

Base Excess: the basics

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Blood gas analysis, which allows assessment of patient acid-base status, involves measurement of the pH and partial pressure (p) of oxygen ($pO_2(a)$) and carbon dioxide ($pCO_2(a)$) in arterial blood. These measurements allow calculation of further parameters that are generated during blood gas analysis, including concentration of plasma bicarbonate [HCO_3^-] and base excess (BE), the subject of this article. BE helps in the assessment of acid-base status because it is a quantitative measure of the non-respiratory (metabolic) component of acid-base balance. Abnormal BE is thus a feature of both metabolic acidosis and metabolic alkalosis; and the extent to which BE deviates from normal is indicative of the severity of these two acid-base disturbances. BE is by definition unaffected by changes in $pCO_2(a)$ (the respiratory component of acid-base balance) and therefore remains within normal limits in respiratory acid-base disturbances unless they have provoked metabolic compensation. This article will include discussion of the concept of base excess, its derivation, and the distinction

between actual base excess (ABE) and standard base excess (SBE). Since an understanding of the clinical utility of base excess depends on appreciating the difference between respiratory and metabolic acid-base disorders and the compensation they invoke, the article begins with a very brief and necessarily simplistic overview of the traditional approach to acid-base pathophysiology and interpretation of blood gas analysis reports.

Health demands that hydrogen ion concentration [H^+], i.e. pH of extracellular fluid is maintained within narrow limits (pH 7.35-7.45) despite normal metabolism being associated with continuous production of volatile acid (carbon dioxide, CO_2) and non-volatile acids (lactic acid, phosphoric acid, acetoacetic acid, β -hydroxybutyric acid, etc.). Three main physiological processes are involved in the maintenance of normal blood pH (termed acid-base balance or acid-base homeostasis). They are respiratory elimination of CO_2 in expired air; blood buffering of hydrogen ions by bicarbonate (and

other chemical buffers, including hemoglobin; and renal regulation of bicarbonate and hydrogen-ion excretion in urine. Acid-base homeostasis is thus dependent on adequate bicarbonate buffer in blood as well as normally functioning lungs and kidneys.

The so-called "*traditional*" approach to acid-base pathophysiology that underlies the application of blood gas analysis in assessment of patient acid-base status developed from the pioneering work of two clinician-physiologists, Henderson and Hasselbalch, a little over a century ago. The familiar modified version of their Henderson-Hasselbalch equation reveals the relationship between blood pH and two other parameters generated during blood gas analysis: $p\text{CO}_2(\text{a})$ and plasma bicarbonate concentration $[\text{HCO}_3^-]$ [1], viz.:

$$\text{pH} = \text{pK} + \log([\text{HCO}_3^-] / p\text{CO}_2(\text{a}) \times 0.03) \quad \text{Eqtn. 1 [1]}$$

Removing constants from this equation we can state

$$\text{pH} \propto [\text{HCO}_3^-] / p\text{CO}_2(\text{a}) \quad \text{Eqtn. 2}$$

or in words: pH is proportional to, or determined by, the ratio of bicarbonate concentration $[\text{HCO}_3^-]$ to $p\text{CO}_2(\text{a})$. So long as the ratio remains within normal limits, pH remains within normal limits. **Equation 2** also allows that acidemia (reduced blood pH) can result from either a decrease in bicarbonate concentration $[\text{HCO}_3^-]$ or increase in $p\text{CO}_2(\text{a})$; whilst alkalemia (increased blood pH) can result from either an increase in bicarbonate concentration $[\text{HCO}_3^-]$ or decrease in $p\text{CO}_2(\text{a})$.

Since $p\text{CO}_2(\text{a})$ is determined by the rate of respiratory ventilation, it is referred to as the respiratory component of acid-base balance, and bicarbonate is referred to as the non-respiratory or metabolic component of acid-base balance. This nomenclature is used to identify the four main classes of primary acid-base disturbance listed in **Table I** below. The third column in this table highlights the quite normal compensatory response to primary acid-base disturbance, which aims to restore normal pH by restoring the ratio described in equation 2 above. For example, the reduced pH that occurs in metabolic acidosis is a consequence of primary reduction

in bicarbonate concentration $[\text{HCO}_3^-]$. The compensatory response is increased respiratory ventilation and thereby reduction in $p\text{CO}_2(\text{a})$. Although both $[\text{HCO}_3^-]$ and $p\text{CO}_2(\text{a})$ are abnormally reduced, the ratio that determines that pH is normal or at least closer to normal was the case prior to compensation. Compensation of acid-base disorders underlines the prime physiological importance of maintaining ECF pH within normal limits.

Metabolic disturbances provoke a respiratory compensatory response, and respiratory disturbances provoke a compensatory metabolic response via renal regulation of bicarbonate and hydrogen-ion excretion. The renal mechanisms involved in metabolic compensation for respiratory acid-base disturbances are slower than those involved in respiratory compensation for metabolic disturbances (days compared to hours). Compensation may be complete (pH restored to normal limits) but more often is partial (pH returns towards normal but remains just outside normal range).

Although each of the four acid-base disturbances can occur in isolation, some patients with multiple medical conditions may be suffering more than one, or even more than two types of acid-base disturbance. So for example, a diabetic patient in ketoacidosis who also has a history of chronic lung disease may well present with a mixed acid-base disorder (compensated metabolic acidosis due to diabetes, and compensated respiratory acidosis due to chronic lung disease).

Base excess – a measure of the metabolic component of acid-base disorders

In accordance with the traditional approach to acid-base physiology, we have seen that blood pH is determined by the respiratory component ($p\text{CO}_2(\text{a})$) and the non-respiratory (metabolic) component ($[\text{HCO}_3^-]$). Elucidation of acid-base disorders, particularly mixed disorders, is helped by quantitating the individual contribution that each of these two components is making to the patient's pH. $p\text{CO}_2(\text{a})$ is a reliable defining index of the respiratory component, but $[\text{HCO}_3^-]$ is an unsatisfactory index of the metabolic component, not least because it can be affected by change in $p\text{CO}_2(\text{a})$ [1].

Acid-base disturbance	Initial (uncompensated) blood gas values	Type of compensation – resulting blood gas values
Metabolic acidosis (primary decrease in $[\text{HCO}_3^-]$)	pH reduced (<7.35) $[\text{HCO}_3^-]$ reduced (<23 mmol/L) $p\text{CO}_2(\text{a})$ normal (4.7-6.0 kPa) (35-45 mmHg)	Respiratory increased ventilation pH now closer to normal, may be low normal $[\text{HCO}_3^-]$ unchanged – still reduced $p\text{CO}_2(\text{a})$ now reduced
Metabolic alkalosis (primary increase in $[\text{HCO}_3^-]$)	pH increased (>7.45) $[\text{HCO}_3^-]$ increased (>28 mmol/L) $p\text{CO}_2(\text{a})$ normal (4.7-6.0 kPa) (35-45 mmHg)	Respiratory decreased ventilation pH now closer to normal $[\text{HCO}_3^-]$ unchanged – still increased $p\text{CO}_2(\text{a})$ now increased
Respiratory acidosis (primary increase in $p\text{CO}_2(\text{a})$)	pH reduced (<7.35) $[\text{HCO}_3^-]$ normal (23-28 mmol/L) $p\text{CO}_2(\text{a})$ increased (>6.0 kPa) (>45 mmHg)	Metabolic – renal adjustments pH now closer to normal, may be low normal $[\text{HCO}_3^-]$ now increased $p\text{CO}_2(\text{a})$ unchanged, still increased
Respiratory alkalosis (primary decrease in $p\text{CO}_2(\text{a})$)	pH increased (>7.45) $[\text{HCO}_3^-]$ normal (23-28 mmol/L) $p\text{CO}_2(\text{a})$ decreased (<4.7 kPa) (<35 mmHg)	Metabolic – renal adjustments pH now closer to normal, may be high normal $[\text{HCO}_3^-]$ now decreased $p\text{CO}_2(\text{a})$ unchanged, still decreased

TABLE I: The four acid-base disturbances (with metabolic component $[\text{HCO}_3^-]$ highlighted)

An alternative to bicarbonate as an index of the metabolic component is base excess (BE), a parameter devised from experimentation and traditional acid-base theory by Siggaard-Andersen in 1960 [2].

BE can be defined as the concentration of strong acid or strong base (expressed in mmol/L) required to return the pH of an *in vitro* sample of whole blood to pH 7.40, whilst $p\text{CO}_2(\text{a})$ of the sample is maintained at 5.32 kPa (40 mmHg) and temperature of the sample is maintained at 37 °C [3]. (Note that the pH and $p\text{CO}_2(\text{a})$ values in this definition are at the midpoint of their respective reference range.)

