Acid Base Balance

45

Kristi D. Langston and Jonathan H. Waters

Management of acute acid-base changes is a common part of the practice of anesthesiology. Historically, analysis of these changes focuses on the Henderson–Hasselbalch equation and the relationship among the three parameters—pH, PCO_2, and HCO_3^-. Respiratory changes are easily recognized and treated by changes in the partial pressure of CO_2. Metabolic changes are easily recognized by bicarbonate or base excess (BE) abnormality; however, the treatment is not simple because the bicarbonate or BE is only a reflection of the actual problem. For example, a lactic acidosis will cause a change in bicarbonate, and if only looking at the bicarbonate, this lactic acidosis cannot be differentiated from a hyperchloremic metabolic acidosis. Unlike PCO_2, HCO_3^- is not an independent determinant of pH. In other words, we know that by changing the ventilator setting we can change the PCO_2 and directly change the pH; however, a similar relationship between HCO_3^- and pH does not exist.

The clinician can gain further information as to the cause of a metabolic problem through use of the anion gap. The anion gap is based on the concept of electroneutrality, that is, the sum of the cations must equal the sum of the anions in solution. The classic acid-base theory focuses on electroneutrality and the Henderson–Hasselbalch equation, but unfortunately, reliance on these two concepts fails to identify the independent determinants of metabolic acid-base change.

In this chapter a brief overview of classic acid-base theory will be discussed, and a new approach, the "physicochemical" acid-base approach will be introduced. This approach incorporates the Henderson–Hasselbalch equation and electroneutrality but rearranges the importance of each in acid-base analysis. This new approach identifies the independent determinants of pH, and by determining these variables, a better understanding is gained of the impact that fluid and electrolyte management have on acid-base status.

K.D. Langston, D.O.
Department of Anesthesiology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA

J.H. Waters, M.D. (✉)
Department of Anesthesiology, Magee Women's Hospital of UPMC, 300 Halket Street, Suite 3510, Pittsburgh, PA 15213, USA
e-mail: watejh@upmc.edu

Classic Acid-Base Theory

Henderson–Hasselbalch Equation

Traditionally, assessment of $[H^+]$ or pH abnormalities has focused on the Henderson–Hasselbalch equation and its two primary components, PCO_2 and HCO_3^-.

$$\mathrm{pH} = \mathrm{p}K_a + \log\left[\mathrm{HCO_3^-}\right] / \left[\mathrm{CO_2}\right]$$

$$\left(\mathrm{pK_a\ is\ the\ negative\ log\ of\ the\ acid\ dissociation\ constant}\right)$$

From this equation, respiratory disorders are defined by changes in CO_2 and metabolic disorders result from changes in the HCO_3^-. Increases in CO_2 cause a respiratory acidosis while decreases in CO_2 cause a respiratory alkalosis. Similarly, an increase in HCO_3^- causes a metabolic alkalosis and a decrease causes a metabolic acidosis. From this it would appear that by this equation, $[H^+]$ is determined by two variables, CO_2 and HCO_3^-.

By reviewing the derivation of the Henderson–Hasselbalch equation we discover that these two variables are interdependent and not independent as these definitions would suggest. The Henderson–Hasselbalch equation is derived from the carbonic acid equilibrium and its associated equilibrium equation.

$$\mathrm{CO_2 + H_2O = H_2CO_3 = HCO_3^- + H^+}$$

$$\left(\mathrm{carbonic\ acid\ equilibrium}\right)$$

$$\mathrm{K\ (equilibrium\ constant) = [CO_2][H_2O]/[H^+][HCO_3^-]}$$

$$\mathrm{(equilibrium\ equation)}$$

From this equilibrium, it is seen that an increase in CO_2 results in hydration of the CO_2 and an increase in H_2CO_3. The

P.K. Sikka et al. (eds.), *Basic Clinical Anesthesia*,
DOI 10.1007/978-1-4939-1737-2_45, © Springer Science+Business Media New York 2015

H_2CO_3 will partially dissociate yielding equimolar quantities of H^+ and HCO_3^-. Both changes will be dictated by the equilibrium equation and its associated constant. As a result a change in CO_2 must be matched by a change in HCO_3^-. Thus, CO_2 and HCO_3^- are dependent on each other and not truly independent determinants of pH as is commonly implied.

