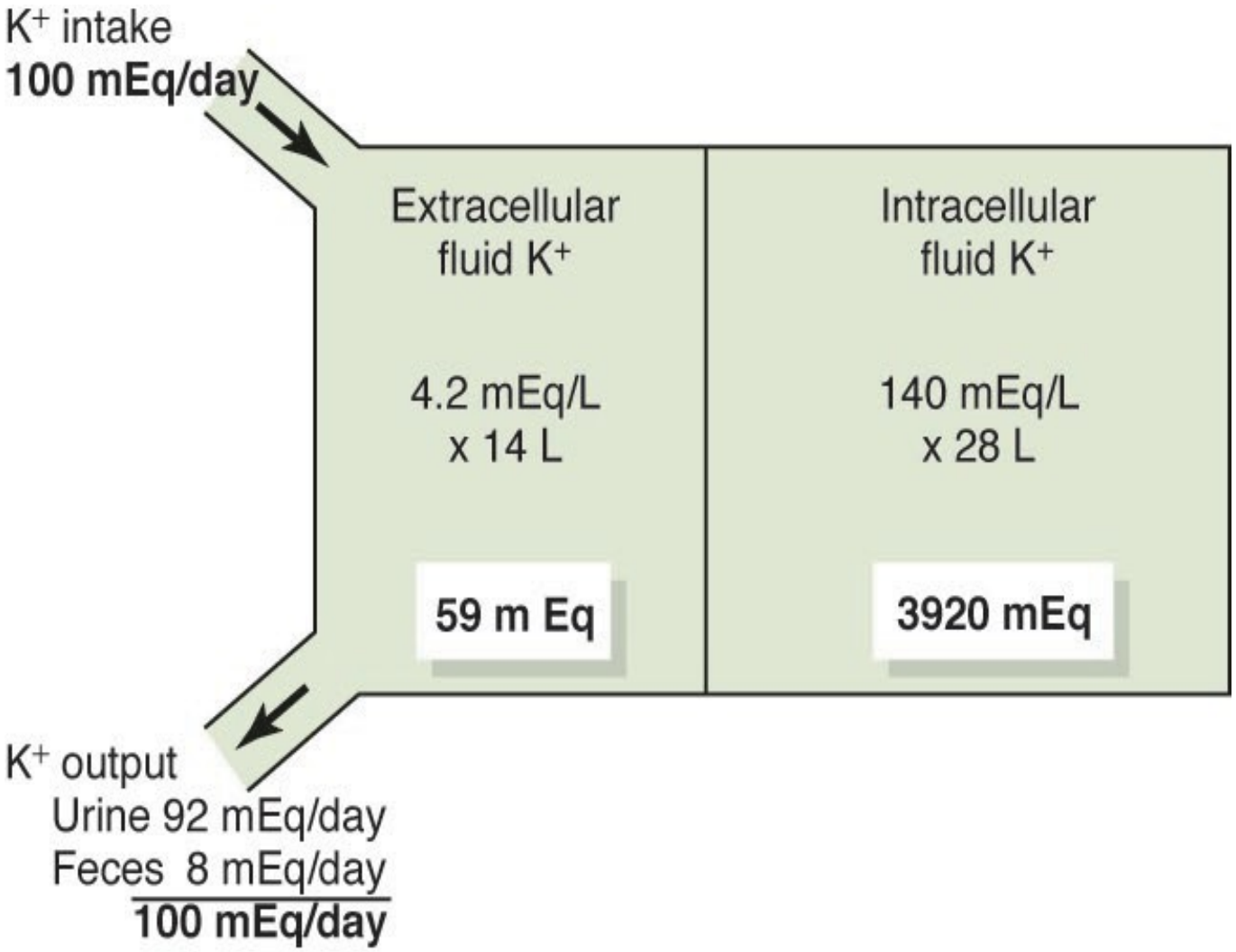


Figure 29-1

- Now let's talk more about homeostasis of K+ in all body compartments and how our body can balance the input and output, daily intake is about100mEq/day.
  In any balance state the input must equal the output and the **main** regulator of the output is urinary excretion.

- We have 2 main Compartments in our body, intracellular and extracellular we know that k+ is the major cation in the intracellular compartment:

3920mEq in 28 liters of water > Which makes a concentration of 140 mEq/L intracellularly
and 59mEq in 14 liters of water > Which makes a concentration of 4.2mEq/L extracellularly

- So any small change in diet may largely affect the concentrations, for example a fruit may have 60 mEq/L of k+ and it can double the extracellular K+ concentration which will lead to bad consequences because the concentration of K+ must be within a very narrow window and the allowed changes are as fractions (أعشار) **(Also decreased conc. May lead to a very bad consequences)**

- So how can our body protect us from the variations of K+ concentration due to K+ intake?
  The first line of defense is actually between intracellular and extracellular which is K+ intake or release between them, And it works until the kidney adjusts excretion which requires hormonal mechanisms

Clinical Perspective

Effects of severe hyperkalemia

- Partial depolarization of cell membranes
- Cardiac toxicity
  ventricular fibrillation or asystole

So that is why it's really important to regulate k+ in the blood or in the extracellular fluid

Effects of severe hypokalemia

- Hyperpolarization of cell membranes
- Fatigue, muscle weakness
- hypoventilation
- delayed ventricular repolarization

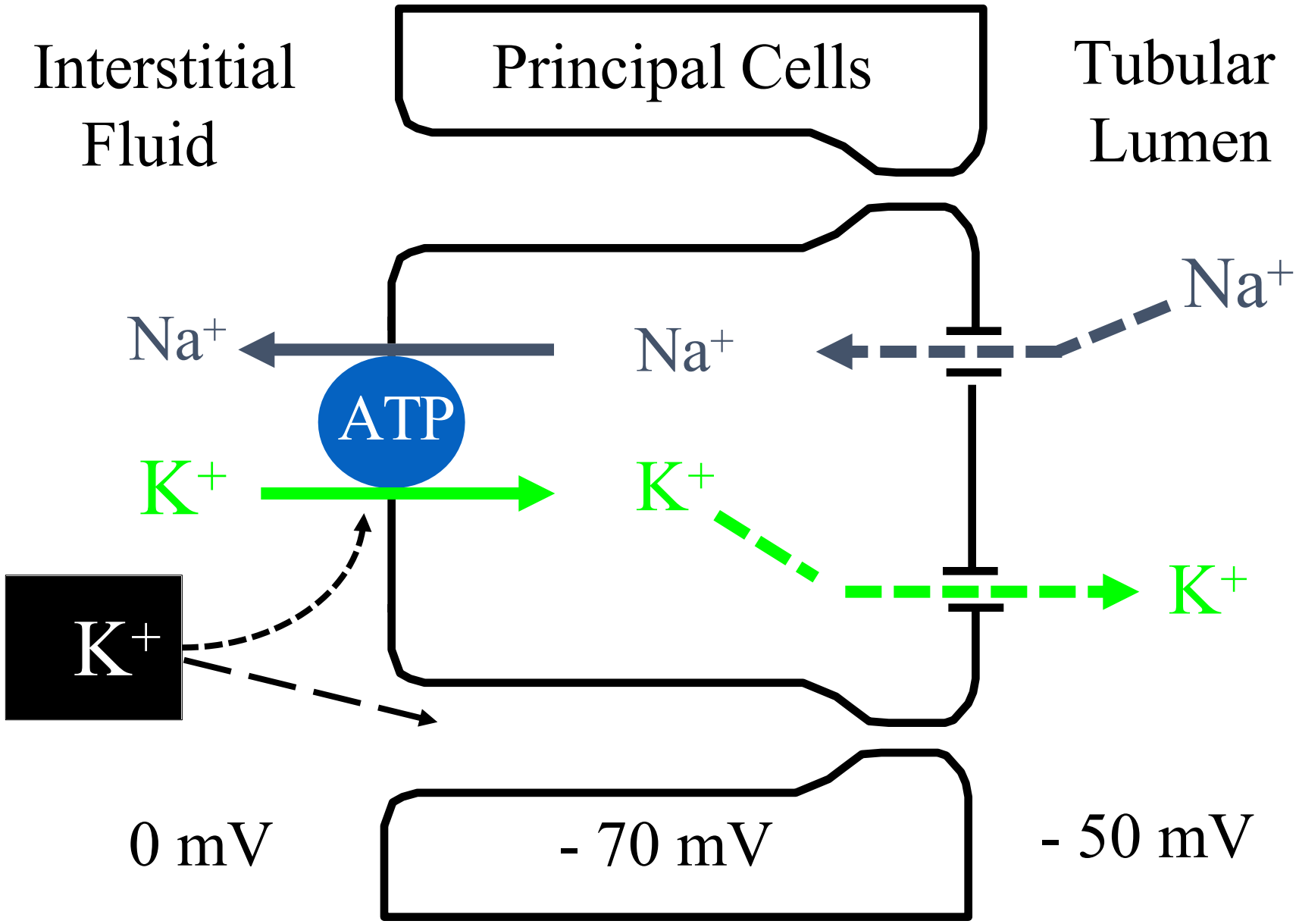
Ok now let's see how they shift between intracellular and extracellular fluid

1- Uptake of k+ by cells which is stimulated by **insulin** and plays a vital role in the regulation process

Insulin stimulates the uptake of glucose which requires the activity of Na+/K+ ATPase which pumps K+ in and Na+ out

So the higher the insulin release the higher the glucose uptake the higher uptake of K+ and usually insulin is released after a meal which probably contains K+

So by that mechanism the insulin reduces the K+

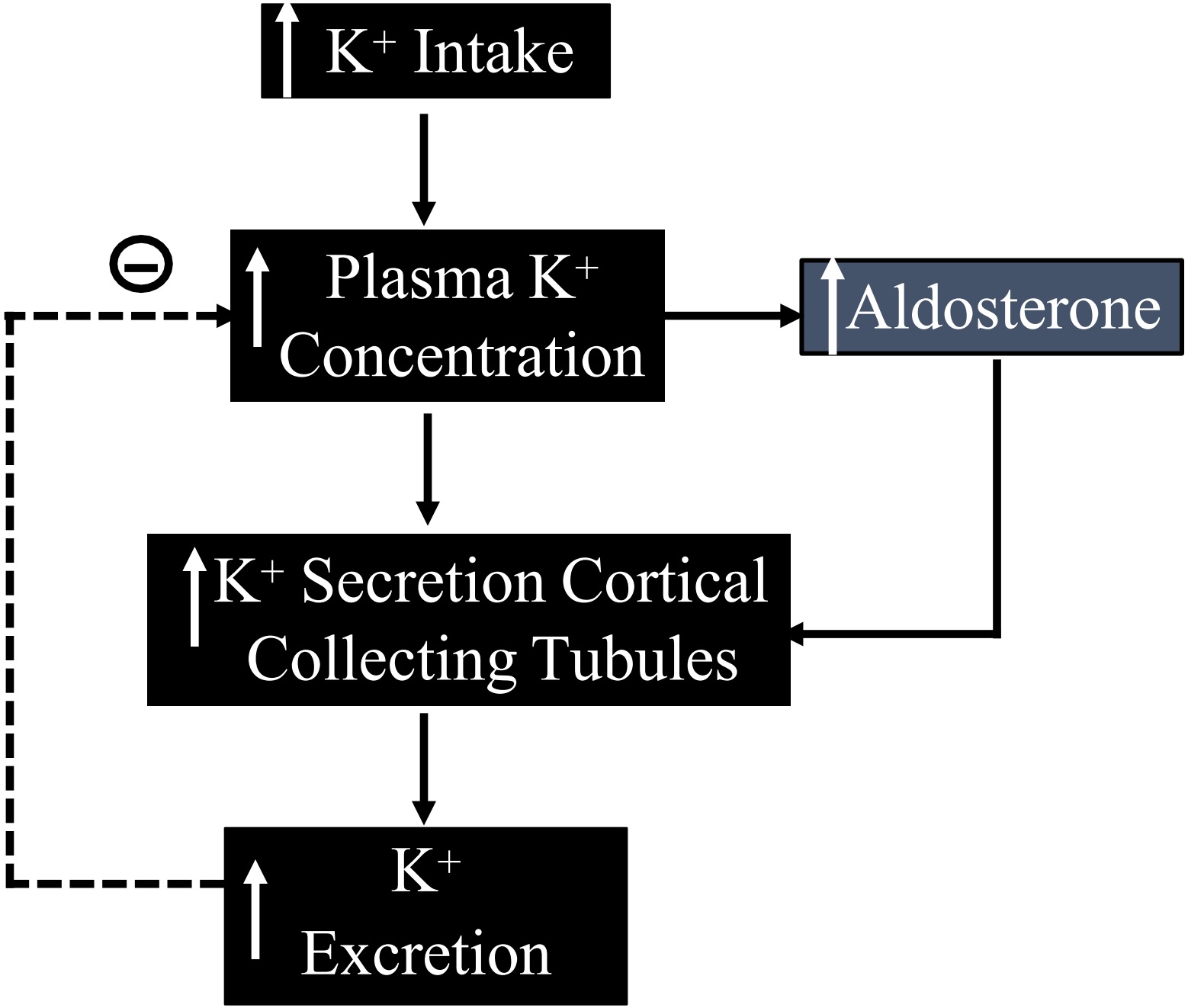

Interstitial Fluid
Principal Cells
Tubular Lumen
Na+
Na+
Na+
ATP
K+
K+
K+
K+
0 mV
- 70 mV
- 50 mV

2- Aldosterone is another important hormone for regulating potassium and it's stimulated by hyperkalemia (slightly increased k+ stimulates *Aldosterone*)

It works on the pumps in principle cells and intercalated cells
increases Na+ reabsorption and k+ secretion
Not only in kidneys but also between other body cells

3- Also there is another stimulus for k+ uptake which **β-adrenergic** receptors stimulations by catecholamines

These 3 factors 1-insulin , 2- aldosterone, 3- β-adrenergic receptors work when there is hyperkalemia and when there is no hyper (normal) they will make hypokalemia
(common sense 👀)


K+ Intake
Plasma K+ Concentration
Aldosterone
K+ Secretion Cortical Collecting Tubules
K+ Excretion

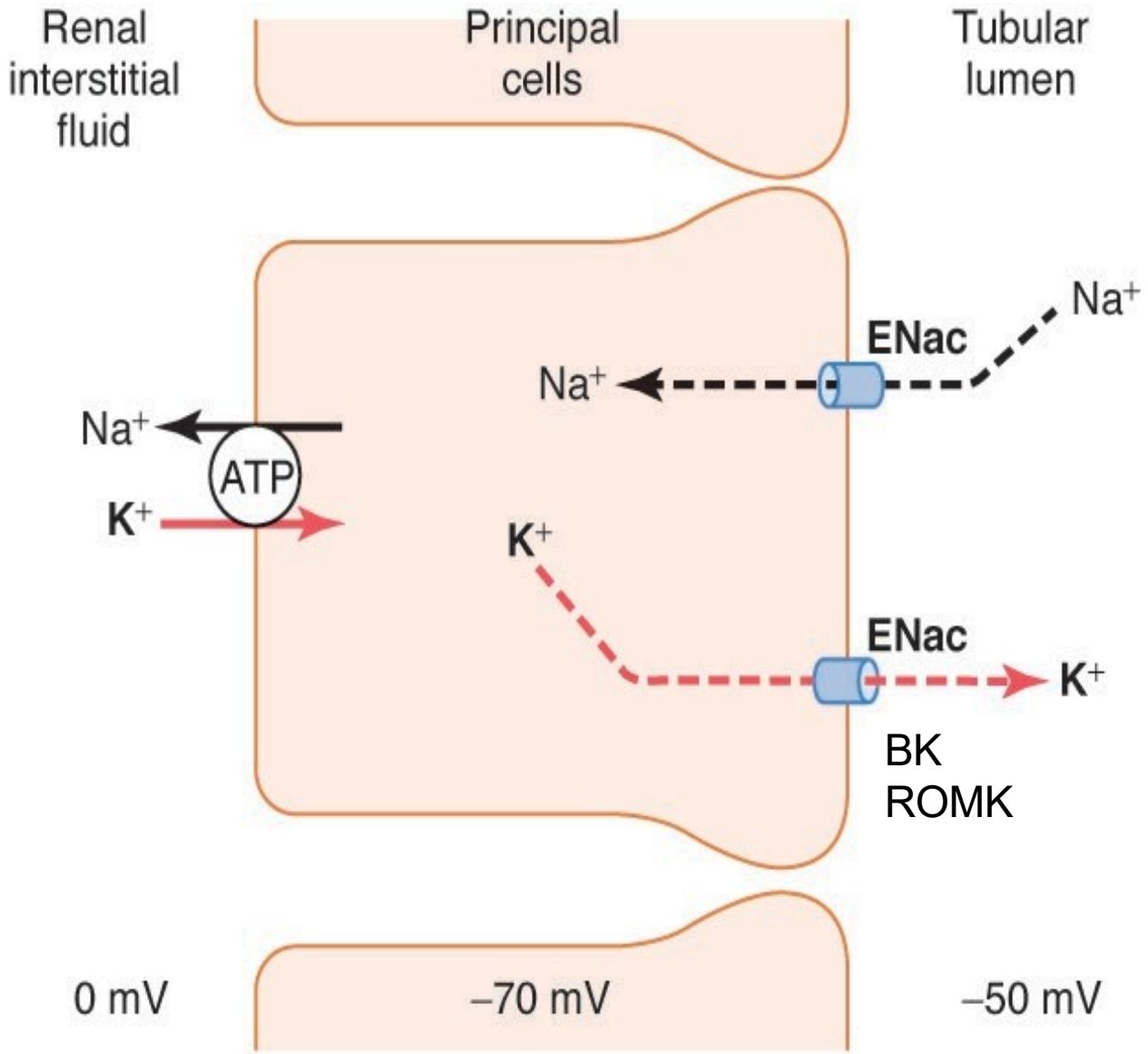
Control of Cortical Collecting Tubule (Principal Cells) K^+ Secretion

