

REVIEW ARTICLE

Julie R. Ingelfinger, M.D., *Editor*

Diagnostic Use of Base Excess in Acid–Base Disorders

Kenrick Berend, Ph.D., M.D.

FOR ALMOST 100 YEARS, CLINICIANS HAVE BEEN TRYING TO ASSESS ACID–base disturbances accurately and to unravel the mechanisms involved.^{1,2} Many schemes have been introduced to describe acid–base disorders. The three most commonly used methods of quantifying these disorders are the physiological approach, based on the renal and lung acid–base interaction³; the physicochemical approach (also called the Stewart method), based on strong ions and pH-related changes in weak ions such as albumin and phosphorus^{4,5}; and the base-excess approach, based on quantification of the change in metabolic acid–base status as provided by the blood gas machine.^{6–12} Standard base excess is one of the most extensively studied prognostic markers used to evaluate patients with trauma in the acute care setting.⁶ Although standard base excess is provided worldwide by most commercial blood gas analyzers,^{6,9–12} many physicians are unaware of its relevance and how to make use of this marker. This review discusses the value of standard base excess and includes several case vignettes that show the benefit of the base-excess approach in clinical practice.

From St. Elisabeth Hospital, Willemstad, Curaçao. Address reprint requests to Dr. Berend at the Department of Nephrology, St. Elisabeth Hospital, J.H.J. Hamelbergweg 193, Willemstad, Curaçao, or at kenber2@me.com.

This article was updated on April 12, 2018, at NEJM.org.

N Engl J Med 2018;378:1419–28.

DOI: 10.1056/NEJMra1711860

Copyright © 2018 Massachusetts Medical Society.

HISTORICAL PERSPECTIVE

To understand the development of standard base excess, one should be familiar with the history of acid–base assessment in the 1950s and 1960s.^{13–23} In 1952, a devastating poliomyelitis epidemic struck Copenhagen. Approximately 3000 affected patients were hospitalized over a period of 4 months; most were admitted to the Blegdam Hospital, an infectious-disease hospital. About 345 of the patients had bulbar poliomyelitis, which affected the respiratory and swallowing muscles. Only one acid–base laboratory test was available when the epidemic began: the total carbon dioxide concentration in blood. Because the partial pressure of carbon dioxide (P_{CO_2}) could not be determined, the high carbon dioxide — or bicarbonate — values were thought to indicate an alkalosis of unclear origin rather than a chronic respiratory acidosis. Over a period of 1 month, at the height of the epidemic, 27 of 31 patients with bulbar poliomyelitis died.

A meeting was held to discuss this disaster; among the attendees were Bjørn Ibsen, an anesthesiologist, and Poul Astrup, chief of the hospital laboratory. Ibsen realized that marked carbon dioxide retention triggered the high blood bicarbonate levels and that these values did not indicate an alkalosis of unknown origin. On the basis of Ibsen's previous experience at Massachusetts General Hospital, where a child with tetanus was treated with curare and ventilated manually through a tracheostomy, he reasoned that artificial ventilation might help patients with poliomyelitis. At Blegdam Hospital, Ibsen used manual bag ventilation to treat a 12-year-old girl whose limbs were paralyzed and who was cyanotic and

gasping for breath.¹³ She was ventilated successfully through a cuffed endotracheal tube after undergoing a tracheotomy. Subsequently, 1500 medical and dental students were recruited to provide ventilation for patients with poliomyelitis at Blegdam Hospital, for a total of 165,000 hours of ventilatory support, and as a result, the lives of about 100 patients were saved.

The selection of candidates for supportive ventilation was largely based on the measurement of P_{CO_2} in blood. A small pH meter was provided by a local company, and by applying the Henderson–Hasselbalch equation, using pH and bicarbonate, P_{CO_2} could be extrapolated with the use of a diagram,¹⁴ heralding a new clinical acid–base era. In 1958, in an attempt to find a simple method to assess the metabolic component of acid–base status, Astrup and Siggaard-Andersen, from Copenhagen, developed the concept of base excess after examining the results of human blood titrations.^{24,25} Their thinking evolved from the concept of whole-blood buffer base, developed by Singer and Hastings in 1948 to describe the metabolic disturbances of acid–base equilibrium.²⁶ The buffer base is considered to be the sum of weak acid (buffer) anions in plasma, including hemoglobin, plasma proteins, phosphate, and bicarbonate.^{25–30} Blood base excess was considered to be a measurement independent of the respiratory component, as well as a measurement that could replace plasma bicarbonate. Base excess is the amount of strong acid (in millimoles per liter) that needs to be added in vitro to 1 liter of fully oxygenated whole blood to return the sample to standard conditions (pH of 7.40, P_{CO_2} of 40 mm Hg, and temperature of 37°C).^{7,25–27} Under these standard conditions, base excess will be 0 mmol per liter by definition.

Base excess was assumed to be the first accurate index of the nonrespiratory component of acid–base balance. Nevertheless, the usefulness of base excess was questioned by an American group, headed by Schwartz and Relman, leading to what was called “the great trans-Atlantic acid–base debate.”^{29,30} They argued that since, in the body, plasma is in continuity with interstitial fluid, which has limited buffer capacity, deriving plasma base excess from blood samples in vitro is inaccurate. Siggaard-Andersen answered this challenge by estimating a hemoglobin concentration of 50 g per liter for calculation, which

would reduce the apparent buffer capacity of a blood sample in vitro. That maneuver provided an assessed base excess now known as standard base excess,^{1,15,27} which reflects the role of hemoglobin as a buffer in the extracellular fluid. Depending on the algorithm used, standard base excess is calculated as 30 to 50 g per liter, which is essentially the estimated hemoglobin concentration in the extracellular fluid (one third of the blood hemoglobin concentration).²⁷ In contrast, the American group offered six steps for calculating changes in the P_{CO_2} or bicarbonate level for changes in, respectively, the bicarbonate level or P_{CO_2} (Table 1) and supported the elimination of standard base excess from printouts.³⁰ Nevertheless, standard base excess is still provided by most blood gas machines and is used widely in clinical studies and in clinical practice throughout the world.^{6,15}

