Acid Base - Vanders Ch. 9, Dibartola Ch. 9

When an acid is dissolved in water, it … dissociates into a proton and a conjugate base.

When a base is dissolved in water, it … combines with a proton to form an acid.

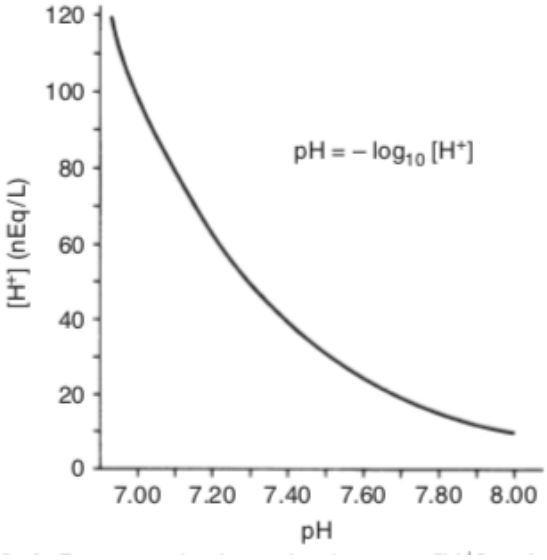
acid <-> conjugate base + H+

An acid is a proton donor, and a base is a proton acceptor.

What is the difference between a weak acid and a strong acid?

Strong acids, such as hydrochloric acid, dissociate fully, releasing all of their hydrogen ions. Eg, 1 mmol of dissolved hydrochloric acid will produce 1 mmol of free hydrogen ions. Whereas acetic acid or lactic acid keep most hydrogen ions bound, so 1 mmol of dissolved acid will not produce the same amount of hydrogen ions.

What is the relationship between pH and [H+]?



Write out the Henderson-Hasselbalch Equation and explain what it means.

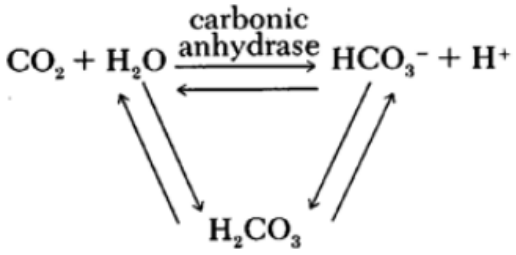
$$pH = pK_a + \log \frac{[\text{conjugate base}]}{[\text{acid}]}$$

[H+] = K [acid] / [base]
K = dissociation constant

A large value for Ka indicates a strong acid and a small value for Ka indicated a weak acid.

Describe the concept of buffering using the CO2-bicarbonate buffer system as an example.

- A buffer is a compound that can accept or donate protons, so a buffer system limits the change in pH regardless of the addition of other acids or bases
- Eg, when an acid is added to a buffer system, most of the hydrogen ions release by that acid combine with the conjugate base of the buffer system, restricting the increase in free hydrogen ions. Similarly, when a base is added, most the free hydrogen ions that combine with the base are replaced by hydrogen ions that dissociate from the acid of the buffer system.
- In the face of persistent imbalance between acid-base input and output, one or the other components of the buffer is gradually reduced in concentration, and eventually, the kidneys have to excrete the acid or bases added to the body.



- CO2 is not technically an acid, but it acts like one as it combines readily with water to form carbonic acid (H2CO3). Carbonic acid then dissociates into a proton and it's conjugate base - bicarbonate. The supply of CO2 is infinite, as it is continuously being produced
- Carbonic anhydrase is an enzyme that greatly speeds up the formation of bicarbonate and H+ from CO2.

In this situation, the concentration of the weak acid (CO2) is held constant, as the rate of respiratory excretion is matched to the rate of metabolic production. Any change in metabolic production is sense by arterial chemoreceptors and chemoreceptors in the brainstem, that alter the rate of ventilation to restore the concentration.

Adding H+ to this system (from a source other than CO2) will drive the equation to the left and reduce bicarbonate on a mole-for-mole basis The pCO2 will not change. Alternatively, removing hydrogen ions will drive the reaction to the right and increase bicarbonate ion concentration.