- Extracellular K^+ concentration : increases K^+ secretion
- Aldosterone : increases K^+ secretion
- Sodium (volume) delivery : increases K^+ secretion
- Acid - base status:
  - acidosis : decreases K^+ secretion
  - alkalosis : increases K^+ secretion

Alkalosis : acid-base imbalance that results in a higher PH than normal
By increasing the Na+/K+ ATPase activity

and Vice Versa for Acidosis

Potassium Secretion by Principal Cells



- On their basolateral surface, principle cells have Na^+/K^+-ATPase channels.
- On their luminal surface, they have ENaC channels for sodium reabsorption, and two types of potassium channels for potassium secretion: Renal Outer Medullary Potassium (ROMK) channels and high conductance/big potassium (BK) channels.
- The greater the availability of these channels, the greater the number and activity of Na^+/K^+-ATPase, which increases both sodium reabsorption and potassium secretion.

Factors that lead to K+ release from the cells
First factor: is cell lysis

Hypotonic solution Which causes swelling and rupture to the cell or damage of the tissue >> Which will lead to a K+ release from ICF to ECF.

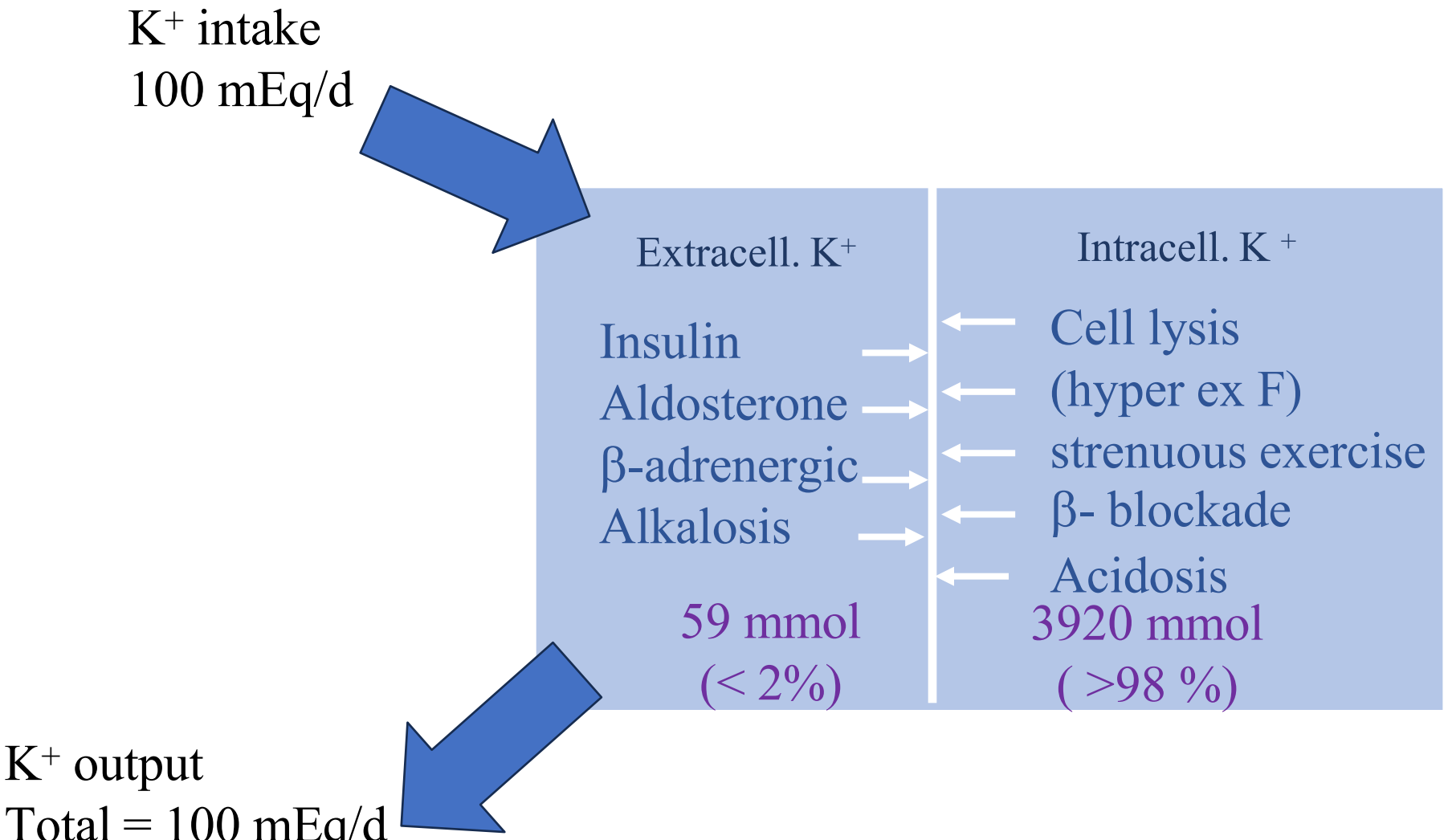
Hypertonic ECF the water will move from intra to extra which will lead to cells shrinkage >> The K+ conc. Intracellularly increases significantly and more K+ diffuses outside the cell (Shift from intra to extra)

Second factor: After a strenuous exercise there is a high release of K+ outside the cells.
Normally exercising doesn't cause a hyperkalemia state unless it's accompanied with other factors that increase the K+ release e.g. (strenuous exercise without drinking water or took β-adrenergic receptors blocker)

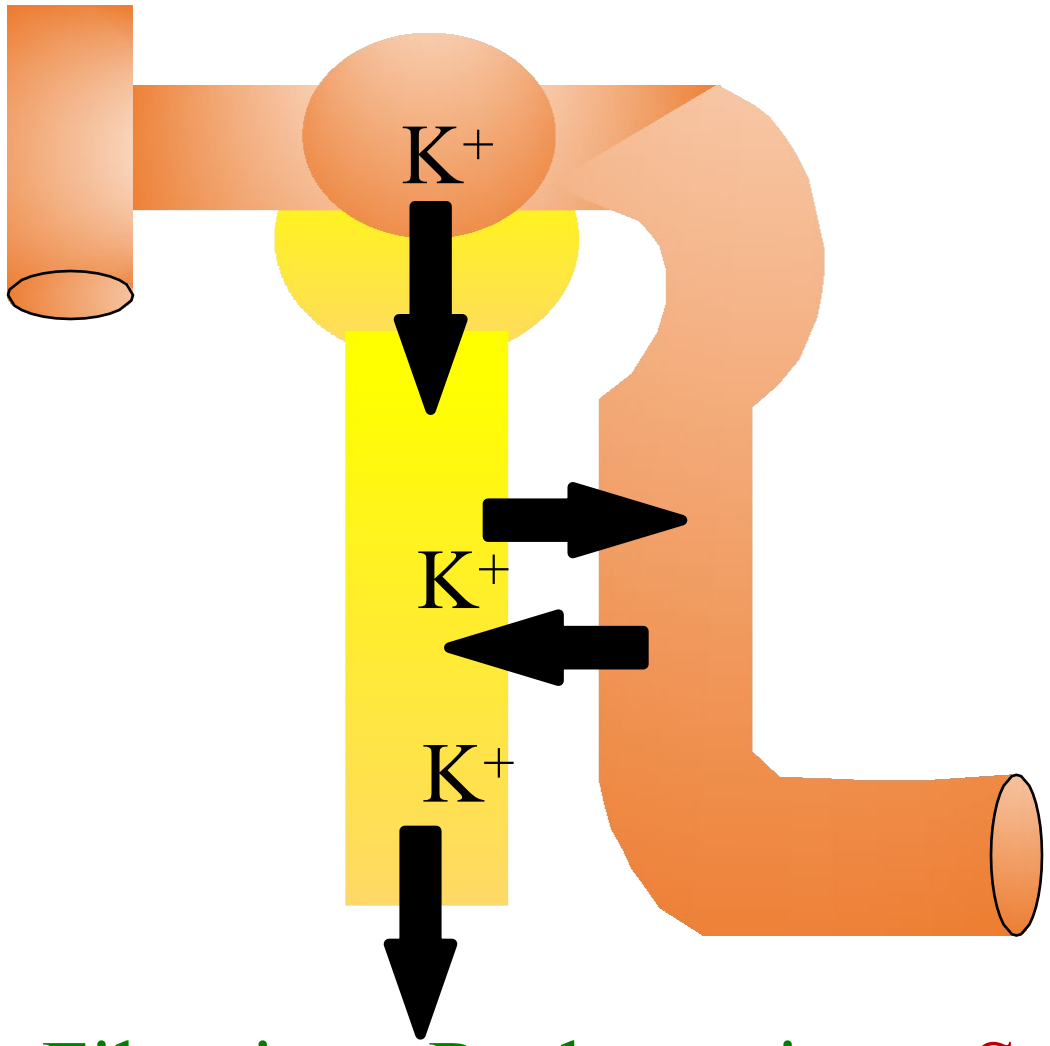
Depletion of K+ without reuptake of it *OR presence of* 2 factors causes severe imbalance of K+

Third factor: if there is a decrease in Na+/K+ ATPase activity (acidosis) this will lead to a decreased uptake of K+ intracellularly and increasing it's conc. Extracellularly (blood)

Potassium Regulation: Internal and External



Control of Potassium Excretion



Excretion = Filtration - Reabsorption + Secretion

How can the kidney control the excretion of K+ (the shift between compartments doesn't correct the imbalance, it only decreases the deviation so we need to preserve/secret K+ to optimally correct it)

The kidney regulates K+ excretion (excretion= filtration – reabsorption + secretion)
so we need to regulate one of these:
1- **Filtration** for K+ depends on (K+ conc. * GFR)
(We can't change the GFR and the K+ conc. Filtration increase/decrease as the K+ increase/decrease directly)
So the filtration aids in the regulation process but it's not enough.

2- **Reabsorption** of K+ occurs in PCT 67% and there is no regulation on it
Thick ascending loop of Henley 25%-27% and also we can't control it
Also in the intercalated cells K+/H+ ATPase but this pump activity is insignificant (discussed later)

3- (**Secretion**) The K+ reabsorption happens in the late DCT and collecting ducts in the principle cells
And secreting K+ from these cells is influenced by Aldosterone so we can regulate K+ secretion by controlling Aldosterone

So the K+ Secretion is the main important factor to regulate K+ excretion 🖐!
(By regulating Aldosterone)

See next slide👇

Renal tubular sites of potassium reabsorption and secretion.

765 mEq/day =
GFR * conc.

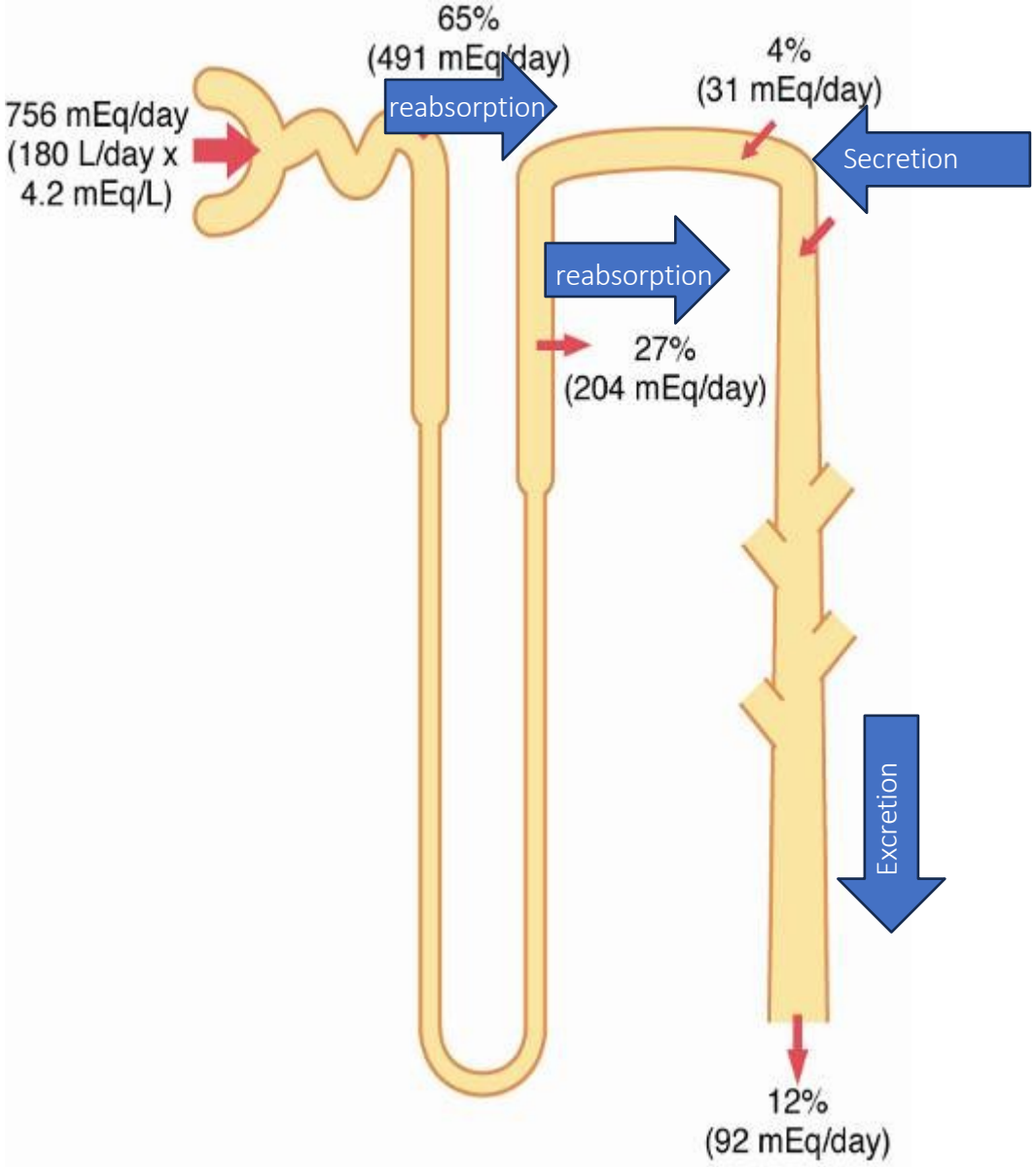
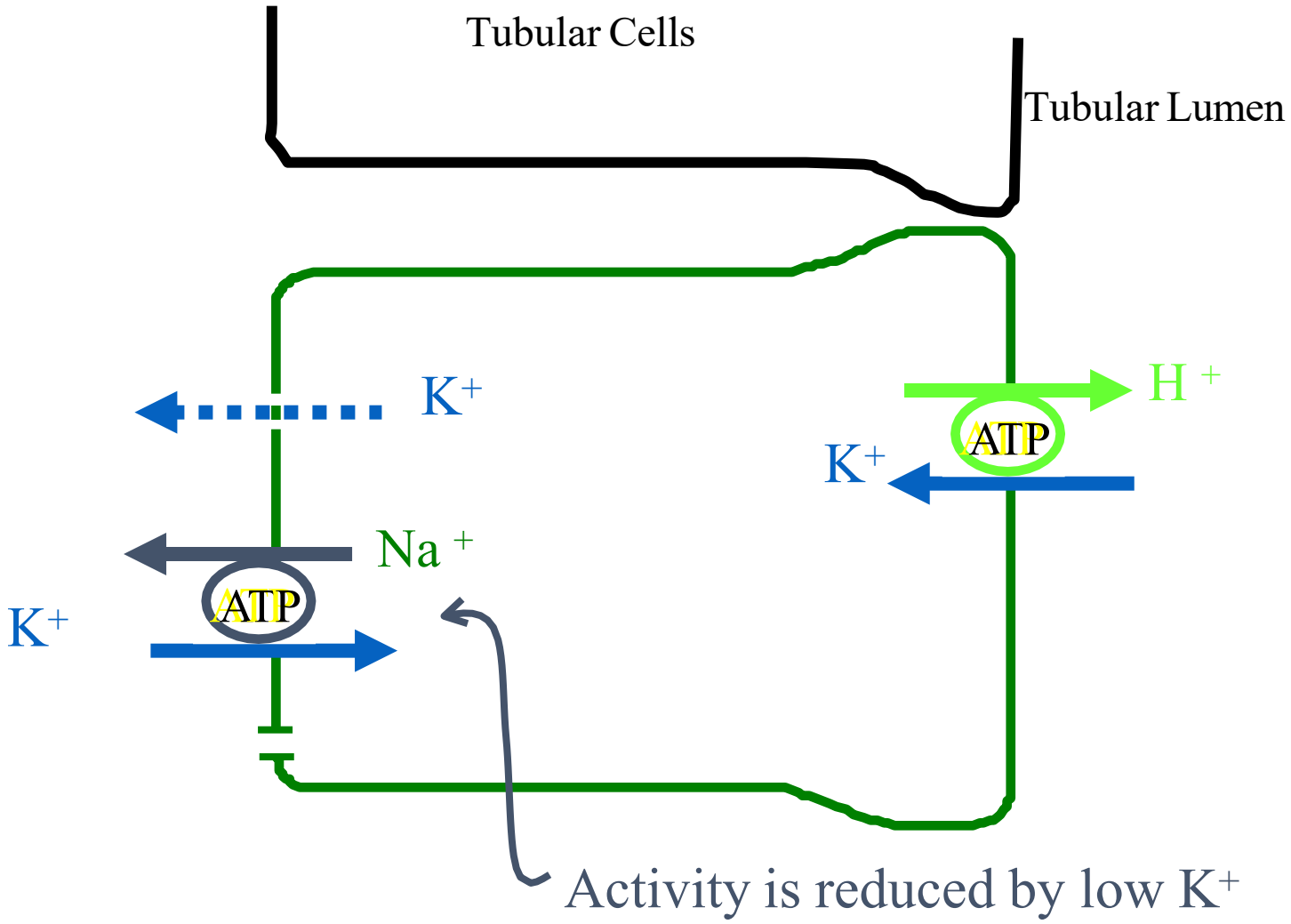


