Case 37

Metabolic Alkalosis: Vomiting

Maria Cuervo is a 20-year-old philosophy major at a state university. When the “24-hour” stomach flu went around campus during final exams, she was one of the unlucky students to become ill. However, instead of 24 hours, Maria vomited for 3 days. During that time, she was unable to keep anything down, and she sucked on ice chips to relieve her thirst. By the time she was seen in the student health center, the vomiting had stopped, but she could barely hold her head up. On physical examination, Maria’s blood pressure was 100/60, and she had decreased skin turgor and dry mucous membranes. The blood values shown in Table 4-15 were obtained.

<table>
<thead>
<tr>
<th>Table 4-15</th>
<th>Maria's Laboratory Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial blood</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.53 (normal, 7.4)</td>
</tr>
<tr>
<td>$\text{HCO}_3$</td>
<td>37 mEq/L (normal, 24 mEq/L)</td>
</tr>
<tr>
<td>$P_{CO_2}$</td>
<td>45 mm Hg (normal, 40 mm Hg)</td>
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<tr>
<td>Venous blood</td>
<td></td>
</tr>
<tr>
<td>Na$^+$</td>
<td>137 mEq/L (normal, 140 mEq/L)</td>
</tr>
<tr>
<td>Cl$^-$</td>
<td>82 mEq/L (normal, 105 mEq/L)</td>
</tr>
<tr>
<td>K$^+$</td>
<td>2.8 mEq/L (normal, 4.5 mEq/L)</td>
</tr>
</tbody>
</table>

Maria was admitted to the infirmary, where she received an infusion of isotonic saline and K$^+$. She was released the next day, after her fluid and electrolyte status had returned to normal.

Q QUESTIONS

1. What acid-base disorder did Maria have after vomiting for 3 days?

2. How does vomiting cause this acid-base disorder? Or, posing the question differently, why does vomiting lead to an increase in the blood $\text{HCO}_3^-$ concentration?

3. Why was Maria’s blood Cl$^-$ concentration decreased?

4. Compared with a healthy person, was Maria’s breathing rate increased, decreased, or the same?

5. Why was Maria’s blood pressure decreased? Why did she have decreased skin turgor and dry mucous membranes?

6. What effect would her decreased blood pressure be expected to have on the renin-angiotensin II-aldosterone system?

7. Why was Maria’s blood K$^+$ concentration so low? (Hint: Identify three separate mechanisms that might have contributed to her hypokalemia.)
8. What effect did Maria’s extracellular fluid (ECF) volume contraction have on her acid–base status? What acid–base disorder is caused by ECF volume contraction?

9. What was the value for Maria’s anion gap? Was it normal, increased, or decreased? What is the significance of her anion gap?

10. Why was it important for Maria to receive an infusion of saline?

11. Why was $K^+$ included in the infusion?
PHYSIOLOGY CASES AND PROBLEMS

ANSWERS AND EXPLANATIONS

1. Maria’s arterial blood values are consistent with metabolic alkalosis: alkaline pH (7.53), increased HCO$_3^-$ concentration (37 mEq/L), and increased P$_{CO_2}$ (45 mm Hg). The primary disturbance in metabolic alkalosis is an increase in the blood HCO$_3^-$ concentration, which increases the pH (according to the Henderson-Hasselbalch equation). The alkalemia is sensed by peripheral chemoreceptors, which direct a decrease in breathing rate (hypoventilation) that causes an increase in P$_{CO_2}$. This hypoventilation is the respiratory compensation for metabolic alkalosis.

\[
pH = 6.1 + \log \frac{HCO_3^-}{P_{CO_2}}
\]

Thus, Maria’s arterial pH was alkaline because her HCO$_3^-$ concentration (in the numerator) was increased. By hypoventilating, Maria’s lungs attempted to increase the P$_{CO_2}$ in the denominator, correcting the ratio of HCO$_3^-$ to CO$_2$ and the pH toward normal.

