PHYSIO

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Urinary System: Renal Physiology for Medical Students, L11

Chapter 30: Acid-Base Regulation in the Kidney

Reference: Guyton & Hall, Jordanian first edition

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Color code

- Slides
- Doctor
- Additional info
- Important

TOPICS OF THIS LECTURE!!

Objectives

- Identify the mechanisms by which the kidney can maintain Acid-Base Balance
- Identify the most important buffers in different body fluids
- Identify the cellular mechanisms of for HCO_3^- reabsorption and Na^+ - H^+ exchange or H+ secretion in the nephron
- Understand the mechanism of renal compensations for

Acid-Base Disorders.

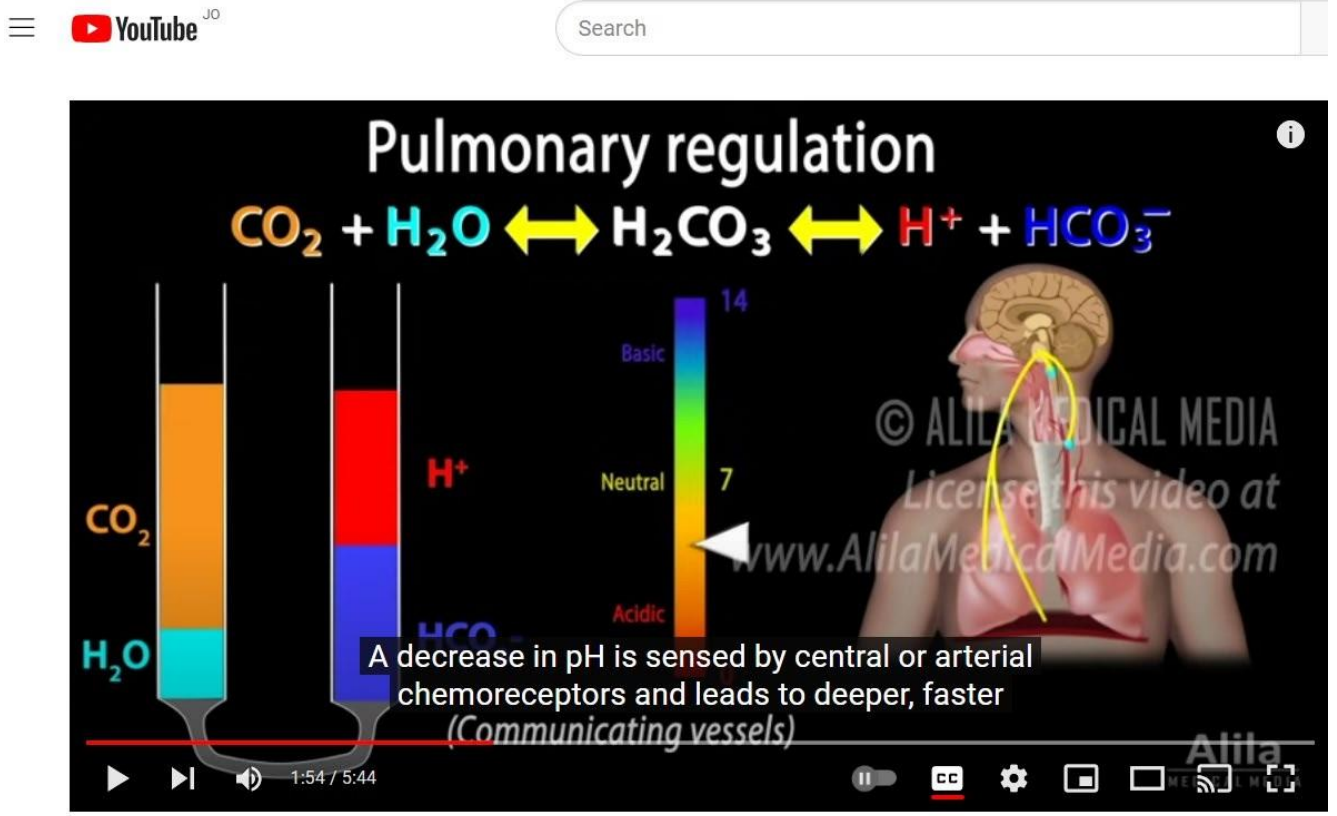
- To be able to determine the type of acid-base imbalance from given lab results and figure out the compensatory changes.
- To know how to use “Anion Gap” as a Diagnostic Tool for Metabolic Acidosis
- Identify main clinical conditions that are accompanied with acid-base imbalance

Audio-Visual Aid

- Please watch this video to help introducing you to the topic of this lecture

[Acid Base Balance, Animation. - YouTube]

The doctor recommended this video for the role of the kidneys and lungs in maintaining acid-base balance



Acid Base Balance, Animation.

- The regulation of **hydrogen ion (H+)** balance is similar in some ways to the regulation of other ions in the body. For example, there must be a balance between the intake or production of H+ and the net removal of H+ from the body to achieve homeostasis. And, as is true for other ions, the kidneys play a key role in regulating H+ removal from the body. **However, precise control of extracellular fluid H+ concentration (it is more complicated)** involves much more than the simple elimination of H+ by the kidneys. **Multiple** acid–base buffering mechanisms involving the blood, cells, and lungs are also essential in maintaining normal H+ concentrations in extracellular and intracellular fluids.

Mechanisms of Hydrogen Ion Regulation

$[H^+]$ is precisely regulated at 3-5 x 10^{-8} moles/L (pH range 7.2 -7.4)

$pH = -\log [H^+]$

1. Body fluid chemical buffers (rapid but temporary)
   - bicarbonate
   - ammonia
   - proteins
   - phosphate

2. Lungs (rapid, eliminates CO_2)

↑$[H^+]$ ⟶ ↑ ventilation ⟶ ↑ CO_2 loss

3. Kidneys (slow, powerful); eliminates non-volatile acids
   - secretes H^+
   - reabsorbs HCO_3^-
   - generates new HCO_3^-

Three primary systems regulate the H+ concentration in the body fluids:

(1) **the chemical acid–base buffer systems of the body fluids**, which immediately combine with an acid or a base to prevent excessive changes in H+ concentration

(2) **the respiratory center**, which regulates the removal of CO2 (and, therefore, H2CO3) from the extracellular fluid

(3) **the kidneys**, which can excrete acidic or alkaline urine, thereby readjusting the extracellular fluid H+ concentration toward normal during acidosis or alkalosis.

The intracellular compartment contains many proteins that act as weak bases by accepting hydrogen ions, **giving it a good buffering capacity**. **However**, its role in acid-base balance is **limited** because H^+ and HCO_3^- cannot easily cross cell membranes, so the effect is slow and takes hours. An important exception is RBCs, where hemoglobin buffers effectively, as H^+ and HCO_3^- can cross more easily.

- Bicarbonate mainly buffers in **plasma.**
- Phosphate is mostly **intracellular**
- Ammonia and phosphate act in the **urine (tubular fluid).**
- Proteins buffer mainly the **intracellular**
- These systems act as a rapid first line of defense, but their effect is **temporary** and doesn't correct the **underlying cause (**they just reduce the pH **fluctuations)**.

▶ We have different body fluid compartments, and each compartment has certain buffers that can work to resist changes in pH

▶ **What is a buffer? A chemical substance that resists changes in pH by accepting or donating hydrogen ions (H^+).**

- When there is a change in H+ concentration, the **buffer systems** of the body fluids react within seconds to minimize these changes. Buffer systems do not eliminate H+ from or add H+ to the body but only keep them tied up until balance can be re-established. The second line of defense, **the respiratory system** **(It works by adjusting the ventilation rate**), acts within a few minutes **(the response is very rapid)** to eliminate CO2 and, therefore, H2CO3 from the body.