Figure 29-2

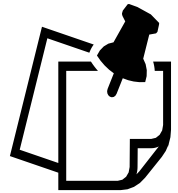
Late Distal and Cortical Collecting Tubules
Intercalated Cells –Reabsorb K^+



So what are the mechanisms that affects K+ Reabsorption In the intercalated cells (Type A) in the late DCT and in the collecting tubules
K+/H+ ATPase (pump On the luminal surface)
the activity of this pump depends on the K+ conc. (it's Primary pump and doesn't need a cotransporter)
Secretion of H+ and reabsorption of K+
This pump has insignificant K+ reabsorption if the individual has hyperkalemia.
In hypokalemia it's active.

Na+/k+ ATPase activity increases when there is hyperkalemia. why? Because it secretes K+ and reabsorb Na+ So pumps get affected by K+ conc.

Control of Cortical Collecting Tubule (Principal Cells) K^+ Secretion

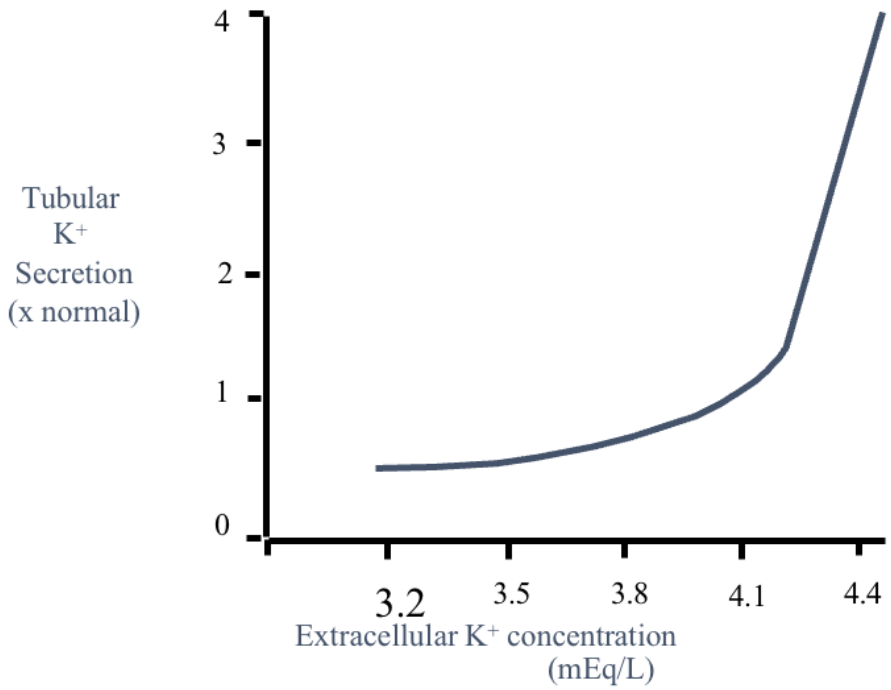


- Extracellular K^+ concentration : increases K^+ secretion
- Aldosterone : increases K^+ secretion
- Sodium (volume) delivery : increases K^+ secretion
- Acid - base status:
  - acidosis : decreases K^+ secretion
  - alkalosis : increases K^+ secretion

The following slides explain how these factors influence potassium secretion and interact with each other:

1. ECF K^+ and its effect on secretion and aldosterone
2. Aldosterone's effect on K^+ secretion
3. Na^+ impact on flow rate and K^+ secretion
4. H^+ influence on K^+ secretion

Effect of Extracellular K^+ on Excretion of K^+



Increased extracellular K^+ promotes K^+ secretion by two ways:
A. Directly by preventing back leak.
B. Indirectly by stimulating aldosterone release.

A. Increased extracellular potassium concentration increases the potassium gradient from the renal interstitial fluid to the interior of the epithelial cell, which reduces backleakage of potassium ions from inside the cells through the basolateral membrane.

Regarding the graph:
Normal ECF potassium concentration = 4.2 mmol/L.
It has been found that the body starts increasing potassium secretion significantly at 4.1 mmol/L (just below the normal level) as a protective mechanism to prevent hyperkalemia.

Increased serum K^+ stimulates aldosterone secretion

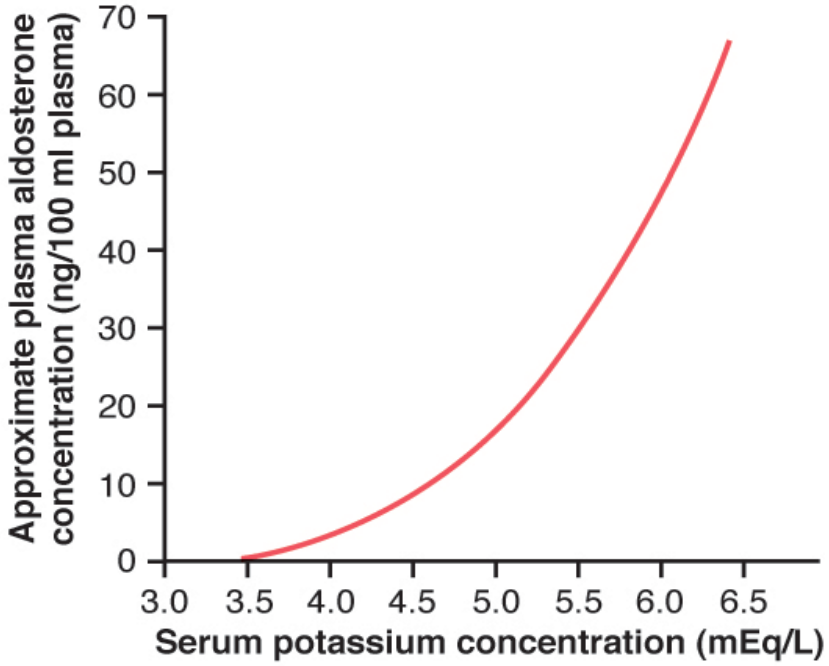
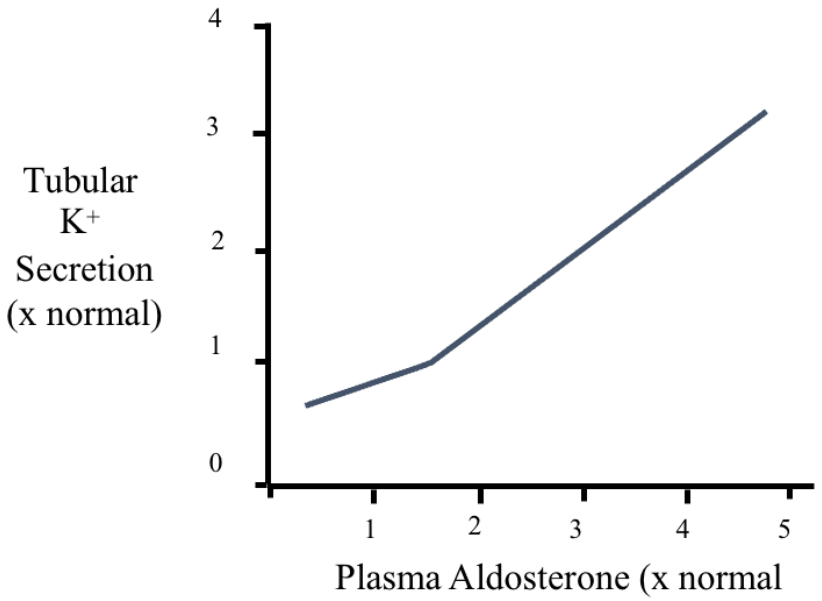


Figure 29-5

B. **Higher ECF potassium stimulates aldosterone secretion**
Effects of high plasma Potassium Concentration on Aldosterone:

At normal potassium levels (4.2 mmol/L), aldosterone is ~4 ng/mL.
Increasing potassium to 4.5 raises aldosterone to ~10 ng/mL.
At 5.0 mmol/L, aldosterone almost reaches 20 ng/mL.
The relationship is direct and nonlinear; higher potassium has progressively stronger effects on aldosterone.

Effect of Aldosterone on K^+ Excretion



Aldosterone increases the activity of Na^+/K^+-ATPase, increasing sodium reabsorption and potassium secretion.

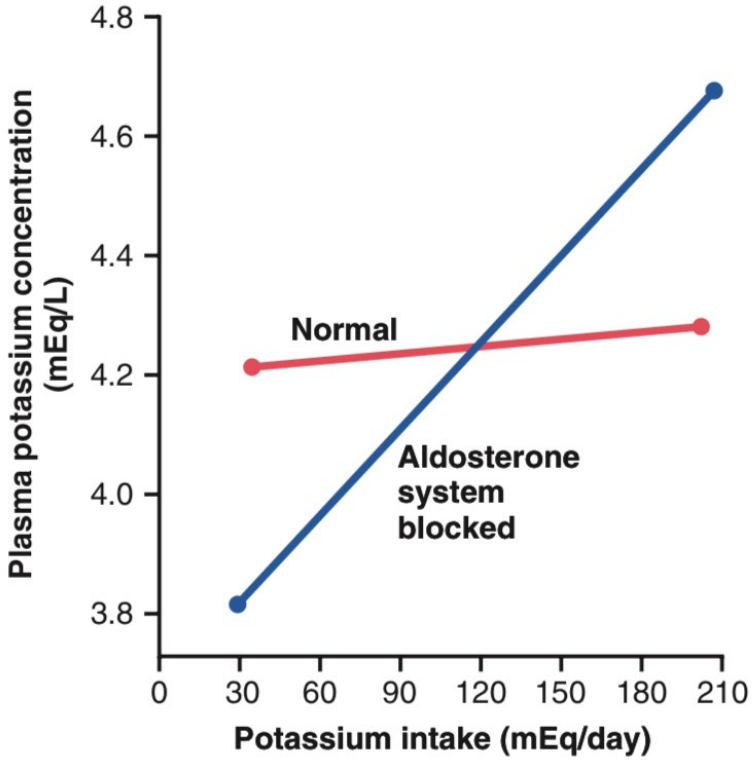
Aldosterone is released during hyperkalemia to promote potassium secretion (mainly) and sodium reabsorption, which makes it a powerful regulator for reducing extracellular potassium levels back to normal.

Hyperkalemia stimulates aldosterone release, and aldosterone in turn enhances the activity of the pump and increases the expression of ENaC, ROMK, and BK channels, boosting potassium secretion and sodium reabsorption.

Conversely, patients with deficient aldosterone production (Addison's disease) often have clinically significant hyperkalemia due to accumulation of potassium in the extracellular space, as well as renal retention of potassium.

Animal studies show that increasing aldosterone (2x, 3x, 5x normal) increases potassium secretion.

K^+ After Blocking Aldosterone System



Feedback Relation Between Potassium and Aldosterone:
High ECF potassium induces aldosterone release → aldosterone increases potassium secretion → ECF potassium decreases → aldosterone release stops.

This negative feedback loop is powerful. Disruption causes wide fluctuations in plasma potassium levels.
Proof: In a study, two animals were compared. In the healthy one, increasing potassium intake (2x or 6x) resulted in plasma K^+ levels remaining within ±0.1 mmol/L of normal due to intact aldosterone feedback.
In another animal with adrenal cortex removal and fixed-rate aldosterone infusion (constant aldosterone level), increasing potassium intake caused much larger increases in plasma potassium concentration.

