27. Effect of Hypoventilation

- Now let's look at how the rate of respiration affects this reaction.
- If the rate of respiration decreases or if the exchange of gases in the lungs is impaired, what happens to the carbon dioxide in the plasma?
  - \( \text{CO}_2 \) increases
  - \( \text{CO}_2 \) decreases

- If the rate of respiration decreases, then carbon dioxide can't leave the plasma and the carbon dioxide builds up.

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3
\]

- **Equilibrium shifts to the right and \( \text{H}^+ \) increases**
- **Equilibrium shifts to the left and \( \text{H}^+ \) decreases**

- If the rate of respiration decreases, what will happen to the equilibrium of this reaction?
- A carbon dioxide build-up in the plasma causes the reaction to proceed to the right and hydrogen ion increases.
- Show what happens in this tank:

- If the rate of respiration decreases, what will happen to the pH of the plasma?
  - \( \text{pH} \) increases
  - \( \text{pH} \) decreases

- Because \( \text{H}^+ \) is being generated, the plasma becomes more acidic and the pH decreases.

28. Effect of Hyperventilation

- If the respiration rate increases to above normal, what happens to the carbon dioxide in the plasma.
  - \( \text{CO}_2 \) increases
  - \( \text{CO}_2 \) decreases
• If the rate of respiration increases, then carbon dioxide readily leaves the plasma and is exhaled.
• What will happen to the equilibrium of this reaction if the rate of respiration increases?

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+
\]

Carbon dioxide Water Bicarbonate Hydrogen ion Carbonic acid

___ Equilibrium shifts to the right and H⁺ increases ___ Equilibrium shifts to the left and H⁺ decreases

• Because carbon dioxide is leaving the plasma, more H⁺ combines with bicarbonate to make more carbon dioxide and the reaction proceeds to the left.
• If the rate of respiration increases, what will happen to the pH of the plasma?
  ___ pH increases ___ pH decreases

• Because H⁺ is being used up to form more CO₂, the plasma becomes more basic and the pH increases.
• You can see how the increased rate of respiration has an effect on the pH of the plasma.
• Because carbonic acid can freely turn into carbon dioxide and can be eliminated through the lungs, it is a volatile acid.
29. Renal Processes

- We will now discuss how renal mechanisms adjust the acid/base balance in the body.

- As you remember, there are three renal processes:
  1. Filtration
  2. Reabsorption
  3. Secretion

- First let's examine what happens during filtration with respect to acid/base balance.

- Label this diagram:

30. Renal Control of pH
• This simplified diagram allows you to observe the non selective filtration of several substances that affect the pH of body fluids from the glomerular capillaries into the glomerular capsule:
  • hydrogen ions, H⁺
  • bicarbonate ions, HCO₃⁻
  • carbon dioxide, CO₂
  • phosphate ions, HPO₄²⁻, H₂PO₄⁻
  • other fixed acids
• Renal tubules selectively reabsorb and secrete these acids and bases to fine-tune the pH of the plasma.
31. Renal Control of Alkalosis

- Now let’s consider what happens when the amount of base increases in the body.
- If the plasma pH is too high, bicarbonate is filtered at the glomerulus, but it is not reabsorbed. Bicarbonate goes into the urine and is eliminated from the body.
- Label this diagram and show what happens to the bicarbonate during alkalosis:

As bicarbonate is eliminated from the body, what happens to the pH of the plasma?

- pH increases
- pH decreases

- Bicarbonate is a base, and as more is eliminated, acid will increase and the pH will decrease.

32. Renal Control of Acidosis

- Now let’s consider what happens when the acid in the body increases.
- When acid increases, there are three major ways that the kidney tubules regulate the pH of the body fluids:
  1. Reabsorption of $\text{HCO}_3^-$
  2. Generation of $\text{HCO}_3^-$ by the kidney tubule cells.
     - By adding new bicarbonate to the blood the pH increases and new buffering power is added to the blood.
  3. Secretion of $\text{H}^+$
- Renal mechanisms are the slowest mechanism and may take hours or days to complete.
- Renal mechanisms are important in the elimination of fixed acids from the body. Fixed acids, are constantly being generated in metabolic reactions and many must be removed from the body in the urine.
- We have just looked at the major functions of the kidney in regulating acid/base balance. The next page will describe these mechanisms in more detail.
- Show what happens to the bicarbonate and hydrogen ion in this diagram:

33. How the Kidneys Combat Acidosis
   • Major ways that the kidneys combat acidosis:
     1. Conserving (Reabsorption) of $\text{HCO}_3^-$
     2. Generation of $\text{HCO}_3^-$
     3. Secretion of $\text{H}^+$
   • First let's take a closer look at how the kidneys combat acidosis by conserving (reabsorbing) bicarbonate ions in the proximal convoluted tubule or PCT.

34. Reabsorption of Bicarbonate
1. Carbon dioxide arrives at the kidney tubule cell in the proximal convoluted tubule from the:
   1. filtrate
   2. plasma
   3. from metabolic reactions within the cell.