Metabolic Indices

The CO_2–HCO_3^- relationship has resulted in the proposal of multiple metabolic indices. These indices are intended to circumvent the CO_2–HCO_3^- relationship. One of these indices is the standard bicarbonate concentration (SBC). The SBC attempts to correct for the interrelationship by standardization of the CO_2. By exposing a blood sample to CO_2 at a partial pressure of 40 mmHg, the sample will equilibrate to this standard CO_2 partial pressure. From this standardization, any deviation of the HCO_3^- from normal will be an indicator of a nonrespiratory problem. In 1960, Siggaard-Andersen proposed that the BE be the standard metabolic index.

Anion Gap

When using the SBC or the BE, the origin of a metabolic deviation is left unexplained. For instance, an abnormal BE would not tell a clinician whether a metabolic acidosis is a result of ketoacidosis, lactic acidosis, or hyperchloremia. For further understanding of a metabolic acidosis, the anion gap is utilized.

The anion gap is based on the concept of electroneutrality. The sum of the positive ions and the negative ions in a solution must be zero, (Σcations = Σanions). In other words, any body fluid will have no net charge. This charge balance means that the charge of Na^+, K^+, Mg^{2+}, Ca^{2+}, and H^+ must be balanced by an equal and opposite charge of Cl^-, SO_4^{2-}, PO_4^{3-}, CO_3^{2-}, HCO_3^-, OH^-, lactate, and the charges on the proteins. The anion gap can be defined as

$$\text{Anion gap} = \left[Na^+\right] - \left(\left[Cl^-\right] + \left[HCO_3^-\right]\right)$$

$$= \text{Unmeasured anions} - \text{Unmeasured cations}$$

By this definition K^+, Ca^{2+}, and Mg^{2+} have been relegated into a grouping of unmeasured cations. Likewise, SO_4^{2-}, PO_4^{3-}, lactate, and the proteins have been grouped into unmeasured anions. An increase in anion gap represents an increase in unmeasured anions or a decrease in unmeasured cations, and a decrease in anion gap can be caused by a decrease in unmeasured anions or an increase in unmeasured cations.

Traditional Approach of Arterial Blood gas Analysis

Arterial blood gases are routinely used to assess acid-base disturbances, which can be analyzed as follows (Fig. 45.1, Table 45.1):

1. pH—The normal pH is 7.35–7.45. A blood pH less than 7.35 is termed as acidosis, while a pH higher than 7.45 is termed as alkalosis.
2. $PaCO_2$—The normal $PaCO_2$ is 35–45 mmHg. A $PaCO_2$ less than 35 mmHg is termed as respiratory alkalosis, while a $PaCO_2$ more than 45 mmHg is termed as respiratory