More ventilation → less CO_2 → less H^+ (fixes acidosis).
Less ventilation → more CO_2 → more H^+ (fixes alkalosis).

- These first two lines of defense keep the H+ concentration from changing too much until the more **slowly responding** third line of defense, **the kidneys**, can eliminate the excess acid or base from the body. Although the kidneys **are relatively slow to respond compared** with the other defenses, over a period of hours to several days, they are by far the **most powerful** of the acid–base regulatory systems.

➡ Kidneys are responsible for eliminating **non-volatile acids**, which cannot be excreted via the lungs. The lungs primarily remove **volatile acids**, derived from carbonic acid (formed when CO_2 and H_2O combine) in a reversible reaction catalyzed by **carbonic anhydrase.**

The kidneys eliminate **Non-volatile acids** through urinary excretion of H^+. Depending on the acid-base status of the body. The kidneys:

- ✓ Secrete varying amounts of H^+ into the urine
- ✓ Reabsorb filtered bicarbonate (HCO_3^-)
- ✓ Generate new HCO_3^-, which helps restore pH balance.

Buffer Systems in the Body

Body fluid chemical buffers

Bicarbonate : **most important ECF buffer**

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

Phosphate : important renal tubular buffer

$$HPO_4^{--} + H^+ \longleftrightarrow H_2PO_4^-$$

Ammonia : important renal tubular buffer

$$NH_3 + H^+ \longleftrightarrow NH_4^+$$

Proteins : important intracellular buffers

$$H^+ + Hb \longleftrightarrow HHb$$

(60-70% of buffering is in the cells)

Bicarbonate is the most important **extracellular buffer**. The reaction between **CO_2 and H_2O**, catalyzed by **carbonic anhydrase**, forms **carbonic acid (H_2CO_3)**, which dissociates into **H^+ and HCO_3^-**. This reaction is reversible and shifts depending on the levels of CO_2 or H^+ in the body.

Phosphate and **ammonia** are key **renal tubular buffers**. Phosphate (HPO_4^{2-}) binds to H^+ to form $H_2PO_4^-$. **Ammonia (NH_3)** can also bind H^+ to form **ammonium (NH_4^+)**. While both are important, **ammonia becomes especially critical during chronic acidosis**, as its production can be upregulated by the body.

Proteins act as major **intracellular buffers**, with **hemoglobin** in red blood cells playing a central role. Hemoglobin can bind H^+ ions, helping to buffer changes in pH inside cells.

Approximately 60% to 70% of the total chemical buffering of the body fluids is inside the cells, and most of this buffering results from the intracellular proteins. However, except for the red blood cells, the slow rate at which H+ and HCO3− move through the cell membranes often delays the maximum ability of the intracellular proteins to buffer extracellular acid–base abnormalities for several hours.

Don't forget that the MOST important ECF buffer is HCO3-

Importance of Buffer Systems

Normal H^+ concentration = 0.00004 mmol/L

Amount of non-volatile acid produced
~ 60-80 mmol/day

80 mmol /42 L = 1.9 mmol/L

= 47,500 times > normal H^+ concentration

PH ----6.8-8 lives for hours

To appreciate the **importance of buffering systems**, consider the normal hydrogen ion concentration in plasma: it is extremely low, approximately **4×10^{-5} mmol/L**, or **0.00004 mmol/L**. When expressed in millimoles, this equals **4×10^{-8} mol/L**. This is a **very tiny concentration**.

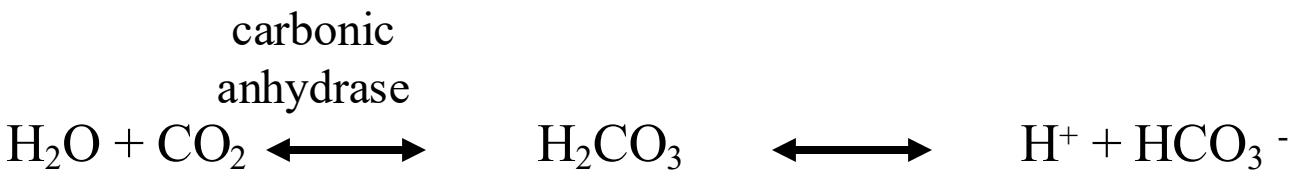
Now compare this to the amount of **non-volatile acids** produced daily by the body, which ranges from **60 to 80 mmol/day**. The amount of H^+ we are physiologically allowed to maintain is **millions of times less than what we produce** 😱.

If you calculate the total hydrogen ion load over the body's **42 liters of water**, it equates to around **1.9 mmol/L** still far above the safe range for plasma H^+ concentration.

This huge discrepancy between acid production and the acceptable plasma H^+ concentration shows how essential strong and efficient buffering systems are. But buffering alone isn't enough ➡️ we also need effective **elimination mechanisms** to get rid of excess hydrogen ions produced daily.

- **Precise H+ regulation** is essential because the activities of almost all **enzyme systems** in the body are influenced by H+ concentration. Therefore, changes in H+ concentration alter virtually all cell and body functions.

Bicarbonate Buffer System



$$pH = pK + \log \frac{HCO_3^-}{\alpha \; pCO_2}$$

$\alpha = 0.03$

$pK = 6.1$

Effectiveness of buffer system depends on:

- concentration of reactants
- pK of system and pH of body fluids

As for the **bicarbonate buffer system**, we refer back to the key chemical equation:

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

Carbonic acid (H_2CO_3) dissociates into **hydrogen ions (H^+)** and **bicarbonate (HCO_3^-)**. To analyze this buffer system, we use the **Henderson-Hasselbalch equation**

This equation allows us to calculate the **plasma pH** if we know the **bicarbonate concentration** and the **partial pressure of CO_2 (pCO_2)**. We plug these into the equation along with the **pKa** of the bicarbonate buffer system, which is **6.1**.

In this equation, **α (alpha)** represents the **solubility coefficient of CO_2 in plasma**, which is approximately **0.03 mmol/L/mmHg**. Since it's easier to measure **pCO_2** than the actual concentration of CO_2, we multiply the solubility factor by the pCO_2 to estimate the concentration of dissolved CO_2.
From this, we can understand how pH changes:
•When **pCO_2 increases**, the blood becomes **more acidic** (acidosis).
•When **HCO_3^- increases**, the blood becomes **more alkaline** (alkalosis).

➡️ Since the equation is **logarithmic**, even small changes in the ratio of bicarbonate to CO_2 can lead to significant shifts in pH.

How can we judge the effectiveness of buffering system?

A buffer is most effective when its **pKa is close to the target pH** of the fluid. The **higher the concentration** of its components, the better its buffering capacity. For example, plasma has a pH of about **7.4**, so the ideal buffer would have a pKa near that.

Although the **HCO3-** has a **pKa of 6.1** (not close to 7.4), it is still the **most important ECF buffer** because its components (CO_2 and HCO_3^-) are **tightly regulated** by the **lungs and kidneys**, making it highly effective.

The phosphate buffer system has a pK of 6.8, which is not far from the normal pH of 7.4 in the body fluids, allows the system to operate near its maximum buffering power. However, its concentration in the extracellular fluid is low, **at only about 8% of the concentration of the bicarbonate buffer**. Therefore, the total buffering power of the phosphate system in the extracellular fluid is **much less** than that of the bicarbonate buffering system.

Titration curve for bicarbonate buffer system.