BASE-EXCESS NOMENCLATURE AND EQUATIONS

The nomenclature for base excess can be confusing^{1,7,15,25,27,32–40} (Table 2; and Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). The term “base excess” is used in clinical practice, but the available blood gas devices calculate either the standard base excess (SBE), also called the base excess of the extracellular fluid (BE_{ECF}), or the base excess of blood (BE_B). The printouts provide BE_{ECF} , BE_B , or both. Unfortunately, BE_{ECF} and BE_B results can vary substantially in severe acid–base disturbances, and it may affect clinical practice if a given institution uses two devices that differ in the reporting of BE_{ECF} and BE_B . Therefore, the National Committee for Clinical Laboratory Standards recommends using devices that calculate standard base excess with a single algorithm and cautions that standard base excess should not be confused with base excess of blood.³³ Another popular term in the literature is base deficit,^{27,32} which is the negative version of base excess and is calculated as $-1 \times SBE$ or $-1 \times BE_B$.

The terms “base deficit” and “base excess” are often used interchangeably, but one should realize that in a patient with metabolic acidosis, a base deficit of 6 mmol per liter is equal to a standard base excess of -6 mmol per liter. Since blood gas machines do not provide base deficit,

Table 1. Secondary (“Compensatory”) Responses in Acid–Base Disorders as Indicated by Standard Base Excess (SBE) or Bicarbonate (HCO₃⁻) Level.*

| Condition | Paco ₂ or SBE Secondary Response | Paco ₂ or HCO ₃ ⁻ Secondary Response |
|---------------------------------------------------------------------------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Acute respiratory acidosis (pH decreased, Paco ₂ increased, SBE=0±2 mmol/liter) | SBE=0±2 mmol/liter | Increase of 1 mmol/liter in HCO ₃ ⁻ for each 10 mm Hg increase in Paco ₂ above 40 mm Hg |
| Acute respiratory alkalosis (pH increased, Paco ₂ decreased, SBE=0±2 mmol/liter) | SBE=0±2 mmol/liter | Decrease of 2 mmol/liter in HCO ₃ ⁻ for each 10 mm Hg decrease in Paco ₂ below 40 mm Hg |
| Chronic respiratory acidosis (pH decreased, Paco ₂ increased, SBE increased) | SBE=0.4 × (Paco ₂ - 40) | Increase of 4–5 mmol/liter in HCO ₃ ⁻ for each 10 mm Hg increase in Paco ₂ above 40 mm Hg |
| Chronic respiratory alkalosis (pH increased, Paco ₂ decreased, SBE decreased) | SBE=0.4 × (Paco ₂ - 40) | Decrease of 4–5 mmol/liter in HCO ₃ ⁻ for each 10 mm Hg decrease in Paco ₂ below 40 mm Hg |
| Metabolic acidosis (pH decreased, Paco ₂ decreased, SBE decreased) | ΔPaco ₂ =SBE | Expected Paco ₂ =1.5 × [HCO ₃ ⁻] + 8±2 mm Hg |
| Metabolic alkalosis (pH increased, Paco ₂ increased, SBE increased) | ΔPaco ₂ =0.6 × SBE | Expected Paco ₂ =0.7 × ([HCO ₃ ⁻] - 24) + 40±2 mm Hg |

* For the partial pressure of arterial carbon dioxide (Paco₂) or SBE secondary response and for the Paco₂ or HCO₃⁻ secondary response, certain changes are expected in primary acid–base disorders according to the calculations shown. Mixed disturbances may be diagnosed if the secondary response to the primary process is outside the expected range³¹ (e.g., in cases of respiratory acidosis, superimposed metabolic alkalosis or acidosis may be diagnosed if the calculated SBE or HCO₃⁻ is greater or less than predicted, respectively). The secondary responses for respiratory acidosis and respiratory alkalosis are metabolic, and the secondary responses for metabolic acidosis and metabolic alkalosis are respiratory. To convert the values for Paco₂ from millimeters of mercury to kilopascals, divide by 7.5006. The delta symbol denotes “change in.”

Table 2. Nomenclature and Equations for Base Excess (BE).*

| Term | Equation | Comments |
|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Buffer base | Normal buffer base in mmol/liter = 41.7 + 0.42 × Hb in g/100 ml | The buffer base (reintroduced in 1983 by Stewart as strong ion difference ⁸) is the sum of weak acid (buffer) anions in plasma, including Hb, plasma proteins, phosphate, and HCO ₃ ⁻ . ²⁵⁻³⁰ |
| Van Slyke equation | BE = (HCO ₃ ⁻ - 24.4) + (2.3 × Hb + 7.7) × (pH - 7.4) × (1 - 0.023 × Hb) | Arterial blood gas analyzers use algorithms mostly based on the Van Slyke equation. ^{1,34} |
| BE _B , actual BE, or in vitro measure | BE _B = (1 - 0.014 × ctHb) × [(HCO ₃ ⁻ act - 24.8) + (7.7 + 1.43 × ctHb) × (pH - 7.40)] | In this equation, ctHb is the total concentration of Hb (deoxyhemoglobin, oxyhemoglobin, carboxyhemoglobin, and methemoglobin) in the blood. ³⁶ |
| Actual HCO ₃ ⁻ | HCO ₃ ⁻ act = 0.0307 × Paco ₂ × 10 ^(pH - 6.105) | Arterial HCO ₃ ⁻ obtained from blood gas analyzers is calculated according to complex formulas, including correction factors for Hb and oxygen saturation. ³³ |
| SBE, BE of the extracellular fluid (BE _{ECF}), or in vivo BE | SBE = HCO ₃ ⁻ act - 24.8 + [16.2 × (pH - 7.40)] | SBE is more representative in vivo than BE _B ; the value of 16.2 is an approximation of the nonbicarbonate buffers in extracellular fluid. ^{30,32-34} |
| Base deficit | BD = -1 × SBE | Base deficit (the negative version of SBE) is not provided by blood gas machines but is often used in the literature instead of SBE. ^{6,27,32} |

* Blood gas devices provide SBE, base excess of blood (BE_B), or both. SBE and BE_B can differ substantially.⁴⁰ The National Committee for Clinical Laboratory Standards recommends using a standard equation for SBE — that is, SBE = HCO₃⁻ act - 24.8 + 16.2 × (pH - 7.40) — and not confusing SBE with BE_B.³³ BD denotes base deficit, ctHb total concentration of hemoglobin, Hb hemoglobin, HCO₃⁻ act actual bicarbonate, and Paco₂ partial pressure of carbon dioxide.

the standard base excess is used in this review. To calculate standard base excess, the commonly used commercially available arterial blood gas analyzers use algorithms that differ slightly according to the manufacturer but are mostly based on the Van Slyke equation (Table 2).^{1,25}

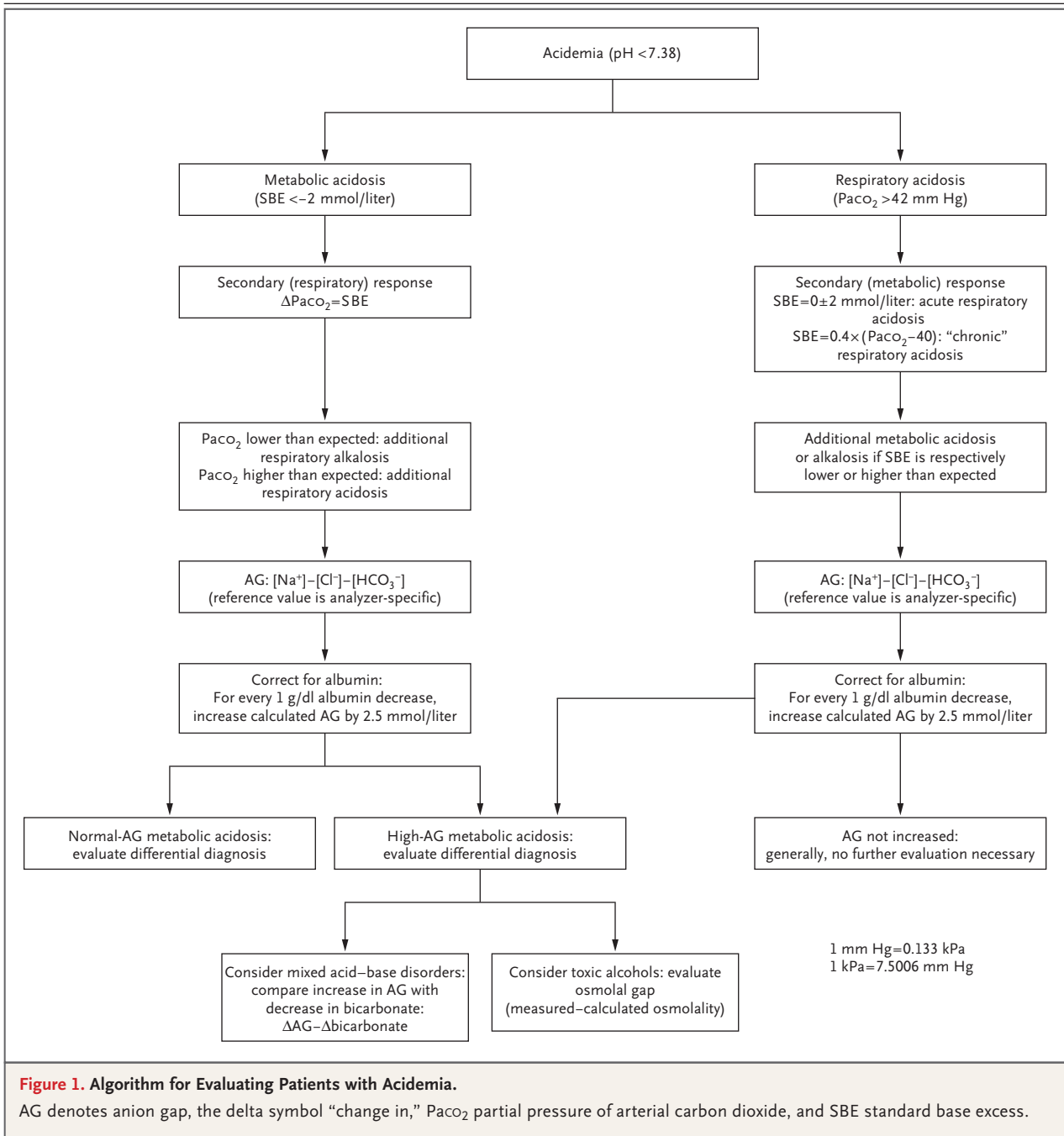


Figure 1. Algorithm for Evaluating Patients with Acidemia.

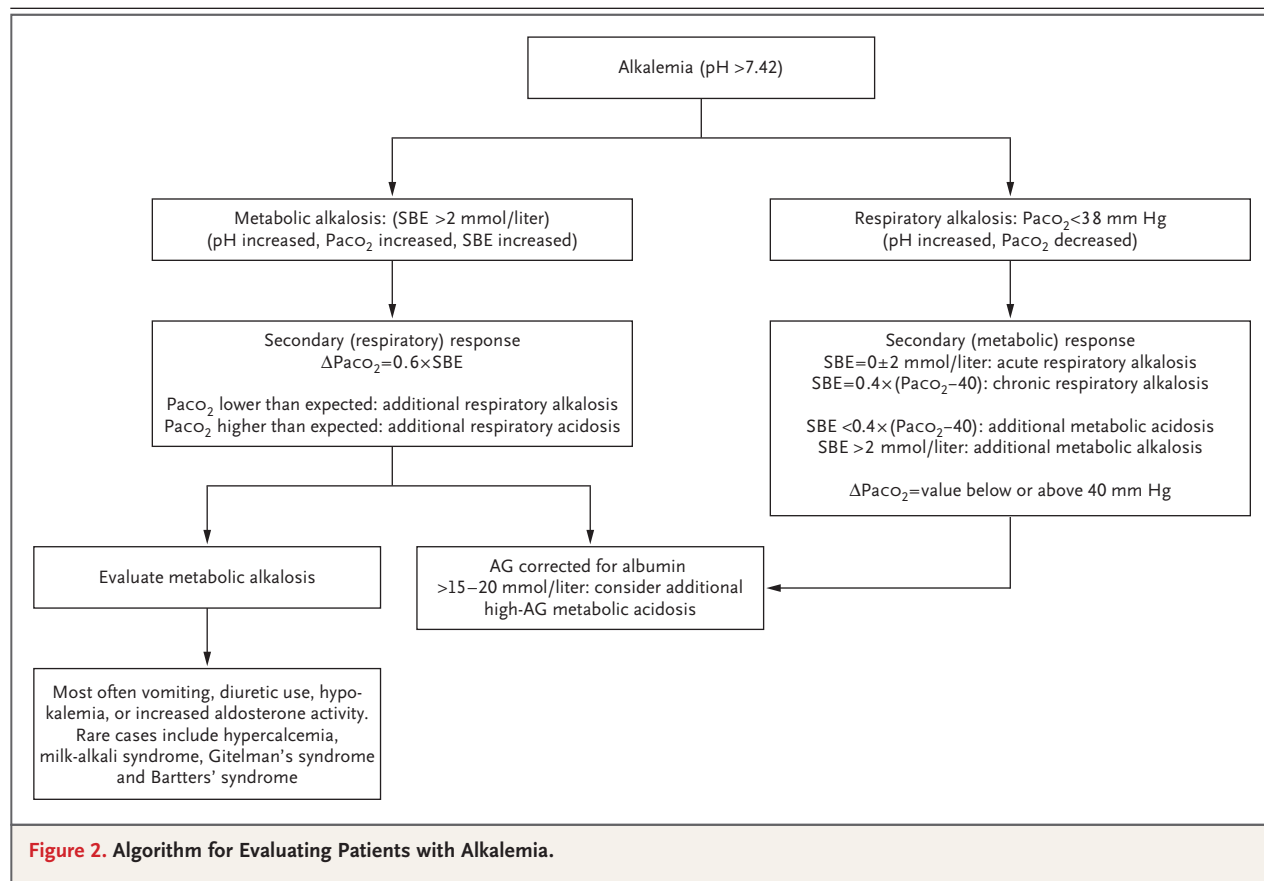
AG denotes anion gap, the delta symbol “change in,” $Paco_2$ partial pressure of arterial carbon dioxide, and SBE standard base excess.

USE OF BASE EXCESS

To diagnose an acid–base disorder, a three-step approach is feasible with the base-excess method. The first step is to evaluate standard base excess in relation to pH and Pco_2 (Figs. 1 and 2 and Table 1). For the purposes of this review, the

reference values are 7.40 for pH, 40 mm Hg for the partial pressure of arterial carbon dioxide ($Paco_2$), and 0 ± 2 mmol per liter for standard base excess. These baseline measures may be different for an individual patient.

The next step is to determine the secondary response (Figs. 1 and 2 and Table 1).^{3,31,38} The



four primary acid–base disorders (respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis) are shown in Table 1. In the presence of an acid–base disorder that alters pH, physiological processes occur that tend to restore pH to normal. These changes are considered compensatory. For instance, a metabolic acidosis causes immediate hyperventilation, and a new steady-state $Paco_2$ is reached within hours. When respiratory abnormalities persist, metabolic compensation occurs slowly, and it takes 2 to 5 days for the plasma bicarbonate level or standard base excess to reach a new steady-state level. A respiratory change is labeled as “acute” or “chronic” on the basis of whether a secondary change in standard base excess meets specific criteria (Table 1 and Figs. 1 and 2).^{3,31,38} Mixed acid–base disorders are those in which the secondary response differs from that which would be expected.³ As an example, a patient with diabetic ketoacidosis and severe vomiting has a mixed metabolic acidosis and alkalosis.

Respiratory disorders should be differentiated as acute, chronic, or mixed disorders. The patient’s history is particularly important in this respect (e.g., a pregnant woman should have a chronic respiratory alkalosis), but often a specific time frame cannot be determined from the patient’s description. In such cases, we assume that calculations will help determine the duration of the respiratory disorder, although these calculations may not always be correct.³

The third step is to partition (divide up) standard base excess or evaluate the anion gap, in order to consider mixed metabolic acid–base disorders (Figs. 1 and 2 and Table 3).^{10,31,41-44} The partitioning approach is illustrated in the case vignette that accompanies Table 3. An easier diagnostic approach, which can replace the comprehensive partitioning calculations, is to evaluate the anion gap. Mixed acid–base disturbances occur frequently, and one should therefore always rule out mixed metabolic acid–base disturbances if the anion gap is increased.^{3,38}

Table 3. Partitioning of SBE.*

| SBE Partition | Equation | Comments |
|--------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| SBE due to free water (SBE _{FW}) | Free water effect (based on sodium) = $0.3 \times (\text{Na} - 140)$ | |
| SBE due to chloride (SBE _{Cl}) | Chloride effect corrected for sodium = $104 - (\text{Cl} \times 140 \div \text{Na})$ | Sodium and chloride change in tandem according to the water content of plasma; therefore, an adjustment for chloride is made when the sodium content is changed. |
| SBE due to albumin (SBE _{alb}) | Albumin effect (mmol/liter) = $(0.148 \times \text{pH} - 0.818) \times (40 - \text{albumin in g/liter})$ | An albumin level of 40 g/liter is used as a normal level. |
| SBE due to unmeasured anions | Unmeasured anion effect = $\text{SBE} - \text{SBE}_{\text{FW}} - \text{SBE}_{\text{Cl}} - \text{SBE}_{\text{alb}}$ | |