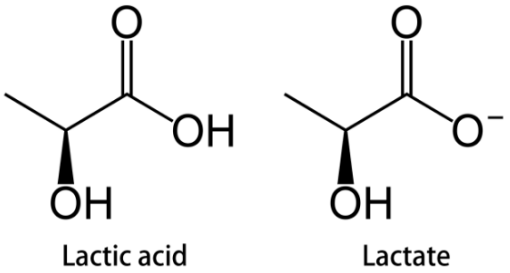
Any metabolic process or reaction that produces hydrogen ions is identical to one that remove bicarbonate, as the end result is always a loss of bicarbonate. And any reaction that consumes hydrogen ions is equivalent to one the produces bicarbonate, as the end result is an increase in bicarbonate. So, when chemical reactions alter the amount of bicarbonate in the blood, the body, specifically the kidneys, must either excrete the excess or replace the lost bicarbonate.

List 5 body buffers:

1. bicarbonate (primary extracellular buffer)
2. hemoglobin (responsible for 80% of non-bicarbonate buffering of whole blood)
    1. imidazole ring of the histidine residue
3. albumin
4. inorganic and organic phosphates
5. bone eg. calcium carbonate, calcium phosphate

Does administration of LRS acidify or alkalinize the blood? How?

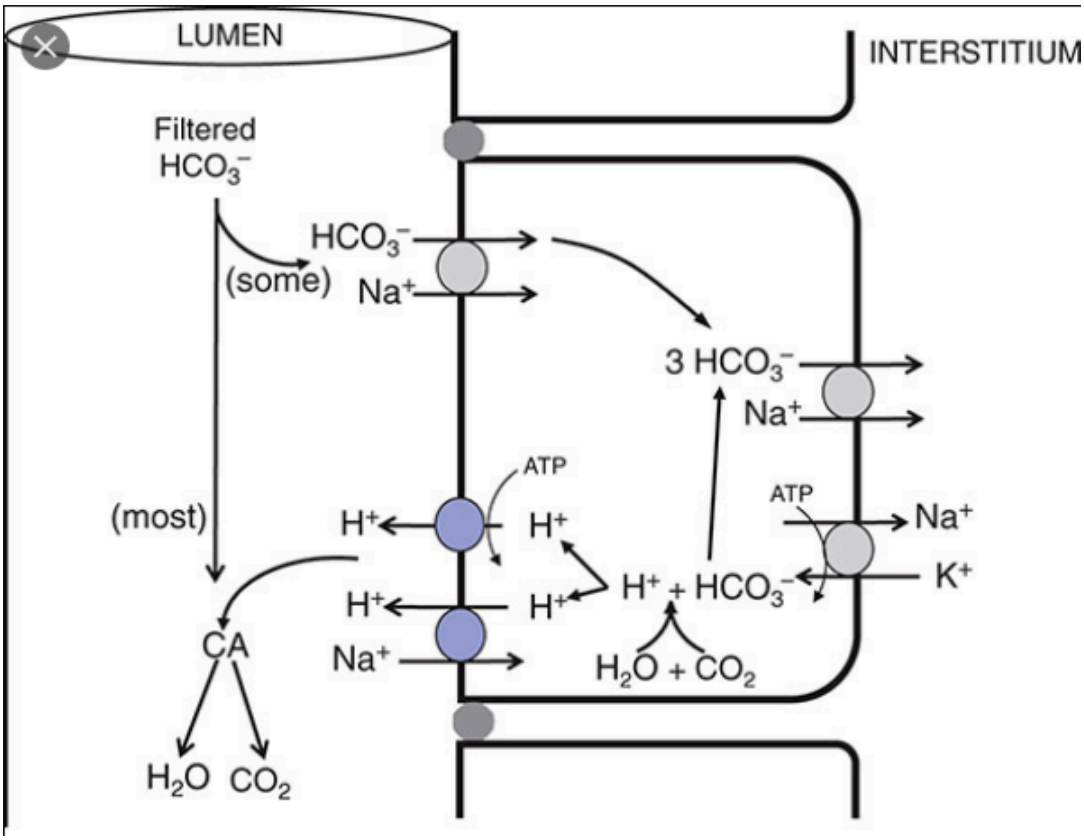
LRS contains 28 mEq/L of lactate with a pH 6.5. Lactate is an organic anion (the conjugate base of lactic acid). When lactate is oxidized to CO2 and water, it consumes a H+ ion and thus produces bicarbonate. LRS should not be confused with lactic acidosis.