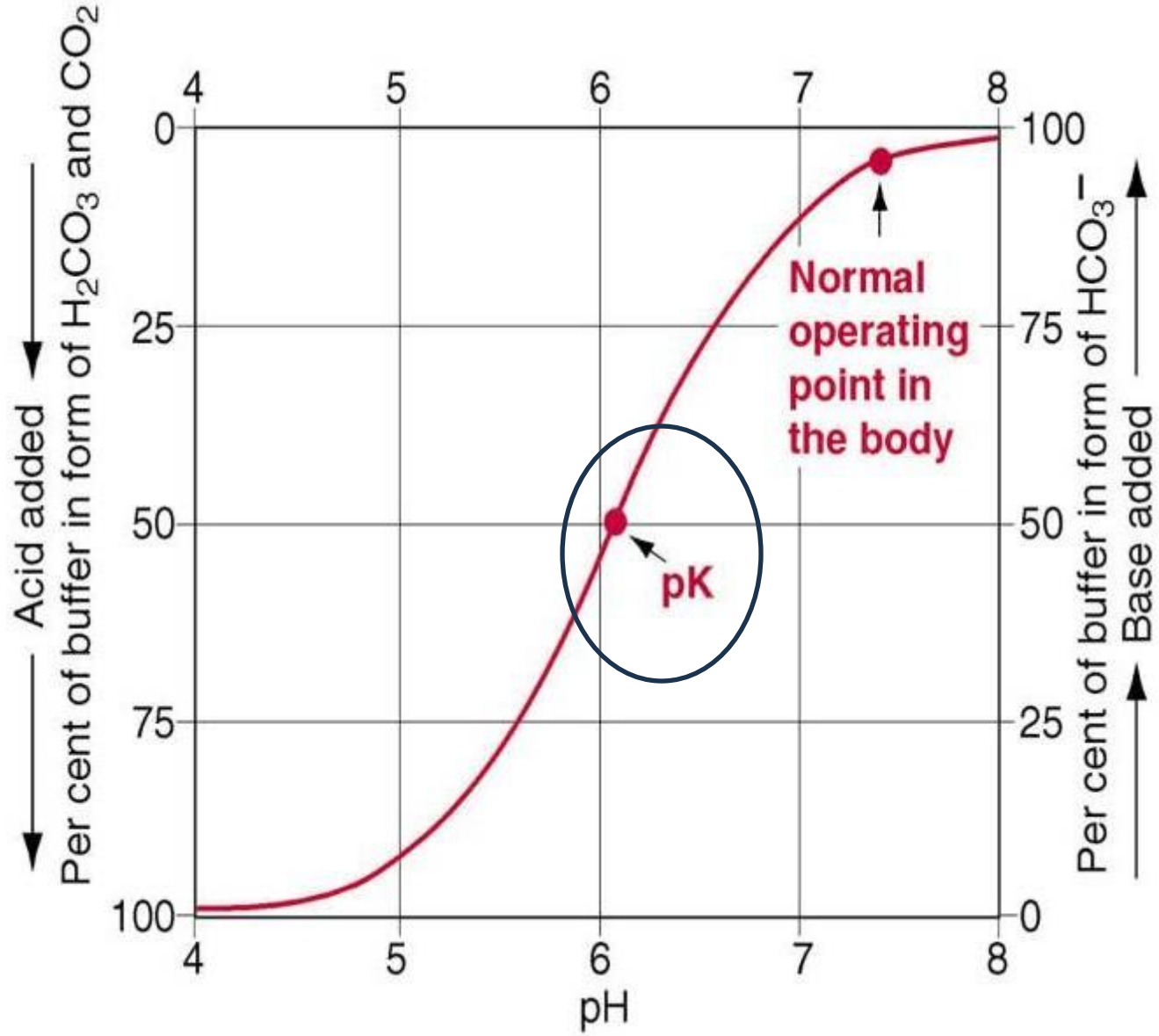


Figure 30-1.

- **Bicarbonate Buffer System Is the Most Important Extracellular Buffer.**

- From the **titration curve**, one would not expect the bicarbonate buffer system to be powerful, for two reasons. **First**, **the pH of the extracellular fluid is about 7.4,** whereas the **pK of the bicarbonate buffer system is 6.1**, which means that there is about 20 times as much of the bicarbonate buffer system in the form of HCO_3^- as in the form of dissolved CO_2.
- For this reason, this system operates on the portion of the buffering curve where the slope is low, and the buffering power is poor**. Second**, the concentrations of the two elements of the bicarbonate system**, CO_2 and HCO_3^-, are not high**.

- **Despite these characteristics, the bicarbonate buffer system is the most powerful extracellular buffer in the body**. This apparent paradox is due mainly to the fact that the two elements of the buffer system, **HCO_3^- and CO_2, are regulated, respectively, by the kidneys and lungs**

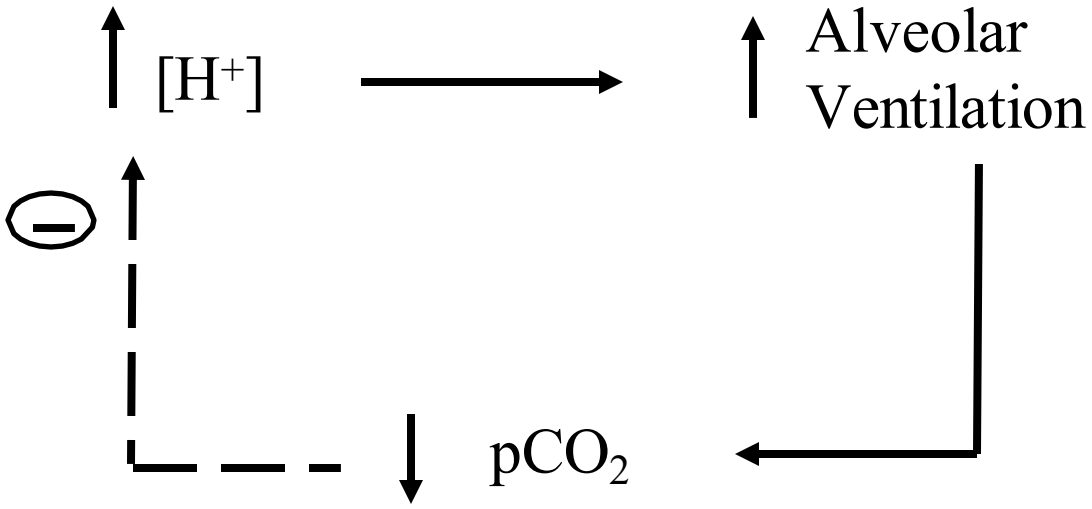
- . As a result of this regulation, the pH of the extracellular fluid can be precisely controlled by the relative rate of removal and addition of HCO_3^- by the kidneys and rate of removal of CO_2 by the lungs.

Bicarbonate Buffer System

Is the most important buffer in extracellular fluid even though the concentration of the components are low and pK of the system is 6.1, which is not very close to normal extracellular fluid pH (7.4).

Reason: the components of the system (CO_2 and HCO_3^-) are closely regulated by the lungs and the kidneys

Respiratory Regulation of Acid-Base Balance



$H_2O + CO_2 \longleftrightarrow H_2CO_3 \longrightarrow H^+ + HCO_3^-$

Feedback Gain = 1.0 to 3.0
(corrects 50 to 75 %)

In acid-base balance, when H^+ increases, it stimulates the respiratory center to increase ventilation. This leads to a decrease in pCO_2. Lower pCO_2 shifts the bicarbonate buffer equation to the left

This shift removes H^+ by converting it into CO_2 and H_2O, which decreases acidity

The respiratory system can correct about **50–75%** of the disturbance (feedback gain of 1–3), but not fully, because it can't eliminate **non-volatile acids** (like lactic acid or ketoacids). Only the **kidneys** can fully correct acid-base imbalances by excreting those acids, though they act more slowly.

