**TITLE: Acid-Base Disorders**

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### Slide 1:

Hello, my name is Brenda Suh-Lailam. I am an Assistant Director of Clinical Chemistry and Mass Spectrometry at Ann & Robert H. Lurie Children's Hospital of Chicago, and an Assistant Professor of Pathology at Northwestern Feinberg School of Medicine. Welcome to this Pearl of Laboratory Medicine on "Acid-Base Disorders."

### Slide 2:

During metabolism, the body produces hydrogen ions which affect metabolic processes if concentration is not regulated. To maintain pH within physiologic limits, there are several buffer systems that help regulate hydrogen ion concentration. For example, bicarbonate, plasma proteins, and hemoglobin buffer systems. The bicarbonate buffer system is the major buffer system in the blood.

### Slide 3:

In the bicarbonate buffer system, bicarbonate, which is the metabolic component, is controlled by the kidneys. Carbon dioxide is the respiratory component and is controlled by the lungs. Changes in the respiratory and metabolic components, as depicted here, can lead to a decrease in pH termed acidosis, or an increase in pH termed alkalosis.

### Slide 4:

Because the bicarbonate buffer system is the major buffer system of blood, estimation of pH using the Henderson-Hasselbalch equation is usually performed, expressed as a ratio of bicarbonate and carbon dioxide. Where pKa is the pH at which the concentration of protonated and unprotonated species are equal, and 0.0307 is the solubility coefficient of carbon dioxide. Four variables are present in this equation; knowing three variables allows for calculation of the fourth. Since pKa is a constant, and pH and carbon dioxide are measured during blood gas analysis, bicarbonate can, therefore, be determined using this equation.

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**Slide 5:**
The acid-base disorders are grouped into two categories, metabolic or respiratory. The difference depends on whether it originated from a metabolic dysfunction, identified by a change in the bicarbonate level; or a ventilatory dysfunction, identified by a change in the carbon dioxide. The metabolic disorders include metabolic acidosis and metabolic alkalosis, while the respiratory disorders include respiratory acidosis and respiratory alkalosis. Nonetheless, mixed acid-base disorders can occur with more than one primary disorders occurring simultaneously.

**Slide 6:**
We will review the primary acid-base disorders starting with metabolic acidosis, which is the result of decreases in bicarbonate. A decrease in bicarbonate can be as a result of one of three things: firstly, it could be due to an excessive production of organic acids at a rate that surpasses elimination; as such, bicarbonate is consumed in the buffering of the excess acid. For example, in diabetic ketoacidosis, there is increased production of the ketones, acetoacetic acid, and β-hydroxybutyric acid, and increased production of lactic acid in lactic acidosis. Secondly, metabolic acidosis can be as a result of reduced acid excretion; for example, in renal failure resulting from uremic acidosis, or in renal tubular acidosis. Thirdly, metabolic acidosis can be due to excessive loss of bicarbonate; for example, when there is increased excretion but decreased renal retention, when bicarbonate-rich fluids are lost such as in diarrhea through loss of duodenal fluid, and when there is drainage from a biliary, pancreatic, or intestinal fistula.

**Slide 7:**
Anion gap refers to the difference between the sum of sodium and potassium and the sum of chloride and bicarbonate. Potassium is not commonly included in this calculation because its concentration is relatively low. In this Pearl, we will use the calculation without the potassium. This difference reflects the unmeasured anions in plasma; for example, proteins, dihydrogen phosphate (H2PO42-), and sulfate (SO42-). Depending on the cause of metabolic acidosis, the anion gap could be increased or normal. As such, calculating the anion gap could be useful in determining the cause of metabolic acidosis. In a situation where there is addition of acid, there is loss of bicarbonate in buffering the excess acid. Electroneutrality is maintained by the retention of the unmeasured conjugate base of the acid resulting in an increase in the anion gap. On the other hand, when there is a loss of bicarbonate, for example in stool (such as in diarrhea) or urine (such as in renal tubular acidosis), electroneutrality is maintained by retaining chloride. As such, even though bicarbonate is being lost, a gain in the measured anion chloride results in a normal anion gap.

