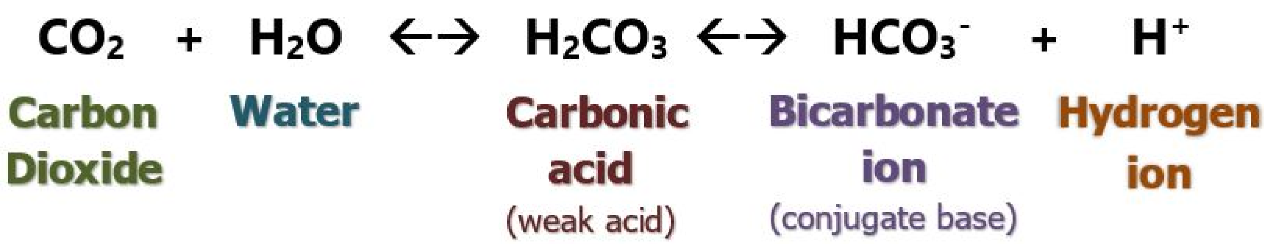
4.3.1

Buffers

Buffers are substance in the body fluids that resist changes in pH. Buffers are composed of weak acids and their conjugate bases. They have the advantage of acting very quickly, almost immediately. So, when you eat citrus fruit and absorb the acids in them, the pH of the blood remains relatively constant because of the action of blood buffers. The weakness of buffers is they only resist changes, they do not prevent changes. Therefore, in a buffered system if you add an acid or a base you will see a small change in pH, but not nearly as large a change as would be observed in the absence of a buffer.

The most important buffer in the blood is the bicarbonate buffer system, see below.



A chemist would tell you that the bicarbonate buffer system should not be very efficient in the body. Indeed, if you placed this buffer into a beaker and tried to maintain a pH of 7.4, it would not do a very good job. Why this is so can be understood a little better by seeing a titration curve that represents how pH changes with the shifting of the amounts of acid (H_2CO_3) and conjugate base (HCO_3^-).

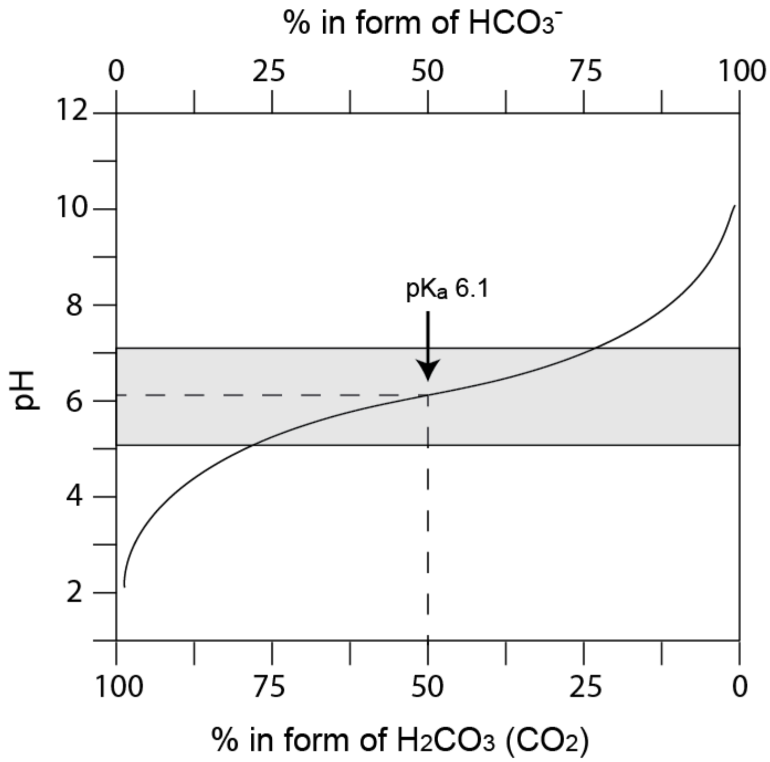


Image by BYU-I JS Spring 2013

If you look at the pKa of the bicarbonate / CO_2 buffer system, it is about 6.1. Notice that while CO_2 is not technically the "acid", it might as well be because it becomes H_2CO_3 when it reacts with water. this means that at body pH of 7.4, there is about 20 times more HCO_3^- than acid (CO_2). Keep in mind that at pH of 6.1, there would be 50% HCO_3^- and 50% acid (CO_2). However, the concentration of both CO_2 and HCO_3^- are regulated which greatly increases the ability of this buffer system. The gray box represents maximal buffering, which is generally considered to be (+ or –) 1 pH unit on a titration curve like this.

Notice that pH changes the least with base or acid added if the pH of the solution is at 6.1. However, the pH of the body is around 7.4. Notice on the titration curve that at a pH of 7.4 we are out of the optimal buffering range (shaded area).

Why then is it so effective in the body? The answer lies in its close ties to the other two lines of defense, the lungs and the kidneys. If we look at just the first part of the equation above, $CO_2 + H_2O \longleftrightarrow H_2CO_3$, we note that one of the key components is carbon dioxide. Therefore, it is directly related to the respiratory system, since the levels of carbon dioxide in the blood can be regulated by increasing or decreasing our respiration. For example, if an acid is added, carbon dioxide is produced which can be excreted in the lungs. The last half of the equation $H_2CO_3 \leftrightarrow H^+ + HCO_3^-$ is linked to the kidneys. The kidneys can either excrete or reabsorb bicarbonate or H^+, as needed. Because the concentrations of both carbon dioxide and bicarbonate can be regulated via the lungs and kidneys, this buffer system becomes the centerpiece of the body's mechanisms for maintaining proper pH.