Renal Regulation of Acid-Base Balance

- **Kidneys eliminate non-volatile acids (H_2SO_4, H_3PO_4) (~ 80 mmol/day)**
  - Filtration of HCO_3^- (~ 4320 mmol/day)
  - Secretion of H^+ (~ 4400 mmol/day)
  - Reabsorption of HCO_3^- (~ 4319 mmol/day)
  - Production of new HCO_3^- (~ 80 mmol/day)
  - Excretion of HCO_3^- (1 mmol/day)

Kidneys conserve HCO_3^- and excrete acidic or basic urine depending on body needs

Each day, about **4320 mmol of HCO_3^-** is filtered from the plasma.

- Most of it is **reabsorbed** to preserve the body's main buffer, and only about **1 mmol/day** is excreted in urine under normal conditions. (Keep in mind that this number varies depending on the body status because reabsorption is variable) ➡ ➡ If we considered **reabsorption=4319 and filtration =4320** ➡ **Excretion= 1mmol / day**

Both the reabsorption of HCO3− and excretion of H+ are accomplished through the process of H+ secretion by the tubules. Because HCO3− must react with a secreted H+ to form H2CO3 before it can be reabsorbed, **4320 mEq of H+** must be secreted each day just to reabsorb the filtered HCO3−. Then, an additional **80 mEq of H+** must be secreted to rid the body of the **non-volatile acids produced each day for a total of 4400 mEq of H+ secreted into the tubular fluid each day.**

In alkalosis, kidneys secrete less H+ and excrete more HCO3−, effectively increasing extracellular H+ concentration.

In acidosis, they secrete more H+, reabsorb HCO3−, and generate new HCO3−, lowering extracellular H+.
Thus, kidneys regulate blood pH through: **(1) H+ secretion, (2) HCO3− reabsorption, and (3) generation of new HCO3−.**

Reabsorption of bicarbonate (and H^+ secretion) in different segments of renal tubule.

Key point:

For each HCO_3^- reabsorbed, there must be a H^+ secreted

- **The majority of HCO_3^-** reabsorption Occurs in the **Proximal tubules** 85%
- **No** HCO_3^- handling in the **thin ascending and descending** loops of Henle

10% of HCO_3 – reabsorbed in the **thick** ascending and H^+ is secreted
4.9% of HCO_3^- is reabsorbed and H^+ is secreted n the distal Convoluted tubeles

Rule of thumb
the REABSORPTION of HCO_3^-, is coupled with the **SECRETION of H^+** in the same amount

The **excretion** of HCO_3^- = 1mEq/day
The **EXCRETION of HCO_3^-** is coupled with the **ADDITION of new H^+** to the blood ,in the same amount

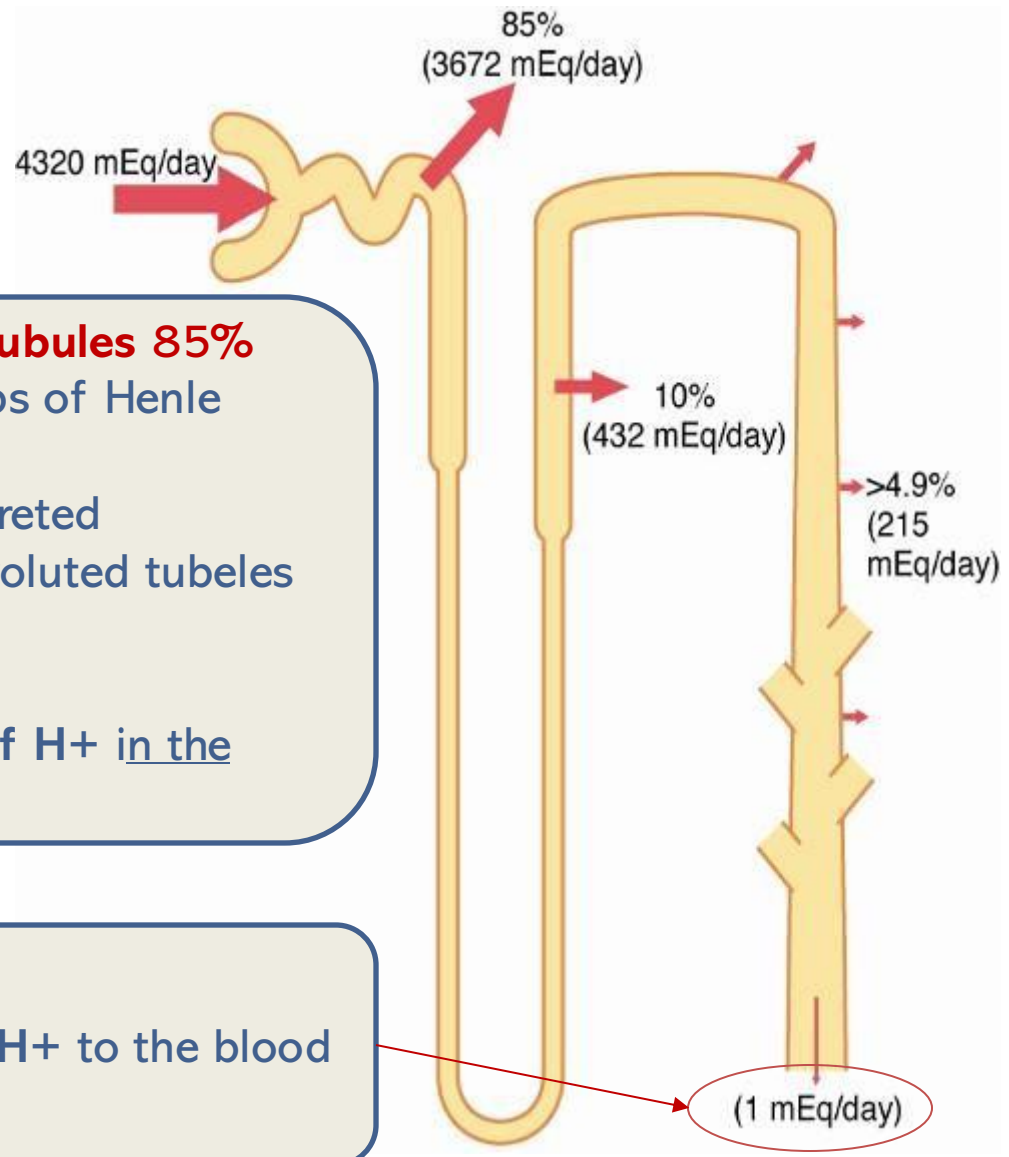


Figure 30-4.