* SBE can be partitioned into its four distinct components in order to determine the combined acid–base disorders.^{10,41,42} In the partitioning equations, one assumes that the patient initially had a sodium level of 140 mmol per liter, a chloride level of 104 mmol per liter, and an albumin level of 40 g per liter. The partitioning approach is illustrated by the following case vignette. A 48-year-old man with type 1 diabetes was admitted with vomiting. The plasma sodium level was 144 mmol per liter, and the chloride level was 93 mmol per liter. Arterial blood gas values were as follows: pH, 7.53; PaCO₂, 32 mm Hg; HCO₃⁻, 27 mmol per liter; and SBE, 4.7 mmol per liter. Other plasma values included a glucose level of 448 mg per deciliter (24.9 mmol per liter) and an albumin level of 30 g per liter. The value for urinary ketones exceeded 80 mg per deciliter. The anion gap ($\text{Na}^+ - \text{Cl}^- - \text{HCO}_3^-$), corrected for albumin, was 26.5 mmol per liter. The increased pH and SBE suggest a metabolic alkalosis. However, the high anion gap reveals an additional metabolic acidosis, despite a pH above 7.4. In this case, two metabolic disorders coexist: diabetic ketoacidosis and metabolic alkalosis due to vomiting. Because of the predominant alkalotic component, the pH exceeded 7.4, indicating ketoalkalosis.^{43,44} In this patient, the components of SBE are as follows: $\text{SBE}_{\text{FW}} = 0.3 \times (\text{Na} - 140) = 0.3 \times (144 - 140) = 1.2$; $\text{SBE}_{\text{Cl}} = 104 - (\text{Cl} \times 140 \div \text{Na}) = 104 - (93 \times 140 \div 144) = 13.6$; $\text{SBE}_{\text{alb}} = 0.296 \times (40 - \text{albumin in grams per liter}) = 0.296 \times (40 - 30) = 2.96$; $\text{SBE due to unmeasured anions} = 4.7 - 1.2 - 13.6 - 2.96 = -13.06$ mmol per liter. The large negative value indicates a high level of anions, suggesting metabolic acidosis in addition to metabolic alkalosis, despite a pH above 7.4 and a positive SBE. Evaluation of the anion gap can be substituted for these comprehensive calculations. The anion gap corrected for albumin is 26.5 mmol per liter. If the initial anion gap in the patient was approximately 12 mmol per liter, there was an increase of 14.5 mmol per liter (which is close to the -13.06 mmol per liter calculated above for SBE due to unmeasured anions); the increase was most likely due to an increase in the beta-hydroxybutyrate level in diabetic ketoacidosis.

TWO CASE EXAMPLES

Patient 1, a 54-year-old man with cirrhosis of the liver, was admitted to the hospital for drainage of ascites. The plasma sodium level was 129 mmol per liter, chloride 101 mmol per liter, and albumin 3.0 g per deciliter. The arterial blood pH was 7.44, and the PaCO₂ was 30 mm Hg. The bicarbonate level was 19.7 mmol per liter, and the standard base excess was -3.8 mmol per liter, with a partial pressure of arterial oxygen (PaO₂) of 80 mm Hg.

In this patient, the high pH, the low PaCO₂, and a standard base excess below -2 mmol per liter suggest a chronic respiratory alkalosis (Table 1). The anion gap corrected for albumin was 10.8 mmol per liter. These results probably indicate a chronic respiratory alkalosis because the anion gap was normal and an expected standard base excess of -4 mmol per liter, calculated as $0.4 \times (\text{PaCO}_2 - 40)$, was close to the measured

standard base excess of -3.8 mmol per liter. The chronic hyperventilation was probably the effect of reduced metabolism of progesterone by the liver, with activated progesterone receptors in the central nervous system leading to increased ventilation.⁴⁵⁻⁴⁷ The hypoxemia may have been caused by a hepatopulmonary syndrome, especially if symptoms of positional dyspnea and hypoxemia occurred when the patient was upright and resolved with recumbency (platypnea and orthodeoxia, respectively).⁴⁷

Patient 2, an 86-year-old woman, was admitted with respiratory failure due to a stroke. The pH was 7.33, the PaCO₂ was 86 mm Hg, and the bicarbonate level was 43.3 mmol per liter. The standard base excess was 16.6 mmol per liter. The plasma sodium level was 146 mmol per liter, and the chloride level was 96 mmol per liter.

The low pH, the high PaCO₂, and a standard base excess above 2 mmol per liter suggest a chronic respiratory acidosis (Table 1). One thus

expects the standard base excess, calculated as $0.4 \times (\text{Paco}_2 - 40)$, to be $0.4 \times (86 - 40)$, or 18.4 mmol per liter. The patient's standard base excess of 16.6 mmol per liter is close to this value, but a lower-than-expected standard base excess may be the result of an additional metabolic acidosis.

BASE EXCESS IN THE ACUTE CARE SETTING

Early recognition of hypovolemic shock in patients with trauma is one of the most challenging tasks in the acute care setting. During shock, anaerobic metabolism is reflected by the serum lactate level. In contrast, the standard base excess is a calculated value, which is influenced not only by lactic acidosis but also by other factors, such as minute ventilation and various therapies, including the administration of sodium bicarbonate and intravenous fluids.⁴⁸ The blood lactate level and standard base excess are the most commonly used circulating markers of systemic metabolic acidosis after an injury. There is still a debate about which measure is more useful in the acute care setting,^{9,12,48,49} but that may be less important for patient care, because blood gas machines often provide both measures so they can be evaluated concurrently.

There is an abundance of literature on the value of standard base excess as one of the most important tools in determining the severity of illness in the acute care setting.⁴⁸⁻⁶⁴ One study, involving more than 16,000 patients, compared standard base excess with the Advanced Trauma Life Support (ATLS) hypovolemic-shock classification, which combines heart rate, systolic blood pressure, and score on the Glasgow Coma Scale.⁵⁰ Standard base excess was found to be superior for detecting hypovolemic shock and stratifying patients in hemorrhagic shock with respect to the need for early transfusion of blood products. Moreover, in patients with trauma, standard base excess predicts the risk of death significantly better than either vital signs or shock index.⁵¹ The use of standard base excess also appears to be superior to measurement of vital signs for rapid physiological assessment of patients with penetrating trauma.⁵¹ These findings suggest that the value for standard base excess may be an indicator of hypoperfusion and a potentially unstable condition in patients who

do not have hypotension on admission; furthermore, it may be an independent predictor of the need for multiple transfusions in patients with major blunt trauma.⁵²