Lactic acid Lactate

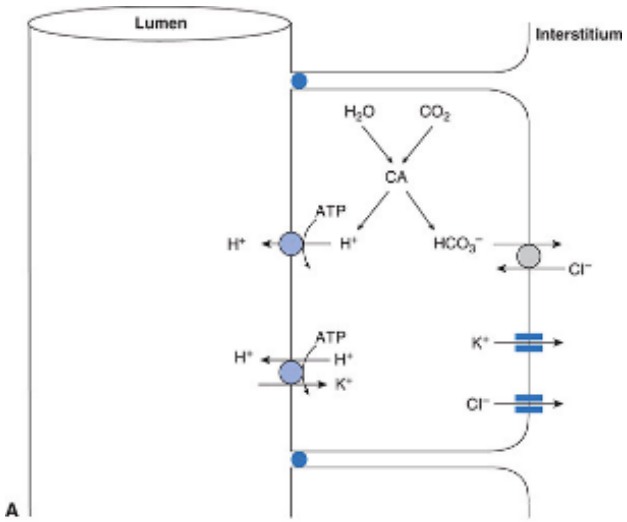
Bicarbonate is freely filtered by the glomerulus and the vast majority is reabsorbed by the <u>proximal tubule</u>. Then, the <u>distal nephron (mostly the collecting tubules)</u> secretes either protons or bicarbonate to balance net acid/ base input into the body.

Describe bicarbonate reabsorption in the proximal tubule.

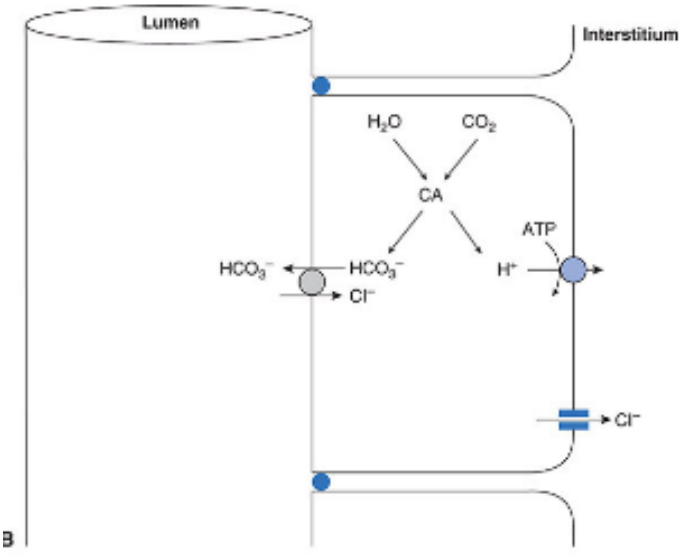


- Within tubular cells: hydrogen ions and bicarbonate are generated from CO2 and water, catalyzed by carbonic anhydrase
- Hydrogen ions are actively secreted into the tubular lumen via an antiporter with Na+ (mostly) or via a primary H-ATPase.
- H+ combines with filtered bicarbonate to form water and CO2. Thus, most of the filtered bicarbonate disappears (requiring an enormous amount of hydrogen ion secretion to occur in the proximal tubule)
- Celluar bicarbonate is transported across the basolateral membrane into the interstitial fluid and then into the peritubular capillary blood.
- i.e. the majority of filtered bicarbonate is converted to CO2 and water, and is replaced by bicarbonate generated inside the cell
- The secondary route for bicarbonate reabsorption is via a Na+/HCO3- symporter that moves bicarbonate from the lumen into the cell. This bicarbonate mixes with cellular bicarbonate and is exported across the basolateral membrane.

Describe the action of Type A and Type B intercalated cells.



Type A intercalated cell:
- apical membrane contains H-ATPases and H-K-ATPases
- bicarbonates moves across the basolateral membrane in antiport with Cl- (AE1)



Type B intercalated cell:
- secretes bicarbonate via HCO3-/Cl- antiporter and transports hydrogen ions into the interstitium

How do the kidneys excrete an acid load (or replace a bicarbonate deficit)?

