SOLUTIONS TO PROBLEMS

Chapter 1

1. An amino or imino group gives a molecule a positive charge; a carboxylate or phosphoryl group gives a molecule a negative charge.

2. **A** Thiol (sulfhydryl) group
   B Carbonyl group
   C Amide linkage
   D Phosphoanhydride (pyrophosphoryl) linkage
   E Phosphoryl group (P_i)
   F Hydroxyl group

3. Hydrolysis reactions tend to occur with an increase in entropy, because the highly ordered polymer is broken down into separate units.

4. Typical prokaryotic cells are 1–10 μm in diameter, so *T. namibiensis* is about 10–300 times larger (or has 1000 to 27 million times the volume). Typical eukaryotic cells are 10–100 μm in diameter, so *T. namibiensis* is about the same size or up to 30 times larger (or has the same to 27,000 times the volume).

5. The data indicate that eukaryotes are more similar to the archaea than to the eubacteria.

6. (a) Liquid water; (b) ice has less entropy at the lower temperature.

7. (a) Decreases; (b) increases; (c) increases; (d) no change.

8. No. When the change in enthalpy is positive and the change in entropy is negative, the free energy change for the process is greater than zero, which makes the process unfavorable.

9. (a) False. A spontaneous reaction occurs in only one direction.
   (b) False. Thermodynamics does not specify the rate of a reaction.
   (c) True. (d) True. A reaction is spontaneous as long as $\Delta S > \Delta H/T$.

10. (a) $T = 273 + 10 = 283$ K
    $\Delta G = \Delta H - T\Delta S$
    $\Delta G = 15$ kJ $- (283$ K$)(0.05$ kJ $\cdot$ K$^{-1})$
    $\quad = 15 - 14.15$ kJ $= 0.85$ kJ

    ΔG is greater than zero, so the reaction is not spontaneous.

    (b) $T = 273 + 80 = 353$ K
    $\Delta G = \Delta H - T\Delta S$
    $\Delta G = 15$ kJ $- (353$ K$)(0.05$ kJ $\cdot$ K$^{-1})$
    $\quad = 15 - 17.65$ kJ $= -2.65$ kJ

    ΔG is less than zero, so the reaction is spontaneous.

11. $\Delta G = \Delta H - T\Delta S$
    $\Delta G = -7000$ J $\cdot$ mol^{-1} $- (298$ K$)(-25$ J $\cdot$ K^{-1} $\cdot$ mol$^{-1})$
    $\Delta G = -7000 + 7450$ J $\cdot$ mol^{-1} $= 450$ J $\cdot$ mol^{-1}

    The reaction is not spontaneous because $\Delta G > 0$. The temperature must be decreased in order to decrease the value of the $T\Delta S$ term.

12. $\Delta G^{\circ\prime} = -RT \ln \dfrac{[C]}{[A][B]}$

    $= -(8.314$ J $\cdot$ K^{-1} $\cdot$ mol$^{-1})(298$ K$) \ln \dfrac{(0.009)}{(0.002)(0.003)}$

    $= -18,000$ J $\cdot$ mol^{-1} $= -18$ kJ $\cdot$ mol^{-1}

13. $\Delta G^{\circ\prime} = -RT \ln K_{eq} = -RT \ln([C][D]/[A][B])$
    $= -(8.314$ J $\cdot$ K^{-1} $\cdot$ mol$^{-1})$ $(298$ K$) \ln[(3 \times 10^{-6}) (5 \times 10^{-6})/$
    $(10 \times 10^{-6}) (15 \times 10^{-6})]$
    $= 5700$ J $\cdot$ mol^{-1} $= 5.7$ kJ $\cdot$ mol^{-1}

Since $\Delta G^{\circ\prime}$ is positive, the reaction is endergonic under standard conditions.

14. $K_{eq} = e^{-\Delta G^{\circ\prime}/RT} = e^{-(-20,900 \text{ J} \cdot \text{mol}^{-1})/(8.314 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1})(298 \text{ K})}$
    $= 4.6 \times 10^3$

15. From Eq. 1-17, $K_{eq} = [G6P]/[G1P] = e^{-\Delta G^{\circ\prime}/RT}$
    $[G6P]/[G1P] = e^{-(-7100 \text{ J} \cdot \text{mol}^{-1})/(8.3145 \text{ J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1})(298 \text{ K})}$
    $[G6P]/[G1P] = 17.6$
    $[G1P]/[G6P] = 0.057$

16. The cell membrane must be semipermeable so that the cell can retain essential compounds while allowing nutrients to enter and wastes to exit.