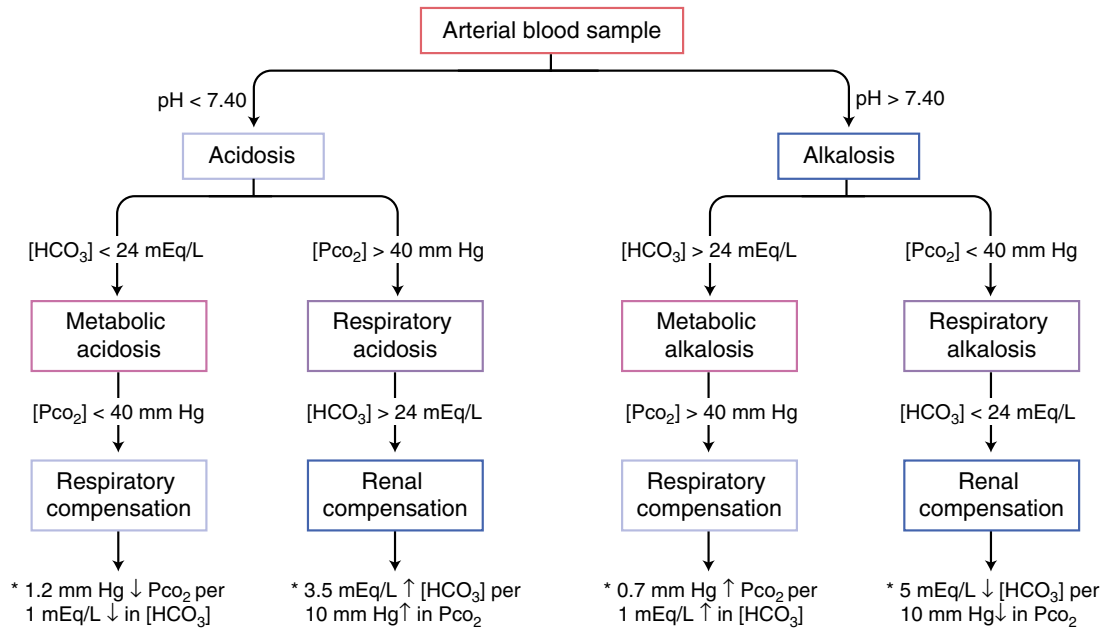

Fig. 45.1 Approach to determine acid-base disorder

acidosis. Adequacy of ventilation can be assessed by calculation of the dead space (V_D) to tidal volume (V_T) ratio, using the Bohr dead space equation:

$$V_D / V_T = \left(P_A CO_2 - ETCO_2\right) / PACO_2,$$

the normal ratio should be less than 0.3

3. PaO_2—Hypoxia is defined as a $PaO_2 < 60$ mmHg. Adequacy of ventilation can be assessed by measuring the
   (a) Alveolar-arterial gradient of oxygen: $PAO_2 - PaO_2$

$$PAO_2 = \left(\begin{array}{l}\text{atmospheric pressure} - \\ \text{water vapor pressure}\end{array}\right) \times FiO_2 - PaCO_2 / 0.8$$

   where 0.8 is the respiratory quotient and is the ratio of CO_2 produced to O_2 consumed. Normally, about 80 % of CO_2 is produced for 100 % O_2 consumed (200 ml CO_2:250 ml of O_2)
   (b) Ratio of PaO_2:FiO_2, the P/F ratio. The lower the ratio, the worse the oxygenation. A P/F ratio less than 300 denotes acute lung injury, whereas a P/F ratio less than 200 denotes ARDS.
4. HCO_3—The normal HCO_3 is 22–26 mmol/L. A HCO_3 less than 22 is termed as metabolic acidosis, while a HCO_3 more than 26 is termed as metabolic alkalosis.
5. Assess compensatory changes.

Regulation of pH in the Body

Regulation of pH or the hydrogen ion concentration in the human body occurs mainly via three processes: the buffer systems, central and peripheral chemoreceptors, and the renal system. Causes and compensatory mechanisms for acid base disturbances are summarized in Tables 45.2 and 45.3. Adverse effects of acid-base disturbances are summarized in Table 45.4.

Buffer Systems

Buffers are chemicals/substances which tend to maintain the pH of the body fluids at 7.4. The main buffer systems in the body are the bicarbonate and the hemoglobin buffer systems. Additionally, some proteins and phosphate also have buffering capabilities.

Table 45.1 Simplified approach to blood gas analysis (approximate equality)

pH, normal 7.4	Is there an acidosis or alkalosis
$PaCO_2$	Is the change in $PaCO_2$ consistent with respiratory component; if not, does the change in HCO_3 indicate a metabolic component
Acute respiratory acidosis	10 units increase in $PaCO_2$ = 1 unit increase in HCO_3
Chronic respiratory acidosis	10 units increase in $PaCO_2$ = 4 units increase in HCO_3
Acute respiratory alkalosis	10 units decrease in $PaCO_2$ = 2 units decrease in HCO_3
Chronic respiratory alkalosis	10 units decrease in $PaCO_2$ = 5 units decrease in HCO_3
Metabolic acidosis	1 unit decrease in HCO_3 = 1 unit decrease in $PaCO_2$
Metabolic alkalosis	10 units increase in HCO_3 = 7 units increase in $PaCO_2$