- All filtered bicarbonate is reabsorbed
- Type A intercalated cells secrete additional H+ via H-ATPases
- these protons attach to bases (other than bicarbonate) in the tubular fluid, allowing for excretion of the proton
- Simultaneously, new bicarbonate is generated in the intercalated cell and transported across the basolateral membrane into the blood via Cl-HCO3 antiporters (AE1)

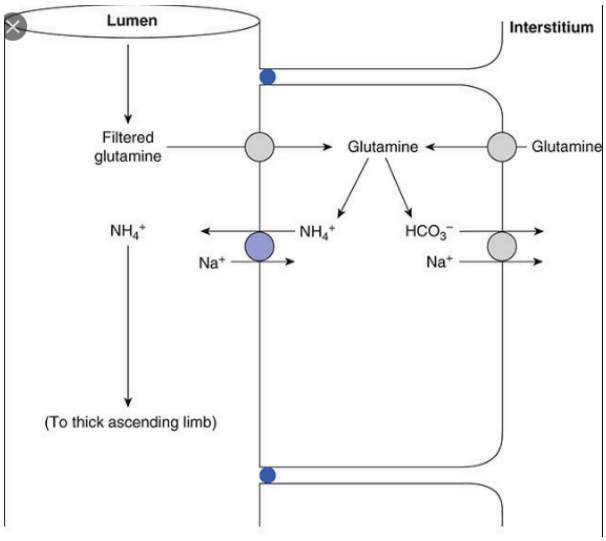
Give two examples of urinary non-bicarbonate bases

1. Phosphate (filtered)
H2PO4- <-> HPO42- + H+

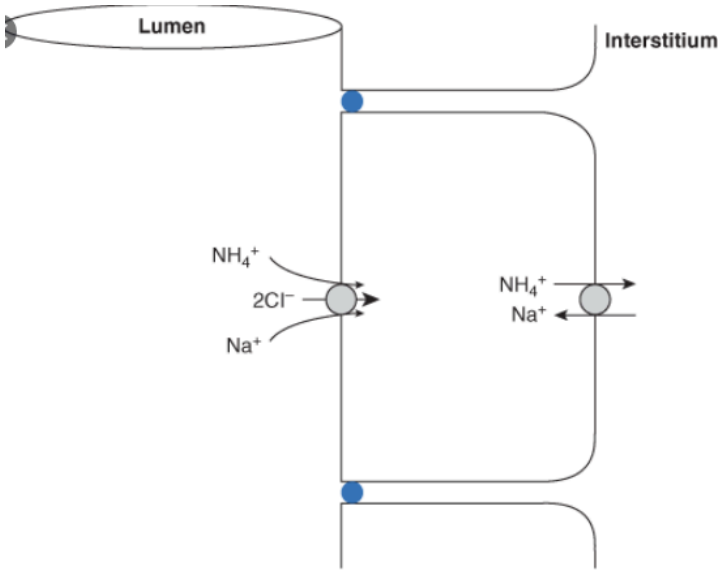
2. Ammonia (synthesized)
Glutamine is synthesized in the liver from NH4+ and bicarbonate. When glutamine reaches the proximal tubule cells, it is converted (via several steps) back into NH4+ and bicarbonate. The bicarbonate is transported back into the blood and the ammonium is secreted.

Describe ammonium handling by the kidneys at the proximal tubule, thick ascending limb, and in the medullary collecting ducts.

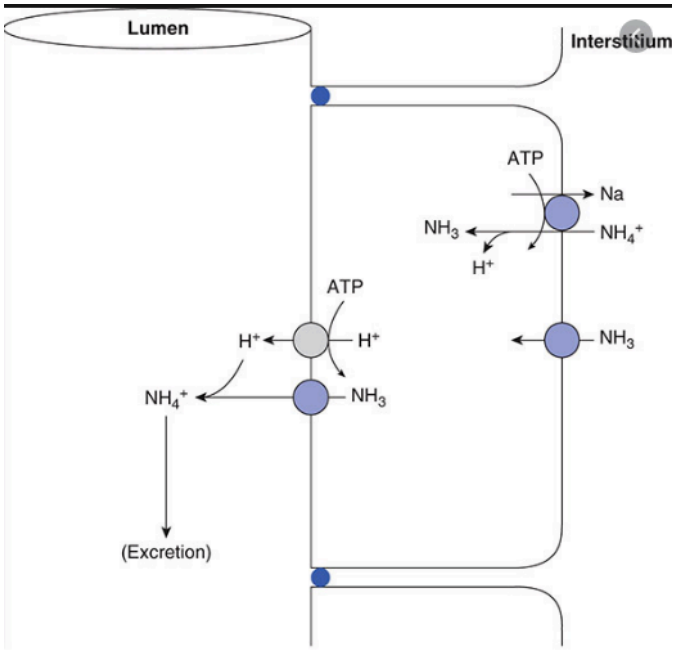
Proximal tubule:
Ammonia is synthesized from glutamine, and is secreted via the NHE3 anti porter in exchange for sodium