2. The question of how vomiting causes metabolic alkalosis (or, how vomiting causes an increase in the blood concentration of HCO$_3^-$) leads us to a discussion of fundamental mechanisms of the gastrointestinal tract.

Gastric parietal cells produce H$^+$ and HCO$_3^-$ from CO$_2$ and water, using the enzyme carbonic anhydrase. The H$^+$ is secreted into the lumen of the stomach to aid protein digestion, and the HCO$_3^-$ enters the blood. After a meal, gastric venous blood pH becomes alkaline because of this addition of HCO$_3^-$ (alkaline tide). In healthy persons, the acidic chyme moves from the stomach to the small intestine, where the H$^+$ stimulates secretion of pancreatic HCO$_3^-$. (Pancreatic HCO$_3^-$ then neutralizes the H$^+$.) Thus, in healthy persons, HCO$_3^-$ that was added to the blood by gastric parietal cells does not remain in the blood; it is secreted into the intestinal lumen via pancreatic secretions.

In persons who are vomiting, the H$^+$ that was secreted in the stomach never reaches the small intestine and therefore never stimulates pancreatic HCO$_3^-$ secretion. Therefore, HCO$_3^-$ that was generated by gastric parietal cells remains in the blood, and, as a result, the blood HCO$_3^-$ concentration increases.

3. Maria’s blood Cl$^-$ concentration was decreased because gastric parietal cells secrete Cl$^-$ along with H$^+$ (HCl). When Maria vomited, both H$^+$ and Cl$^-$ were lost from her body, and her blood Cl$^-$ concentration decreased.

4. Maria’s breathing rate must have been decreased (hypoventilation) because her arterial P$_{CO_2}$ was increased. (Recall, from respiratory physiology, the inverse relationship between alveolar ventilation and P$_{CO_2}$.) As discussed earlier, Maria was hypoventilating because peripheral chemoreceptors sensed the alkalemia that was caused by her increased HCO$_3^-$ concentration.

5. Maria’s blood pressure was decreased because she lost ECF volume when she vomited. Decreased ECF volume led to decreased blood volume and decreased venous return to the heart. Decreased venous return caused a decrease in cardiac output (through the Frank-Starling mechanism) and decreased arterial pressure. Maria’s decreased skin turgor and dry mucous membranes were further signs of decreased ECF volume (specifically, of decreased interstitial fluid volume).

6. Decreased arterial pressure should have activated Maria’s renin-angiotensin II-aldosterone system as follows. Decreased arterial pressure leads to decreased renal perfusion pressure, which stimulates renin secretion. Renin catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin-converting enzyme catalyzes the conversion of angiotensin I to angiotensin II. Angiotensin II causes vasoconstriction of arterioles and secretion of aldosterone.
7. Maria had severe hypokalemia. Recall, from our previous discussions of $K^+$ homeostasis in Cases 31, 34, and 35, that hypokalemia can result either from a shift of $K^+$ into cells or from increased $K^+$ loss from the body.

First, consider the major factors that cause a $K^+$ shift from ECF to ICF: insulin, $\beta$-adrenergic agonists, and alkalosis. Of these factors, metabolic alkalosis could have contributed to Maria's hypokalemia; as $H^+$ left her cells, $K^+$ entered her cells to maintain electroneutrality.

Next, consider the factors that might result in increased $K^+$ loss from the body, through either the gastrointestinal tract or the kidneys. Certainly, some $K^+$ was lost in gastric juice when Maria vomited. In addition, and most importantly, Maria's renin-angiotensin II-aldosterone system was activated by ECF volume contraction. A major action of aldosterone is to increase $K^+$ secretion by the principal cells of the late distal tubule and collecting ducts, resulting in increased $K^+$ loss in urine.

8. In Question 5, we discussed the fact that vomiting causes ECF volume contraction. However, we have not considered the possibility that this ECF volume contraction might cause its own acid-base disturbance. Maria had metabolic alkalosis because she lost $H^+$ by vomiting. To compound the problem, ECF volume contraction caused its own metabolic alkalosis (called contraction alkalosis) [Figure 4–13].