**Slide 8:**
The mnemonic MUDPILES is helpful in remembering substances that cause high anion gap metabolic acidosis. Normal anion gap metabolic acidosis is mainly due to the loss of bicarbonate such as in gastrointestinal fluid loss and renal tubular acidosis.

## Slide 9:

Metabolic alkalosis results from an increase in bicarbonate. There are three main ways by which this can happen. One way is through the addition of excess base to the system. For example, the administration of an alkali (such as sodium bicarbonate) and the ingestion of bicarbonate-producing salts (such as antacids) can lead to an excess of base in blood. Also, bicarbonate concentration can be increased by loss of acid-rich fluids through vomiting, nasogastric suctioning, or prolonged use of diuretics that increase acid loss. In addition, any situation that will decrease the elimination of base can lead to an increase in bicarbonate.

## Slide 10:

Now shifting gears to ventilatory dysfunctions, respiratory acidosis results when there is an increase in carbon dioxide which is due to a decrease in the elimination of carbon dioxide. This can be due to conditions that result in the direct depression of the respiratory center such as centrally acting drugs, trauma, and infection affecting the CNS, and primary central hypoventilation. It can also be due to conditions that disrupt the elimination of carbon dioxide by the lungs, such as diseases that affect lung function including chronic obstructive pulmonary disease, severe pulmonary fibrosis, and status asthmaticus. There are other conditions not discussed here that can also decrease elimination of carbon dioxide leading to respiratory acidosis such as extreme obesity.

## Slide 11:

Respiratory alkalosis results when there is a decrease in carbon dioxide. This is as a result of excessive carbon dioxide elimination by the lungs caused by an increase in the rate and/or depth of breathing. Factors that cause respiratory alkalosis do so either by directly stimulating the respiratory center or by affecting lung function. Some of these factors include hypoxia, drugs such as salicylates and progesterone, Gram-negative septicemia, a febrile state, and pulmonary disorders such as pulmonary emboli and pneumonia.

## Slide 12:

Compensation is an attempt to restore acid-base homeostasis whenever an imbalance occurs. The primary goal of compensation is to normalize pH. Typically, this is achieved by altering the factor that is not initially disturbed. For example, if the metabolic component is primarily affected, the respiratory component will be altered. Respiratory compensation is rapid and the maximal compensation is achieved in 12 to 24 hours. If the respiratory component is primarily affected, the metabolic component will be altered. Metabolic compensation is slow and maximal compensation is achieved in 3 to 4 days.

## Slide 13:

Here is a summary of compensatory mechanisms in acid-base disorders. In metabolic acidosis, the respiratory compensatory mechanism kicks in causing hyperventilation which leads to increased elimination of carbon dioxide with an expected outcome of an increase in pH. In metabolic alkalosis, respiratory compensation is by hypoventilation which results in increased carbon dioxide retention leading to a decrease in pH. In respiratory acidosis, renal compensation is by increased excretion of acid and increased reclamation of bicarbonate by the kidneys, resulting in an increase in pH. In respiratory alkalosis, renal compensation is by increased excretion of bicarbonate and increased reclamation of acid by the kidneys, resulting in a decrease in pH.

**Slide 14:**
We will review acid-base disorders using two cases. The first case is that of a 13-year-old girl who was brought to the emergency room after being found in her room. She was minimally responsive and blood gas analysis showed that: pH was 7.1, carbon dioxide – 29 mmHg, bicarbonate – 9 mmol/L, sodium – 144 mmol/L, and chloride – 103 mmol/L. Considering these laboratory values, what is the acid-base disorder in this patient?

**Slide 15:**
First, we evaluate the pH. A pH of 7.1 is low compared to the reference interval pointing to an acidemia. Then, we look at the bicarbonate and carbon dioxide to determine the acid-base process (acidosis or alkalosis). Bicarbonate is low suggesting an acidotic process which supports the acidemia revealed by the pH. As such, this acidosis is of metabolic origin; hence, the primary disorder in this patient is metabolic acidosis. The carbon dioxide is also low, changing in the same direction as the bicarbonate. This decrease in carbon dioxide points to an alkalotic process which is an attempt to raise the pH as such is a respiratory compensation.

Next, we calculate the anion gap. Calculation of the anion gap yielded a value of 23 which is high. A high anion gap indicates the presence of an unmeasured anion pointing to the possibility that the metabolic acidosis may be due to the addition of an acid into the patient’s system.

Further laboratory testing revealed that this patient had ethylene glycol poisoning. Ethylene glycol metabolizes into several acids, primarily glycolic acid and thus, the acidemia.

**Slide 16:**
Assessing the completeness of compensation in an acid-base disorder can provide useful information for the management of the patient. Mathematical formulas have been published which aid in predicting the expected compensation. This table shows the primary acid-base disorders and corresponding formulas which can be used to calculate the expected compensation.

**Slide 17:**
In Case 2, a 6-year-old boy with acute, severe diarrhea presented to the emergency room. Laboratory results revealed a pH of 7.29, carbon dioxide of 30 mmHg, bicarbonate of 15 mmol/L, sodium of 132 mmol/L, and a chloride of 103 mmol/L. How would you describe the acid-base disorder in this patient?

### Slide 18:
First, we evaluate the pH. A pH of 7.29 is low compared to the reference interval pointing to an acidemia. Then, we look at the bicarbonate and carbon dioxide to determine the acid-base process (acidosis or alkalosis). Bicarbonate is low suggesting an acidotic process which supports the acidemia revealed by the pH. As such, this acidosis is of metabolic origin; hence, the primary disorder in this patient is metabolic acidosis. The carbon dioxide is also low, changing in the same direction as the bicarbonate. This decrease in carbon dioxide points to an alkalotic process which is an attempt to raise the pH as such is a respiratory compensation.

Next, we calculate the anion gap. Calculation of the anion gap yielded a value of 14 which is normal. Hence, this is a normal anion gap metabolic acidosis with compensatory respiratory alkalosis.

Then, we check if the degree of compensation is adequate. To assess the adequacy of the compensation, the expected compensation is calculated. This yields an expected carbon dioxide concentration of 29.2 plus or minus 2 and since the measured carbon dioxide is 30, which is in this range, compensation is maximal.

### Slide 19:
In summary, to evaluate acid-base disorders, start by evaluating the pH. If acidemia is present, it indicates that the primary disorder is an acidosis and if alkalemia is present, it indicates that the primary disorder is an alkalosis.

Second, determine the primary disorder by evaluating the respiratory and metabolic components of the bicarbonate buffer system. The component that changes in a direction as to support the acid-base state determined by the pH is indicative of what the primary disorder is. If there is acidemia and the bicarbonate is low or the carbon dioxide is elevated, then the primary disorder is a metabolic acidosis or respiratory acidosis, respectively. Similarly, if there is alkalemia and the bicarbonate is elevated or the carbon dioxide is low, then the primary disorder is a metabolic alkalosis or respiratory alkalosis, respectively.

Next, compute the anion gap. The anion gap can be useful in identifying the cause of metabolic acidosis as different differential diagnosis exist for processes that result in an increased versus normal anion gap. Check for mixed disorders when anion gap is elevated. One way to do this is by calculating the delta gap. This will help determine the presence of additional metabolic alkalosis or normal anion gap metabolic acidosis.

Lastly, assess the adequacy of the compensation. A good rule of thumb is, if compensation is present, carbon dioxide and bicarbonate change in the same direction. Calculate the expected compensation and determine if it is adequate. Absence of compensation represents an additional disorder.

### Slide 20: References

### Slide 21: Disclosures

**Slide 22: Thank You from www.TraineeCouncil.org**

Thank you for joining me, Brenda Suh-Lailam, on this Pearl of Laboratory Medicine on "Acid-Base Disorders."