17. Membrane-enclosed cellular compartments are typical of eukaryotic but not prokaryotic cells.

18. Concentration = (number of moles)/(volume)
    Volume $= (4/3)\pi \, r^3 = (4/3)\pi(5 \times 10^{-7}$ m$)^3$
    $\quad = 5.24 \times 10^{-19}$ m$^3 = 5.24 \times 10^{-16}$ L

    Moles of protein = (2 molecules)/(6.022 $\times 10^{23}$ molecules $\cdot$ mol^{-1})
    $\quad = 3.32 \times 10^{-24}$ mol

    Concentration $= (3.32 \times 10^{-24}$ mol$)/(5.24 \times 10^{-16}$ L$)$
    $\quad = 6.3 \times 10^{-9}$ M $= 6.3$ nM

19. Number of molecules = (molar conc.)(volume) (6.022 $\times$
    10^{23} molecules $\cdot$ mol^{-1})
    $= (1.0 \times 10^{-3}$ mol $\cdot$ L$^{-1})(5.24 \times 10^{-16}$ L$)$
    $(6.022 \times 10^{23}$ molecules $\cdot$ mol^{-1})
    $= 3.2 \times 10^5$ molecules

20. In order for ΔG to have a negative value (a spontaneous reaction), $T\Delta S$ must be greater than ΔH.

    $T\Delta S > \Delta H$
    $T > \Delta H/\Delta S$
    $T > 7000$ J $\cdot$ mol$^{-1}/20$ J $\cdot$ K^{-1} $\cdot$ mol^{-1}
    $T > 350$ K or 77°C

21. (a) Because $K_{eq} = \dfrac{[R]}{[Q]} = 25$, at equilibrium, the concentration of

    R is 25 times greater than the concentration of Q. When equal concentrations of Q and R are mixed, molecules of Q will be converted to molecules of R.

    (b) Let x = amount of Q converted to R, so that [R] will be 50 μM +

    x and [Q] will be 50 μM $-x$. Since $K_{eq} = \dfrac{[R]}{[Q]} = 25$,

    $50 + x = 25(50 - x)$
    $50 + x = 1250 - 25x$
    $26x = 1200$
    $x = 46.15$
    $[R] = 50 \mu M + 46.15 \mu M = 96.15 \mu M$
    $[Q] = 50 \mu M - 46.15 \mu M = 3.85 \mu M$

22. At 10°C = 283 K (1/T = 0.00353), $K_{eq} = 100$ and ln $K = 4.61$.
    At 30°C = 303 K (1/T = 0.00330), $K_{eq} = 10$ and ln $K = 2.30$.

    These two points generate a line on a van't Hoff plot (ln K_{eq} versus 1/T) with a positive slope that is equal to $(-\Delta H^{\circ}/R)$. ΔH must therefore be negative, indicating that enthalpy decreases during the reaction (heat is given off).

23. This strategy will *not* work because Reaction 1 has a negative enthalpy change, releasing heat, and will therefore become more favorable with decreasing temperature, whereas Reaction 2, which has a positive enthalpy change, will become less favorable. Thus decreasing the temperature will favor Reaction 1, not Reaction 2. To make Reaction 2 more favorable, the temperature must be raised.

    To calculate the amount that the temperature must be raised, Equation 1-18 may be used as follows:

$$\ln K_{eq} = \frac{-\Delta H^\circ}{R}\left(\frac{1}{T}\right) + \frac{\Delta S^\circ}{R}$$

$$\ln\frac{K_1^{T_1}}{K_1^{T_2}} = \frac{-\Delta H_1^\circ}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

$$\ln\frac{K_2^{T_1}}{K_2^{T_2}} = \frac{-\Delta H_2^\circ}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

On subtraction of the previous two equations, and taking into account that $\frac{K_2^{T_1}}{K_1^{T_1}} = 1$, we get

$$\ln\left[\frac{K_1^{T_1}K_2^{T_2}}{K_1^{T_2}K_2^{T_1}}\right] = \ln\frac{K_2^{T_2}}{K_1^{T_2}} = \frac{\Delta H_2^\circ - \Delta H_1^\circ}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

