Physiology of Urinary system

By

Dr. Mossa M. Marbut

Dr. Hassan Y. Hassan

3rd Year/ Lecture 5

Acids, Bases, and Buffers

- **One of the most important aspects of homeostasis**
  - Metabolism depends on enzymes, and enzymes are sensitive to pH
  - Slight deviation from the normal pH can shut down entire metabolic pathways
  - Slight deviation from normal pH can alter the structure and function of macromolecules

Acids, Bases, and Buffers

- pH of a solution is determined solely by its **hydrogen ions (H^+)**
- **Acids**—any chemical that releases H^+ in solution
  - A **strong acid** such as hydrochloric acid (HCl) ionizes freely
    - Gives up most of its H^+
    - Markedly lowers pH of a solution
  - A **weak acid** such as carbonic acid (H_2CO_3) ionizes only slightly
    - Keeps most H^+ chemically bound
    - Does not affect pH much

Acids, Bases, and Buffers

- **Bases**—any chemical that accepts H^+
  - **Strong bases,** such as the hydroxide ion (OH^-), have a strong tendency to bind H^+, markedly raising pH
  - **Weak bases,** such as the bicarbonate ion (HCO_3^-), bind less of the available H^+ and have less effect on pH

Acids, Bases, and Buffers

- **7.35 to 7.45 is the normal pH range** of blood and tissue fluid

- **Challenges to acid–base balance**
  - Metabolism **constantly produces acid**
    - **Lactic acids** from anaerobic fermentation
    - **Phosphoric acid** from nucleic acid catabolism
    - **Fatty acids and ketones** from fat catabolism
    - **Carbonic acid** from carbon dioxide

Acids, Bases, and Buffers

- **Buffer**—any mechanism that resists changes in pH
  - Convert strong acids or bases to weak ones
- **Physiological buffer**—system that controls output of acids, bases, or CO_2
  - **Urinary system** buffers greatest quantity of acid or base
    - Takes several hours to days to exert its effect
  - **Respiratory system** buffers within minutes
    - Cannot alter pH as much as the urinary system

Acids, Bases, and Buffers

- **Chemical buffer**—a substance that binds H^+ and removes it from solution as its concentration begins to rise, or releases H^+ into solution as its concentration falls
  - Restores normal pH in fractions of a second
  - **Buffer systems** are mixtures composed of weak acids and weak bases
  - **Three major chemical buffers: bicarbonate, phosphate,** and **protein systems**
    - Amount of acid or base neutralized depends on the concentration of the buffers and the pH of the working environment

The Bicarbonate Buffer System

- **Bicarbonate buffer system**—a solution of carbonic acid and bicarbonate ions
  - **Carbonic acid** and **bicarbonate ions** participate in a reversible reaction
    - $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$
  - The direction of the reaction determines whether it raises or lowers pH
    - $CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
      - Lowers pH by releasing H^+
    - $CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$
      - Raises pH by binding H^+

The Bicarbonate Buffer System

- The bicarbonate buffer system coordinates with the **lungs** and **kidneys** to help control pH and CO_2
  - To lower pH, kidneys excrete HCO_3^-
  - To raise pH, kidneys excrete H^+ and lungs excrete CO_2

The Phosphate Buffer System

- **Phosphate buffer system**—a solution of HPO_4^{2-} and $H_2PO_4^-$
- $\mathbf{H_2PO_4^- \leftrightarrow HPO_4^{2-} + H^+}$
  - As in the bicarbonate system, reactions that proceed to the right liberate H^+ and decrease pH, and those to the left increase pH
- **Important buffering in the ICF and renal tubules**
  - In these places, phosphates are more concentrated and the buffer can function closer to its optimum pH of 6.8
    - Constant production of metabolic acids creates pH values from 4.5 to 7.4 in the ICF, avg. 7.0