In a recent systematic review of trauma studies that were conducted over a period of 25 years, a negative value for arterial standard base excess was consistently associated with clinically important injuries, major complications, and increased mortality.⁶ The odds ratio for the risk of death during hospitalization increased by 8 to 14% for each unit decrease in the value for arterial standard base excess. Despite advances in trauma care over the past 20 years, the arterial standard base excess remains useful in patients with trauma.⁶ Furthermore, in such patients, a standard base excess that is negative or becoming increasingly negative is considered to be predictive of transfusion requirements,^{53,54} as well as of numerous shock-related complications, including a prolonged stay in the intensive care unit, renal failure, the acute respiratory distress syndrome, multiorgan failure, and acute lung injury.^{27,54-58} In the acute setting, standard base excess may also be correlated with the risk of potentially fatal coagulation disturbances in patients with trauma.⁵⁸ Measurement of standard base excess in patients with multiple sources of trauma has become common practice in emergency rooms, since many trauma specialists see it as predictive and crucial for guiding resuscitation efforts.⁶⁰ In patients with burns, standard base excess may be useful both prognostically and in determining the end point of resuscitation efforts.^{27,61} Key to the use of standard base excess is an assessment of the metabolic component of acid-base abnormalities through the estimation of the level of metabolic acidosis. A negative value below -6 mmol per liter indicates severe metabolic acidosis.^{6,57,62}

Unfortunately, the studies of standard base excess in patients with trauma have several limitations. First, randomized, controlled trials have not been performed; thus, evidence is available solely from observational studies.⁶ Second, most studies have had a substantial selection bias; for example, arterial standard base excess was often measured in less than 30% of patients.^{6,63,64} In addition, standard base excess values are influenced by hyperchloremic acidosis after the administration of isotonic saline, as

well as by renal failure, diabetic ketoacidosis, and prolonged carbon dioxide retention.⁵⁴ In patients who have undergone fluid resuscitation in an ambulance and in those with preexisting renal failure, chronic respiratory disorders, or mixed acid–base disturbances, standard base excess values are easy to misinterpret. As an example, a patient with chronic respiratory acidosis will have a standard base excess of 4 mmol per liter when the P_{aCO_2} has been increased by 10 mm Hg for a few days. If shock and additional metabolic acidosis develop, the standard base excess may become about 0 mmol per liter, suggesting the absence of a metabolic acid–base problem. In such cases, an increased anion gap may direct the clinician to diagnose a high-anion-gap metabolic acidosis in combination with the respiratory acidosis. Therefore, if the acid–base disorder is carefully evaluated in individual cases, studies regarding standard base excess and trauma may be helpful in guiding clinical decision making.

The use of standard base excess has also been studied extensively in neonates and children, including neonates with asphyxia-related encephalopathy⁶⁵ and children with trauma.^{33,50,66} Additional remarks about standard base excess in the pediatric setting are beyond the scope of this review.

In summary, standard base excess continues to be among the most commonly used markers in critical care units, both to diagnose metabolic acidosis and to guide resuscitation or therapy.⁶⁷ In trauma care, standard base excess is rapidly obtainable, has been well studied, and seems to be superior to vital signs or pH as a resuscitation end point; however, any single acid–base value alone cannot be used as an end point. With the increased availability of blood gas analysis in point-of-care settings, standard base excess can be assessed simply and within

minutes after a patient has been admitted to the emergency department.^{50,51} Measurement of standard base excess usually requires arterial blood, which may be difficult to obtain in the acute care setting. Venous blood can be obtained more easily and more rapidly, and values for venous standard base excess generally correlate well with arterial values.^{11,68} The reason for this close correlation is that the arterial bicarbonate level is only slightly lower than the venous bicarbonate level and the difference between arterial and venous pH is too small to cause substantial changes in standard base excess.

CONCLUSIONS

The standard base excess is a useful construct for evaluating acid–base disorders. Standard base excess is readily available from most blood gas printouts, and the four calculations of P_{aCO_2} and standard base excess that are used to evaluate the secondary response in acid–base disorders are easier to remember and perform than the calculations in the physiological method. The usefulness of the standard base excess method in acid–base evaluation is improved when combined with the anion gap. Standard base excess may have a role in the initial assessment of and prognosis for acutely ill patients. The terminology surrounding base excess may be confusing, but with some background knowledge, the concept is easy to apply in clinical practice. Clinicians should remember that standard base excess calculations are accurate, but manufacturers of blood gas devices should standardize the standard base excess equation and use only the standard base excess calculation recommended by the National Committee for Clinical Laboratory Standards.³³

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

REFERENCES

- Kofstad J. Base excess: a historical review — has the calculation of base excess been more standardised the last 20 years? *Clin Chim Acta* 2001;307:193-5.
- Prough DS, White RT. Acidosis associated with perioperative saline administration: dilution or delusion? *Anesthesiology* 2000;93:1167-9.
- Berend K, de Vries APJ, Gans ROB. Physiological approach to assessment of acid–base disturbances. *N Engl J Med* 2014;371:1434-45.
- Stewart PA. Modern quantitative acid–base chemistry. *Can J Physiol Pharmacol* 1983;61:1444-61.
- Seifter JL. Integration of acid–base and electrolyte disorders. *N Engl J Med* 2014;371:1821-31.
- Ibrahim I, Chor WP, Chue KM, et al. Is arterial base deficit still a useful prognostic marker in trauma? A systematic review. *Am J Emerg Med* 2016;34:626-35.
- Schiraldi F, Guiotto G. Base excess, strong ion difference, and expected compensations: as simple as it is. *Eur J Emerg Med* 2014;21:403-8.
- Park M, Maciel AT, Noritomi DT, Pontes de Azevedo LC, Taniguchi LU, da Cruz Neto LM. Effect of P_{aCO_2} variation on standard base excess value in criti-