We would like $\frac{K_2^{T_2}}{K_1^{T_2}} = 10$. Substituting in all values and solving for T_2 we get

$$\ln\frac{K_2^{T_2}}{K_1^{T_2}} = \ln 10 = 2.3 = \frac{28{,}000 + 28{,}000}{8.31}\left(\frac{1}{298} - \frac{1}{T_2}\right)$$

Solving for T_2 we get

$$T_2 = \frac{1}{\dfrac{1}{298} - \dfrac{2.3 \times 8.31}{56{,}000}} = 332\ K$$

Hence, to increase K_2/K_1 from 1 to 10, the temperature must be raised from 298 K to 332 K.

Chapter 2

1. (a) Donors: NH1, NH$_2$ at C2, NH9; acceptors: N3, O at C6, N7.

    (b) Donors: NH$^+$, NH$_2$ at C4; acceptors: O at C2, N3. (c) Donors: NH$_3^+$ group, OH group; acceptors: COO$^-$ group, OH group.

2. From most soluble (most polar) to least soluble (least polar): c, b, e, a, d.

3. 18 mL of water has a mass of about 18 g; one mole contains about 6×10^{23} molecules, and the molecular mass of H$_2$O is about 18 g · mol^{-1}. Therefore, the spoon holds (18 g)(6 × 10^{23} molecules · mol^{-1})/(18 g · mol^{-1}) = 6 ×10^{23} molecules.

4. (a) (2.6 × 10^8 ions)(40 g · mol^{-1})(1 mol/6 × 10^{23} ions) = 1.7 × 10^{-14} g. Because the mass of the ions is 1% the mass of the cell, the mass of the cell is 100 times greater, or about 1.7 × 10^{-12} g.

    (b) (2 × 10^8 molecules)(1 mol/6 × 10^{23} molecules)(150 g · mol^{-1}) = 5 × 10^{-14} g

    The fraction of the cell's mass due to carbohydrates is (5 × 10^{-14} g)/(1.7 ×10^{-12} g) = 0.03 or about 3%.

    (c) (0.006)(1.7 × 10^{-12} g)(6 × 10^{23} molecules · mol^{-1})(1 mol/5.6 × 10^9 g) = 1

5. (a) Water; (b) water.

6. (a) Micelle, with the polar carboxylate group on the surface; (b) in the interior of the micelle.

7. Water molecules move from inside the dialysis bag to the surrounding seawater by osmosis. Ions from the seawater diffuse into the dialy-sis bag. At equilibrium, the compositions of the solutions inside and outside the dialysis bag are identical. If the membrane were solute-impermeable, essentially all the water would leave the dialysis bag.

8. (a) Water will move out of the cell by osmosis, from an area of high concentration (low solute concentration) to an area of low concentration (high solute concentration). (b) Salt ions would undergo a net movement by diffusion from the surrounding solution (high salt concentration) into the cell (low salt concentration).

9. (a) COO$^-$ (b) COO$^-$

10. (a) COO$^-$ (b) COO$^-$
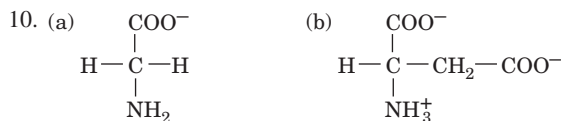
11. pH 4, NH$_4^+$; pH 8, NH$_4^+$; pH 11, NH$_3$.

12. pH 4, H$_2$PO$_4^-$; pH 8, HPO$_4^{2-}$; pH 11, HPO$_4^{2-}$.

13. The increase in [H$^+$] due to the addition of HCl is (50 mL)(1 mM)/(250 mL) = 0.2 mM = 2 × 10^{-4} M. Because the [H$^+$] of pure water, 10^{-7} M, is relatively insignificant, the pH of the solution is equal to $-\log(2 \times 10^{-4})$ or 3.7.

14. (a) (0.010 L)(5 mol · L^{-1} NaOH)/(1 L) = 0.05 M NaOH ≡ 0.05 M OH$^-$

    [H$^+$] = K_w/[OH$^-$] = (10^{-14})/(0.05) = 2 × 10^{-13} M

    pH = $-\log$[H$^+$] = $-\log(2 \times 10^{-13})$ = 12.7

    (b) (0.020 L)(5 mol · L^{-1} HCl)/(1 L) = 0.1 M HCl ≡ 0.1 M H$^+$

    Because the contribution of 0.010 L × 100 mM/(1 L) = 1 mM glycine is insignificant in the presence of 0.1 M HCl,

$$pH = -\log[H^+] = -\log(0.1) = 1.0$$

    (c) pH = pK + log([acetate]/[acetic acid])

    [acetate] = (5 g)(1 mol/82 g)/(1 L) = 0.061 M

    [acetic acid] = (0.010 L)(2 mol · L^{-1})/(1 L) = 0.02 M

    pH = 4.76 + log(0.061/0.02) = 4.76 + 0.48 = 5.24

15. The pK corresponding to the equilibrium between H$_2$PO$_4^-$ (HA) and HPO$_4^{2-}$ (A$^-$) is 6.82 (Table 2-4). The concentration of A$^-$ is (50 mL)(2.0 M)/(200 mL) = 0.5 M, and the concentration of HA is (25 mL)(2.0 M)/(200 mL) = 0.25 M. Substitute these values into the Henderson–Hasselbalch equation (Eq. 2-10):

$$pH = pK + \log\frac{[A^-]}{[HA]}$$
$$pH = 6.82 + \log\frac{0.5}{0.25}$$
$$pH = 6.82 + \log 2$$
$$pH = 6.82 + 0.30 = 7.12$$

16. Use the Henderson–Hasselbalch equation (Eq. 2-10) and solve for pK:

$$pH = pK + \log\frac{[A^-]}{[HA]}$$
$$pK = pH - \log\frac{[A^-]}{[HA]}$$
$$pK = 6.5 - \log\frac{0.2}{0.1}$$
$$pK = 6.5 - 0.3 = 6.2$$

Case 1
Acute Aspirin Overdose:
Relationship to the Blood Buffering System

Focus concept
The response of the carbonic acid/bicarbonate buffering system to an overdose of aspirin is examined.

Prerequisites
- · Principles of acids and bases, including pK_a and the Henderson-Hasselbalch equation.
- · The carbonic acid/bicarbonate blood buffering system.

Background
You are an emergency room physician and you have just admitted a patient, a 23-year-old female, who had been hospitalized for psychiatric treatment for the past six months. She was out on a day pass when she was brought to the emergency room around 9 pm. The patient was disoriented, had trouble speaking, and was suffering from nausea and vomiting. She was also hyperventilating. The patient admitted to taking an entire bottle of aspirin, which contained 250 tablets. The patient said that she took the tablets around 7 pm that evening. You draw blood from the patient and the laboratory performs the analyses shown in Table 1.1.   The patient is experiencing mild respiratory alkalosis.

**Table 1.1**: Arterial blood gas concentration in patient

	Patient, two hours after aspirin ingestion	Patient, ten hours after aspirin ingestion	Normal values
p_{CO_2}	26 mm Hg	19 mm Hg	35-45 mm Hg
HCO_3^-	18 mM	21 mM	22-26 mM
p_{O_2}	113 mm Hg	143 mm Hg	75-100 mm Hg
pH	7.44	7.55	7.35-7.45
Blood salicylate concentration, mg/dL	57	117	

In the emergency room, the patient is given a stomach lavage with saline and two doses of activated charcoal to adsorb the aspirin. Eight hours later, nausea and vomiting became severe, and her respiratory rate increased; she was in severe respiratory alkalosis, and further treatment was required. You carry out a gastric lavage at pH = 8.5 and administer further activated charcoal treatments, one every 30 minutes. A bicarbonate drip was required to prevent the blood bicarbonate concentration from dropping below 15 mM. After 12 hours, blood salicylate concentrations began to decrease. The patient's blood pH begins to drop around 24 hours after the aspirin ingestion and finally returned to normal at 60 hours after the ingestion, although salicylate concentrations did not fall to zero until about 80 hours after aspirin ingestion.

Questions

1. Aspirin, or acetylsalicylic acid (structure shown in Figure 1.1), is hydrolyzed in the presence of aqueous acid and stomach esterases (which act as catalysts) to salicylic acid (the pharmacologically active form of the drug) and acetic acid. Write the balanced chemical reaction for this transformation.