• The more carbon dioxide in the blood, as in the case of respiratory acidosis, the faster it enters the cell.

• Label this diagram and show how the carbon dioxide enters the cell:
2. Within the proximal tubule cell, carbon dioxide and water form carbonic acid. This reaction is catalyzed by carbonic anhydrase, shown here as CA.

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3
\]

Carbon dioxide       Water       Carbonic acid

• Then the carbonic acid splits into hydrogen ions and bicarbonate.

\[
\text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-
\]

Carbonic acid       Hydrogen ion      Bicarbonate

• Show what happens to the carbon dioxide:

3. The hydrogen ion moves into the filtrate in exchange for Na\(^+\), to maintain electrical neutrality, through a sodium ion/hydrogen ion antiport transport protein, or countertransport, which is a type of secondary active transport.

• The concentration of sodium ion inside the cell is kept low by the sodium/potassium pump on the surface of the cell facing the plasma.

• This low concentration of sodium ion inside the cell drives the sodium ion/hydrogen ion antiport system.

• Show what happens to the hydrogen ion and how the sodium ion concentrations remain low within the cell:
4. In the filtrate, $H^+$ combines with filtered bicarbonate to form carbonic acid.

$$\text{H}^+ + \text{HCO}_3^- \rightarrow \text{H}_2\text{CO}_3$$

Hydrogen ion  Bicarbonate  Carbonic acid

- Carbonic anhydrase then breaks apart the carbonic acid into carbon dioxide and water.

$$\text{H}_2\text{CO}_3 \rightarrow \text{CO}_2 + \text{H}_2\text{O}$$

Carbonic acid  Carbon dioxide  Water

- The carbonic anhydrase may be attached to the brush border (microvilli) of the PCT cell.
- The carbon dioxide diffuses into the kidney tubule cell, removing bicarbonate from the filtrate. Note that bicarbonate can't move back to the filtrate itself, it must be moved back in the form of carbon dioxide.
- This carbon dioxide can reform bicarbonate within and the process repeats.
- Show what happens to the hydrogen ion within the filtrate on this diagram:

5. Much of the water generated also gets reabsorbed.

- The bicarbonate generated within the cells of the proximal convoluted tubule diffuses into the plasma.
- Sodium ion also moves into the plasma via the sodium/potassium pump to maintain electrical neutrality.
- Show what happens to the water, sodium, and bicarbonate ions in this diagram:

- What is the result of this whole process?
  1. $\text{HCO}_3^-$ is reabsorbed into the plasma. Typically 80-90% of filtered bicarbonate is reabsorbed in the PCT.
2. You end up with more sodium ions getting reabsorbed back into the plasma.

In severe acidosis, this process continues until all the bicarbonate is reabsorbed from the filtrate.
• Now let’s see how additional bicarbonate can be generated in the intercalated cells of the distal convoluted tubule and cortical collecting duct.

35. Generation of Bicarbonate
• In order to combat acidosis, the cells of the late distal convoluted tubule and cortical collecting duct will generate bicarbonate which is taken back up into the plasma.
• At the same time hydrogen ions are secreted into the filtrate.
• The hydrogen ions attach to buffers and are eliminated from the body. Let’s see how this process occurs.

1. Carbon dioxide arrives at the kidney tubule cell in the late distal convoluted tubule and cortical collecting duct from the plasma or from metabolic reactions within the cell.

• Label this diagram and show this process on the diagram to the right:
2. In the kidney tubule cell carbon dioxide and water form carbonic acid. The reaction is catalyzed by carbonic anhydrase:

\[
\text{CO}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3
\]

- Carbon dioxide          Water          Carbonic acid

• Then the carbonic acid splits into hydrogen ions and bicarbonate.

\[
\text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-
\]

- Carbonic acid          Hydrogen ion        Bicarbonate

• Show this process on the diagram to the right:
3. The hydrogen ion goes into the filtrate via primary active transport.

- ATP is used up.
- Hydrogen ion is secreted against the gradient and there can be a thousand times more hydrogen ion in the filtrate than in the plasma.
- Show this process on the diagram to the right:

4. Bicarbonate is scarce in the filtrate at this point because it is reabsorbed in the proximal convoluted tubule, so the hydrogen ion will combine with a buffer such as hydrogen phosphate, which is the most important buffer in the urine.

$$\text{HPO}_4^{2-} + \text{H}^+ \rightarrow \text{H}_2\text{PO}_4^{-1}$$

- Dihydrogen phosphate + Hydrogen ion = Hydrogen phosphate
- The resulting dihydrogen phosphate is unable to go back into the cell and is trapped in the filtrate and excreted.
- By attaching the hydrogen ion to hydrogen phosphate the pH of the filtrate is kept above 4.5. In fact, hydrogen ion secretion will stop if the pH of the filtrate goes below 4.5.
- Show this process on the diagram to the right: