



LUND UNIVERSITY

Determination of base excess in umbilical cord blood at birth: accessory or excess?

Olofsson, Per

Published in:
American Journal of Obstetrics and Gynecology

DOI:
[10.1016/j.ajog.2015.06.037](https://doi.org/10.1016/j.ajog.2015.06.037)

2015

Document Version:
Peer reviewed version (aka post-print)

[Link to publication](#)

Citation for published version (APA):
Olofsson, P. (2015). Determination of base excess in umbilical cord blood at birth: accessory or excess? *American Journal of Obstetrics and Gynecology*, 213(3), 259-261. <https://doi.org/10.1016/j.ajog.2015.06.037>

Total number of authors:
1

General rights

Unless other specific re-use rights are stated the following general rights apply:
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

EDITORIAL

Am J Obstet Gynecol. 2015 Sep;213(3):259-61. doi: 10.1016/j.ajog.2015.06.037.

Determination of base excess in umbilical cord blood at birth – accessory or excess?

Per Olofsson, MD, PhD, BSc

Professor, Senior Consultant

Department of Obstetrics and Gynecology, Skåne University Hospital, Malmö, and Institution of Clinical Sciences, Lund University, Malmö, Sweden

Email per.olofsson@med.lu.se

The author reports no conflict of interest and no financial support associated with this article

To maintain acid-base homeostasis in the body, a series of buffering systems work to counteract the large and continuously ongoing metabolic production of hydrogen ions. The major buffering systems are bicarbonate in plasma and proteins in erythrocytes, among which hemoglobin is prime. The carbonic acid-bicarbonate equilibrium is of utmost importance because by the reaction $H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$ an excess of H^+ is neutralized and disposed as carbon dioxide and water. The fetus is then dependent of a CO_2 escape across the placenta and a further disposal by the maternal respiration.

The placental circulation is to some degree always affected in labor and a benign fetal respiratory acidemia due to hypercapnia normally develops. In contrast, acidemia due to hypoxia with anaerobic metabolism may develop into metabolic acidosis with disturbances of cellular functions and enzyme activity with potentially deleterious effects on the newborn. It is therefore of value in acidemic newborns to determine the type of acidemia.

In the 1950s Siggaard-Andersen and Engel proposed the use of base excess (BE) as a measure of the non-respiratory component in acid-base status, the metabolic acid accumulation (1). Siggaard-Andersen (2) later presented a Van Slyke equation to calculate BE, where BE is defined as the amount of base or acid needed to restore the pH to a physiological level of 7.4 at a pCO_2 of 5.33 kPa (40 mmHg) at 37 °C (98.6 °F). Thus, BE is an artificial measure that is calculated but not analyzed in the blood gas analyzer. BE is calculated either in blood as actual BE, or in the extracellular fluid (ecf) compartment as standard BE. At birth most BE values are negative and the term base deficit (BD) is then synonymously used.

The rationale for adding BD to pH determinations is to distinguish between respiratory and metabolic acidemia. In the early stage of an impaired placental circulation, hypoxemia and hypercapnia result in a decrease in pH with BD maintained normal (respiratory acidemia), whereas if the hypoxic process develops into a sustained anaerobic metabolism the BD rises secondary to lactic acidosis and consumption of buffer. Metabolic acidosis is in obstetrics defined as a low umbilical cord pH (usually <7.1, <7.05 or <7.0) plus a high BD (usually >12.0 or >16.0 mmol/L). The threshold BD >12.0 mmol/L, with no reference to blood or ecf, was established by Low et al. (3).

Many physicians might be unaware of the fundamental principle of fluid compartment when assessing cord blood BD. In contrast to adults, in the hypoxic fetus there could be a fairly large difference in BD value when calculated in blood and when calculated in ecf, but few

researchers have recognized that BD in blood (BD_{blood}) and BD in ecf (BD_{ecf}) are calculated differently and that different blood gas analyzers use different algorithms to calculate BD (4,5). The intra-analyzer difference between BD_{blood} and BD_{ecf} might be up to 426% (5). Similarly, the resultant metabolic acidosis prevalence will vary between different blood gas analyzers (5).