As Figure 4–13 shows, the metabolic alkalosis produced by vomiting has two components. The first component, or the "generation phase," is due to the initial loss of gastric $HCl$. The second component is due to ECF volume contraction, which causes a "maintenance phase," as follows. Vomiting causes ECF volume contraction, which activates the renin-angiotensin II-aldosterone system (as discussed earlier). Activation of the renin-angiotensin II-aldosterone system causes an increase in blood $HCO_3^-$ concentration (metabolic alkalosis) in two ways.
(1) Angiotensin II stimulates Na\textsuperscript{+}-H\textsuperscript{+} exchange in the proximal tubule and leads to an increase in the reabsorption of filtered HCO\textsubscript{3}\textsuperscript{-} (Figure 4-14).

Figure 4-14  Mechanism for reabsorption of filtered HCO\textsubscript{3}\textsuperscript{-} in the proximal tubule. CA, carbonic anhydrase. (Reprinted with permission from Costanzo LS: BRS Physiology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 2003, p 193.)

(2) Aldosterone stimulates the H\textsuperscript{+} pump (H\textsuperscript{+} ATPase) of the intercalated cells of the late distal tubule and collecting ducts. Increased secretion of H\textsuperscript{+} by this pump is accompanied by re-absorption of "new" HCO\textsubscript{3}\textsuperscript{-}, which leads to a further increase in the blood HCO\textsubscript{3}\textsuperscript{-} concentration (Figure 4-15).

Figure 4-15  Mechanism for excretion of H\textsuperscript{+} as titratable acid. CA, carbonic anhydrase. (Reprinted with permission from Costanzo LS: BRS Physiology, 3rd ed. Baltimore, Lippincott Williams & Wilkins, 2003, p 194.)

9. Maria's anion gap was:

\[
\text{Anion gap} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-]) \\
= 137 \text{ mEq/L} - (37 \text{ mEq/L} + 82 \text{ mEq/L}) \\
= 18 \text{ mEq/L}.
\]

As discussed in Cases 34 and 35, the normal range for the anion gap is 8–16 mEq/L, with an average value of 12 mEq/L. Maria's anion gap was elevated at 18 mEq/L. You have learned that an increased anion gap accompanies some forms of metabolic acidosis. Since Maria's overriding acid-base disorder was metabolic alkalosis, how can an increased anion gap be explained? It is likely that a second acid-base disorder (metabolic acidosis) was probably developing. For 3 days, she could not keep any food down; during this period of starvation, she was hydrolyzing
fat and generating fatty acids. The fatty acids were metabolized to ketoacids and caused a meta-
olic acidosis that was superimposed on Maria’s metabolic alkalosis.

10. It was important to correct Maria’s ECF volume contraction with a saline infusion. Recall that
activation of her renin-angiotensin II-aldosterone system secondary to volume contraction had
two very detrimental effects. (1) It maintained her metabolic alkalosis (contraction alkalosis),
and (2) it contributed to her hypokalemia. Even if the vomiting stopped, the metabolic alkalo-
sis and hypokalemia would have persisted until her ECF volume was returned to normal.

11. K⁺ was included in the infusion solution because Maria was in negative K⁺ balance. Recall from
the earlier discussion that two of the three etiologies of her hypokalemia involved K⁺ loss from
the body (gastric secretions and urine). Thus, to restore K⁺ balance, Maria needed to replace the
K⁺ that she lost.

Key topics
β-Adrenergic agonist
Aldosterone
Alkaline tide
Contraction alkalosis
Extracellular fluid (ECF) volume contraction
Gastric H⁺ secretion
H⁺-K⁺-ATPase
Hypokalemia
Insulin
Intercalated cells
K⁺ shifts
Metabolic alkalosis
Pancreatic HCO₃⁻ secretion
Parietal cells
Principal cells
Renal H⁺ secretion
Renin-angiotensin II-aldosterone system