The Protein Buffer System

- **Proteins** are more concentrated than bicarbonate or phosphate systems, especially in the ICF
- **Protein buffer system** accounts for about three-quarters of all chemical buffering in the body fluids
- **Proteins' buffering ability is due to certain side groups of their amino acid residues**
  - **Carboxyl (−COOH) side groups** release H^+ when pH begins to rise
  - Others have **amino ($-NH_2$) side groups** that bind H^+ when pH gets too low

Respiratory Control of pH

- **The bicarbonate buffer system is the basis for the strong buffering capacity of the respiratory system**
  - The addition of CO_2 to the body fluids raises the H^+ concentration and lowers pH
  - The removal of CO_2 has the opposite effects
- **Neutralizes two or three times as much acid as the chemical buffers can**

Respiratory Control of pH

- **CO_2 is constantly produced by aerobic metabolism**
  - – Normally eliminated by the lungs at an equivalent rate
  - – CO_2 (from metabolism) + $H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$
    - Lowers pH by releasing H^+
  - – CO_2 (expired) + $H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + H^+$
    - Raises pH by binding H^+
- **Increased CO_2 and decreased pH stimulate pulmonary ventilation, while an increased pH inhibits pulmonary ventilation**

Renal Control of pH

- **The kidneys can neutralize more acid or base than either the respiratory system or chemical buffers**

- **Renal tubules secrete H^+ into the tubular fluid**
  - Most bind to bicarbonate, ammonia, and phosphate buffers
  - Bound and free H^+ are excreted in the urine actually expelling H^+ from the body
  - Other buffer systems only reduce its concentration by binding it to other chemicals

Secretion and Neutralization of Hydrogen Ions in the Kidney

1. H^+ in blood reacts with HCO_3^- to form H_2CO_3.
2. H_2CO_3 decomposes into H_2O and CO_2, which enter the tubule cell.
3. Tubule cells acquire CO_2 from blood, tubular fluid, and their own aerobic respiration.
4. Carbonic anhydrase (CAH) combines H_2O and CO_2 to re-form H_2CO_3.
5. H_2CO_3 ionizes to form HCO_3^- (which returns to the blood) and H^+.
6. Na^+–H^+ antiport exchanges H^+ for Na^+.
7. $NaHCO_3$ from glomerular filtrate decomposes into Na^+ and HCO_3^-. Na^+ is pumped into tubule cell.
8. Na^+ is removed by Na^+–K^+ pump at the base of the cell.
9. HCO_3^- reacts with H^+ from tubule cell to form H_2CO_3.
10. CAH on brush border decomposes H_2CO_3 to H_2O and CO_2 again.
11. CO_2 enters the tubular cell and H_2O passes in the urine (carrying the H^+ that was originally in the blood).