Acetylsalicylic acid (aspirin)

Figure 1.1: Structure of aspirin.
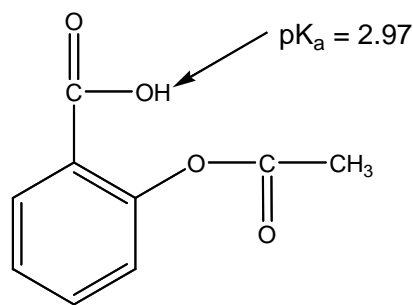
2. Since the patient was brought into the emergency room only two hours after the overdose, you suspect that her stomach might contain undissolved aspirin that is continuing to be absorbed. The fact that she is experiencing severe respiratory alkalosis 10 hours after the ingestion confirms your suspicion and you decide to use a gastric lavage at pH 8.5 to effectively remove any aspirin that still remains in the stomach.
   a. Calculate the percentage of protonated and unprotonated forms of salicylic acid at the pH of the stomach, which is usually around 2.0.
   b. Calculate the percentage of protonated and unprotonated forms of salicylic acid at the pH of the gastric lavage. How does the gastric lavage at pH 8.5 facilitate removal of aspirin from the stomach? Explain. (Note: Assume that the pK_a values for the carboxylate group in salicylic acid and acetylsalicylic acid are the same.)

3. It has been shown that salicylates act directly on the nervous system to stimulate respiration. Thus, our patient is hyperventilating due to her salicylate overdose.
   a. Explain how the salicylate-induced hyperventilation leads to the values of pO_2 and pCO_2 symptoms seen in the patient.
   b. Explain how the salicylate-induced hyperventilation causes the pH of the patient's blood to increase. Illustrate your answer with the appropriate equations.

c. Why was the bicarbonate drip necessary?

4.   a.   Determine the ratio of HCO_3^- to H_2CO_3 in the patient's blood 10 hours after aspirin ingestion. How does this compare to the ratio of HCO_3^- to H_2CO_3 in normal blood? Can the H_2CO_3/HCO_3^- system work effectively as a buffer in this patient under these conditions? Explain.
   b.   Compare the concentration of HCO_3^- in a normal person and in our patient. Then calculate the concentration of H_2CO_3 in the patient's blood 10 hours after aspirin ingestion. Again, compare this value to the concentration of H_2CO_3 found normally, and again address the question of buffer effectiveness in the patient.

5.   Sixty hours after aspirin ingestion, the patient's blood pH returned to normal (pH = 7.4). By what mechanism(s) was the patient's blood pH return to normal?

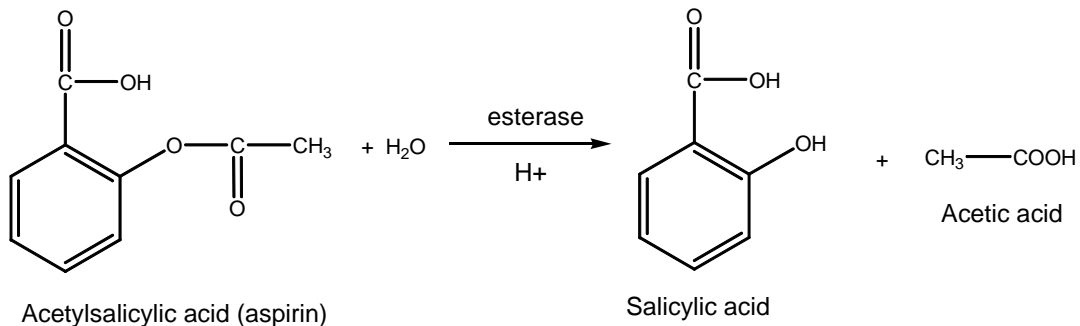6.   Are there other substances in the blood that can serve as buffers?

Reference
Krause, D. S., Wolf, B. A., and Shaw, L. M. (1992) *Therapeutic Drug Monitoring* **14**, pp. 441-451.