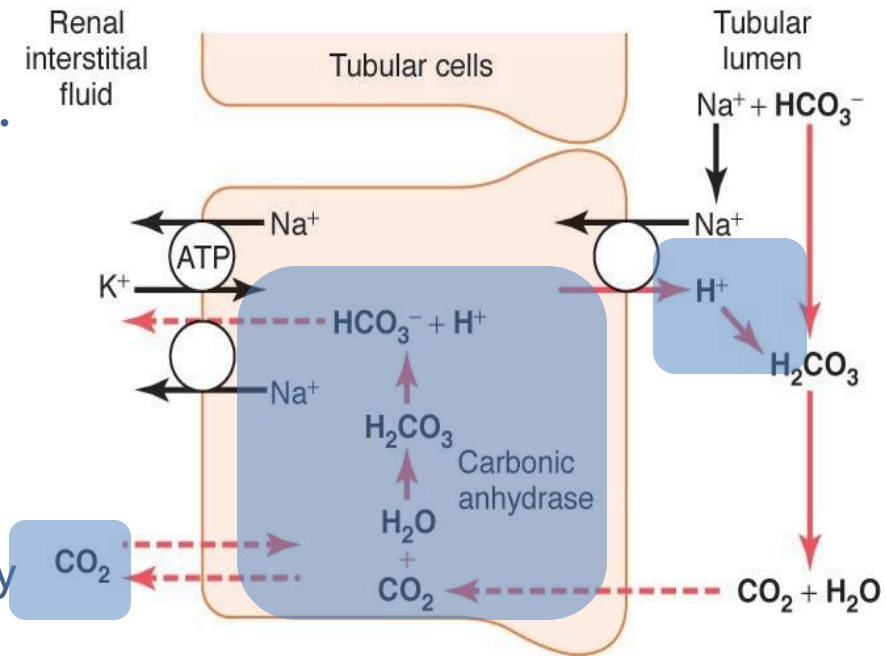
Mechanisms for HCO_3^- reabsorption and Na^+ - H^+ exchange in proximal tubule and thick loop of Henle

- secrete H+ into the tubular fluid by **Na+/ H+ counter-transport**, it depends the gradient which is established by (Na+/K+ ATPase) pump in the **basolateral membrane.**

- **What is the source of H+ ?**
  The secretory process begins when CO2 diffuses into the tubular cells . Under the influence of the enzyme carbonic anhydrase, CO2, combines with H2O to form H2CO3, which dissociates into HCO3− and H+.

- The **H+** is secreted from the cell into the **tubular lumen** by Na/H+ counter-transport. The **HCO3−** generated in the cell (when H+ dissociates from H2CO3) then moves downhill across the basolateral membrane, into the renal interstitial fluid and peritubular capillary **blood**.

- The **net result** is that for every H+ secreted into the tubular lumen, an HCO3− enters the blood.



Minimal pH ~ 6.7

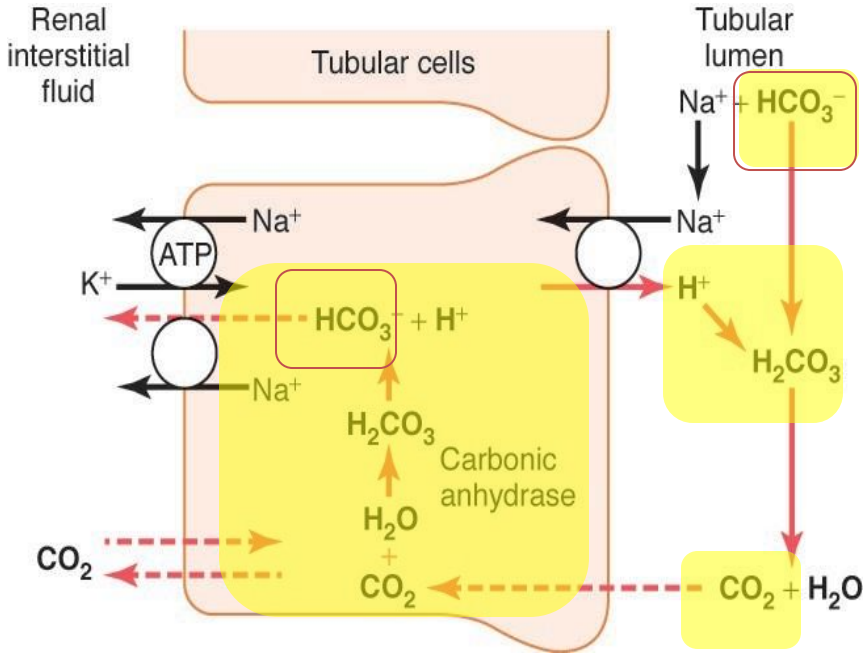
Figure 30-5.

Mechanisms for HCO_3^- reabsorption and Na^+ - H^+ exchange in proximal tubule and thick loop of Henle

FILTERED HCO3− IS REABSORBED BY INTERACTION WITH H+ IN THE TUBULES

Bicarbonate ions do not readily permeate the luminal membranes of the renal tubular cells; therefore, HCO3− that is filtered by the glomerulus cannot be directly reabsorbed.

This reabsorption of HCO3− is initiated by a reaction in the tubules between HCO3− filtered at the glomerulus and H+ secreted by the tubular cells. The H2CO3 formed then dissociates into CO2 and H2O. The CO2 can move easily across the tubular membrane; therefore, it instantly diffuses into the tubular cell, where it recombines with H2O, under the influence of carbonic anhydrase, to generate a new H2CO3 molecule.



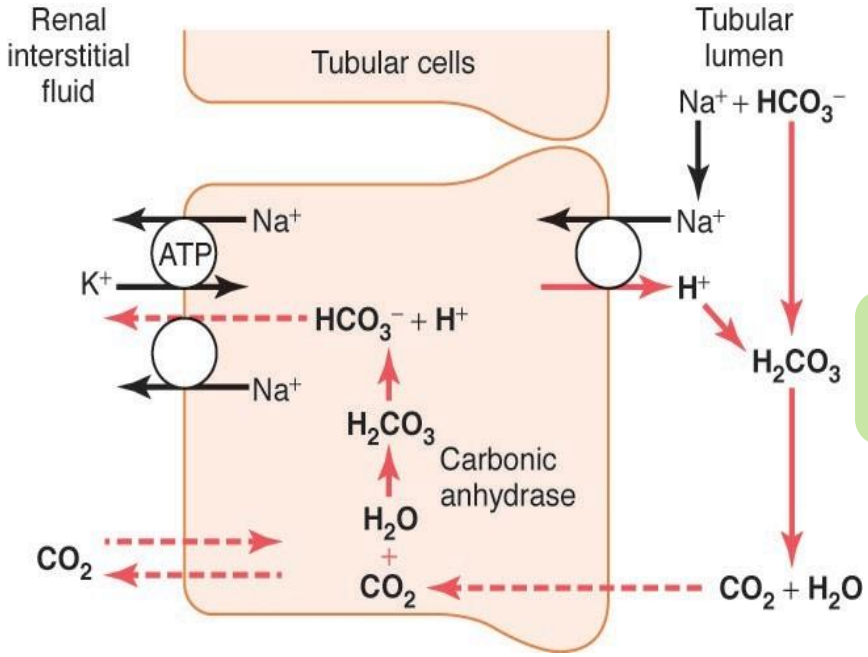
Minimal pH ~ 6.7

Mechanisms for HCO_3^- reabsorption and Na^+ - H^+ exchange in proximal tubule and thick loop of Henle

- This mechanism continues till all HCO3− filtered at the glomerulus is titrated with H+ Therefore, it is said that HCO3− and H+ normally "titrate" each other in the tubules.

- In acidosis, there is excess H+ relative to HCO3−, causing complete reabsorption of the HCO3−; the excess H+ passes into the urine in combination with urinary buffers, especially phosphate and ammonia, and eventually is excreted as salts. And minimal amount stay as free H+ limited by minimal PH

- **This mechanism, however, can establish a minimum pH of only about 6.7;** as the Na^+/H^+ exchanger operates against a limited electrochemical gradient.