Although the bicarbonate system is the most important blood buffer, other buffer systems play important roles in other parts of the body. Acid-base changes inside cells are buffered by the intracellular proteins as well as the phosphate buffer system. The phosphate buffer system also plays an important role in the urine, along with the ammonia/ammonium ion buffer system.

Respiratory System

As mentioned above, the respiratory system plays a key role in regulating the body's pH due to its ability to alter the levels of carbon dioxide in the blood and excrete volatile acids. Like buffers, the respiratory system reacts quickly to changes in pH and can bring about a response within a few minutes. Its limitation is that it cannot restore the components of the system to their normal values. For example, suppose the concentration of non-volatile acids increased, causing the pH to go down. Bicarbonate ions would combine with the excess hydrogen ions to buffer the pH change resulting in the production of more carbon dioxide. The extra carbon dioxide would then be excreted via the respiratory system and the pH change would be minimized. However, the respiratory system cannot replace the bicarbonate that was used to buffer the acid. Even though the pH may have been maintained within the normal range, bicarbonate levels are now low. The only way to restore all parameters to their normal levels is through the third component of our defenses, the kidneys.

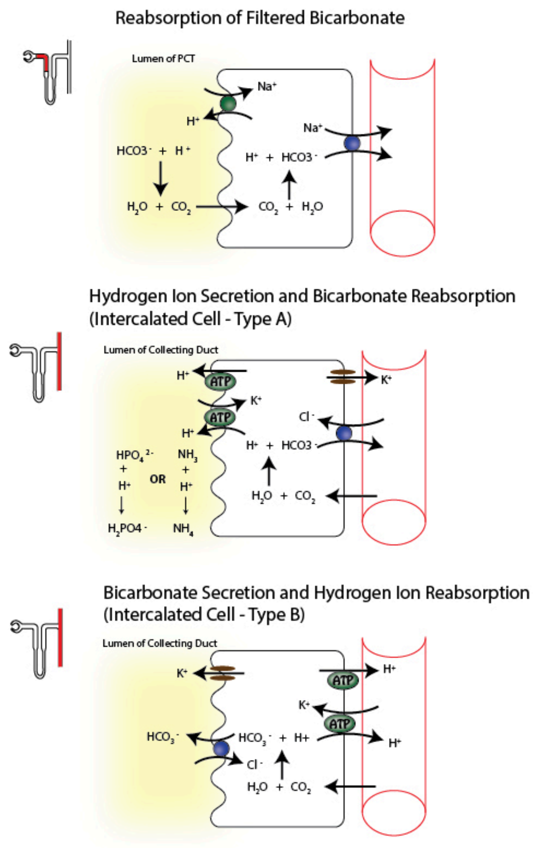
Kidneys

Our most powerful long term defense against changes in pH is the urinary system, specifically the kidneys. Of our three lines of defense, the urinary system is the only one that can restore all of the components to their normal values. It does this by either excreting or reabsorbing bicarbonate ions and hydrogen ions or through the production of new bicarbonate ions. Also, the kidney is responsible for excreting the non-volatile acids that are produced in the body each day. Unlike the blood buffers and the respiratory system which can respond within seconds or minutes to acid-base disturbances, the response of the kidneys takes more time, ranging from hours to days. The kidneys perform several important tasks in terms of regulating acid-base balance. First, they must reabsorb all of the bicarbonate that is filtered each day (see the first image below). In the cells of the kidney tubules, carbon dioxide reacts with water in the presence of the enzyme carbonic anhydrase resulting in the formation of hydrogen ions and bicarbonate ions. The hydrogen ion is secreted into the kidney tubule in exchange for sodium. Once in the tubule, the hydrogen ion can combine with the filtered bicarbonate and be converted to carbon dioxide and water. The carbon dioxide diffuses into the tubule cell and combines with water, producing hydrogen ions and bicarbonate. The bicarbonate can then be reabsorbed into the blood. The end result is the reabsorption of the filtered bicarbonate. Under normal conditions, virtually all of the filtered bicarbonate can be reabsorbed back into the blood. This process takes place primarily in the proximal convoluted tubules.

The kidneys are also able to produce new bicarbonate from carbon dioxide in the blood using carbonic anhydrase, or from the metabolism of the amino acid glutamate.

The other important functions of the kidneys pertain to their ability to either excrete hydrogen ions while reabsorbing bicarbonate ions or excrete bicarbonate ions while reabsorbing hydrogen ions. The newly formed HCO_3^- can then buffer the non-volatile acid. In the collecting ducts of the nephrons, there are two types of cells that are involved in regulating acid/base balance designated as Type A and Type B intercalated cells (bottom two images below). The type A cells are able to secrete H+ while absorbing HCO_3^-. The Type B cells do just the opposite, they absorb H+ while secreting HCO_3^-.

If you look closely at the two diagrams below you will notice that there is a difference in the location of the carriers that transport the various ions across the membranes. The factor that determines which cell is active is the pH of the blood. In conditions of acidosis, the cells that secrete H+ into the nephron lumen are active, while in conditions of alkalosis, the cells that reabsorb H+ into the blood vessels are active. Notice that as H+ is moving across the membranes, K+ is moving the opposite direction. Another consequence of acid-base imbalances is that it can cause a disruption of normal K+ concentrations in the body. Acidosis can result in hyperkalemia (too much extra cellular K+) and alkalosis can result in hypokalemia (too little extracellular K+). Either condition can have tragic effects due to their effect on membrane potentials. It is important that the excreted H+ be buffered in the urine. This is accomplished either by phosphate buffer or by ammonia. This prevents the pH of the urine from becoming too low, which could damage the cells of the kidney tubules.



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