Acute Aspirin Overdose: Relationship to the Blood Buffering System

1.

esterase
H+

Acetylsalicylic acid (aspirin)   Salicylic acid   Acetic acid

2. These questions can be answered by using the Henderson-Hasselbalch equation:
   a.

$$pH = pK_a + \left(\log \frac{[salicylate]}{[salicylic\ acid]} \right)$$

$$2.0 = 2.97 + \left(\log \frac{[salicylate]}{[salicylic\ acid]} \right)$$

$$\frac{0.11}{1} = \frac{[salicylate]}{[salicylic\ acid]}$$

At pH = 2, the percentage of salicylate (unprotonated) is 9.9% (0.11/1.11) and the percentage of salicylic acid (protonated) is 90.1% (1/1.11).
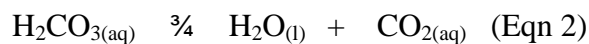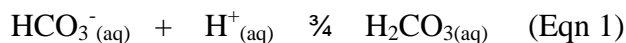
b.

$$pH = pK_a + \left(\log \frac{[salicylate]}{[salicylic\ acid]} \right)$$

$$\frac{10^{5.5} = 3.0 + \left(\log \frac{[salicylate]}{[salicylic\ acid]} \right)}{1} = \frac{[salicylate]}{[salicylic\ acid]}$$

1

At pH = 8.5, virtually 100% of the salicylate is in the unprotonated form. The gastric lavage increases the solubility of the drug because at this pH, the salicylate is unprotonated and negatively charged. At the pH of the stomach, pH = 2, about 90% of the salicylic acid is in the protonated, or uncharged, form. This form is more lipid-soluble and will be able to pass through the membranes of the cells lining the stomach, facilitating its absorption into the bloodstream (an undesirable result). On the other hand, charged species are among the most polar, and as such, they dissolve in water very well and in lipids, not well at all. Negatively charged species can form ion-dipole interactions with water and are generally more polar (and water soluble) than neutral species, so the gastric lavage increases the solubility of the drug by converting the neutral salicylic acid to the negatively charged salicylate. This facilitates the removal of the aspirin from the stomach. At the same time, the decreased lipid solubility of the charged salicylate results in decreased absorption from the stomach into the bloodstream.

3. a. The patient's p_{O_2} pressure increases between two hours and ten hours, and the pCO_2 decreases in the same time period, indicating the excessive oxygen intake and excessive CO_2 exhalation that would be expected in a hyperventilating patient. (An additional note: In addition to causing hyperventilation, salicylates act as uncouplers of electron transport and oxidative phosphorylation; this also explains the patient's abnormal blood gas values.) Salicylates are clearly the stimulus for this hyperventilation, as their concentration increases from 57 mg/dL to 117 mg/dL from two hours to ten hours after aspirin ingestion. The patient's laboratory values show a low p_{CO_2} value (26 mm Hg two hours after aspirin ingestion and 19 mm Hg after 10 hours of aspirin ingestion) and a high p_{O_2} value (113 mm Hg two hours after aspirin ingestion and 143 mm Hg after 10 hours of aspirin ingestion), indicating that oxygen is being taken in and carbon dioxide is being exhaled at a greater rate than normal as expected during hyperventilation (normal values for p_{CO_2} are 35-45 mm Hg and for p_{O_2} the normal value is 75-100 mm Hg).

    b. The carbonic acid/bicarbonate buffering system relies on these three equilibria:

$$HCO_3^-{}_{(aq)} \ + \ H^+{}_{(aq)} \ \rightleftharpoons \ H_2CO_{3(aq)} \quad \text{(Eqn 1)}$$
$$H_2CO_{3(aq)} \ \rightleftharpoons \ H_2O_{(l)} \ + \ CO_{2(aq)} \quad \text{(Eqn 2)}$$
$$CO_{2(aq)} \ \rightleftharpoons \ CO_{2(g)} \quad \text{(Eqn 3)}$$

The patient experiences salicylate-induced hyperventilation, which means that carbon dioxide is being rapidly removed from the lungs. The removal of $CO_{2(g)}$ shifts the equilibrium of the third equation above to the right, which means that carbon dioxide moves out of the bloodstream and into the lungs. This causes $CO_{2(aq)}$ to be depleted, so the equilibrium of the second equation also

shifts to the right. This depletes the carbonic acid, so the equilibrium of the first equation also shifts right to produce more carbonic acid. The result is that hydrogen ions are depleted and the blood becomes more basic. This is verified by looking at the laboratory values, which show that the patient's blood pH after 10 hours of aspirin ingestion is 7.55 (normal is 7.35-7.45). The shift of the first equation to the right causes bicarbonate ions to be depleted. This is why the bicarbonate concentration in the patient is lower than normal (as discussed below).

c. The shift of the first equation to the right depletes both hydrogen ions and bicarbonate ions, as discussed above. If the shift is too dramatic, bicarbonate ions will be depleted and the ability of the carbonic acid/bicarbonate buffering system will be compromised.   Both conjugate base and weak acid forms of a buffer are needed to "mop up" protons and hydroxide ions, respectively. A bicarbonate drip replaced the bicarbonate ions that were being depleted until the salicylates could be removed from the patient's system and thus remove the stimulus for hyperventilation.