BD is a measure of acid-base shift not only in the carbonic acid-bicarbonate system, but also in all other buffering systems in the body. Compared to the adult, the fetus has a higher hemoglobin and a lower plasma protein concentration and a relatively larger extravascular fluid compartment; as H^+ ions are produced in the tissues and mostly exist outside the blood compartment, several researchers agree on that BD_{ecf} best represents the fetal exposure and response to hypoxia by its capacity to buffer H^+ ions, but hitherto the calculation algorithm has not been standardized. The probably most frequently used BD_{ecf} algorithm is derived from the Siggaard-Andersen acid-base chart (2): BD_{ecf} (in SI units) = $-0.9149 \times (0.23 \times pCO_2 \times 10^{[pH-6.1]} - 24.1 + 16.21 \times [pH - 7.4])$ (4).

Umbilical cord blood gas analysis at birth provides a retrospective objective measure of the fetus' aerobic and anaerobic intrauterine metabolism, used not only to assess the course of labor and management in individual births, but it is also as an important measure in cases of litigation, in education, for quality assurance of maternity units, and as an outcome parameter in clinical research. However, there is no consensus on whether to perform the analysis in selected births or as a routine. In support of routine analyses, Malin et al. (6) have pointed out that the association between a low cord artery pH and neonatal mortality is stronger in an unselected population than in a high-risk population. A policy of routine umbilical cord acid-base assessment at birth has been in effect at James Low's maternity unit since 1984 (3) and at the author's unit since 1981. In Sweden cord blood acid-base status at birth is routine care, with an 84% average determination rate among deliveries in 2013 (7). In a recent inquiry, only 1% of parturients found the sampling procedure disturbing and a majority was not aware of it being done (8).

Unless severely affected, there is a poor correlation between the newborn's vitality and acid-base status, and only a minority of cerebral palsies is caused by intrapartum hypoxic events. In cases of litigation, a cord blood gas analysis can more often help than trouble the blamed; if no blood gases are available it is difficult to prove that an adverse outcome was not due to intrapartum asphyxia, if blood gases exist and they are abnormal it makes little difference, but if blood gases exist and they are more or less normal it strongly tells against mismanagement of labor.

It is unanimously accepted that it is the metabolic component of acidemia that associates with neonatal morbidity, but in this issue of the *Journal* Knutzen et al. (9) challenge the concept that determination of BD in umbilical cord blood adds to pH in the evaluation and management of acidemic newborns. In a study of 8797 term, singleton, non-anomalous neonates, where 520 were acidemic ($pH < 7.1$) and 84 were severely acidemic ($pH < 7.0$), they found in associations with Apgar score < 7 at 5 minutes, hypoxic-ischemic encephalopathy Sarnat stage 2 or 3, neonatal intensive care unit admission, and a composite adverse outcome parameter, that adding BD_{ecf} to pH did not improve the prediction of adverse outcomes once pH was taken into account. The apparently worse outcomes associated with a higher BD_{ecf} simply reflect a greater degree of acidemia.

The ability of pH and BD to reflect a depressed vitality at birth has been addressed also in other studies, where some have shown pH to be better than BD, some studies equally good (or bad), but no study that BD is better than pH. In contrast to Knutzen et al. (9), Ramin et al. (10) in a recent review argue that BD is the most important variable for reflecting neonatal morbidity. They state that a cord artery pH of <7.0 is a practical threshold for defining pathological fetal acidemia, but that pH alone is not a strong interpreter of neonatal outcome because only acidosis with a metabolic component is associated with an increased risk of neonatal morbidity or mortality. Supporting the findings of Knutzen et al. (9), Wiberg et al. (11) and Georgieva et al. (12) in series of 13,735 and 34,510 deliveries, respectively, found that addition of BD to pH did not improve the predictability of an adverse perinatal outcome. Wiberg and coworkers have pointed out that the power of BD to indicate neonatal distress decisively depends on the choice of fetal fluid compartment and the choice of algorithm to calculate BD (4).

The accuracy of the BD algorithms is apparently a problem and it has been suggested that the actual oxygen saturation and the type of hemoglobin should be included in the algorithm, and that lactate should replace BD. A fact that has been ignored in the literature is that cord lactate and blood gases, except venous pCO_2 , change by progression of pregnancy (13,14). Therefore, gestational age-adjusted values, including BD, have a better congruence with Apgar score than traditional stationary cutoff values (11).