Effect of collecting tubule flow rate on K^+ secretion

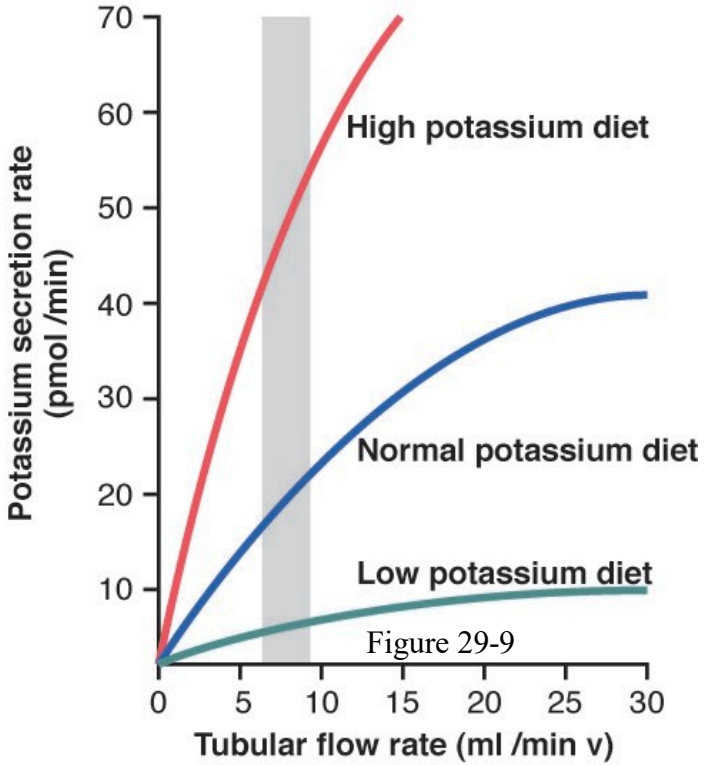
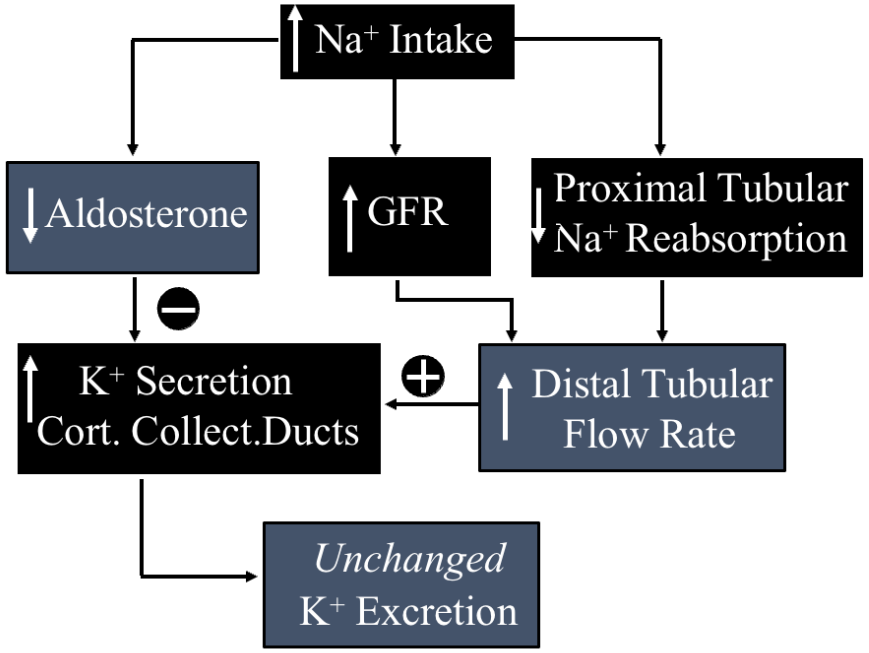


Figure 29-9

Increasing tubular flow rate enhances potassium secretion.
When potassium is secreted into the tubular fluid, the luminal concentration of potassium increases, thereby reducing the driving force for potassium diffusion across the luminal membrane. With increased tubular flow rate, the secreted potassium is continuously flushed down the tubule, so the rise in tubular potassium concentration becomes minimized and net potassium secretion is increased.
In experiments dividing animals into three dietary groups: high, normal, and low potassium:
In those with normal potassium diets, high tubular flow increased potassium secretion.
In the high potassium diet group, secretion was even greater due to both high ECF potassium and high flow rate.
Therefore, elevated ECF K^+ amplifies the effect of increased flow rate on potassium secretion and filtration.

Effect of Sodium on Potassium secretion

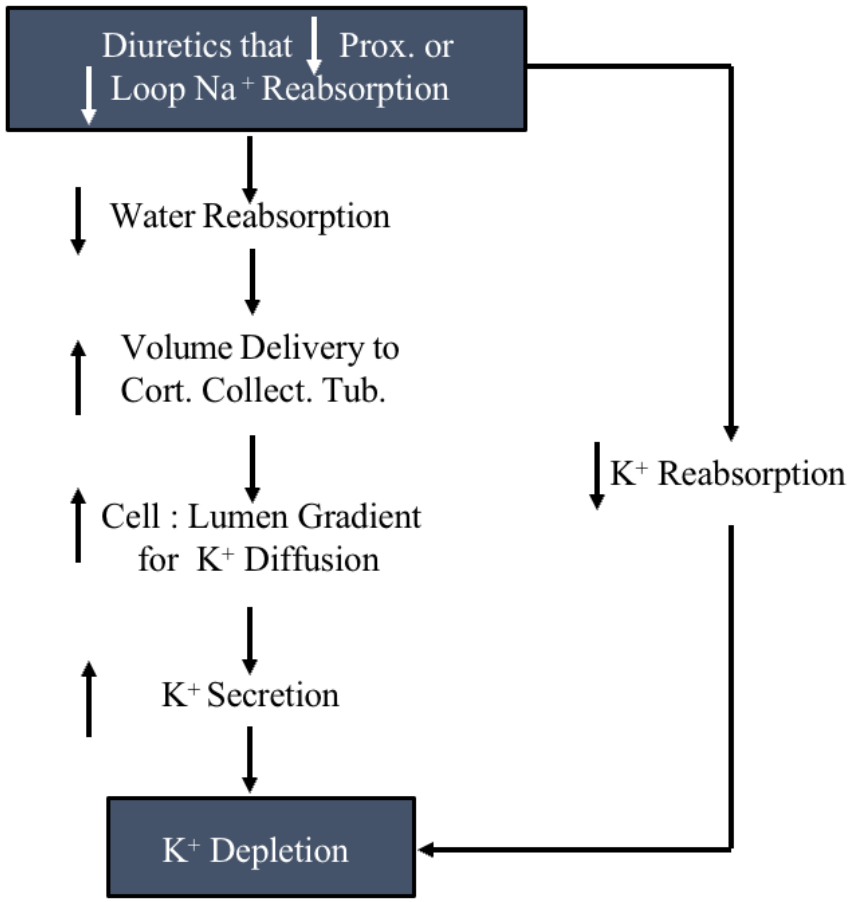


You can see in this diagram how increased sodium intake influences potassium excretion through two opposing mechanisms that balance each other out.

High Na^+ intake increases ECF volume due to salt and water retention, this raises GFR, which increases the pressure and amount of fluid filtered into the nephron, leading to a higher tubular flow rate. The increased flow reduces sodium and water reabsorption in PCT (since Na^+ reabsorption is time -and gradient- dependent) and delivers more fluid to the distal tubule. There, the elevated flow rate enhances potassium secretion by washing out secreted K^+ and preventing its backleak into the ECF, maintaining a strong concentration gradient that favors continued secretion. This flow-dependent mechanism is of greater importance in patients on diuretics, who are at higher risk of potassium depletion due to further increases in tubular flow.

At the same time, high Na^+ intake suppresses the RAAS, resulting in decreased aldosterone secretion. Since aldosterone normally enhances K^+ secretion, its reduction counteracts the flow-induced increase in secretion. As a result of these two opposing influences potassium excretion remains relatively unchanged.

Clinical perspective

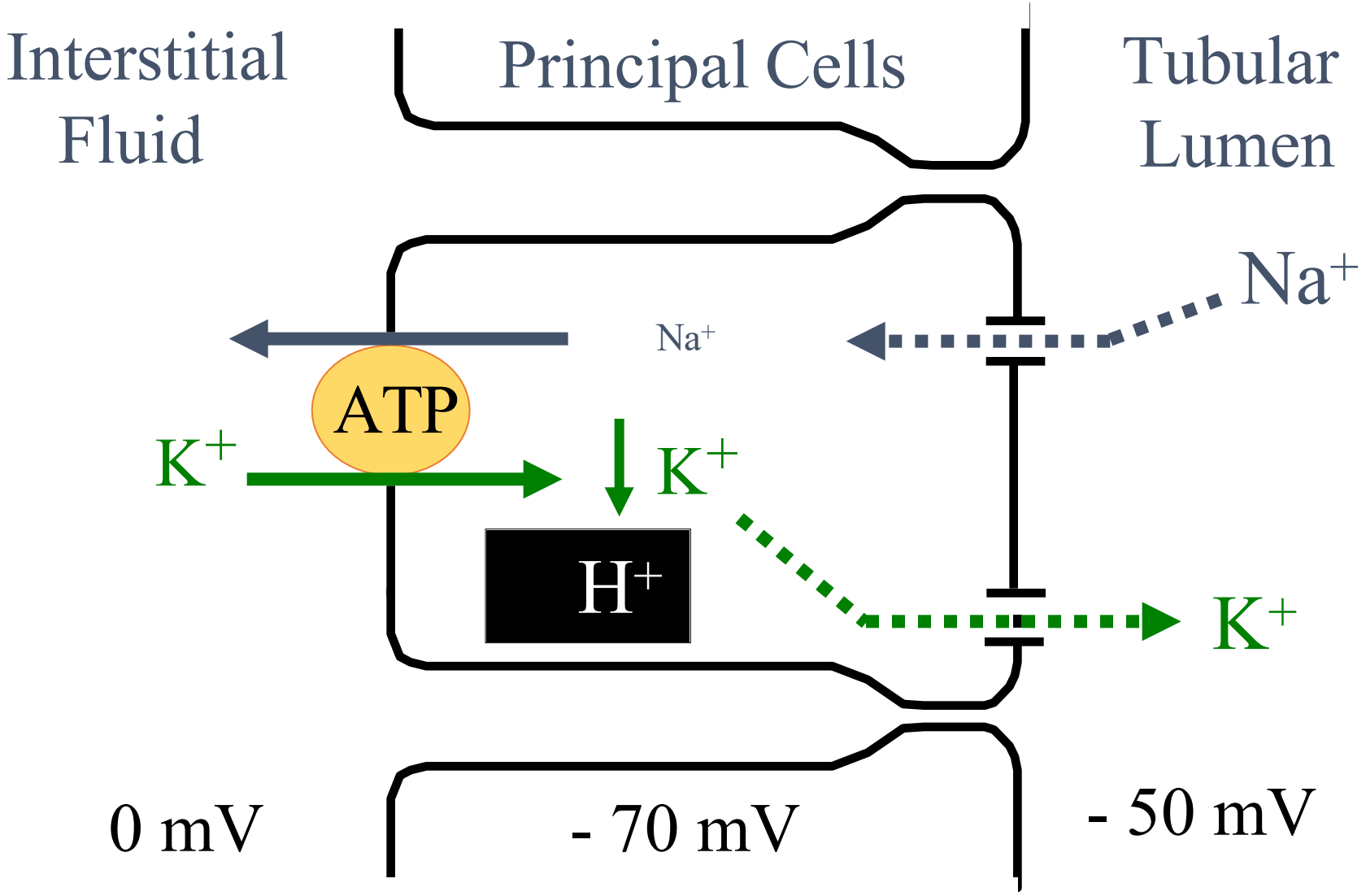


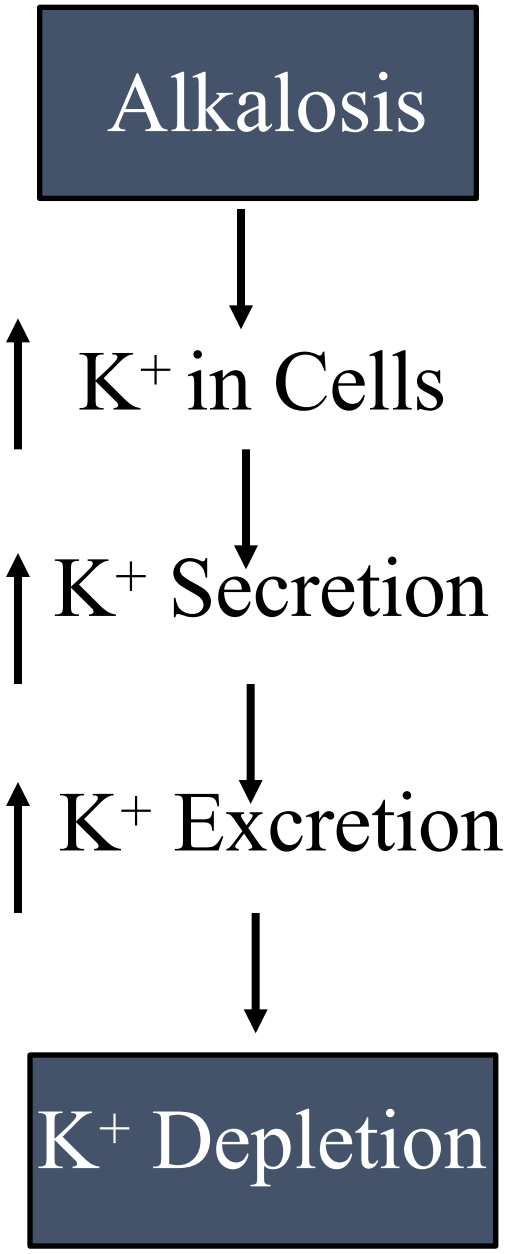
Diuretics that inhibit sodium reabsorption in the proximal tubule or loop of Henle cause decreased water reabsorption. This increases fluid volume delivered to the cortical collecting tubule. The elevated tubular flow rate enhances the gradient between the intracellular and luminal potassium concentrations, resulting in potassium diffusion from the cell into the lumen (K^+ secretion). As mentioned before, the increased flow rate washes potassium out of the lumen too, limiting the opportunity for K^+ reabsorption and further increasing urinary potassium loss. Certain diuretics may also directly reduce potassium reabsorption by increasing the velocity of tubular fluid, leaving no enough time for K^+ to be reabsorbed.

Diuretics that inhibit sodium reabsorption in PCT increase the tubular flow rate and potassium washout in DCT, which resulting in greater potassium secretion.

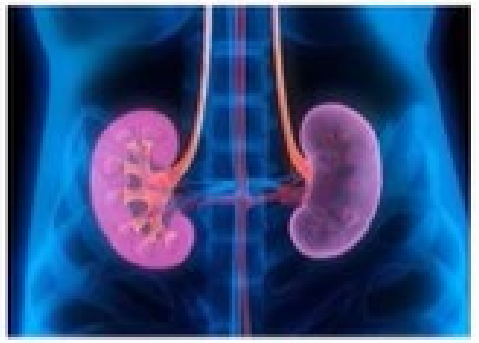
Diuretics targeting sodium transport in the thick ascending limb of the loop of Henle also reduce potassium reabsorption because sodium and potassium are reabsorbed by the same transport channels in this segment.

Acidosis Decreases Cell K^+





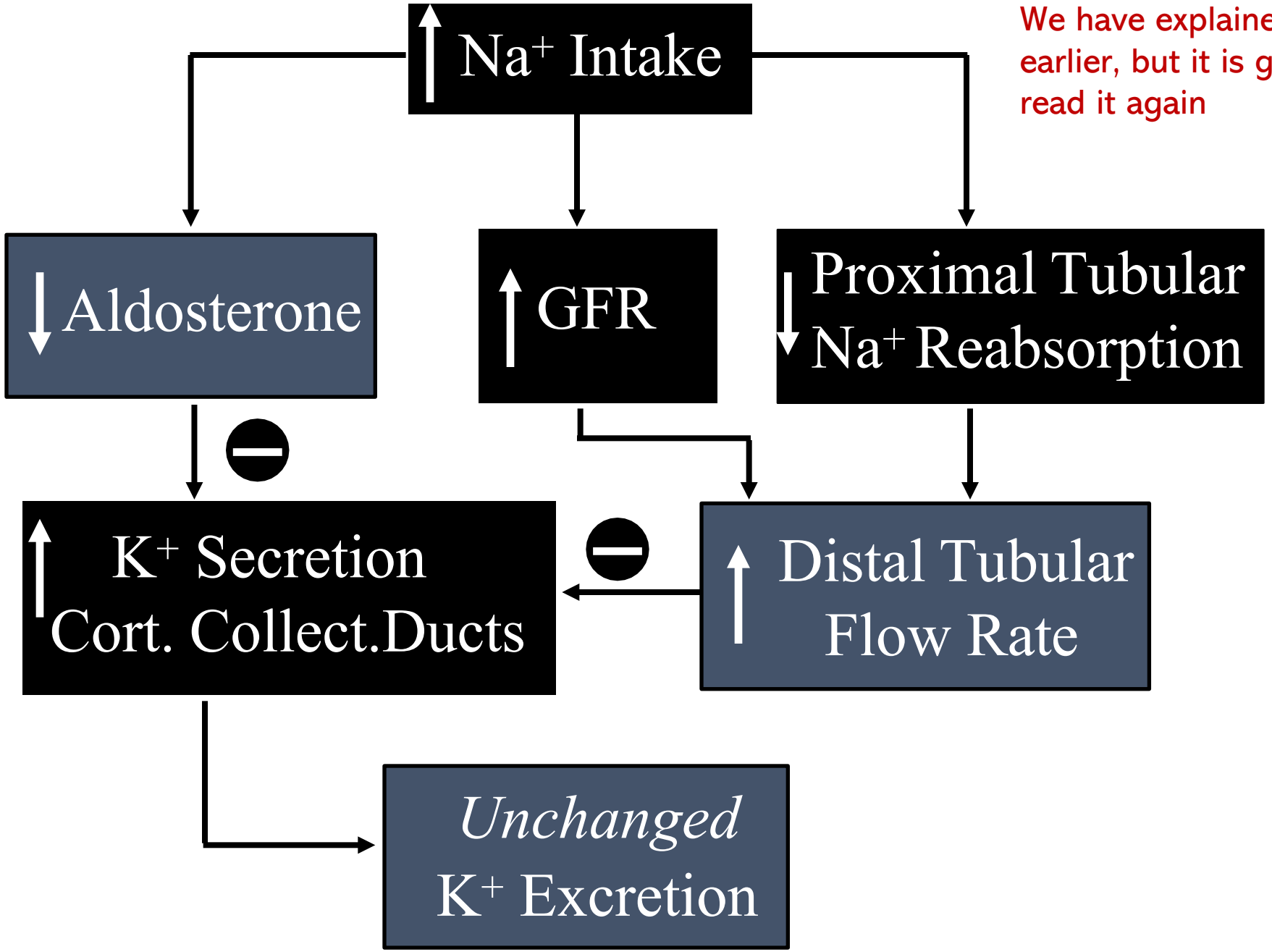
Acidosis (H^+ to be specific) inhibits Na^+/K^+-ATPase, reducing potassium secretion. Alkalosis increases its activity, enhancing secretion.



Homeostasis of K part II

Guyton and Hall, ch 30
Ebaa M Alzayadneh, PhD
2024

We have explained this earlier, but it is good to read it again



What are the consequences of increasing sodium in the diet, and how does that affect potassium excretion?

- When sodium intake is increased, the glomerular filtration rate (GFR) tends to increase. This leads to an increase in distal tubular flow rate, resulting in volume expansion within the distal tubules. At the same time, increased sodium intake reduces proximal tubular sodium reabsorption, which also contributes to increased fluid delivery and volume expansion in the distal tubule.

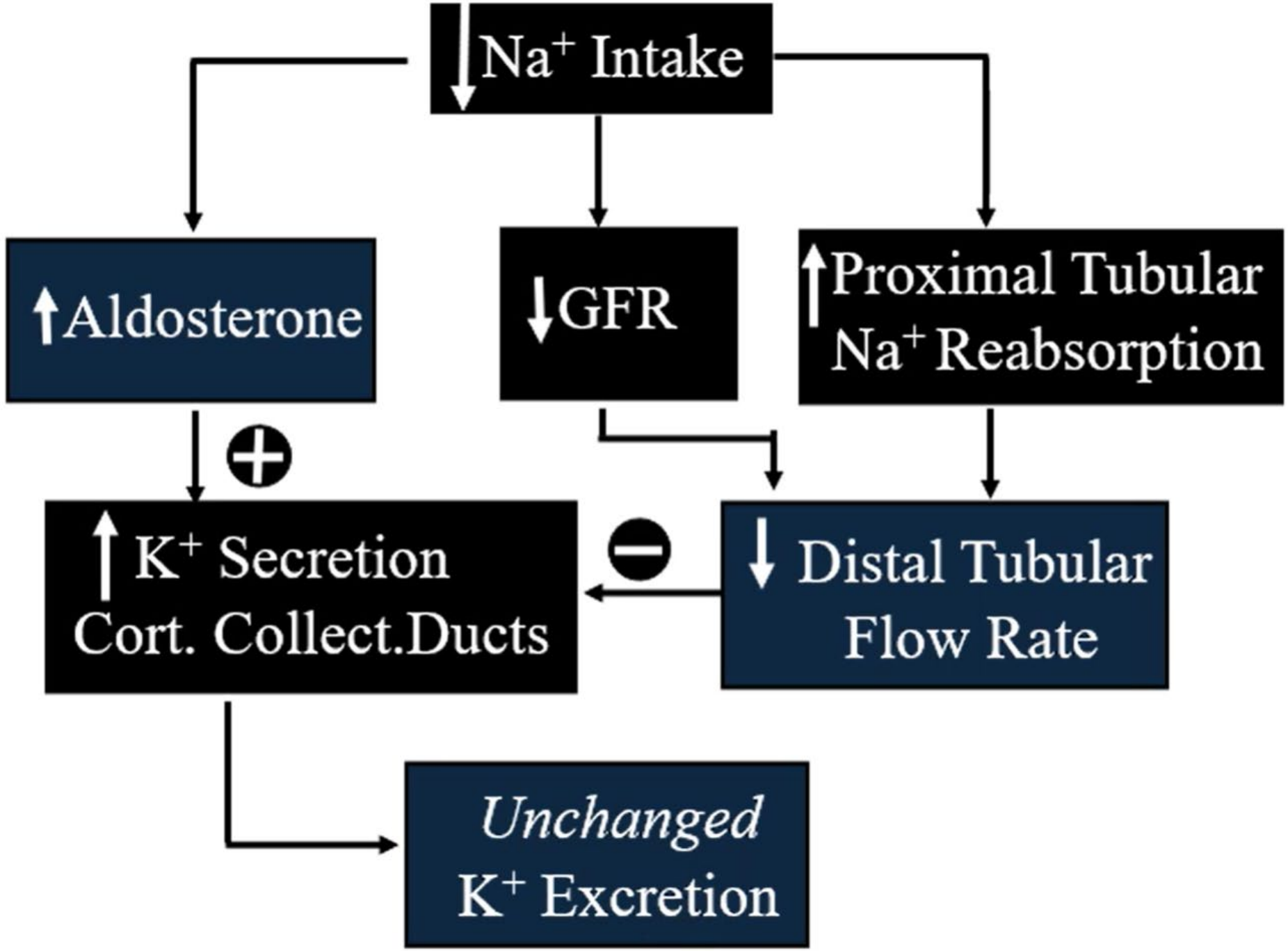
- This elevated distal tubular flow rate directly increases potassium secretion. This is an important effect of increased sodium intake. However, increased sodium intake also inhibits aldosterone secretion. A reduction in aldosterone levels normally leads to **decreased** potassium secretion.

- So here, we have **two opposing effects** on potassium excretion:

1- Decreased potassium secretion due to reduced aldosterone.
2- Increased potassium secretion due to elevated distal tubular flow rate.

- These opposing effects tend to counterbalance each other, leading to **no significant change in overall potassium excretion**.

- This balance is important because it explains why, under conditions of high sodium intake, potassium excretion may remain relatively unchanged despite reduced aldosterone activity. The increase in tubular flow compensates for the inhibitory effect of aldosterone suppression, allowing sufficient potassium to be secreted.


↓ Na+ Intake
↑ Aldosterone
↓ GFR
↑ Proximal Tubular Na+ Reabsorption
+
↑ K+ Secretion Cort. Collect.Ducts
−
↓ Distal Tubular Flow Rate
Unchanged K+ Excretion

The Opposite is Also True: Low Sodium Intake and Potassium Excretion

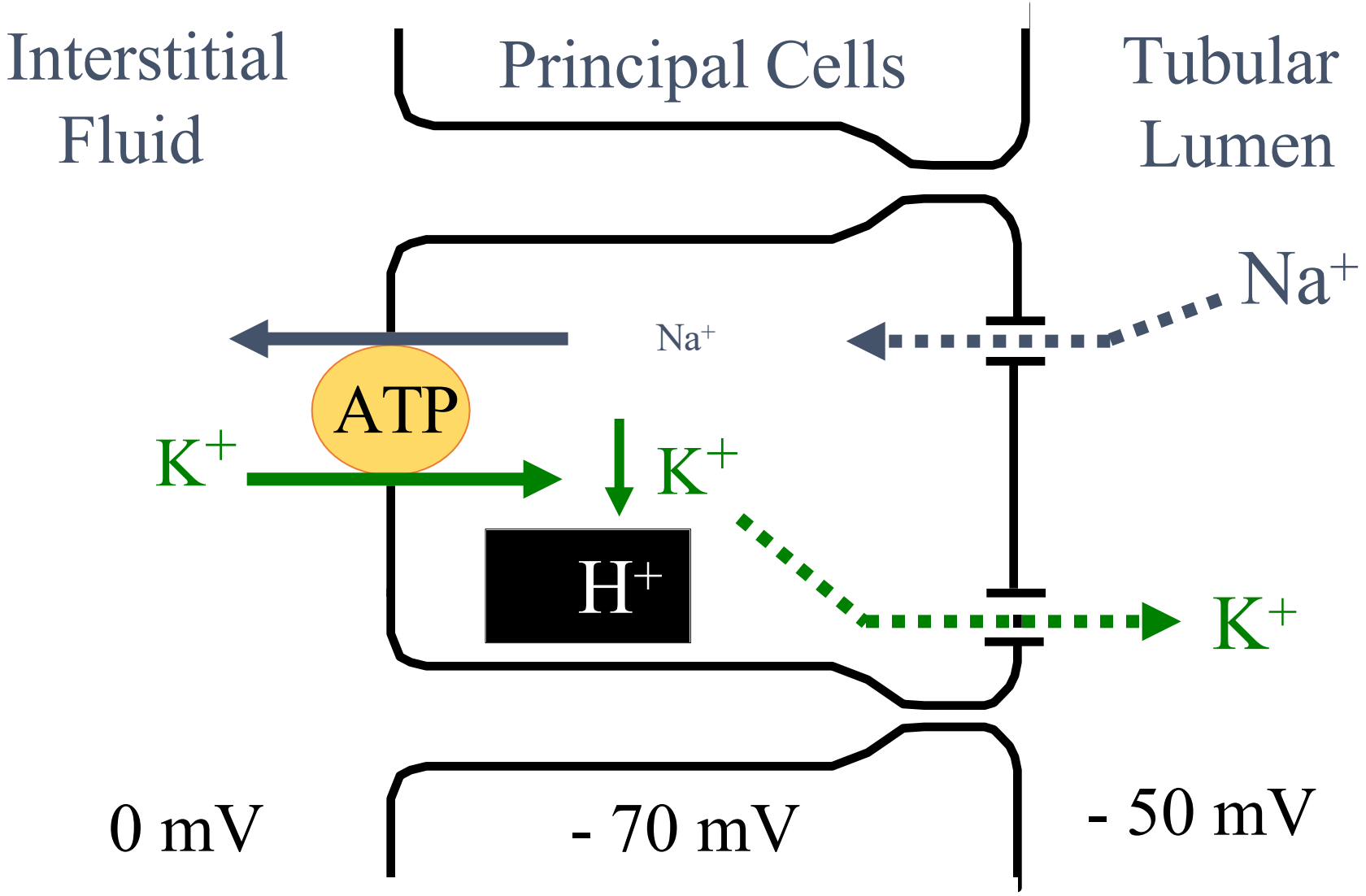
- When sodium intake is low, there is also **little change in potassium excretion**. This is due to a counterbalancing effect between two opposing mechanisms:

- **Low sodium intake increases aldosterone secretion**, which **stimulates potassium secretion**

- However, low sodium intake also leads to **a reduction in GFR** and **increased proximal tubular sodium reabsorption**, which in turn **reduces distal tubular flow rate**. A lower flow rate **decreases potassium secretion**.

- These opposing effects—stimulation of potassium secretion by aldosterone and inhibition of secretion due to reduced flow—counterbalance each other, resulting in **no change in overall potassium excretion**.

Acidosis Decreases Cell K^+



Effect of Acidosis on Potassium Secretion

- From previous discussions, we know that **acidosis decreases potassium secretion**, particularly in the case of **acute acidosis**. This occurs due to:

1- **Inhibition of the Na^+/K^+-ATPase activity**, and
2- **Decreased permeability to potassium on the luminal membrane**.

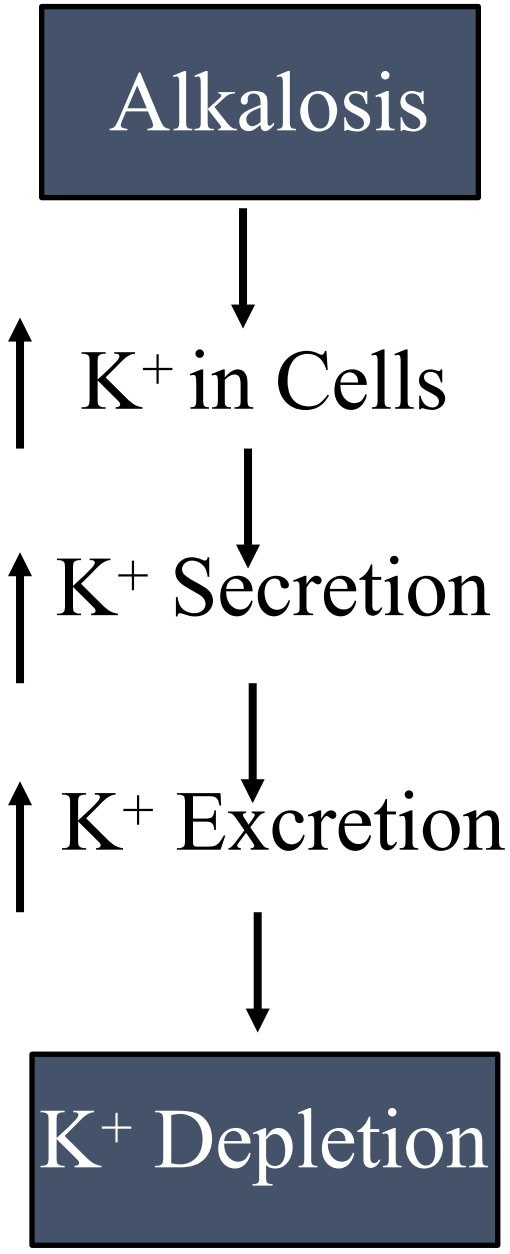
- However, in the case of **chronic acidosis** (lasting several days or more), the effect is different.

Chronic acidosis:

- **Inhibits proximal tubular reabsorption of sodium, chloride, and water**,
- Leading to an **increase in tubular flow rate**,
- Which **stimulates potassium secretion**.

- Thus, in **chronic acidosis**, the net effect is **increased potassium secretion** due to enhanced flow-dependent mechanisms, despite the acidotic state.

- In contrast, **acute acidosis inhibits potassium secretion**, primarily due to reduced transporter activity and membrane permeability.



Effect of Alkalosis on Potassium Secretion

- In **alkalosis**, the opposite effect occurs compared to acidosis. There is an **increase in Na^+/K^+-ATPase activity**, which leads to:
- Increased uptake of potassium into the **intracellular compartment** of tubular cells,
- Higher **intracellular potassium concentration**, and
- Enhanced **potassium secretion** into the tubular lumen.
- As a result, **potassium excretion increases**, which can contribute to **potassium depletion** in the body.
- So, in alkalosis, the stimulation of potassium secretion and excretion may lead to or worsen **hypokalemia**.

Clinical Perspective — Causes of Hyperkalemia

- Renal failure

  Reduction in tubular flow rate

- Decreased distal nephron flow (heart failure, severe volume depletion, NSAID, etc)
- Decreased aldosterone or decreased effect of aldosterone
  - adrenal insufficiency
  - K^+ sparing diuretics (spironolactone, eplerenone)
- Metabolic acidosis (hyperkalemia is mild)
- Diabetes (kidney disease, acidosis, ↓ insulin)

Clinical Perspective

Causes of Hypokalemia

- Very low intake of K^+
- GI loss of K^+ - diarrhea
- Metabolic alkalosis
- Excess insulin
- Increased distal tubular flow /
  - salt wasting nephropathies
  - osmotic diuretcs
  - loop diuretics
- Excess aldosterone or other mineralocorticoids

Can have similar effects on potassium secretion.