4. a. The ratio of bicarbonate to carbonic acid in the patient's blood:

$$pH = pK_a + \left(\log \frac{[bicarbonate]}{[carbonic\ acid]} \right)$$

$$7.55 = 6.4 + \left(\log \frac{[bicarbonate]}{[carbonic\ acid]} \right)$$

$$\frac{14}{1} = \frac{[bicarbonate]}{[carbonic\ acid]}$$

The ratio of bicarbonate to carbonic acid in normal blood:

$$pH = pK_a + \left(\log \frac{[bicarbonate]}{[carbonic\ acid]} \right)$$

$$7.4 = 6.4 + \left(\log \frac{[bicarbonate]}{[carbonic\ acid]} \right)$$

$$\frac{10}{1} = \frac{[bicarbonate]}{[carbonic\ acid]}$$

What makes an effective buffer?

a. The concentration of the conjugate base to weak acid should range from 0.1/1 to 10/1 to ensure that there is some of each species, weak acid and conjugate base, present. Ratios lying outside of this range have an abundance of either the conjugate base or the weak acid alone. In order to

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serve as an effective buffer (ie, absorb both added H^+ and OH^-), both a conjugate base and a weak acid must be present. In our patient, the ratio of conjugate base to weak acid does not lie within the effective buffering range. The bicarbonate concentration (conjugate base) is too high relative to the carbonic acid (weak acid) concentration; thus the relative amount of weak acid is insufficient.

b. It is not just the ratio of conjugate base to weak acid that is important–it's the <u>absolute concentration</u> of each that is also important.   We are given the concentration of HCO_3^- and can calculate the concentration of H_2CO_3 using the Henderson-Hasselbalch equation:

$$pH = pK_a + \left(\log \frac{[bicarbonate]}{[carbonic\ acid]} \right)$$
$$7.55 = 6.4 + \left(\log \frac{(21\ x\ 10^{-3}\ M)}{[carbonic\ acid]} \right)$$

$$[H_2CO_3] = 1.49\ mM$$

The carbonic acid concentration in our patient is 1.49 mM. We can infer that in a normal patient, the carbonic acid concentration is 2.2-2.6 mM, since there is a 10:1 ratio between bicarbonate and carbonic acid. Thus both the carbonic acid and bicarbonate concentrations are lower than normal in our patient. If the concentration of buffering species is low, then the ability of the buffer to work effectively is compromised. The greater the concentration of weak acid and conjugate base, the greater the ability of the buffer to absorb added amounts of strong acid and strong base, ie, <u>the greater the buffer capacity</u>. Buffers with higher buffering capacities (ie, higher concentrations) can absorb greater amounts of added acid or added base and can therefore buffer more effectively.

5. As the salicylate is removed, the stimulus for salicylate-induced hyperventilation will decrease as a result. At time = 60 hours, the salicylate concentrations have not fallen to zero, but the concentrations are much decreased. In the basic blood, OH^- reacts with the H^+ to form water. This depletes the H^+ so that the first equation (shown in Question 3b) shifts left to produce more hydrogen ions. This in turn depletes H_2CO_3, so the second equation shifts left. This depletes $CO_{2(aq)}$, which shifts the third equation to the left. This results in shallow breathing. The shallow breathing results in a greater concentration of $CO_{2(aq)}$ in the blood which can ultimately produce more hydrogen ions, which will bring the blood pH back to normal.

6. Yes, phosphate ($H_2PO_4^-$/HPO_4^{2-}, $pK_a = 7.2$), and proteins like hemoglobin which can bind protons can also serve as buffers. Organic acids and proteins also have a buffering role. However, unlike the bicarbonate/carbon dioxide buffer system, these buffering systems are not linked to respiration.