For example, a patient with a pH of 7.27, $PaCO_2$ 60, HCO_3 25, has respiratory acidosis. If the HCO_3 would have been 29, the patient would have chronic (compensated) respiratory acidosis

Table 45.2 Causes and compensation of respiratory acidosis and alkalosis

Respiratory acidosis—increased $PaCO_2$ causing an increase in carbonic acid and hydrogen ions		
Hypoventilation (decreased CO_2 elimination	COPD, asthma, sleep apnea, restrictive lung diseases (fibrosis, sarcoidosis), anesthetics, opioids, scoliosis, obesity, pneumothorax, pulmonary edema	Metabolic compensation • (Acute) Change in pH = 0.008 × change in $PaCO_2$ • (Chronic) Change in pH = 0.003 × change in $PaCO_2$ The kidneys increase H^+ ion secretion and bicarbonate reabsorption over the course of few days to bring the pH to near normal
Increased CO_2 production	Hyperthyroidism, exhausted soda lime CO_2 absorbent, pneumoperitoneum from laparoscopic surgery	
Respiratory alkalosis—decreased $PaCO_2$ relative to bicarbonate		
Hyperventilation (increased CO_2 elimination)	Pain, anxiety, pregnancy, hypoxemia, sepsis, hyperthermia, mechanical ventilation	Metabolic compensation • (Acute) Change in pH = 0.008 × change in $PaCO_2$ • (Chronic) Change in pH = 0.017 × change in $PaCO_2$ – The kidneys compensate by a decrease in bicarbonate reabsorption and an increase in H^+ excretion to bring the pH back to normal in a few days – Increased glycolysis leads to generation of lactic acid – Respiratory alkalosis can cause hypocalcemia and tetany, as plasma proteins bind more calcium in an alkaline pH
Decreased CO_2 production	Hypothyroidism, hypothermia	

Table 45.3 Causes and compensation of metabolic acidosis and alkalosis

Metabolic acidosis—serum anion gap (SAG) is calculated as Na^+-($Cl^- + HCO_3$)		
High anion gap acidosis (>12 meq/L)	Diabetic ketoacidosis, lactic acidosis, cirrhosis of liver, uremia or poisoning due to cyanide, ethanol and salicylates	*Ventilatory compensation* Expected $PaCO_2 = 1.5 \times HCO_3 + 8$ (±2). Increase H^+ ions stimulate the carotid bodies to increase alveolar ventilation, the kidneys increase the secretion of H^+ ions to bring the pH back to normal Measure serum albumin. Hypofibroginemia decreases the anion gap Severe acidosis can be temporarily treated with alkanizing agents, such as sodium bicarbonate, Carbicarb, or THAM
Normal anion gap acidosis (3–12 meq/L)	Excess saline administration, hyperparathyroidism, renal tubular acidosis (bicarbonate loss), diarrhea, pancreatic fistula, or drugs, such as spironolactone and acetazolamide	
Metabolic alkalosis	Loss of hydrogen, chloride and potassium ions, increased metabolism to bicarbonate ions (lactate, citrate, acetate), hypovolemia, hyperaldosteronism, hypercapnia	*Ventilatory compensation* Expected $PaCO_2 = 0.7 \times HCO_3 + 20$ (±1.5) Compensation with alveolar hypoventilation, increased renal tubule reabsorption and decreased secretion of H^+. Kidney needs sodium, potassium and chloride ions (infusions) to effectively excrete excess bicarbonate

Table 45.4 Deleterious effects of respiratory and metabolic acidosis/alkalosis

Respiratory and metabolic acidosis	Hyperkalemia CNS vasodilation, increased ICP Decrease in cardiac contractility, cardiac arrhythmias Increased sympathetic activity (tachycardia, vasoconstriction) Rightward shift of oxyhemoglobin dissociation curve
Respiratory and metabolic alkalosis	Hypokalemia, hypocalcemia Hypoxia Central nervous system excitation Decrease myocardial contractibility, cardiac arrhythmias Neuromuscular irritability Leftward shift of oxyhemoglobin dissociation curve