By artificially maintaining the $p\text{CO}_2(\text{a})$ of an *in vitro* blood sample within normal limits, any deviation from normal pH 7.40 must be due to the total effect of the non-respiratory metabolic component (which includes the bicarbonate contribution). If there is no deviation, i.e. the *in vitro* sample with $p\text{CO}_2(\text{a})$ 5.32 kPa already has a pH of 7.40, no added strong acid or base is required and base excess is therefore zero.

Normal base excess, i.e. 0 mmol/L (range -3 mmol/L to $+3$ mmol/L), indicates that any deviation from normal pH (i.e. <7.35 or >7.45) is due solely to deviation from normal of the respiratory component, $p\text{CO}_2(\text{a})$.

Returning to the definition above: “BE is the concentration of acid or base required to etc. etc.” explains why BE could have a positive or negative value. If the *in vitro* sample was >7.40 (relatively alkalotic), then acid would be needed to return pH to 7.40, whereas if the sample was <7.40 (relatively acidotic), then base would be needed to return the pH to 7.40. In the first case BE would have a positive value (i.e. the sample has relatively too much base), and in the second case, BE would have negative value (i.e. the sample has not enough base). Thus, an abnormally negative base excess (e.g. BE -8 mmol/L) indicates metabolic acidosis and an abnormally positive base excess (e.g. BE $+8$ mmol/L) indicates metabolic alkalosis. The higher the number (integer), the more severe is the metabolic disturbance. A negative BE is sometimes referred to as a base deficit (BD).

Calculation of BE – distinction between Actual BE (ABE) and Standard (SBE)

From his original *in vitro* titration work on whole-blood samples Siggaard-Andersen developed a complex equation which he named the Van Slyke equation in honor of the US luminary of acid-base physiology, Donald Van Slyke [4]. This equation allows calculation of whole-blood base excess from plasma pH, plasma bicarbonate [HCO_3^-] and blood hemoglobin concentration [Hb] in mmol/L:

$$\text{BE} = \{[\text{HCO}_3^-] - 24.4 + (2.3 \times [\text{Hb}] + 7.7) \times (\text{pH} - 7.4)\} \times (1 - 0.023 \times [\text{Hb}]) \quad (\text{Eqtn. 3})$$

The base excess derived from this equation is, confusingly, variously described in the literature as:

- base excess (BE)
- actual base excess (ABE),
- whole-blood base excess (BE_{blood}) or
- concentration of base in blood(B), cBase(B).

Although the *in vitro* accuracy of this expression of base excess has been confirmed [5], it is less satisfactory than this implies because it has been shown to be affected by extreme *in vivo* change in $p\text{CO}_2(\text{a})$ [6, 7] – it is apparently not a truly CO_2 -invariant parameter, as it ideally needs to be.

The CO_2 invariance of this expression of base excess *in vitro* but not *in vivo* is attributed to the fact that *in vivo* buffering occurs throughout the total ECF (i.e. intravascular plus interstitial) and not just the intravascular ECF as reflected in isolated (*in vitro*) blood samples. This whole-blood base excess effectively overestimates the buffering effect of hemoglobin *in vivo*.

To overcome this problem a modified version of the Van Slyke equation was devised [7] which better simulates the buffering effect of hemoglobin throughout the whole ECF. Rather than input the patients actual blood hemoglobin concentration, a standardized hemoglobin concentration of a third of normal value (15 g/dL

or 150 g/L) is used (i.e. 5 g/dL or 50 g/L). All other elements of the Van Slyke equation (Eqtn. 3 above) remain unchanged. The simple expedient of using a standardized low hemoglobin concentration (5 g/dL) or, as in some algorithms, (3 g/dL) rather than the patient's actual hemoglobin concentration renders a base excess value that is CO_2 -invariant, i.e. not affected by change in $p\text{CO}_2(\text{a})$.

The base excess derived from this modified equation is, confusingly, variously described in the literature as:

- base excess (BE)
- standard base excess (SBE),
- base excess of extracellular fluid (BE_{ecf}), or
- concentration of base in extracellular fluid (ECF), cBase(ECF).