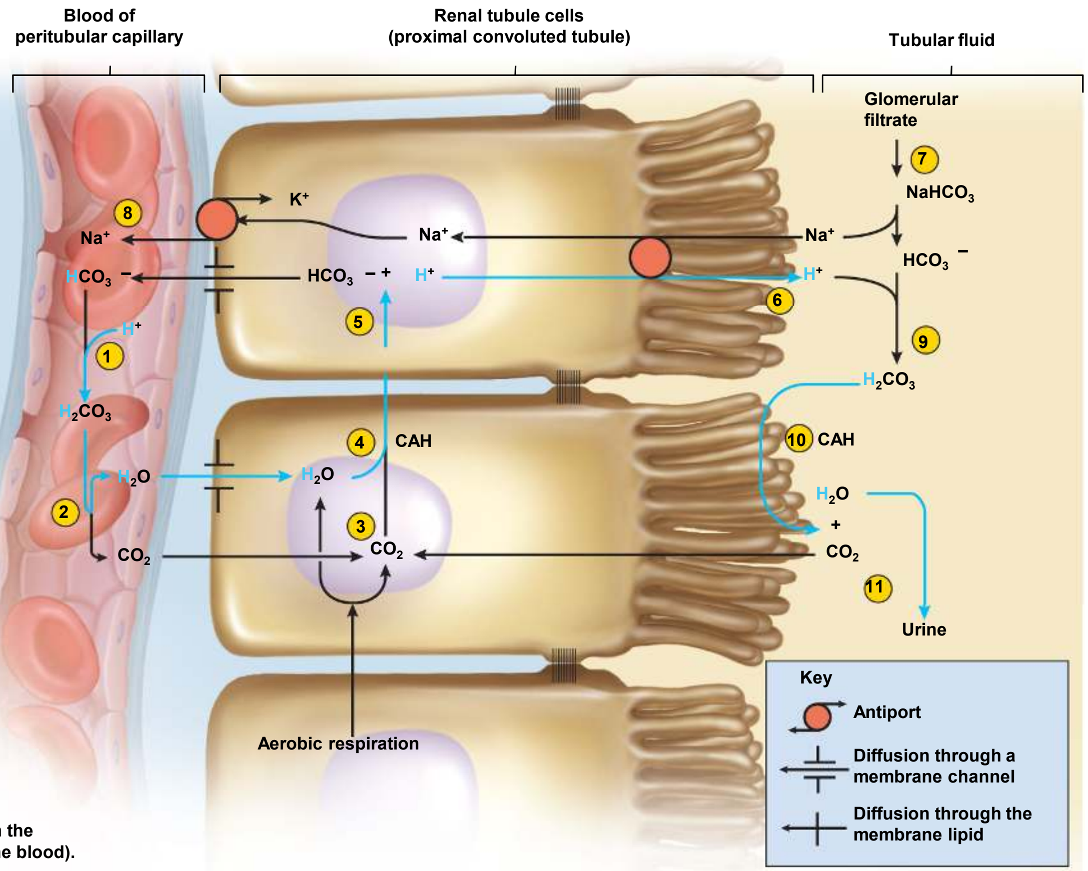

Figure 24.10

Renal Control of pH

- **Tubular secretion of H^+ (step 6)**
  - Continues only with a steep concentration gradient of H^+ between tubule cells and tubular fluid
  - If H^+ concentration increases in tubular fluid, (to pH of 4.5), secretion of H^+ stops, **limiting pH** for secretion

- **This is prevented by buffers in tubular fluid**
  - **Bicarbonate system:** all bicarbonate ions in tubular fluid are consumed, neutralizing H^+
    - So there is no HCO_3^- in the urine
    - The more acid the kidneys secrete, the less sodium is in the urine

Renal Control of pH

Tubular buffers (Continued)

- **Phosphate system:** dibasic sodium phosphate is contained in glomerular filtrate
  - Reacts with some of the H^+ replacing a Na^+ in the buffer which passes into the urine
  - $Na_2HPO_4 + H^+ \rightarrow NaH_2PO_4 + Na^+$
- **Ammonia (NH$_3$):** from amino acid catabolism acts as a base to neutralize acid
  - $NH_3 + H^+$ and $Cl^- \rightarrow NH_4Cl$ (ammonium chloride: weak acid)