The controversy about the additional value of umbilical cord BD is not yet sorted out, though much data indicate that BD is not an asset relative to pH in reflecting perinatal outcome. As BD is calculated from pH and pCO_2 values, BD is not an independent parameter and a negative linear relation exists to pH (Fig. 1), illustrating the statement by Knutzen et al. (9) that a high BD_{ecf} in cases of low pH simply reflect a greater degree of acidemia. However, the cord artery BD value is valuable for the neonatologist in assessment and management of the asphyxiated newborn and therefore cannot be omitted from the panel of cord blood acid-base parameters. In any case, a large majority of acidemic newborns are vigorous and in the absence of neurological symptoms they appear not to run an increased risk of developing neurologic or behavioral problems later in life (15).

REFERENCES

1. Siggaard-Andersen O, Engel K. A new acid-base nomogram: and improved method for calculation of the relevant blood acid-base data. *Scand J Clin Lab Invest* 1960;12:177-186.
2. Siggaard-Andersen O. The Van Slyke equation. *Scand J Clin Lab Invest* 1977;37:15-20.
3. Low JA, Lindsay BG, Derrick EJ. Threshold of metabolic acidosis associated with newborn complications. *Am J Obstet Gynecol* 1997;177:1391-1394.
4. Wiberg N, Källén K, Olofsson P. Base deficit estimation in umbilical cord blood is influenced by gestational age, choice of fetal fluid compartment, and algorithm for calculation. *Am J Obstet Gynecol* 2006;195:1651-1656.

5. Mokarami P, Wiberg N, Olofsson P. An overlooked aspect on metabolic acidosis at birth: blood gas analyzers calculate base deficit differently. *Acta Obstet Gynecol Scand* 2012;91:574-579.
6. Malin GL, Morris RK, Khan KS. Strength of association between umbilical cord pH and perinatal and long term outcomes: systematic review and meta-analysis. *BMJ* 2010;340:c1471. doi:10.1136/bmj.c1471.
7. Nyberg C, Falck S, Saltvedt S, Nordström L. Kvinnor positiva till rutinmässig provtagning från navelsträngen vid förlossning. [Women are positive to routine umbilical cord blood acid-base analysis at birth]. *Swedish Society of Obstetrics and Gynecology, Medlemsbladet* 2015;3:34-5. www.sfog.se/medlemsblad/MB35f330ba1-af4d-4c6a-9c5b-a98bbd54ab84.pdf. Accessed July 17, 2015.
8. Swedish Society of Obstetrics and Gynecology. Summarisk rapport för verksamhetsåret 2013. [Summary of Women's Clinics annual report 2013]. *Figure* 2013:45/26, page 29. www.sfog.se/media/193032/summarisk_rapport_sfog_2013.pdf. Accessed July 17, 2015.
9. Knutzen L, Svirko E, Impey L. The significance of base deficit in academic term neonates. *Am J Obstet Gynecol* 2015;213:373.e1-7. doi: 10.1016/j.ajog.2015.03.051.
10. Ramin SM, Lockwood CJ, Barss VA. Umbilical cord acid-base analysis at delivery. UpToDate, Inc. <http://www.uptodate.com/contents/umbilical-cord-blood-acid-base-analysis-at-delivery#> (Accessed June 10, 2015).
11. Wiberg N, Källén K, Herbst A, Olofsson P. Relation between umbilical cord blood pH, base deficit, lactate, 5-minute Apgar score and development of hypoxic ischemic encephalopathy. *Acta Obstet Gynecol Scand* 2010;89:1263-1269.
12. Georgieva A, Moulden M, Redman CWG. Umbilical cord gases in relation to the neonatal condition: the EverEst plot. *Eur J Obstet Gynecol Repr Biol* 2013;168:155-160.
13. Laczna Kitlinski M, Källén K, Marsál K, Olofsson P. Gestational age-dependent reference values for pH in umbilical cord arterial blood at term. *Obstet Gynecol* 2003;102:338-345.
14. Wiberg N, Källén K, Olofsson P. Physiological development of a mixed metabolic and respiratory umbilical cord blood acidemia with advancing gestational age. *Early Hum Dev* 2006;82:583-589.
15. Hafström M, Ehnberg S, Blad S, Norén H, Renman C, Rosén KG, Kjellmer I. Developmental outcome at 6.5 years after acidosis in term newborns: a population-based study. *Pediatrics* 2012;129(6):e1501.

Figure 1. Base deficit relative to pH in umbilical cord blood.

Relation between pH and base deficit in extracellular fluid (BD_{ecf}) in umbilical cord arterial blood at birth ($N=15,354$; cubic polynomial regression, $P<0.0001$, $|R|=0.62$). For BD_{ecf} calculation algorithm, see text (4). Data retrieved from the author's database.