To illustrate the practical significance of the difference between the two expressions of base excess, consider the blood gas results from a patient with Type 2 respiratory failure and fluctuating $p\text{CO}_2(\text{a})$ (Table II below) reported by Morgan [8]. If base excess is a truly CO_2 -invariant parameter, then this patient's base excess should not have been affected by the 2 hour decrease in $p\text{CO}_2(\text{a})$ from 172 mmHg to 124 mmHg since his metabolic acid-base status ([HCO_3^-]) was unchanged. In fact, actual base excess increased significantly (>4 mmol) but standard base excess increased very little (1.6 mmol/L).

Because standard base excess is less affected by *in vivo* change in $p\text{CO}_2(\text{a})$ than actual base excess, it is widely considered to be the preferable index of the metabolic component [7, 9, 10, 11]. Results of a 2009 study [12], however, suggest that in critically ill patients, standard base excess may not be as independent of $p\text{CO}_2(\text{a})$ as was once supposed.

Base excess, compensation and mixed acid-base disorders

By definition base excess remains normal (in the range of -3 to +3) in the two acute (uncompensated) respiratory acid-base disorders: acute respiratory acidosis and

	Reference range	Patient's initial results	Results 2 hours later
pH	7.35-7.45	7.16	7.30
$p\text{CO}_2(\text{a})$ (mmHg)	35-45	172	124
$[\text{HCO}_3^-]$ (mmol/L)	22-28	59	59
Actual Base Excess (mmol/L)	-3 to +3	19.1	23.5
Standard Base Excess (mmol/L)	-3 to +3	29.1	30.7

TABLE II: Blood gas results from a patient with Type 2 respiratory failure [adapted from ref 8]

Acid-base disturbance	Initial (uncompensated) blood gas values	Type of compensation – resulting blood gas values
Metabolic acidosis (primary decrease in $[\text{HCO}_3^-]$)	pH reduced (<7.35) BE abnormal (<-3 mmol/L) $p\text{CO}_2(\text{a})$ normal (4.7-6.0 kPa) (35-45 mmHg)	Respiratory increased ventilation pH now closer to normal, may be low normal BE remains unchanged and abnormal $p\text{CO}_2(\text{a})$ now reduced
Metabolic alkalosis (primary increase in $[\text{HCO}_3^-]$)	pH increased (>7.45) BE abnormal ($>+3$ mmol/L) $p\text{CO}_2(\text{a})$ normal (4.7-6.0 kPa) (35-45 mmHg)	Respiratory decreased ventilation pH now closer to normal BE remains unchanged and abnormal $p\text{CO}_2(\text{a})$ now increased
Respiratory acidosis (primary increase in PaCO_2)	pH reduced (<7.35) BE normal (-3 to $+3$ mmol/L) $p\text{CO}_2(\text{a})$ increased (>6.0 kPa) (>45 mmHg)	Metabolic – renal adjustments pH now closer to normal, may be low normal BE abnormal ($>+3$ mmol/L) $p\text{CO}_2(\text{a})$ unchanged, still increased
Respiratory alkalosis (primary decrease in $p\text{CO}_2(\text{a})$)	pH increased (>7.45) BE normal (-3 to $+3$ mmol/L) $p\text{CO}_2(\text{a})$ decreased (<4.7 kPa) (<35 mmHg)	Metabolic – renal adjustments pH now closer to normal, may be high normal BE abnormal (<-3 mmol/L) $p\text{CO}_2(\text{a})$ unchanged, still decreased

TABLE III: The four acid-base disturbances (with metabolic index, base excess (BE) highlighted)

acute respiratory alkalosis. Base excess is abnormal (<-3) in primary metabolic acidosis and abnormal ($>+3$) in primary metabolic alkalosis. Base excess is also abnormal during metabolic compensation for primary respiratory disorders. **Table III** is a summary of this information with BE values (highlighted).

The four equation rules in **Table IV** below, developed from a 1998 study [13], help in predicting appropriate compensation for primary acid-base disturbance. If these rules are not reflected in patient results, it suggests either incomplete compensation or that more

complex, mixed acid-base disorders are contributing to the patient's acid-base status.

These derived equation rules allow calculation of the approximate expected compensatory response to primary acid-base disorders.