Acid Buffering in the Urine

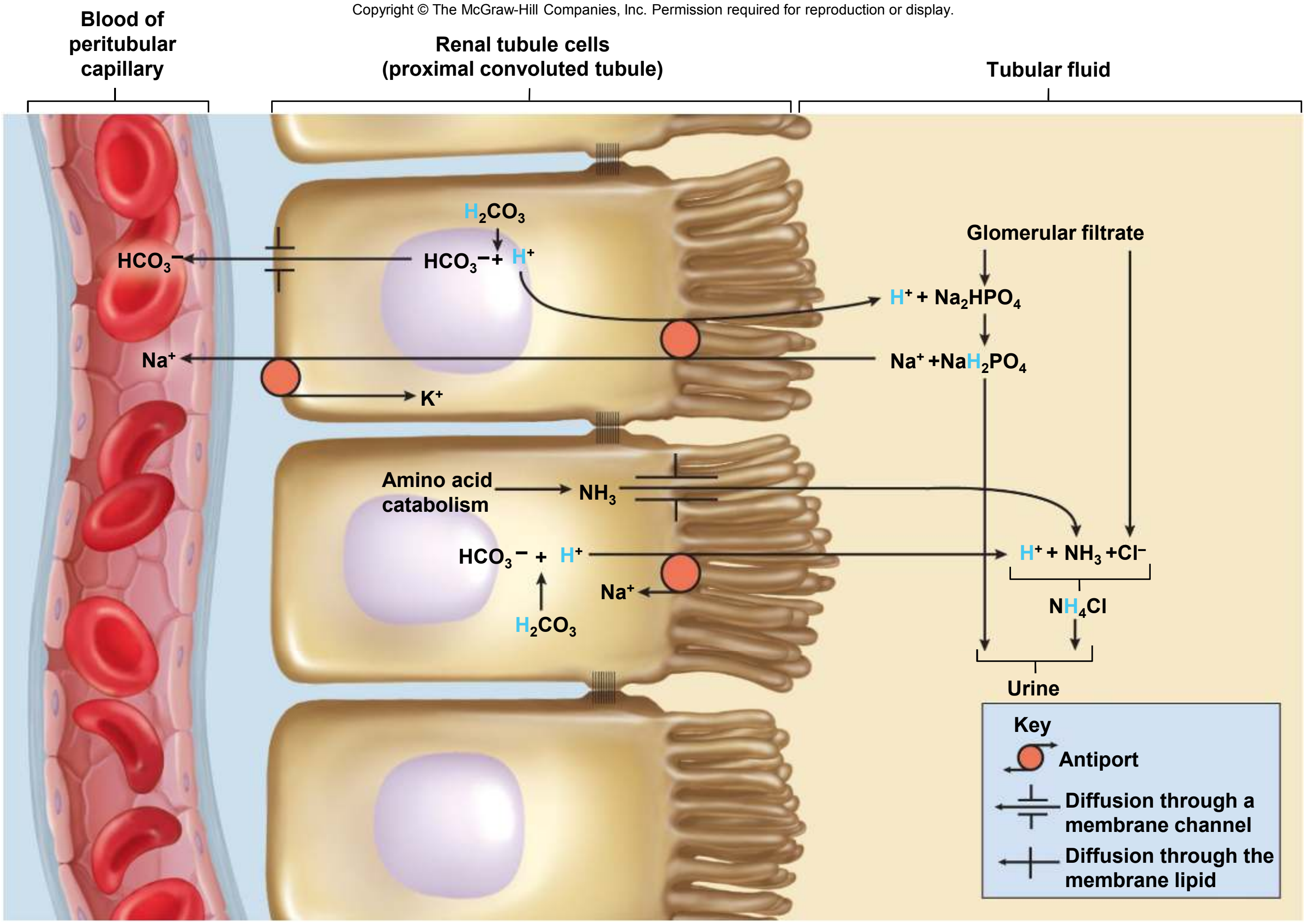

Figure 24.11

The Relationship of Bicarbonate–Carbonic Acid Ratio to pH

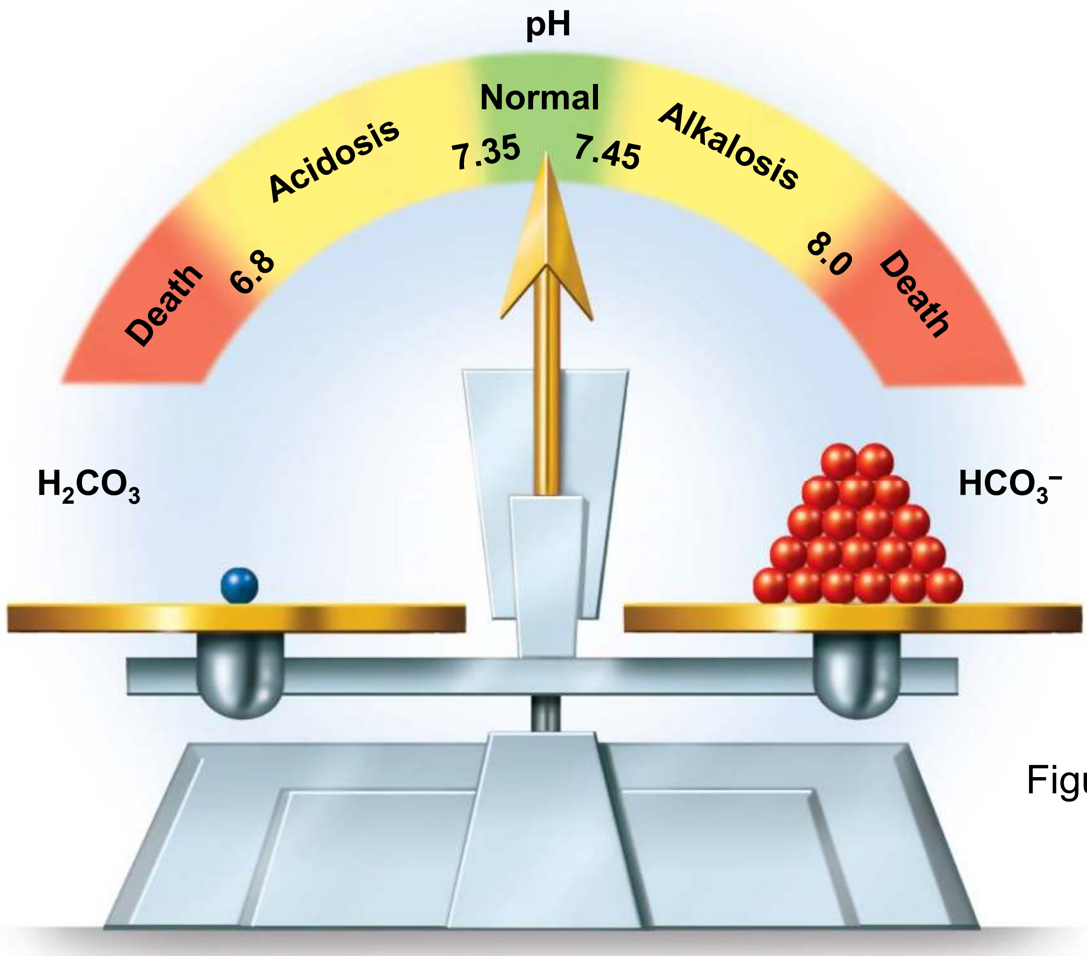

Figure 24.12

Disorders of Acid–Base Balance

- **Acidosis**—pH of ECF below **7.35**
  - H^+ diffuses into cells and drives out K^+, elevating K^+ concentration in ECF
    - H^+ buffered by protein in ICF, so net result is cation loss
