Acid-Base Balance and Renal Acid Excretion

Objectives

By the end of this chapter, you should be able to:

1. Cite the basic principles of acid-base physiology.
2. Understand the bicarbonate-carbon dioxide buffer system and its role in regulating acid-base balance.
3. List the 2 mechanisms by which the kidney excretes the daily “fixed” acid load.
4. Define and explain the term “net acid excretion”

Outline

I. Acid-Base Balance
II. The Carbonic acid/Bicarbonate buffer system
III. Characteristics of Bicarbonate Reabsorption
IV. Urinary acidification
V. Formation and Excretion of Titratable Acid (TA)
VI. Formation and Excretion of Ammonium (NH₄⁺)
VII. Net Acid Excretion
ACID BASE BALANCE AND RENAL ACID EXCRETION

I. Acid Base Balance

The concentration of H+ relative to other electrolytes is extremely low and is typically expressed in nanoequivalents per liter. At a pH 7.40, the H+ concentration is only 40 nEq/L. The normal range for pH is narrow at 7.37-7.43, which corresponds to a H+ concentration of 37-43 nEq/L.

The metabolism of typical diet generates approximately 50 to 100 mEq of H+ (fixed acid) per day, which must be excreted in the urine in order for acid-base balance to be maintained. Acid-base balance also depends on reabsorption of almost all of the filtered bicarbonate in the proximal tubule.

II. The Carbonic acid/Bicarbonate buffer system

The lung eliminates CO\(_2\) (volatile acid) and determines the concentration of H\(_2\)CO\(_3\) by regulating the partial pressure of CO\(_2\). The pCO\(_2\) determines dissolved CO\(_2\) that is in equilibrium via hydration with H\(_2\)CO\(_3\). The kidney maintains the [HCO\(_3^-\)] at 24 mEq/L. Ventilation normally maintains the PCO\(_2\) at 40 mmHg. The resulting pH is 7.40.

The proton concentration can be related to the pCO\(_2\) and HCO\(_3^-\) concentration by the following equation, where 24 represents a modified dissociation constant:

\[
[H^+] = \frac{pCO_2}{[HCO_3^-]} \times 24
\]

or conceptually:

\[
[H^+] = 24 \frac{\text{Lung}}{\text{Kidney}} \frac{\text{Respiratory}}{\text{Metabolic}}
\]

III. Proximal Tubular Bicarbonate Reabsorption

Approximately 4000 mEq of bicarbonate a day are filtered in the kidneys of an average sized adult. Virtually all of this bicarbonate is reabsorbed in the proximal tubule. Failure of this mechanism would obviously result in an enormous acid burden that would exceed the acid excretion capacity of the kidneys. The process of bicarbonate resorption in the proximal tubule results in no net acid excretion, but importantly serves to prevent urinary bicarbonate losses.

Bicarbonate reabsorption occurs mainly in the proximal tubule indirectly via Na+/H+ exchange (Figure 1). There is a minimal fall in urine pH since the weak acid buffer formed (H\(_2\)CO\(_3\)) does not accumulate in the lumen (with C.A. it dissociates to CO\(_2\) and H\(_2\)O). There is no net change in H+ balance since each H+ secreted is recycled via carbonic anhydrase into water, which is deprotonated in the proximal tubular cells and is again available for secretion. Thus, although large amounts of H+ are secreted, none of this H+ is excreted in the urine.
A further decline in urinary pH to levels less than 4.5 does not occur because of the finite activity of the H+-ATPase, as well as the limited impermeability of the tubular epithelium to H+. Decreased H+-ATPase activity or disruption of the epithelial barrier to H+ backleak, as may occur in distal renal tubular acidosis, generally leads to formation of a less than maximally acidified urine with a pH of >5.5.

Note that the amount of fixed acid that can be excreted as free H+ is limited by the minimal urine pH. The concentration of H+ at a pH of 4.5 is only 0.03 mEq/L. Excretion of the 70 mEq daily non-volatile acid as free H+ would then require more than 2000 liters of urine output per day. This problem is overcome through excretion of H+ in the form of two urinary buffers:

1. Titratable acid (HPO$_4^{2-}$/H$_2$PO$_4^-$)
2. NH$_4^+$

V. Formation and Excretion of Titratable Acid (TA)

Dibasic phosphate (HPO$_4^{2-}$) freely filtered at the glomerulus acts as a buffer for protons in the proximal and distal tubule (Figures 3 and 4).

The efficacy of dibasic phosphate as a buffer is a function of the urinary pH in relation to the pK of HPO$_4^{2-}$. The pK of HPO$_4^{2-}$/H$_2$PO$_4^-$ is 6.8, and most (90%) of the buffering by HPO$_4^{2-}$ occurs above a pH of 5.8. The 30-40 mEq of dibasic phosphate that is filtered each day accounts for the excretion of approximately one half of the daily fixed H+ excretion. The buffering activity of dibasic phosphate is referred to as titratable acid, because it is measured by back titration of the urine with NaOH to a pH of 7.40.

The capacity for H+ excretion as titratable acid is limited by the quantity of dibasic phosphate that is filtered. For each secreted H+ buffered by a weak acid and excreted in the urine as titratable acid (TA), a HCO$_3^-$ is released into the plasma.
VI. Formation and Excretion of Ammonium ($\text{NH}_4^+$)

Under normal physiologic conditions, approximately 30-40 mEq of fixed acid per day is excreted in the form of ammonium. Unlike titratable acid, however, the kidney has the capacity under conditions of increased acid burden to excrete as much as 300 mEq per day of fixed acid as ammonium.

Ammonium is primarily synthesized in the proximal tubular cells by the deamination of glutamine to glutamate and ammonium cation (Figure 5). It is transported into the interstitium in the thick ascending limb substituting for K+ on the Na+-K+-2Cl- carrier. Ammonium then dissociates to ammonia in the medullary interstitium under the influence of a relatively higher pH.

![Figure 5: Ammonia Synthesis and Transport](image-url)
Ammonia subsequently diffuses into the medullary collecting duct, and is “trapped” in the increasingly acidic urine as NH$_4^+$ (Figure 6). A HCO$_3^-$ is released into the systemic circulation for each ammonium cation is excreted in the urine.

VII. Net Acid Excretion

Net acid excretion (NAE) can be calculated by the following equation:

$$\text{NAE} = (\text{TA} + \text{NH}_4^+ - \text{HCO}_3^-)$$

(in the urine)

Normally there is no HCO$_3^-$ in the urine. The loss of HCO$_3^-$ in the urine represents the loss of buffer for H$^+$ and thus it is subtracted. For each mEq of TA and NH$_4^+$ excreted in the urine, a new HCO$_3^-$ is generated into the plasma. Normally, the H$^+$ dissociated from the fixed acid end products of metabolism (which are buffered and consume HCO$_3^-$) are excreted as TA and NH$_4^+$, a process which also replaces, one-for-one the HCO$_3^-$ thus consumed.