- cally ill patients. *J Crit Care* 2009;24:484-91.
9. Seo MH, Choa M, You JS, et al. Hypoalbuminemia, low base excess values, and tachypnea predict 28-day mortality in severe sepsis and septic shock patients in the emergency department. *Yonsei Med J* 2016;57:1361-9.
 10. Yasuda K, Hayashi M, Murayama M, Yamakita N. Acidosis-induced hypochloremic alkalosis in diabetic ketoacidosis confirmed by the modified base excess method. *J Clin Endocrinol Metab* 2016;101:2390-5.
 11. Wijaya R, Ng JH, Ong L, Wong AS. Can venous base excess replace arterial base excess as a marker of early shock and a predictor of survival in trauma? *Singapore Med J* 2016;57:73-6.
 12. Davis JW, Dirks RC, Kaups KL, Tran P. Base deficit is superior to lactate in trauma. *Am J Surg* 2018 January 31 (Epub ahead of print).
 13. West JB. The physiological challenges of the 1952 Copenhagen poliomyelitis epidemic and a renaissance in clinical respiratory physiology. *J Appl Physiol* (1985) 2005;99:424-32.
 14. Astrup PB, Severinghaus JW. The history of blood gases, acids and bases. Copenhagen: Munksgaard, 1986.
 15. Story DA. Bench-to-bedside review: a brief history of clinical acid-base. *Crit Care* 2004;8:253-8.
 16. Van Slyke DD. Some points of acid-base history in physiology and medicine. *Ann N Y Acad Sci* 1966;133:5-14.
 17. Andersen EW, Ibsen B. The anaesthetic management of patients with poliomyelitis and respiratory paralysis. *Br Med J* 1954;1:786-8.
 18. Astrup P, Gøtzche H, Neukirch F. Laboratory investigations during treatment of patients with poliomyelitis and respiratory paralysis. *Br Med J* 1954;1:780-6.
 19. Bower AG, Bennett VR, Dillon JB, Axelrod B. Investigation on the care and treatment of poliomyelitis patients. *Ann West Med Surg* 1950;4:561-82.
 20. Bower AG, Bennett VR, Dillon JB, Axelrod B. Investigation on the care and treatment of poliomyelitis patients. II. Physiological studies of various treatment procedures and mechanical equipment. *Ann West Med Surg* 1950;4:686-716.
 21. Ibsen B. The anaesthetist's viewpoint on the treatment of respiratory complications in poliomyelitis during the epidemic in Copenhagen, 1952. *Proc R Soc Med* 1954;47:72-4.
 22. Jungner I, Laurent B. The poliomyelitis epidemic in Stockholm 1953: biochemical laboratory investigations. *Acta Med Scand Suppl* 1956;316:71-9.
 23. Lassen HCA. A preliminary report on the 1952 epidemic of poliomyelitis in Copenhagen with special reference to the treatment of acute respiratory insufficiency. *Lancet* 1953;1:37-41.
 24. Severinghaus JW. The invention and development of blood gas analysis apparatus. *Anesthesiology* 2002;97:253-6.
 25. Siggaard-Andersen O, Fogh-Andersen N. Base excess or buffer base (strong ion difference) as measure of a non-respiratory acid-base disturbance. *Acta Anaesthesiol Scand Suppl* 1995;107:123-8.
 26. Singer RB, Hastings AB. An improved clinical method for the estimation of disturbances of the acid-base balance of human blood. *Medicine (Baltimore)* 1948;27:223-42.
 27. Juern J, Khatri V, Weigelt J. Base excess: a review. *J Trauma Acute Care Surg* 2012;73:27-32.
 28. Andersen OS. The pH-log pCO₂ blood acid-base nomogram revised. *Scand J Clin Lab Invest* 1962;14:598-604.
 29. Severinghaus JW. Siggaard-Andersen and the "Great Trans-Atlantic Acid-Base Debate." *Scand J Clin Lab Invest Suppl* 1993;214:99-104.
 30. Schwartz WB, Relman AS. A critique of the parameters used in the evaluation of acid-base disorders — whole-blood buffer base and standard bicarbonate compared with blood pH and plasma bicarbonate concentration. *N Engl J Med* 1963;268:1382-8.
 31. Schlichtig R, Grogono AW, Severinghaus JW. Human PaCO₂ and standard base excess compensation for acid-base imbalance. *Crit Care Med* 1998;26:1173-9.
 32. Knutzen L, Svirko E, Impey L. The significance of base deficit in acidemic term neonates. *Am J Obstet Gynecol* 2015;213(3):373.e1-373.e7.
 33. Blood gas and pH analysis and related measurements: approved guideline. NCCLS document no. C46. Wayne, PA: National Committee for Clinical Laboratory Standards, 2001.
 34. Morgan TJ, Clark C, Endre ZH. Accuracy of base excess — an in vitro evaluation of the Van Slyke equation. *Crit Care Med* 2000;28:2932-6.
 35. Ross MG, Jessie M, Amaya K, et al. Correlation of arterial fetal base deficit and lactate changes with severity of variable heart rate decelerations in the near-term ovine fetus. *Am J Obstet Gynecol* 2013;208(4):285.e1-285.e6.
 36. Mokarami P. Pitfalls in interpreting umbilical cord blood gases and lactate at birth (Ph.D. thesis). Malmo, Sweden: Lund University, 2013.
 37. Astrup P, Jørgensen K, Andersen OS, Engel K. The acid-base metabolism: a new approach. *Lancet* 1960;1:1035-9.
 38. Adrogué HJ, Gennari FJ, Galla JH, Madias NE. Assessing acid-base disorders. *Kidney Int* 2009;76:1239-47.
 39. Peake MJ, White GH. Arterial blood gas analysis: selecting the clinically appropriate option for calculating base excess. *Ann Clin Biochem* 2002;39:614-5.
 40. Nakamaru K, Hatakeyama N, Yamada M, Yamazaki M. Comparison of bicarbonate and base excess values analyzed by four different blood gas analyzers. *J Anesth* 2007;21:429-32.
 41. Funk GC, Doberer D, Kneidinger N, Lindner G, Holzinger U, Schneeweiss B. Acid-base disturbances in critically ill patients with cirrhosis. *Liver Int* 2007;27:901-9.
 42. Maciel AT, Park M. Differences in acid-base behavior between intensive care unit survivors and nonsurvivors using both a physicochemical and a standard base excess approach: a prospective, observational study. *J Crit Care* 2009;24:477-83.
 43. Jensen IW, Jensen S. Diabetic ketoacidosis. *Diabetes Care* 1988;11:368-9.
 44. Pape A, Nguyen HV, Flack JR. Recurrent diabetic ketoacidosis in a patient with Type 1 diabetes mellitus and severe gastroparesis. *Diabet Med* 2010;27:607-8.
 45. Bayliss DA, Cidlowski JA, Millhorn DE. The stimulation of respiration by progesterone in ovariectomized cat is mediated by an estrogen-dependent hypothalamic mechanism requiring gene expression. *Endocrinology* 1990;126:519-27.
 46. Passino C, Giannoni A, Mannucci F, et al. Abnormal hyperventilation in patients with hepatic cirrhosis: role of enhanced chemosensitivity to carbon dioxide. *Int J Cardiol* 2012;154:22-6.
 47. Tumgor G. Cirrhosis and hepatopulmonary syndrome. *World J Gastroenterol* 2014;20:2586-94.
 48. Gale SC, Kocik JF, Creath R, Crystal JS, Dombrovskiy VY. A comparison of initial lactate and initial base deficit as predictors of mortality after severe blunt trauma. *J Surg Res* 2016;205:446-55.
 49. Maegele M, Lefering R, Wafaisade A, et al. Revalidation and update of the TASH-Score: a scoring system to predict the probability for massive transfusion as a surrogate for life-threatening haemorrhage after severe injury. *Vox Sang* 2011;100:231-8.
 50. Mutschler M, Nienaber U, Brockamp T, et al. Renaissance of base deficit for the initial assessment of trauma patients: a base deficit-based classification for hypovolemic shock developed on data from 16,305 patients derived from the Trauma-Register DGU. *Crit Care* 2013;17(2):R42.
 51. Dunham MP, Sartorius B, Laing GL, Bruce JL, Clarke DL. A comparison of base deficit and vital signs in the early assessment of patients with penetrating trauma in a high burden setting. *Injury* 2017;48:1972-7.
 52. Söderlund T, Ikonen A, Pyhäntö T, Handolin L. Factors associated with in-hospital outcomes in 594 consecutive patients suffering from severe blunt chest trauma. *Scand J Surg* 2015;104:115-20.