Bicarbonate: CO_2 combines with water to form carbonic acid; the reaction accelerated by the enzyme carbonic anhydrase. The carbonic acid then dissociates into hydrogen and bicarbonate ions. The bicarbonate reaches the lung, where an opposite reaction occurs. Hydrogen ions are added to the bicarbonate to form carbonic acid, which dissociated into CO_2 and water. The CO_2 is then exhaled.

$$CO_2 + H_2O \xleftarrow{\text{Carbonic anhydrase}} H_2CO_3$$
$$(\text{occurs in the tissues})$$

$$HCO_3^- + H^+ \rightarrow H_2CO_3 \rightarrow CO_2 + H_2O$$
$$(\text{occurs in the lungs and kidneys})$$

Hemoglobin: Hemoglobin also plays a role in buffering CO_2. A similar reaction, as above, takes place in erythrocytes. CO_2 diffuses freely into the erythrocytes, where it combines with water to form carbonic acid. The latter then dissociates into hydrogen and bicarbonate ions. The hydrogen ions are absorbed by the hemoglobin, and the bicarbonate ions are exchanged for chloride (Chloride shift) to maintain electroneutrality. A reverse reaction happens in the pulmonary capillaries, where bicarbonate combines with the hydrogen ions to form carbonic acid and ultimately CO_2, which is exhaled. Also hemoglobin, especially deoxyhemoglobin, can directly combine with CO_2 to form carbaminohemoglobin, which facilitates removal of CO_2 from peripheral tissues.

Chemoreceptors

CO_2 freely passes the plasma membrane of cells. In the brain it decreases the pH of CSF, thereby stimulating the central chemoreceptors causing an increase in minute ventilation. The increase in minute ventilation decreases the $PaCO_2$ and maintains the pH. In addition, the peripheral chemoreceptors, which are present in the carotid bodies and the aortic arch, sense a decrease in blood pH or a decrease in PaO_2 and stimulate the respiratory center in the brain to increase the minute ventilation.

Renal Buffering

Proximal tubule cells of the kidney absorb most of the bicarbonate from the glomerular filtrate and secrete hydrogen ions into the tubules. The kidneys thus regulate the pH by altering the absorption of bicarbonate and the secretion of hydrogen ions. Renal tubal acidosis results from wasting of bicarbonate ions due to a defect in the absorption of bicarbonate. The drug acetazolamide can cause a normal anion gap acidosis by inhibiting the reabsorption of bicarbonate ions in the renal proximal tubule.

The PhysicoChemical Approach

In 1981, Stewart proposed a change in the approach to acid-base problems. He recognized that multiple chemical interactions affect [H^+] and that the carbonic acid equilibrium was just one of these interactions (Fig. 45.2). The focus of

his approach is on the concept of electroneutrality, the basis of the anion gap. He incorporated the multiple chemical equilibria that affect [H^+], including the carbonic acid equilibrium, into a single electroneutrality equation.

From this mathematical development, he found that [H^+] is dependent on three independent variables: (1) the strong ion difference (SID) which is a modified anion gap, (2) the PCO_2, and (3) the total weak acid concentration [A_{tot}], which is primarily composed of protein and phosphate. For most purposes, the weak acid concentration does not change during a surgical procedure, so we can define the CO_2 as the respiratory component which drives pH and the SID as the metabolic component which changes pH.

For simplicity, the SID = [Na^+] + [K^+] − [Cl^-] − [lactate$^-$]

Remembering the law of electroneutrality, we can think of H^+ and OH^- as charge buffers. As the relationship of the strong ions changes, so does the H^+ and OH^- change, as reflected in Fig. 45.2. For instance, an increase in the negatively charged chloride will result in a decrease in the SID and an increase in H^+ to maintain electroneutrality, which results in acidosis. Because of the inverse relationship between H^+ and OH^-, it is sometimes easier to assess pH changes through changes in the basic OH^-. Increased OH^- leads to alkalosis, decreased OH^- results in acidosis.