Minimal pH ~ 6.7

HCO_3^- reabsorption and H^+ secretion in intercalated cells of late distal and collecting tubules

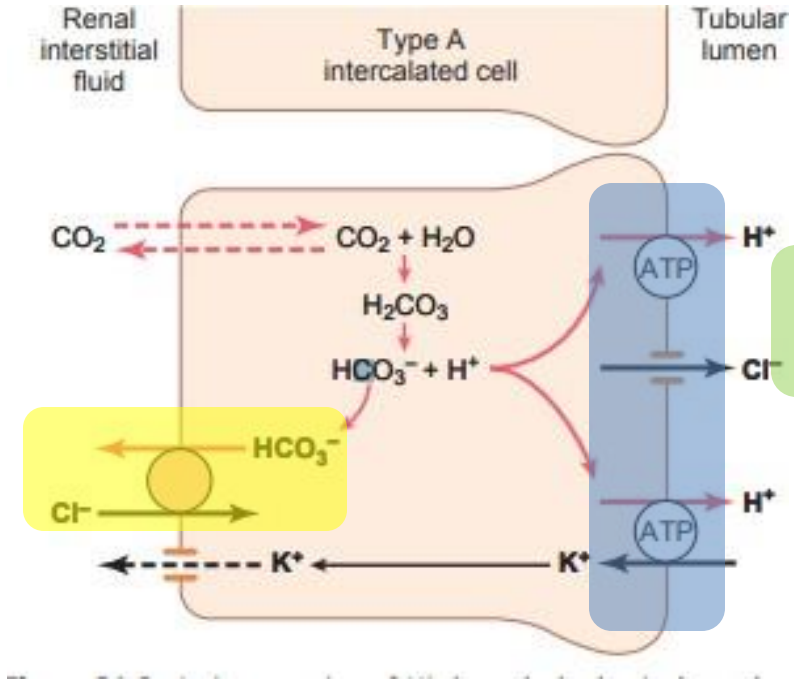


Figure 30-6.

Type A intercalated cells contain **hydrogen–ATPase** and **hydrogen-potassium-exchanger in the luminal membrane, to secret H+**

H+/K+ exchanger is active when there is hypokalemia , while hydrogen–ATPase is always active

Minimal pH ~4.5

The tubular fluid becomes highly acidic only in the collecting tubules and collecting ducts, where the urine pH can drop to as low as 4.5. This is possible because H^+- ATPase can pump against an electrochemical gradient as great as 1000-fold.

The other difference is that **HCO3- is reabsorbed** by **HCO3-/ Cl- exchanger**

same concept here each 1xH+ secreted is coupled with 1× HCO3- reabsorption the titration continues till all the filtered HCO3 is reabsorbed.

Renal Regulation of Acid-Base Balance

- ✅ Kidneys eliminate non-volatile acids (H_2SO_4, H_3PO_4) (~ 80 mmol/day)
- ✅ Filtration of HCO_3^- (~ 4320 mmol/day)
- ✅ Secretion of H^+ (~ 4400 mmol/day)
- ✅ Reabsorption of HCO_3^- (~ 4319 mmol/day)
- ❓ Production of **new** HCO_3^- (~ 80 mmol/day)
- Excretion of HCO_3^- (1 mmol/day)

Kidneys conserve HCO_3^- and excrete acidic or basic urine depending on body needs

Regulation of H^+ secretion

Check next slide

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

$$pH = pK + \log \frac{HCO_3^-}{\alpha \; pCO_2}$$

- Increased pCO_2 increases H^+ secretion

  i.e. respiratory acidosis

- Increased extracellular H^+ increases H^+ secretion

  i.e. metabolic or respiratory acidosis

- Increased tubular fluid buffers increases H^+ secretion

  i.e. metabolic or respiratory acidosis

Acidosis :

- **lung disease** → hypoventilation → Increase in pCO2 → decrease PH → **respiratory acidosis** → increase H+ secretion and HCO3- reabsorption by kidney (Kidney Compensation)
- **decrease in HCO3- Production → Metabolic acidosis**

Alkalosis :

- **increase in HCO3 - levels → Metabolic alkalosis**
- **decrease in PCO2 → Respiratory alkalosis**

***Note :**

- the **metabolic** type is always related to the levels **of HCO3-**
- while **respiratory** type is related **to PCO2**
- increased **extracellular H+** could be related to **respiratory or metabolic acidosis**

how kidneys can compensate the acidosis ?

1. Increased tubular fluid buffers other than the filtered HCO3 ,which could be completely consumed,
other buffers includes Ammonia (NH3) and phosphate
Phosphate has limited Stores in Kidney,
NH3 has also limited stores,however in chronic acidosis, kidney can synthesize Amonia to increase the capacity of titrating H+ and
then increase H+ secretion.

2. increases H+ secretion
3. increase HCO3 reabsorption or production

Renal Compensations for Acid-Base Disorders

- Acidosis:
  - increased H^+ secretion
  - Increased HCO_3 –reabsorption
  - production of new HCO_3 - Check next slide

- Alkalosis:
  - decreased H^+ secretion
  - Decreased HCO_3 - reabsorption
  - loss of HCO_3^- in urine

in alkalosis, **HCO3**– is removed from the extracellular fluid by renal **excretion**, which has the same effect as **adding an H+** to the extracellular fluid. This process helps return the H+ concentration and pH toward normal.
انتبه للمصطلحات المستخدمة

In acidosis all HCO_3^- is titrated and excess H^+ in tubule is buffered

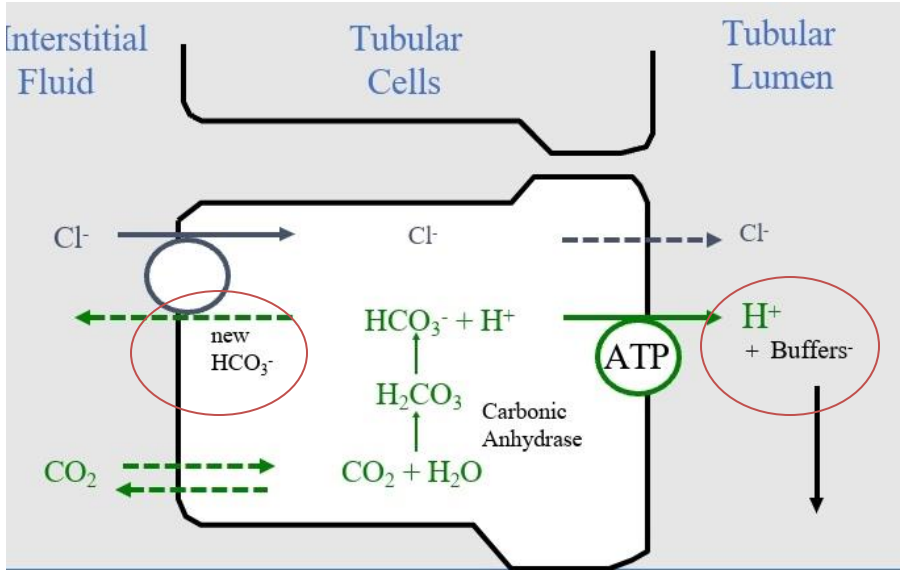
how new HC03 is produced ?

H+ is titrated in the tubular fluid with HCO3 this leads to reabsorption of one HCO3− for each H+secreted, as discussed earlier.

However, once all the HCO3− has been reabsorbed and is no longer available to combine with H+, any excess H+ can combine with **buffers other than HCO3- such as Phosphate and ammonia , and this leads to generation of new HCO3-** that can also enter the blood.