    - This causes membrane hyperpolarization, nerve and muscle cells are hard to stimulate; CNS depression may lead to confusion, disorientation, coma, and possibly death

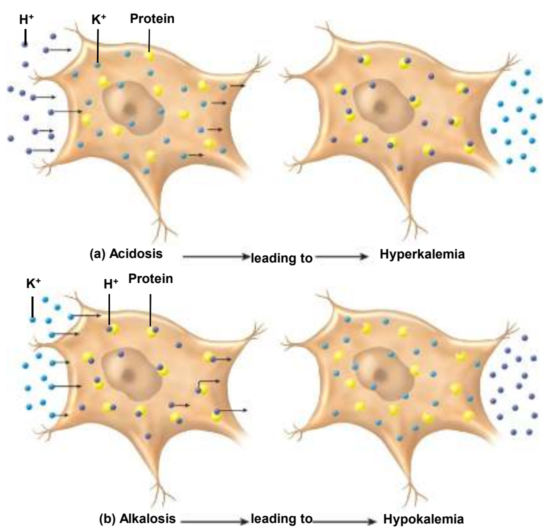

Figure 24.13

Disorders of Acid–Base Balance

- **Alkalosis** – pH above **7.45**
  - H^+ diffuses out of cells and K^+ diffuses in, membranes depolarized, nerves overstimulated, muscles causing spasms, tetany, convulsions, respiratory paralysis
  - A person cannot live for more than a few hours if the blood pH is below 7.0 or above 7.7