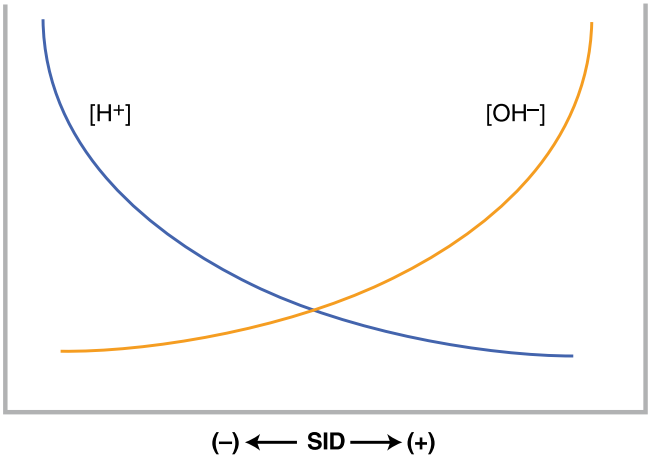

Fig. 45.2 Relationship of SID change and H^+ and OH^- change (SID-strong ion difference)

Specific Metabolic Abnormalities

From this general approach more specific metabolic problems can be addressed. There are three general mechanisms by which SID changes: changing the water content of plasma (contraction alkalosis and dilutional acidosis), changing the Cl^- (hyperchloremic acidosis and hypochloremic alkalosis), and increasing the concentration of unidentified anions (organic acidosis).

SID Free Water Change

Dilutional Acidosis

Development of a dilutional acidosis is best illustrated by an example. If a liter of water contains 140 mEq/L of sodium and 110 mEq/L of chloride then the SID of that solution is 30 mEq. This represents a positive charge excess which needs to be balanced by a negative charge of 30 mEq. Hydroxyl ions (OH^-) act as this charge equalizer. If we were to add another liter of water without adding any more electrolytes, the solution would contain 70 mEq/L of sodium and 55 mEq/L of chloride (Fig. 45.3). Now the SID is 15 mEq. Because we have decreased the positive charge contribution of the SID from 30 to 15 mEq, a fall in OH^- would occur and a "dilutional" acidosis would be seen. In the operating room, dilutional acidosis can theoretically occur as part of the Trans Urethral Resection of the Prostate (TURP) syndrome.

Contraction Alkalosis

Contraction alkalosis can be seen in the perioperative patient who has been fluid restricted or treated with diuretics. It can

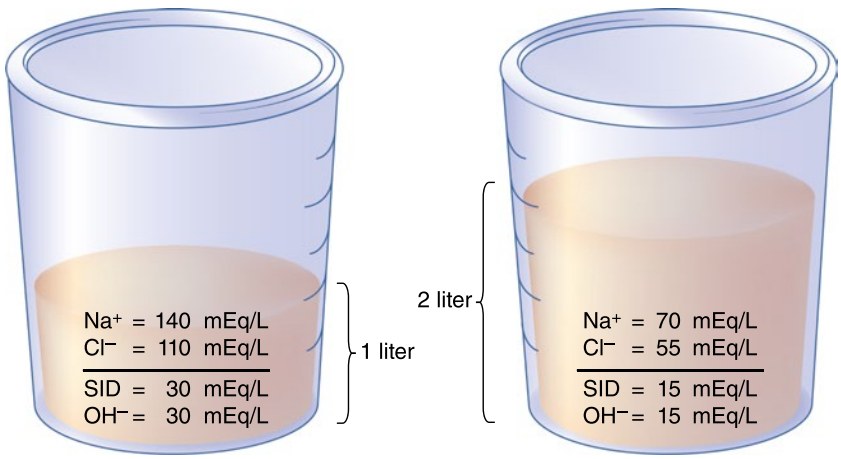

Fig. 45.3 Dilutional acidosis

also be seen intraoperatively if evaporative loss of free water is not replaced. Similar to dilutional acidosis, this problem arises from free water and SID changes. If we return to the original volume of water containing 140 mEq/L of sodium and 110 mEq/L of chloride (as above), and boil off half of the water, it would result in a sodium concentration of 280 mEq/L and a chloride concentration of 220 mEq/L. Now the SID is 60 mEq, and the OH^- "buffer" would increase so that the solution would remain electrically neutral.