Thus, when there is excess H+ in the extracellular fluid, the kidneys not only reabsorb the filtered HCO3 but also generate new HCO3 , thereby helping replenish the HCO3 lost from the extracellular fluid in acidosis.

only a small part of the excess H+ can be excreted in the Free ionic form (H+) in the urine.This is because the minimal urine pH is about 4.5.



Importance of Renal Tubular Buffers

Minimum urine pH = 4.5 $= 10^{-4.5}$

i.e. the maximal $[H^+]$ of urine is 0.03 mmol/L$= 3 \times 10^{-5}$ moles/L

Yet, the kidneys must excrete, under normal conditions, at least 60 mmol non-volatile acids each day. **To excrete this as free H^+ would require :**

$$\frac{60 \text{ mmol}}{.03 \text{mmol/L}} = 2000 \text{ L per day !!!}$$

2000L is needed to excrete H+ in the absence of tubular buffers, to maintain the PH as 4.5
Which is impossible to excrete that amount of urine

Buffering of secreted H^+ by filtered phosphate ($NaHPO_4^-$) and generation of "new" HCO_3^-

However, once all the HCO3– has been reabsorbed and is no longer available to combine with H+, any excess H+ can combine with HPO4 = and other tubular buffers.

After the H+ combines with HPO4= to form H2PO4–, it can be excreted as a sodium salt (NaH2PO4), carrying with it the excess H+.

Note that a **new HCO3–** is returned to the blood for each NaHPO4 that reacts with a secreted H+.

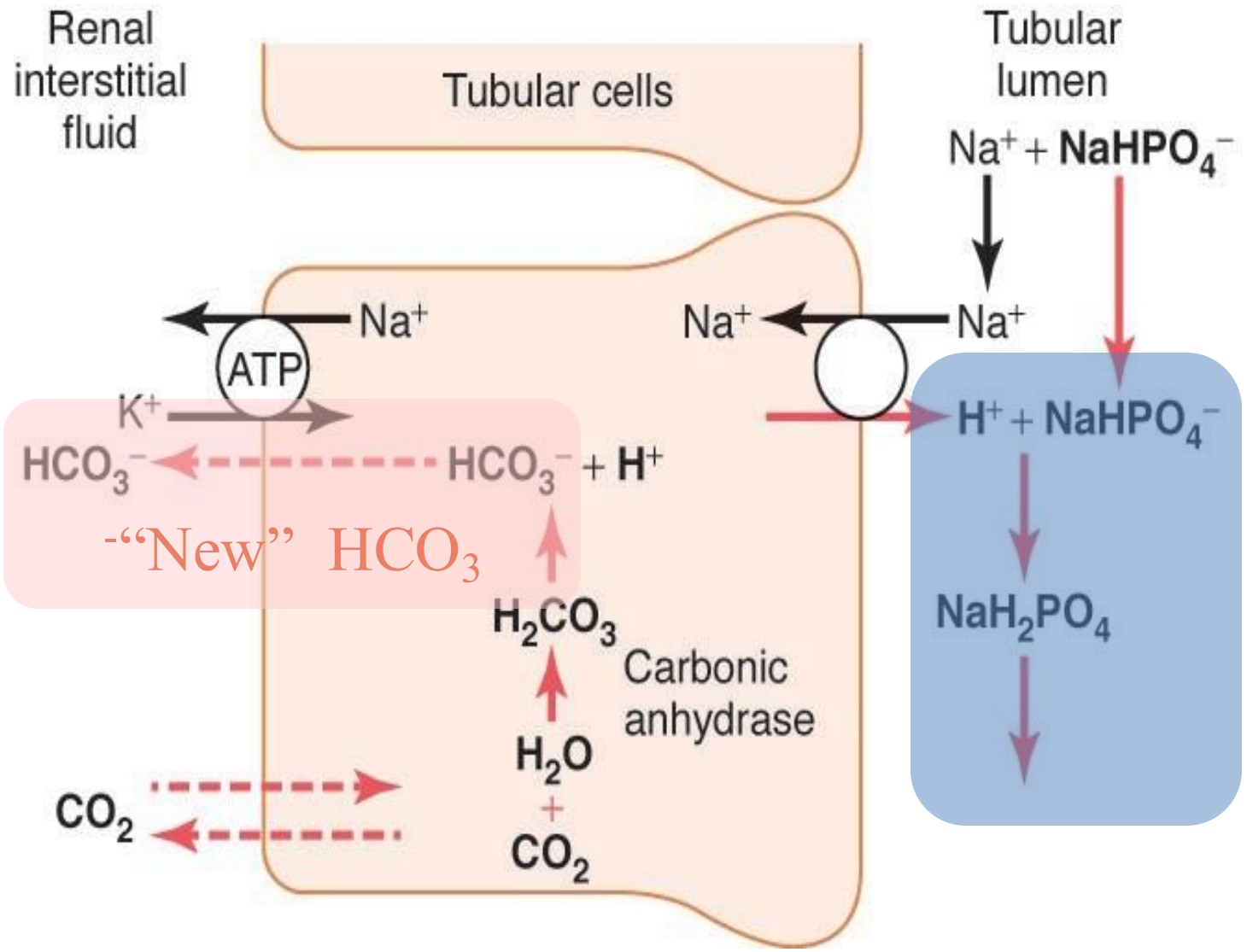


Figure 30-7.

Phosphate as a Tubular Fluid Buffer

- There is a high concentration of phosphate in the tubular fluid; pK = 6.8

Phosphate pka is close to the urine ph, however, its filtred amount in the lumen is low and can't be controlled, thus, it has limited capacity.

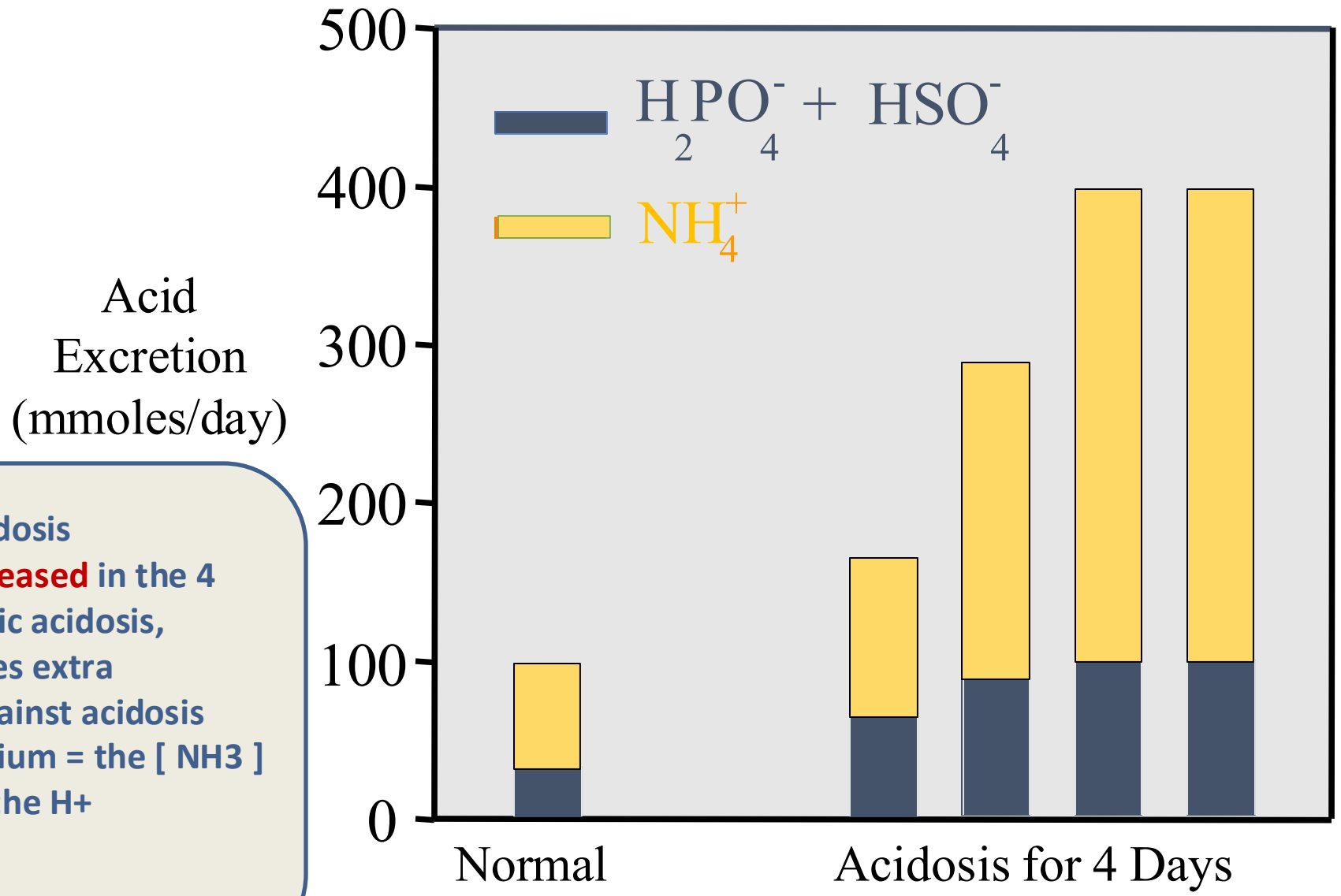
- Phosphate normally buffers about 30 mmol/day H^+
(about 100 mmol/day phosphate is filtered but 70 % is reabsorbed)

- Phosphate buffering capacity does not change much with acid-base disturbance. (phosphate is not the major tubular buffer in chronic acidosis

Because kidney **can't increase phosphate Concentration** in the urine

$$NaHPO_4^- + H^+ \longrightarrow NaH_2PO_4$$

Phosphate and Ammonium Buffering In Chronic Acidosis



in chronic acidosis
[NH3] is increased in the 4 days of chronic acidosis, which provides extra protection against acidosis
[NH4+] amonium = the [NH3] that titrated the H+

Test your knowledge

Which of the following statements is true regarding the regulation of extracellular fluid pH during acidosis or alkalosis?

A. The respiratory center is the primary long-term regulator of pH, adjusting CO_2 levels instantly and permanently correcting imbalances.

B. The chemical acid-base buffer systems eliminate excess H^+ or OH^- from the body rapidly to restore pH.

C. Intracellular proteins act as the main regulators of extracellular pH by quickly removing H^+ from the blood.

D. The kidneys restore extracellular fluid pH over hours to days by excreting acidic or alkaline urine, making them the most powerful long-term regulators.

Hypoventilation is associated with which acid-base disturbance?

a. Increased plasma pH, increased plasma HCO3, alkaline urine
b. Increased plasma pH, decreased plasma HCO3, alkaline urine
C. Decreased plasma pH, increased plasma HCO3, acidic urine
d. Decreased plasma pH, decreased plasma HCO3, acidic urine
e. Decreased plasma pH, decreased plasma HCO3, alkaline urine

In the context of renal function, why is the phosphate buffer system more effective as a tubular fluid buffer compared to its role in extracellular fluid?

A. The pH of extracellular fluid is closer to the pk of the phosphate buffer system.
B. Phosphate becomes highly concentrated in the tubules, and the tubular fluid has a lower pH than extracellular fluid, optimizing the buffer's function.
C. Phosphate is less concentrated in tubular fluid, reducing its buffering capacity.
D. The phosphate buffer system does not play a role in buffering tubular fluid.

D
C
B

In the context of renal tubular function, how is bicarbonate (HCO_3^-) reabsorption achieved, considering that bicarbonate ions do not readily permeate the tubular cell membranes?

Bicarbonate ions are directly transported across the luminal membrane through a bicarbonate transporter.
Bicarbonate ions are reabsorbed via a paracellular route between the tubular cells.
Bicarbonate ions are actively transported across the membrane by a hydrogen-potassium ATPase transporter.
Filtered bicarbonate combines with secreted H^+ to form H_2CO_3, which dissociates into CO_2 and H_2O; CO_2 then diffuses into the cell.

In the context of type A intercalated cells in the late distal tubule and collecting tubules, how is H^+ secreted into the tubular lumen, and what is the significance of this mechanism?

Via primary active transport using H^+-ATPase and H^+-K^+-ATPase transporters, facilitating the formation of maximally acidic urine.
Via a secondary active transport mechanism coupled with chloride ion transport.
Via Na^+-H^+ counter-transport, allowing for the direct excretion of H^+ ions.
Via passive diffusion, relying on a concentration gradient to move H^+ into the lumen.

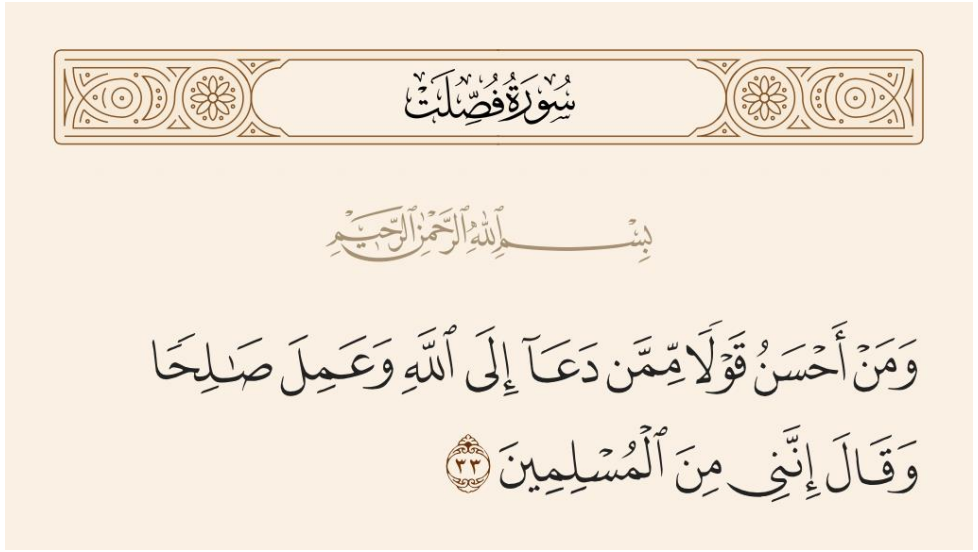
How does chronic acidosis impact renal ammonium excretion, and why is this process significant for long-term acid-base balance?

Chronic acidosis inhibits NH_4^+ excretion, leading to an accumulation of acid in the body and exacerbating the acidotic state.
Chronic acidosis increases renal NH_4^+ excretion, which serves as the dominant mechanism for acid elimination and new bicarbonate generation.
Chronic acidosis decreases renal glutamine metabolism, reducing the formation of NH_4^+ and limiting its role in acid excretion.
Chronic acidosis has no significant impact on renal NH_4^+ excretion.

This response to acid-base imbalances requires several days to be marginally effective:

A. Respiratory compensation
B. Renal compensation
C. Intracellular buffering system
D. Extracellular buffering system

D
A
B
B



VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!