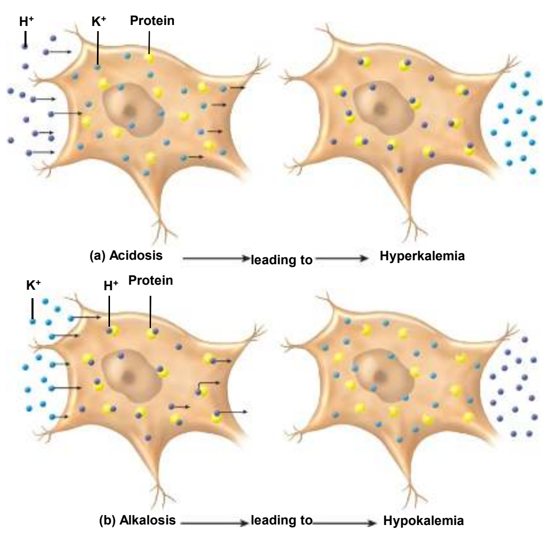

Figure 24.13

Disorders of Acid–Base Balance

- **Acid–base imbalances fall into two categories**
  - **Respiratory** and **metabolic**
- **Respiratory acidosis**
  - Occurs when rate of alveolar ventilation fails to keep pace with the body's rate of CO_2 production
  - Carbon dioxide accumulates in the ECF and lowers its pH
  - Occurs in emphysema where there is a severe reduction of functional alveoli
- **Respiratory alkalosis**
  - Results from hyperventilation
  - CO_2 eliminated faster than it is produced

Disorders of Acid–Base Balance

- **Metabolic acidosis**
  - Increased production of organic acids such as lactic acid in anaerobic fermentation, and ketone bodies seen in alcoholism, and diabetes mellitus
  - Ingestion of acidic drugs (aspirin)
  - Loss of base due to chronic diarrhea, laxative overuse
- **Metabolic alkalosis**
  - Rare, but can result from:
    - Overuse of bicarbonates (antacids and IV bicarbonate solutions)
    - Loss of stomach acid (chronic vomiting)

Compensation for Acid–Base Imbalances

- **Compensated** acidosis or alkalosis
  - Either the **kidneys** compensate for pH imbalances of **respiratory origin,** or
  - The **respiratory system** compensates for pH imbalances of **metabolic origin**
- **Uncompensated** acidosis or alkalosis
  - A pH imbalance that the body cannot correct without clinical intervention

Compensation for Acid–Base Imbalances

- **Respiratory compensation—**changes in pulmonary ventilation to correct changes in pH of body fluids by expelling or retaining CO_2
  - If there is **hypercapnia,** (excess CO_2) it stimulates pulmonary ventilation eliminating CO_2 and allowing pH to rise
  - If there is **hypocapnia,** (deficiency of CO_2) ventilation is reduced to allow CO_2 to accumulate and thereby lowering pH

Compensation for Acid–Base Imbalances

- **Renal compensation**—adjustment of pH by changing rate of H^+ secretion by renal tubules
  - Slow, but better at restoring a fully normal pH
  - In **acidosis,** urine pH may drop to 4.5 due to excess H^+
    - Renal tubules increase rate of H^+ secretion (and ammonia to buffer it) elevating pH in the body
  - In **alkalosis** urine pH as high as 8.2 due to excess HCO^{3-}
    - Renal tubules decrease rate of H^+ secretion, and allow neutralization of bicarbonate, lowering pH in body
  - Kidneys cannot act quickly enough to compensate for short-term pH imbalances
  - Effective at compensating for pH imbalances that last for a few days or longer