Treatment of contraction alkalosis simply requires free water administration in the form of hypotonic solutions. Using the beaker model, treatment can be explained mechanistically. We would now add one liter of 0.45 % NaCl solution containing 77 mEq of Na^+ and 77 mEq of Cl^-. The final electrolyte concentration would contain 238 mEq of Na^+ and 198 mEq of Cl^-, and a SID of 40 mEq. By the use of this hypotonic fluid, we have changed the SID from 60 to 40 mEq resulting in a decrease in the OH^- and a correction of the alkalosis.

SID Chloride Change

Hypochloremia

Chloride shifts occur in relation to gastrointestinal abnormality. If the hyperchloremic gastric contents are lost through vomiting or through gastric tube suction then a hypochloremia can result. Hypochloremia leads to an increase in SID. The positive charge increase associated with the SID must be balanced by an increase OH^-. Treatment can be with normal saline administration. The treatment can be illustrated in the same fashion as free water changes. If we have a 1 L of water with 140 mEq/L of Na^+ and a "hypochloremic" 95 mEq/L of Cl^- then the SID is 45 mEq. If 1 L of normal saline is added, the beaker would then contain 147 mEq/L of Na^+ and 125 mEq/L of Cl^-, with the SID being 22 mEq/L. By shifting the SID, we have shifted the pH in the normal direction.

Hyperchloremia

Hyperchloremia results in an increase in H^+. Hyperchloremia typically results from aggressive normal saline administration. Treatment of the elevated Cl^- and decreased SID would be done by increasing the SID. This could be accomplished through sodium bicarbonate administration. Here, the Na^+ is the effector agent and not the HCO_3^-. The HCO_3^- is a dependent variable and is rapidly excreted as CO_2. Other ways of administering Na^+ with a metabolizable anion are through the use of the sodium salts of lactate, gluconate, acetate, or citrate.

SID Unidentified Anions

SID can also be affected by the presence of organic acids such as lactate or ketoacids. Again, because these negatively charged molecules lower the SID, they result in an acidosis. Treatment is usually focused on stopping the development of acid. Resolution of the abnormal H^+ can also be achieved by increasing the SID using $NaHCO_3$.

Further Reading

1. Astrup P, Severinghaus JW. The history of blood gases, acids and bases. Copenhagen: Munksgaard. 1986;16:257–76.
2. Bunker JP. The great trans-Atlantic acid-base debate. Anesthesiology. 1965;26:591–4.
3. Cameron JN. Acid-base homeostasis: past and present perspectives. Physiol Zool. 1989;62:845–65.
4. Fencl V, Rossing T. Acid-base disorders in critical care medicine. Annu Rev Med. 1981;40:17–29.
5. Figge J, Rossing TH, Fencl V. The role of serum proteins in acid-base equilibria. J Lab Clin Med. 1991;117:453–67.
6. Fogt EJ. Continuous ex vivo and in vivo monitoring with chemical sensors. Clin Chem. 1990;36:1573–80.
7. Garella S, Chang BS, Kahn SI. Dilution acidosis and contraction alkalosis: review of a concept. Kidney Int. 1975;8:279–83.
8. Jorgensen K, Astrup P. Standard bicarbonate, its clinical significance and a new method for its determination. Scand J Clin Lab Invest. 1957;9:122.
9. Oh MS, Carroll HJ. The anion gap. N Engl J Med. 1977;297:814–7.
10. Schwartz WB, Relman AS. A critique of the parameters used in the evaluation of acid-base disorders. N Engl J Med. 1963;268:1382–8.
11. Siggaard-Andersen O. Titratable acid or base of body fluid. Ann N Y Acad Sci. 1966;33:41–58.
12. Stewart PA. Modern quantitative acid-base chemistry. Can J Physiol Pharmacol. 1983;61:1444–61.