Thus, for example, supposing we have a patient whose clinical history (chronic obstructive pulmonary disease (COPD)), and blood gas results (pH 7.34, $p\text{CO}_2(\text{a})$ 60 mmHg (7.98 kPa), SBE +7.6 mmol/L) indicate chronic (compensated) respiratory acidosis. We can use the

Acid-base disturbance	Equation rule
1. Acute respiratory acidosis/alkalosis	$\Delta\text{SBE} = 0 \times \Delta\text{PaCO}_2$
2. Chronic respiratory acidosis/alkalosis	$\Delta\text{SBE} = 0.4 \times \Delta\text{PaCO}_2$
3. Metabolic acidosis	$\Delta\rho\text{CO}_2(\text{a}) = \Delta\text{BE}$
4. Metabolic Alkalosis	$\Delta\rho\text{CO}_2(\text{a}) = 0.6 \times \Delta\text{BE}$

TABLE IV: The four $\rho\text{CO}_2(\text{a})/\text{SBE}$ rules [13]

Note: ΔSBE = amount that patient's standard base excess (SBE) deviates from normal (0 mmol/L);

$\Delta\rho\text{CO}_2(\text{a})$ = amount that patient's $\rho\text{CO}_2(\text{a})$ deviates from normal (40 mmHg).

above **rule 2** to confirm that the abnormal SBE is due to metabolic compensation alone. In this case $(0.4 \times \Delta\rho\text{CO}_2(\text{a})) = 0.4 \times 20 = 8$, which is, more or less, equal to the patient's SBE. We can therefore conclude that the metabolic compensation reflected in the SBE is appropriate, and that these blood gas results are internally consistent with a single acid-base disorder, namely chronic (i.e. compensated) respiratory acidosis. If the SBE were in fact significantly less or more than +7.6 mmol/L, then consideration should be given to the possibility that the acid-base status of this patient is more complex than previously thought, and might reflect a mixed disturbance (e.g. chronic respiratory acidosis and metabolic acidosis or chronic respiratory acidosis and chronic respiratory alkalosis).

Rule 3 states that in metabolic acidosis, the compensatory change in $\rho\text{CO}_2(\text{a})$ (measured in mmHg) is approximately identical to the change in SBE that induced it. Thus, consider a case of metabolic acidosis in which SBE is -15 mmol/L, i.e. ΔSBE is 15. Respiratory compensation for this degree of metabolic acidosis should, according to the rule, result in a $\Delta\rho\text{CO}_2(\text{a})$ of 15. This represents a measured $\rho\text{CO}_2(\text{a})$ of $(40 - 15) 25$ mmHg. Thus, a single acid-base disorder (namely, compensated metabolic acidosis) is confirmed in a patient with SBE -15 mmol/L, if $\rho\text{CO}_2(\text{a})$ is approximately equal to 25 mmHg (3.32 kPa).

Rule 1 reminds that acute (as opposed to chronic) respiratory acid-base disorders are not associated with significant metabolic compensation (because the renal mechanism involved is relatively slow), and in such cases BE remains within normal limits, i.e. $\Delta\text{SBE} = 0$, irrespective of the $\rho\text{CO}_2(\text{a})$.

Summary

- Base excess is a calculated parameter generated during blood gas analysis.
- The clinical utility of base excess is as an index of the metabolic (non-respiratory) component of acid-base balance; it is therefore helpful in assessing patient acid-base status.
- There are two expressions of base excess: actual base excess (ABE) and standard base excess (SBE) that differ very slightly in the way they are calculated.
- SBE (alternative nomenclature: BE_{ecf} and cBase(ECF)) is widely considered to be preferable to ABE because it is less affected by change in $\rho\text{CO}_2(\text{a})$.
- In health, base excess (SBE and ABE) is maintained within the approximate reference range of minus (-)3 mmol/L to plus (+)3 mmol/L.
- Base excess (SBE and ABE) is abnormal in metabolic acidosis and metabolic alkalosis – abnormally negative value in metabolic acidosis and abnormally positive value in metabolic alkalosis.
- The magnitude of the deviation from normal (reference) range of base excess (SBE and ABE) is indicative of the severity of metabolic acidosis and metabolic alkalosis.
- Base excess (ABE and SBE) is unaffected by respiratory acid-base disturbances unless they provoke metabolic compensation.
- Compensation for respiratory acidosis is associated with abnormally positive base excess value (ABE and SBE). Compensation for respiratory alkalosis is associated with abnormally negative base excess value (ABE and SBE).
- Base excess (SBE) results are used in "rule of thumb" calculations to assess compensation for acid-base disturbances.

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