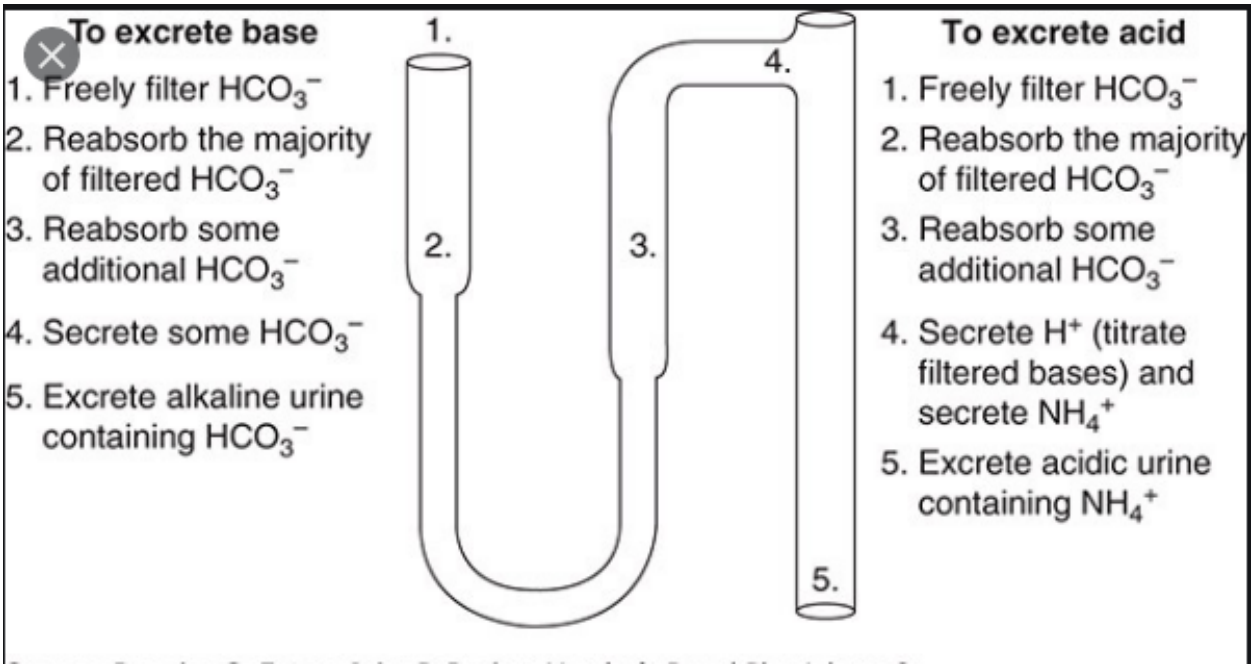
Thick ascending limb:
80% of tubular ammonium is reabsorbed, mostly by the Na-K-2Cl multi porter (with ammonia substituting for K+) and exits via the anti porter in exchange for Na+



Medullary collecting ducts:
Ammonia is taken up from the interstitium and exits into the lumen, to combine with a hydrogen ion



Label what happens at each segment of the kidney to (A) Excrete base; (B) Excrete acid



Fill out the following chart regarding renal tubular acidosis

	Type 1	**Type 2**	**Type 4**
Defect in …	"Classic distal RTA" Defect in acid secretion by the type A intercalated cells in the distal nephron, typically due to defects in the basolateral HCO3-Cl antiporter (AE1) or the apical H-ATPase	“Proximal RTA” Defect in bicarbonate reabsorbing capacity in the proximal tubule, allowing for a large amount of bicarbonate flow that overwhelms the distal nephron	Hypoaldosteronism or failure to respond to aldosterone, reducing the ability to take up glutamine and synthesize ammonium in the proximal tubule. Ammonia excretion can not be increased enough to manage acid load
Mild/ mod or severe acidosis	Severe acidosis	Moderate acidosis	Mild acidosis
Effect on K+	Hypokalemia (severe)	Hypokalemia (moderate)	Hyperkalemia
Acidic or alkaline urine?	Typically > 6.0	Acidic, typically <6.0	Acidic urine
		Fanconi syndrome	

*Type 3 - rare, combination of type 1 and 2