Question

- Which of the following would cause the most serious hypokalemia?
  A) A decrease in potassium intake from 150 mEq/day to 60 mEq/day
  B) An increase in sodium intake from 100 to 200 mEq/day
  C) Excessive aldosterone secretion plus high sodium intake
  D) Excessive aldosterone secretion plus low sodium intake
  E) A patient with Addison's disease
  F) Treatment with a beta-adrenergic blocker
  G) Treatment with spironolactone

Compensatory responses to decreased plasma ionized calcium

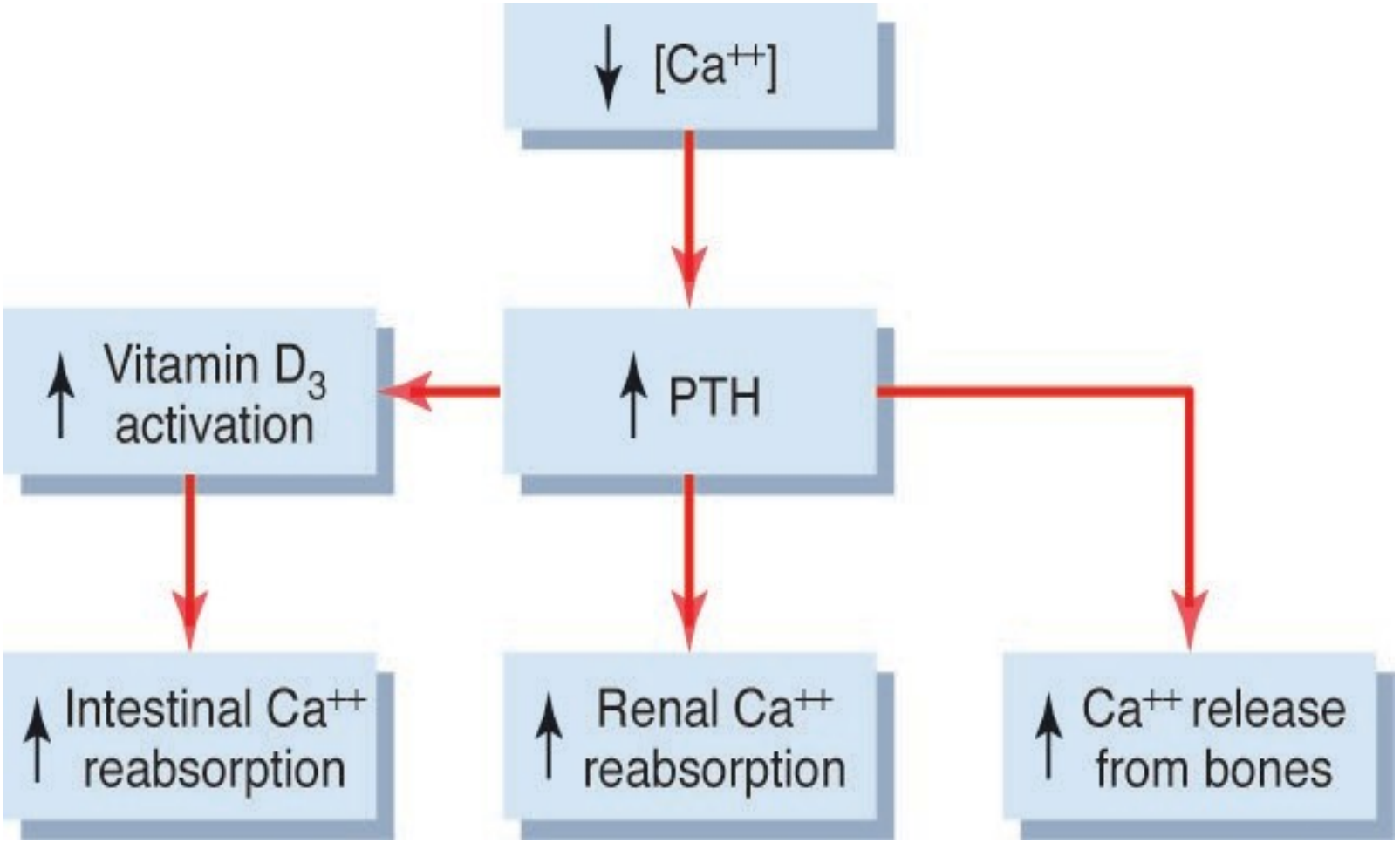


Figure 29-11

Calcium Regulation

- The concentration of calcium ions in the extracellular fluid is **tightly regulated**, typically maintained around **2.4 mEq/L**.

- Approximately **50% of the total calcium in plasma exists in the ionized (free) form**, which is biologically active. The remaining calcium is either:
- **Bound to plasma proteins**, or
- **Complexed with anions** such as phosphate or citrate.

Role of Parathyroid Hormone (PTH)

- The **major regulator** of plasma calcium levels is **parathyroid hormone (PTH)**. PTH acts primarily to **increase blood calcium levels** through three key mechanisms:

Kidneys:

- PTH **increases calcium reabsorption** in the distal tubules, reducing urinary calcium excretion.

Bones:

- PTH **stimulates osteoblastic activity**, which in turn promotes **osteoclastic bone resorption**, releasing calcium into the bloodstream.

Digestive System (Indirectly via Vitamin D):

- PTH stimulates the **activation of vitamin D (calcitriol)**, which enhances **intestinal calcium absorption** from the digestive tract. This occurs through increased expression of calcium-binding proteins and transporters.

Proximal tubular calcium reabsorption

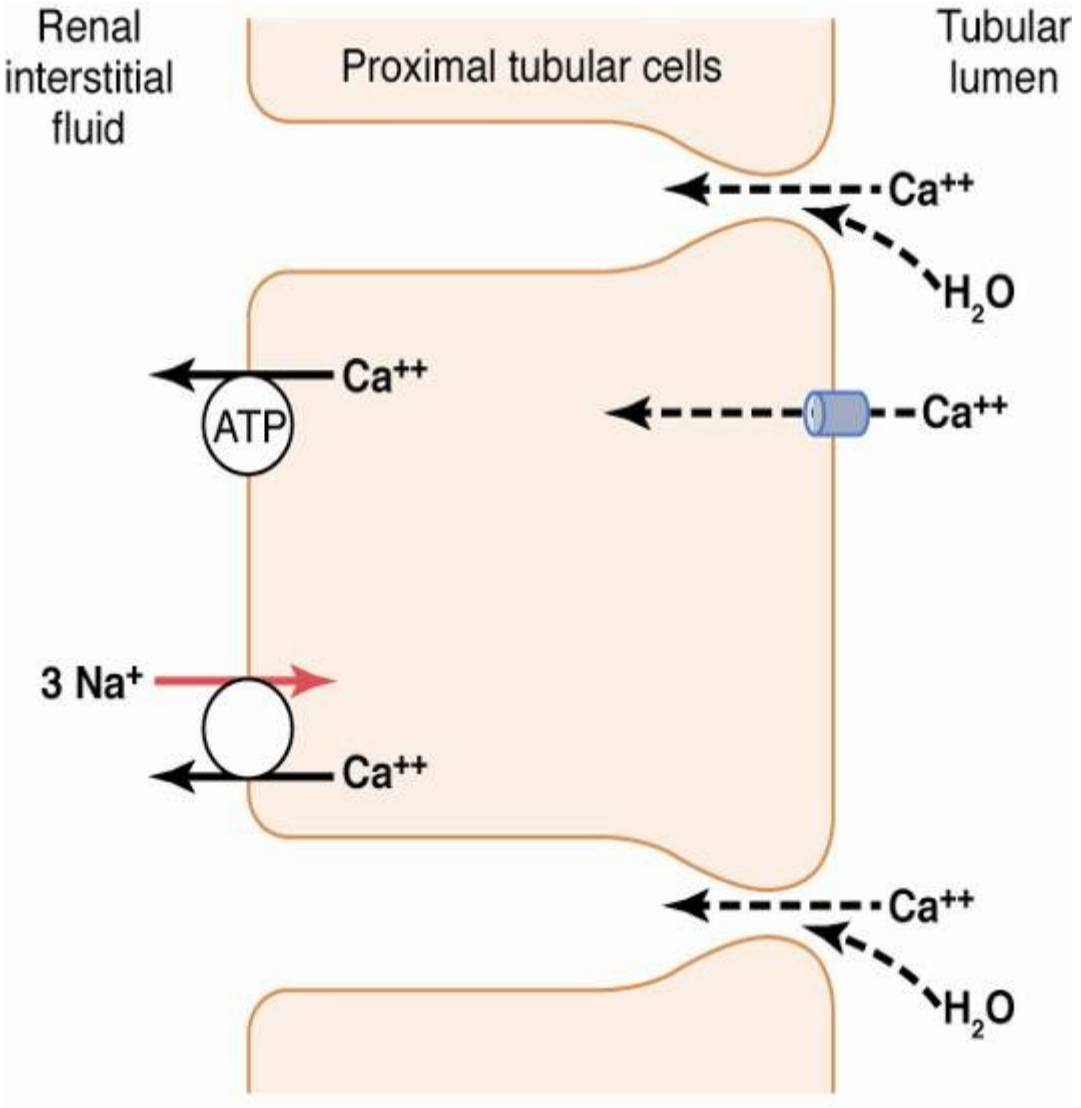


Figure 29-12

Calcium Reabsorption in the Nephron

- Calcium reabsorption in the **proximal convoluted tubule (PCT)** occurs **mainly via the paracellular pathway**. In this pathway, calcium is **carried along with water** between tubular epithelial cells.

- Only about **20% of calcium reabsorption in the PCT occurs via the transcellular route**. In this pathway:

- Calcium **diffuses down its electrochemical gradient** from the tubular lumen into the epithelial cell.

- It is then transported out of the cell into the **interstitial fluid** by:
- The **calcium ATPase** pump, and
- The **sodium-calcium exchanger (Na^+/Ca^{2+} antiporter)**, both of which promote calcium reabsorption into the blood.

- In the **thick ascending limb of the loop of Henle**, calcium is also reabsorbed **predominantly via the paracellular pathway**

- Also, there is calcium reabsorption in the **distal convoluted tubule**

Parathyroid hormone plays a crucial role in regulating calcium reabsorption.

Integration of Renal Mechanisms for Regulation of Body Fluids as well as electrolytes

Excretion = Filtration - Reabsorption + Secretion

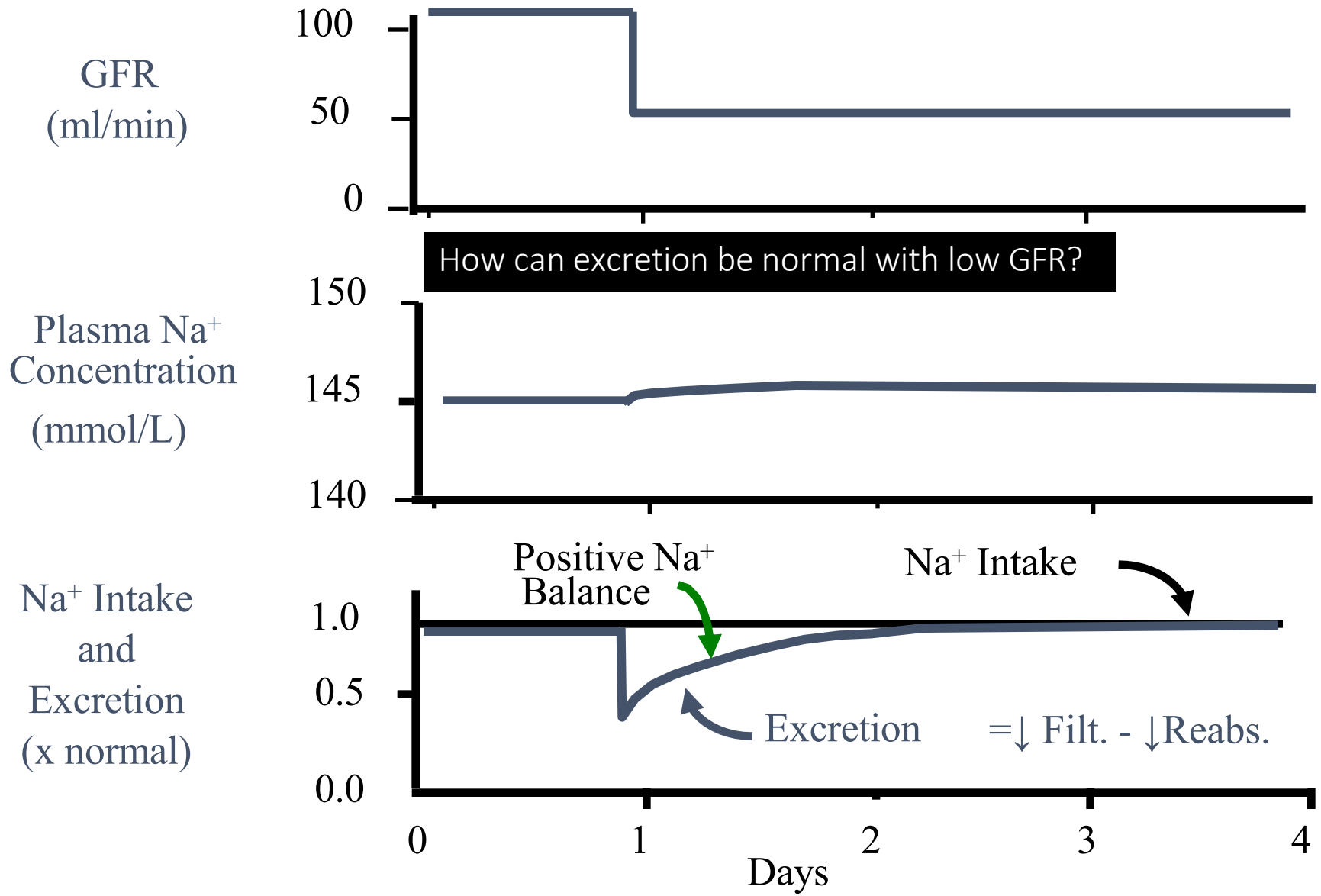
If there is a steady - state :

Fluid Excretion = Fluid Intake

Electrolyte Excretion = Electrolyte intake

Because we know that the osmolarity of electrolytes affect the volumes of fluids

Effect of Decreased GFR on Sodium



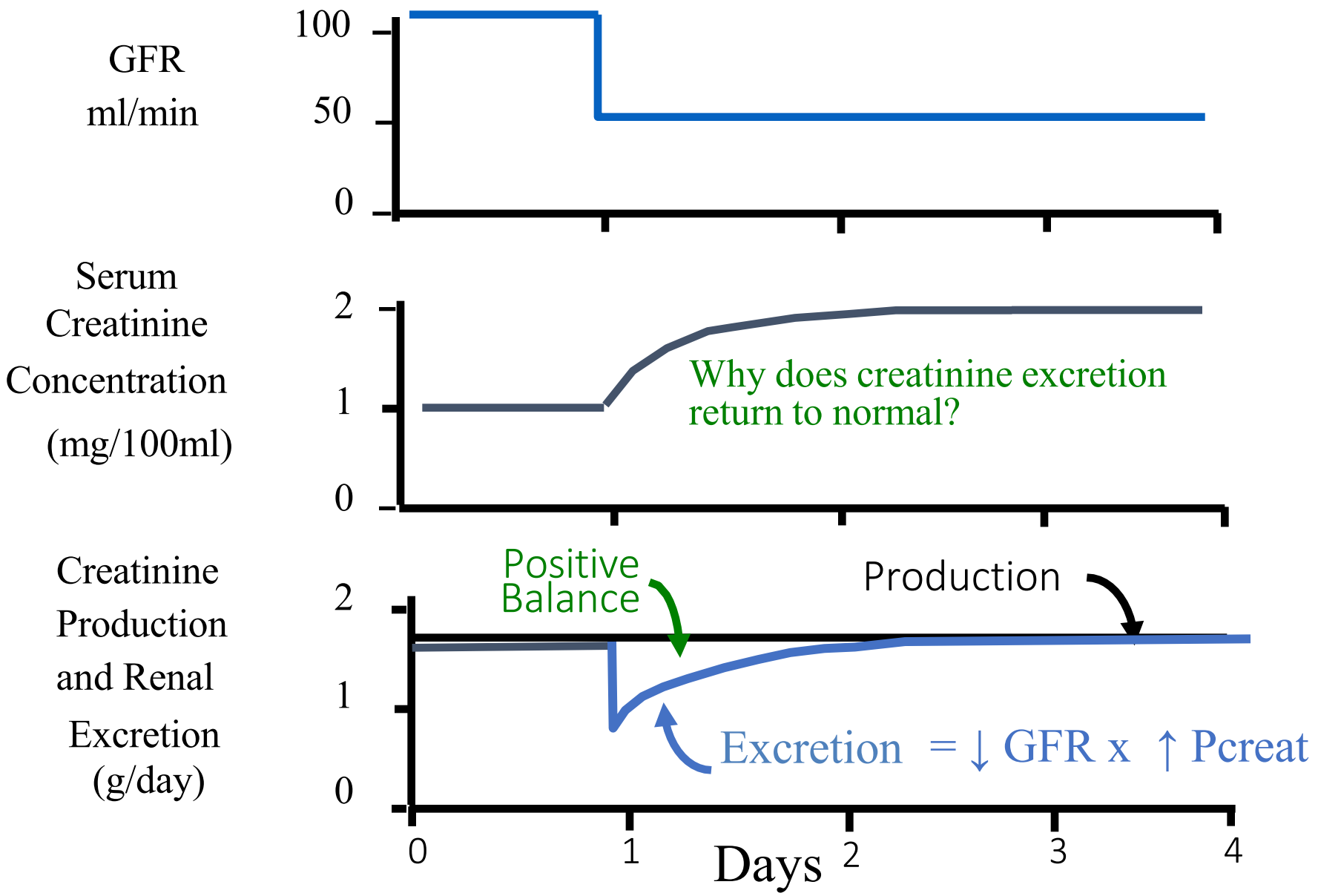
Effect of Reduced GFR on Sodium Excretion

- A **reduction in GFR to half its normal level** results in only a **slight increase in plasma sodium concentration**. However, if we look at the sodium **intake and excretion curve**, we observe a **sudden drop in sodium excretion**, which then **gradually returns to balance with sodium intake** over time.

- The reason sodium excretion eventually returns to normal—**despite the sustained reduction in GFR**—is that **tubular reabsorption adjusts**. Specifically, **sodium reabsorption decreases** in response to the lower filtration rate.

- Since sodium **excretion = filtration − reabsorption**, the **reduction in both filtration and reabsorption** maintains sodium excretion at a level **similar to normal**. This adjustment typically occurs **over the course of a few days** as the kidneys adapt to the new steady state.

Effect of Decreased GFR on Creatinine



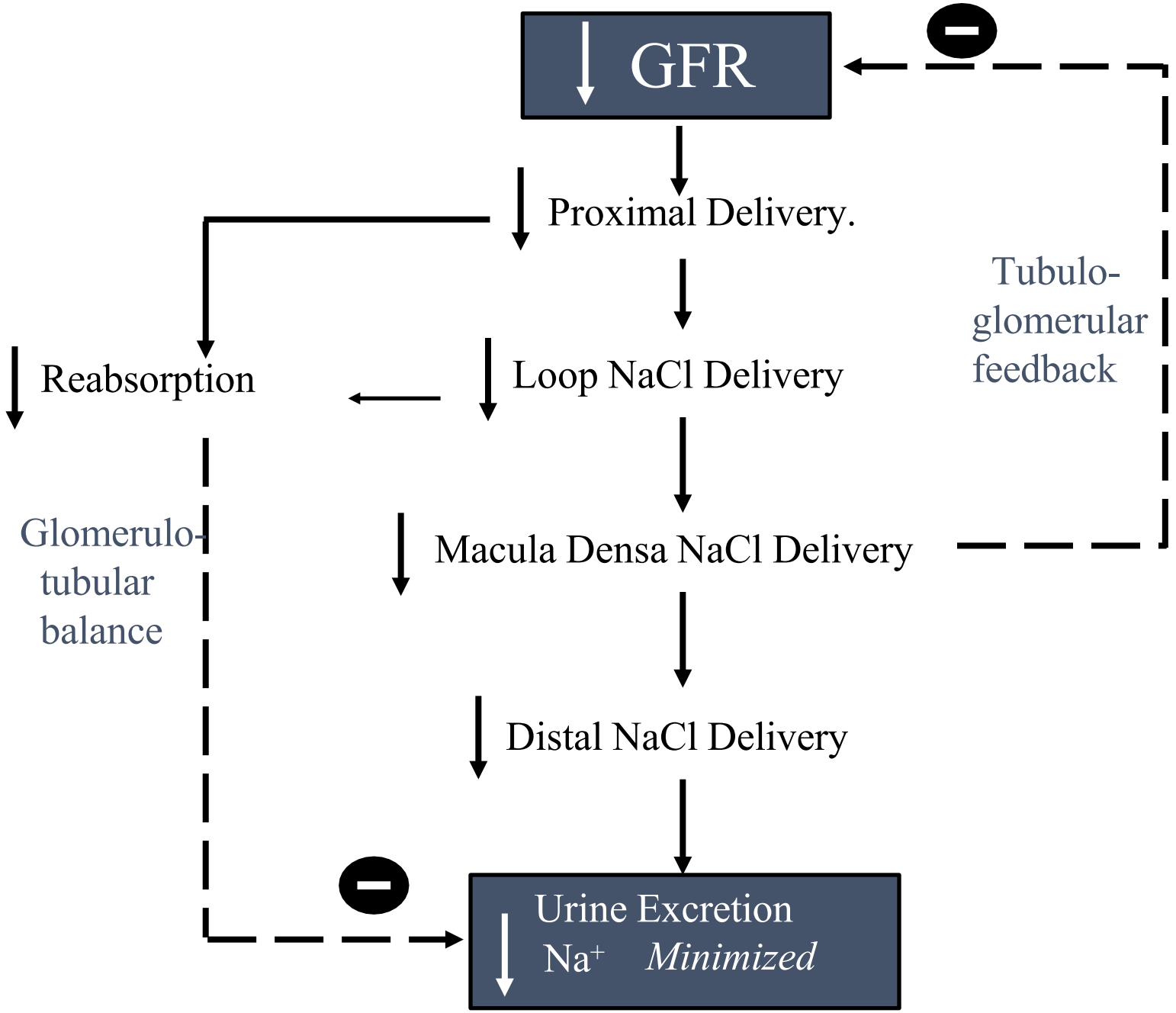
Effect of Decreased GFR on Creatinine and Its Excretion

- As discussed in previous lectures, a **reduction in GFR to half its normal value** will lead to an **increase in plasma creatinine concentration**. This increase occurs because **creatinine is poorly reabsorbed** and is only **minimally secreted**. When GFR decreases, **creatinine is not filtered and eliminated efficiently**, so it begins to **accumulate in the plasma**.

- Despite this reduction in GFR, **creatinine excretion eventually increases** and returns to match its **production rate**, maintaining balance. This happens because the **elevated plasma creatinine concentration increases the filtered load**, even though GFR is reduced. As a result, the amount of creatinine excreted becomes **similar to pre-GFR-decline levels**.

- We also recall that **creatinine clearance is used as an estimate of GFR**. When GFR declines, clearance decreases, and plasma creatinine rises. The **increase in plasma creatinine**, combined with the **reduced GFR**, **counterbalances** to maintain a **relatively normal excretion rate**.

- This adaptive mechanism ensures that **creatinine excretion equals creatinine production**, even in the setting of impaired kidney function.


GFR
Proximal Delivery.
Reabsorption
Loop NaCl Delivery
Tubulo-
glomerular
feedback
Glomerulo-
tubular
balance
Macula Densa NaCl Delivery
Distal NaCl Delivery
Urine Excretion
Na+ Minimized

Summary: Effect of Reduced GFR on Sodium Handling

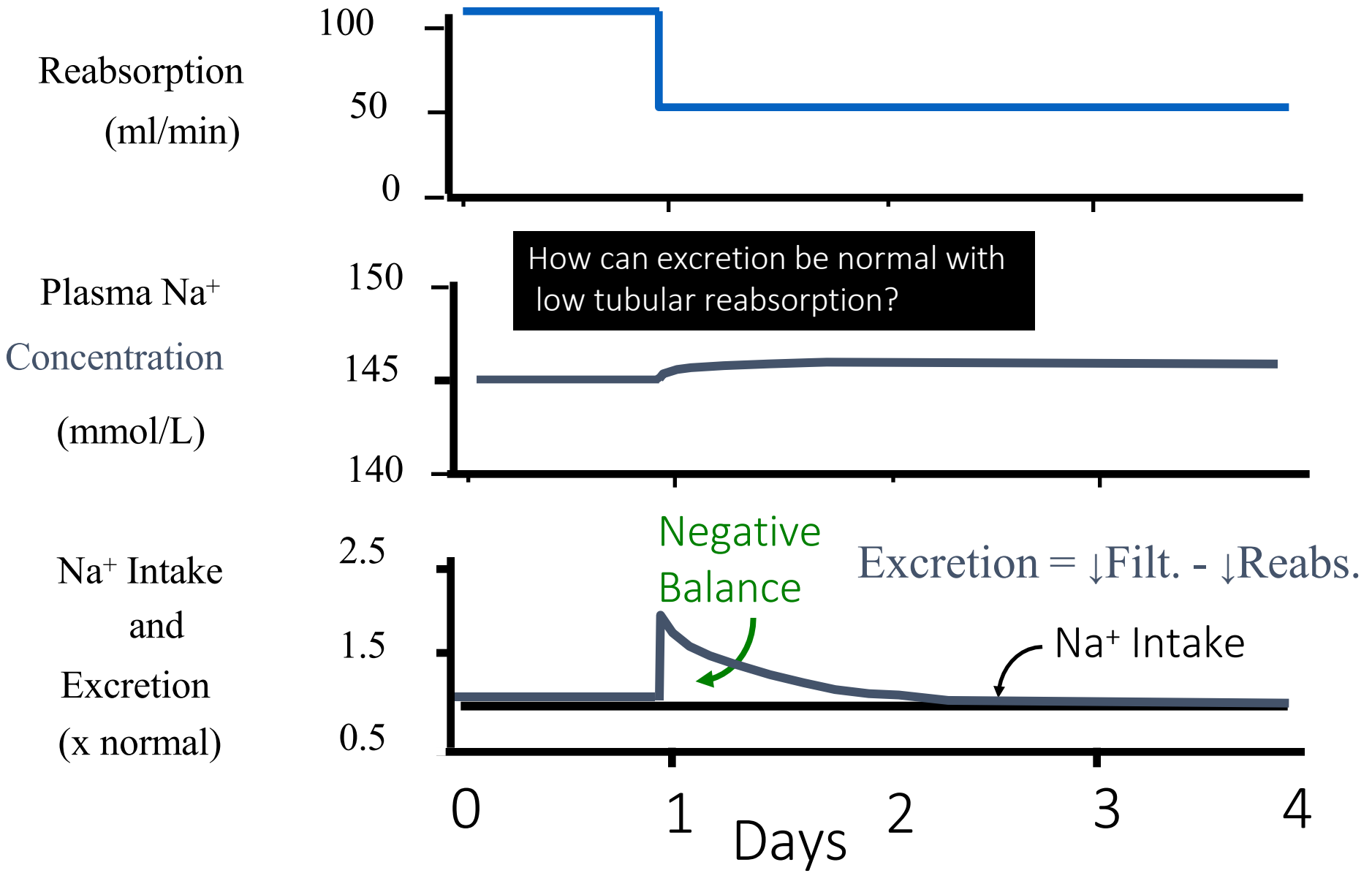
- A **reduction in GFR** is accompanied by a **decrease in sodium and chloride delivery** to the **proximal convoluted tubule**, the **loop of Henle**, and continuing to the **macula densa** and the **distal convoluted tubule**.

Two key regulatory mechanisms are activated to correct for this:
1- Tubuloglomerular Feedback: The macula densa senses the reduced sodium chloride levels and initiates feedback mechanisms to **increase GFR**.

2- Regulation of Reabsorption (Glomerulotubular Balance): Due to the lower GFR and reduced sodium chloride delivery to the proximal tubules, **tubular reabsorption decreases proportionally**. This adjustment ensures that reabsorption matches the reduced filtration rate—a process known as **glomerulotubular balance**.

Together, these two mechanisms help to **minimize the reduction in urinary sodium excretion**, ensuring that sodium excretion remains relatively stable despite the drop in GFR.

Effect of Decreased Reabsorption on Sodium Balance on the proximal tubules



- Initially, when **tubular reabsorption drops to half**, there will be an **increase in sodium excretion**. However, over time, sodium excretion will **gradually return to normal**, balancing with sodium intake, and **excretion will decrease** accordingly.

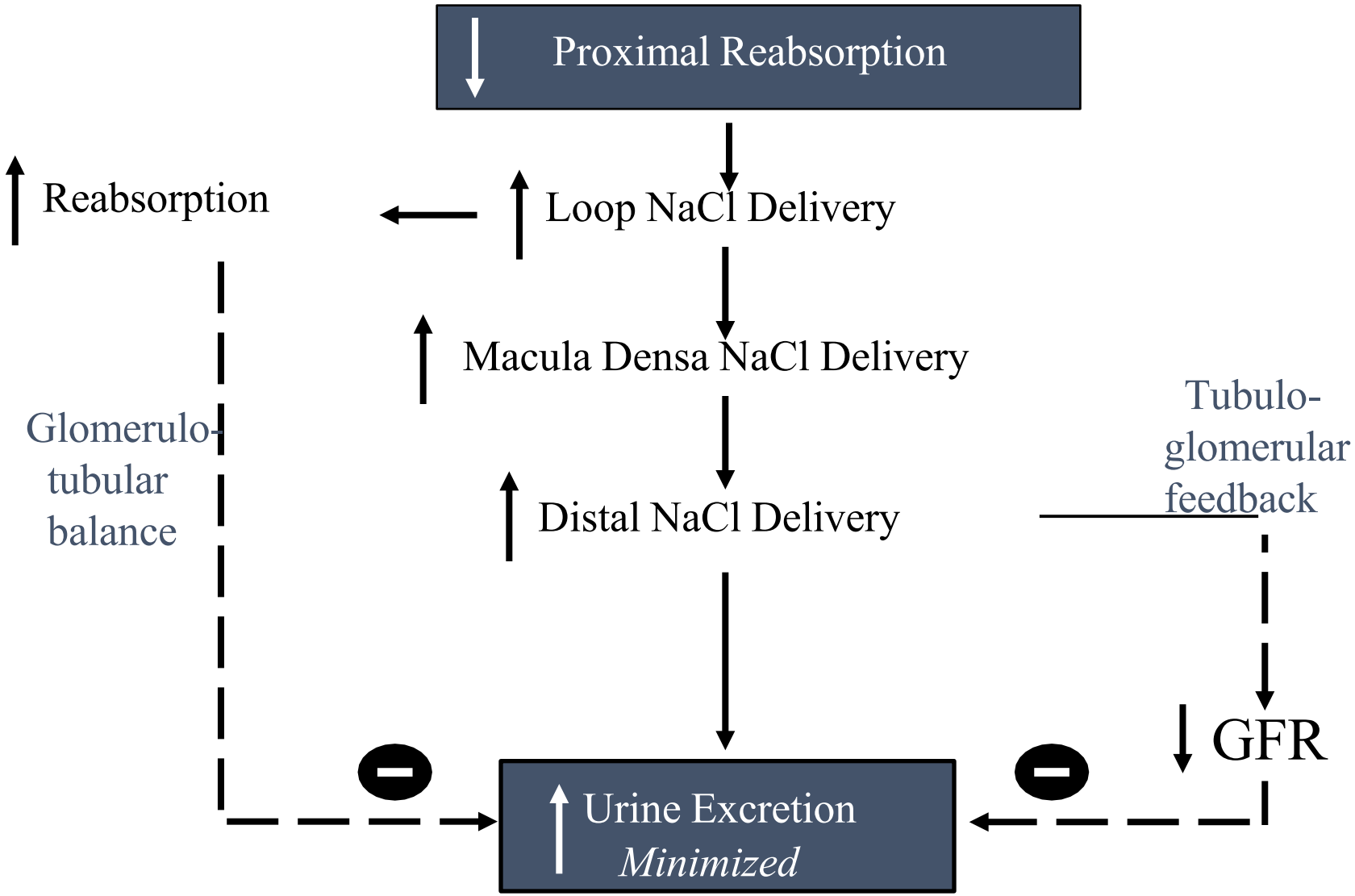
- The reason sodium excretion eventually decreases is based on the relationship:

Excretion = Filtration − Reabsorption

- When **reabsorption decreases**, this triggers **autoregulation** of filtration via the **tubuloglomerular feedback mechanism**. This mechanism leads to a **further reduction in GFR**, which helps **match the lowered reabsorption capacity**.

- As a result, **sodium excretion stabilizes**, returning to near-normal levels **despite the continued reduction in tubular reabsorption**.