53. Davis JW, Kaups KL, Parks SN. Base deficit is superior to pH in evaluating clearance of acidosis after traumatic shock. *J Trauma* 1998;44:114-8.
54. Connelly CR, Schreiber MA. End-points in resuscitation. *Curr Opin Crit Care* 2015;21:512-9.
55. Davis JW, Parks SN, Kaups KL, Gladen HE, O'Donnell-Nicol S. Admission base deficit predicts transfusion requirements and risk of complications. *J Trauma* 1996;41:769-74.
56. Davis JW, Shackford SR, Mackersie RC, Hoyt DB. Base deficit as a guide to volume resuscitation. *J Trauma* 1988;28:1464-7.
57. Callaway DW, Shapiro NI, Donnino MW, Baker C, Rosen CL. Serum lactate and base deficit as predictors of mortality in normotensive elderly blunt trauma patients. *J Trauma* 2009;66:1040-4.
58. Eberhard LW, Morabito DJ, Matthey MA, et al. Initial severity of metabolic acidosis predicts the development of acute lung injury in severely traumatized patients. *Crit Care Med* 2000;28:125-31.
59. Cheddie S, Muckart DJ, Hardcastle TC. Base deficit as an early marker of coagulopathy in trauma. *S Afr J Surg* 2013;51:88-90.
60. Shallwani H, Waqas M, Waheed S, Siddiqui M, Froz A, Bari ME. Does base deficit predict mortality in patients with severe traumatic brain injury? *Int J Surg* 2015;22:125-30.
61. Cancio LC, Galvez E Jr, Turner CE, Kypreos NG, Parker A, Holcomb JB. Base deficit and alveolar-arterial gradient during resuscitation contribute independently but modestly to the prediction of mortality after burn injury. *J Burn Care Res* 2006;27:289-96.
62. Peñasco Y, González-Castro A, Rodríguez-Borregán JC, Llorca J. Base excess, a useful marker in the prognosis of chest trauma in the geriatric population. *Rev Esp Anestesiol Reanim* 2017;64:250-6.
63. Ouellet JF, Roberts DJ, Tiruta C, et al. Admission base deficit and lactate levels in Canadian patients with blunt trauma: are they useful markers of mortality? *J Trauma Acute Care Surg* 2012;72:1532-5.
64. Tremblay LN, Feliciano DV, Rozycki GS. Assessment of initial base deficit as a predictor of outcome: mechanism of injury does make a difference. *Am Surg* 2002;68:689-93.
65. American College of Obstetricians and Gynecologists, American Academy of Pediatrics. Neonatal encephalopathy and neurologic outcome. 2nd ed. Washington, DC: American College of Obstetricians and Gynecologists, 2014.
66. Randolph LC, Takacs M, Davis KA. Resuscitation in the pediatric trauma population: admission base deficit remains an important prognostic indicator. *J Trauma* 2002;53:838-42.
67. Martin MJ, FitzSullivan E, Salim A, Berne TV, Towfigh S. Use of serum bicarbonate measurement in place of arterial base deficit in the surgical intensive care unit. *Arch Surg* 2005;140:745-51.
68. Middleton P, Kelly AM, Brown J, Robertson M. Agreement between arterial and central venous values for pH, bicarbonate, base excess, and lactate. *Emerg Med J* 2006;23:622-4.

Copyright © 2018 Massachusetts Medical Society.

IMAGES IN CLINICAL MEDICINE

The *Journal* welcomes consideration of new submissions for Images in Clinical Medicine. Instructions for authors and procedures for submissions can be found on the *Journal's* website at NEJM.org. At the discretion of the editor, images that are accepted for publication may appear in the print version of the *Journal*, the electronic version, or both.