Maintenance of Sodium Balance After Decreased Proximal Reabsorption



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Plasma concentrations of solutes in chronic renal failure

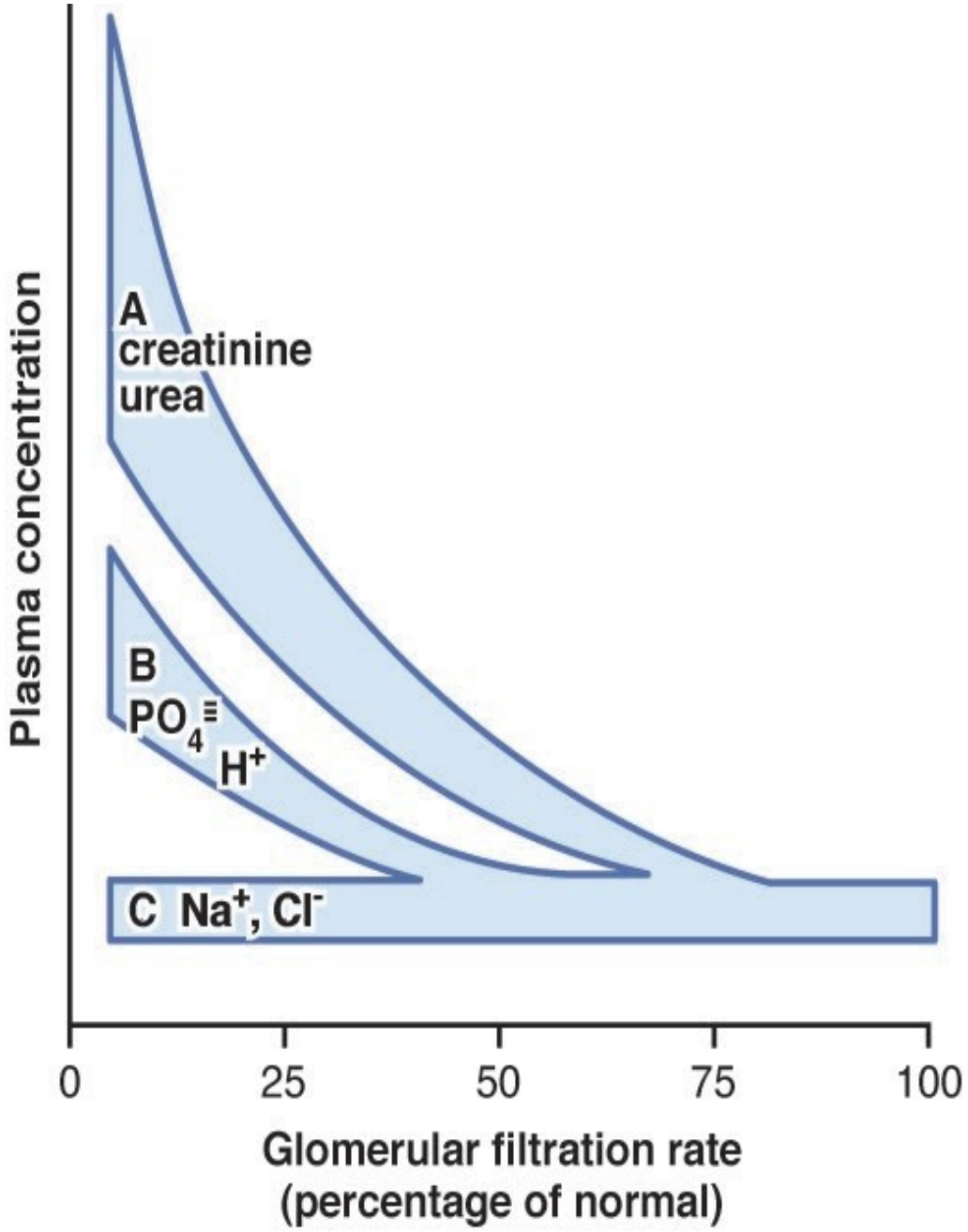

Figure 31-5

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Hierarchy of Responses to Disturbances of Body Fluid Regulation

1. Local renal mechanisms
   - changes in GFR
   - changes in tubular reabsorption
   - changes in tubular secretion
2. Systemic mechanisms (which can affect the whole body)
   - changes in hormones
   - changes in sympathetic activity
   - changes in blood pressure
   - changes in blood composition

Doctor didn't explain this slide

Hierarchy of Responses to Disturbances of Body Fluid Regulation

In steady-state, Intake = Output

1. Local renal responses
   - changes in GFR
   - changes in tubular reabsorption
   - changes in tubular secretion

2. Systemic mechanisms (which can affect the whole body)
   - changes in hormones
   - changes in sympathetic activity
   - changes in blood pressure
   - changes in blood composition

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explain this slide

Sodium excretion and extracellular fluid volume during diuretic administration.

Compensations that Permit Na^+ balance:

- ↓ blood pressure
- ↑ renin, angiotensin II
- ↑ aldosterone

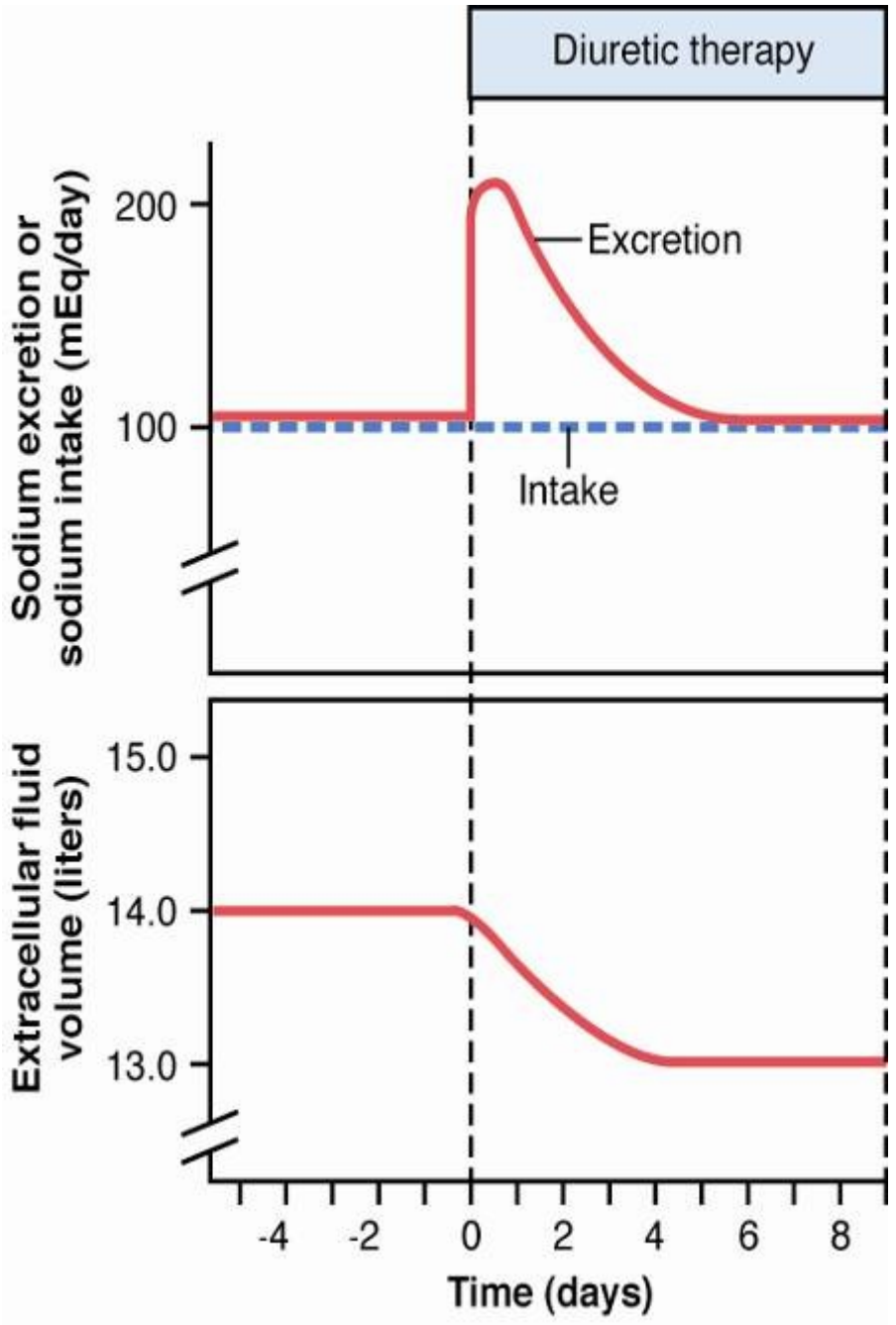

Figure 31-1

Hormonal Response to Chronic Renal Disease - PTH

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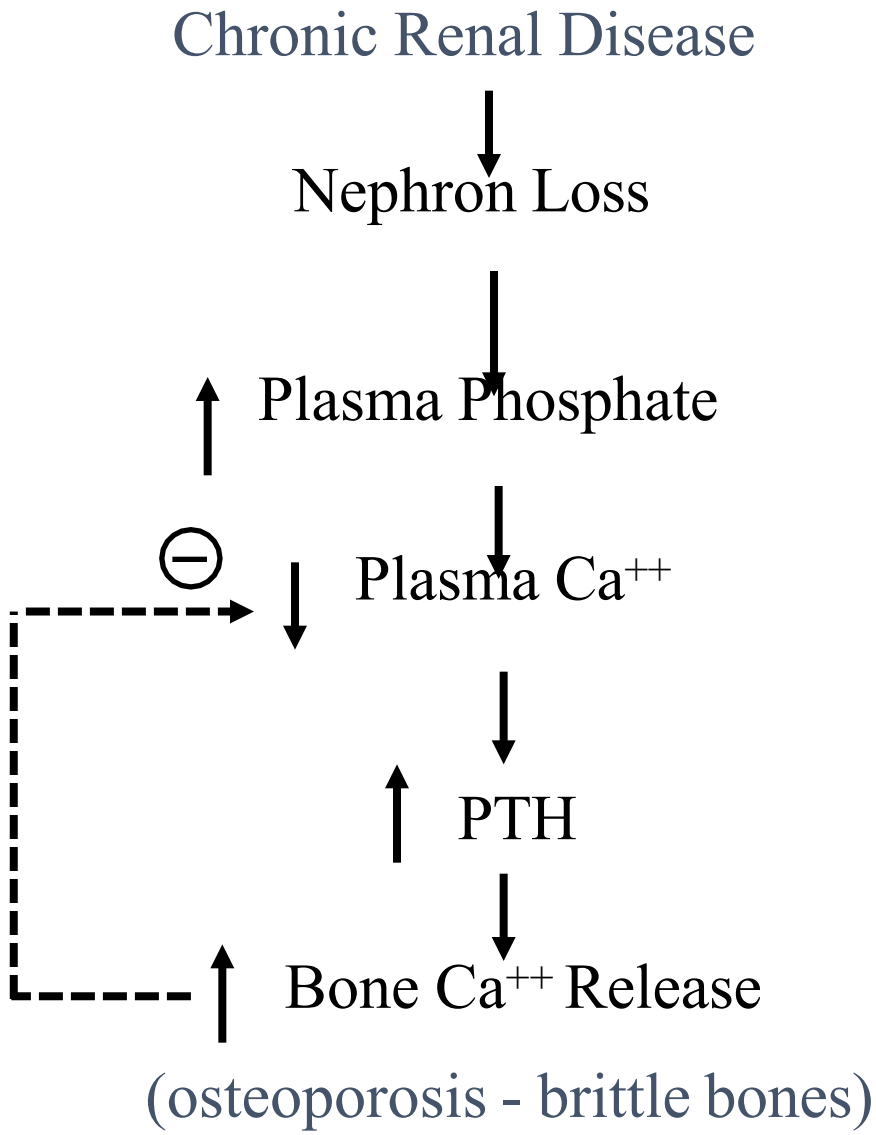

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Hierarchy of Responses to Disturbances of Body Fluid Regulation

In steady-state, Intake = Output

1. Local renal responses
   - changes in GFR
   - changes in tubular reabsorption
   - changes in tubular secretion
2. Systemic mechanisms (which can affect the whole body)
   - changes in hormones
   - changes in sympathetic activity
   - changes in blood pressure
   - changes in blood composition

Renal-Body Fluid Feedback- Increased Fluid (Na^+) Intake

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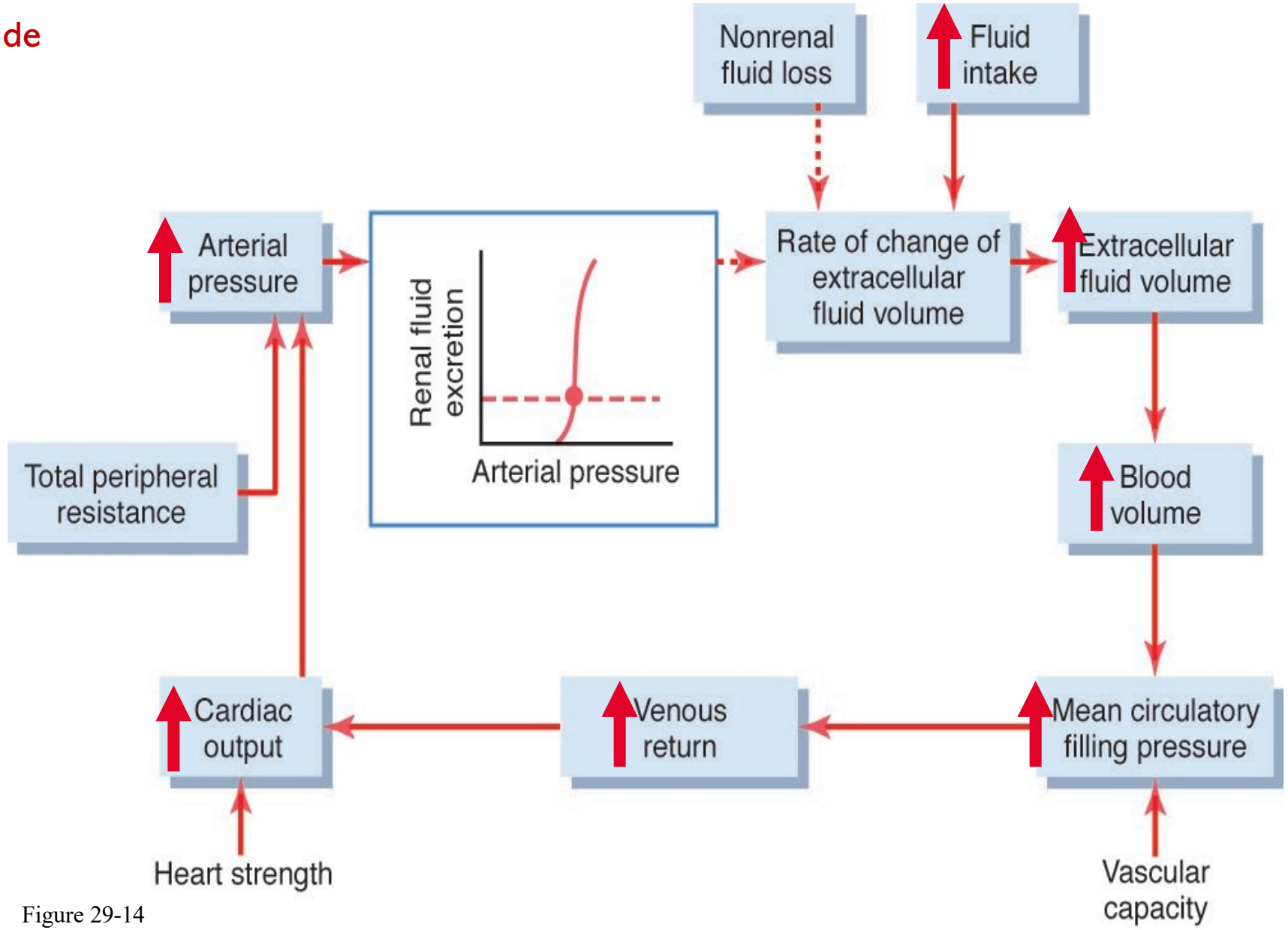

Figure 29-14

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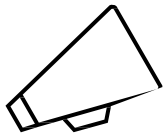
Integrated Responses to High Na^+ Intake

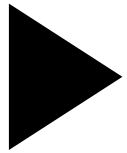
Excretion Na^+ = Filtration Na^+ - Reabsorption Na^+

1. Small increase in GFR
2. Decreased Na^+ Reabsorption is caused by:
   - small increase in blood pressure
   - increased peritubular capillary pressure
   - decreased angiotensin II
   - decreased aldosterone
   - Increased natriuretic hormones (e.g. ANP)

Net effect = increased Na^+ excretion



Audio-Visual Aid



Link to recoded lecture

[UGS physiology lecture 10 - YouTube]

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VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2	8	K out Na in	K in Na out
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!