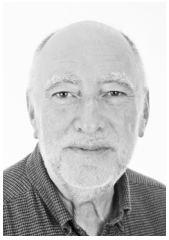
Why measure blood gases? A three-part introduction for the novice - Part 1

January 2012



Chris Higgins
Little Acre, Main Road
Shurdington
Nr Cheltenham
Gloucester
GL51 4XF, UK
E-mail: cjhiggins@hotmail.co.uk

Summary

Arterial blood gas (ABG) analysis generates a number of parameters (listed in BOX 5) that together allow assessment of pulmonary gas exchange, blood oxygenation and acid-base balance. These physiological functions of the blood, respiratory and renal systems are disturbed in a range of respiratory and non-respiratory diseases.

The application of ABG analysis in diagnosis and monitoring of these diseases will be considered in two future articles, where the focus will be the clinical significance of abnormal ABG results.

Abstract

Arterial blood gases (ABG), a clinical test that involves measurement of the pH of arterial blood and the amount of oxygen and carbon dioxide dissolved in arterial blood, is routinely used in the diagnosis and monitoring of predominantly critically/acutely ill patients being cared for in emergency rooms and intensive care units. Additionally, ABG is useful in delivery of clinical care to some patients with acute and chronic respiratory disease in medical wards and outpatient departments.

In broad terms the test allows assessment of two related physiological functions: the facility of the lungs to simultaneously add oxygen to blood and remove carbon dioxide from blood (the dual process called pulmonary gas exchange), and the ability of the body to maintain the pH of blood within narrow healthy limits (acid-base balance). This is the first of three articles intended to explain the clinical value of ABG to those with little or no experience of the test.

In two future articles the focus will be the clinical significance of abnormal ABG results, but this first article is concerned with the physiological aspects that underpin the understanding of patient ABG results. The ABG parameters generated during analysis will be defined here and their relationship to pulmonary gas exchange and acid-base balance discussed. The article begins with consideration of some relevant aspects of respiratory physiology.

Respiratory physiology

Oxygen is fundamental to life. The cells of all human tissues derive the energy they require to survive and function from the continuous aerobic metabolism of dietary-derived nutrients (carbohydrates, fats, etc.).

This aerobic metabolism requires a constant supply of oxygen and results in a continuous production of carbon dioxide, a waste product that must be eliminated from the body.

The delivery of oxygen to, and removal of carbon from tissue cells is a major function of blood that occurs in tissues where the smallest blood vessels (microcapillaries) surround each tissue cell.

Blood returning in veins to the heart from this tissue microvasculature (i.e. venous blood) is thus oxygen depleted and relatively rich in carbon dioxide.

By contrast, arterial blood, which flows in arteries from the heart back to the microvasculature of tissues, is rich in oxygen (said to be oxygenated) and relatively depleted of carbon dioxide due to the pulmonary gas exchange that occurs when venous blood is diverted from the heart to the lungs (via the pulmonary artery), before return to the heart (via the pulmonary vein), and then onward journey, via the aorta and arterial system, to the tissues.

Pulmonary gas exchange, central to the process of respiration, accounts for the vital role that the lungs play in the delivery of oxygen to tissue cells and the elimination of carbon dioxide from the body.

The dual objective of respiration is transfer of oxygen present in inspired air to venous blood (blood oxygenation) and elimination of carbon dioxide from venous blood to the environment in expired air.

The site of gaseous exchange between blood and air within the lungs is the alveolar-capillary membrane, which comprises two elements: the alveolar membrane that lines the microscopic, bubble-like, cul-de-sacs of lung structure called alveoli; and the endothelium (wall) of blood microcapillaries.

The millions of alveoli and their network of tiny blood capillaries provide a massive membrane surface area for gas exchange: around 80 sq. meters in each adult lung. On one side of the alveolar-capillary membrane is alveolar air (essentially inspired air); on the other is venous blood.

The membrane is very thin (of the order 0.3 µm) allowing gases (oxygen and carbon dioxide) to diffuse easily from alveoli to blood and blood to alveoli.

The direction and rate of this diffusion is governed by the amount or partial pressure of each gas on either side of the membrane.

Gases diffuse from areas of high partial pressure to areas of low partial pressure. (For an explanation of partial pressure, essential for understanding ABG results, see Box 1).

The partial pressure of oxygen (pO_2) in alveolar air is higher (~13 kPa or 100 mmHg) than that of the venous blood (~5.3 kPa or 40 mmHg) flowing on the other side of the membrane, so oxygen diffuses from the alveoli to blood.

Conversely, the partial pressure of carbon dioxide ($pCO2$) of alveolar air (~5 kPa) is lower than that of venous blood (~6 kPa) so CO_2 diffuses from blood to the alveoli.

Maintenance of two measured ABG parameters, $pO_2(a)$ and $pCO_2(a)$ within normal limits implies effective pulmonary gas exchange, **which is dependent on**:

- Adequate alveolar ventilation. This is the movement of air in and out of alveoli due to the mechanical process of breathing that depends on the chest musculature and elastic recoil of the lungs.
- Normal numbers of functioning alveoli.
- Normal thickness of alveolar-capillary membrane.

The amount of gas in any system is defined by the pressure it exerts, traditionally measured as height in millimeters (mm) of a column of mercury (Hg). For example, the pressure of atmospheric air (i.e. barometric pressure) at sea level is 760 mmHg. This means that at sea level, the gases contained in the air we breathe have a combined pressure sufficient to support a column of mercury 760 mm high.

In a mixture of gases, as air is, the total pressure is simply the sum of the partial pressures (represented by the symbol p) of each gas. Air comprises 21 % oxygen, 0.03 % carbon dioxide and 78% nitrogen so partial pressure of oxygen (pO_2) in inspired air is 21 % of total atmospheric pressure (21/100x760) i.e. 150mmHg and the partial pressure of carbon dioxide pCO_2 is 0.03 % of 760, i.e. 0.02 mmHg.

The SI unit of pressure used in clinical medicine outside of North America is the kilopascal (kPa). To convert values in the traditional unit (mmHg) to the equivalent SI unit (kPa) value, simply multiply by 0.133.

It is important to note that these are a measure only of the amount of gas that is dissolved in arterial blood (or venous blood), not the total amounts. For example, most of the oxygen in blood is bound to the protein hemoglobin. This protein-bound oxygen is not included in the pCO_2 measurement (see text).

Box 1: A note on partial pressure (*p*)

- Sufficient blood flow through pulmonary capillaries (i.e. adequate alveolar perfusion).
- No significant ventilation / perfusion mismatch (mismatch occurs, for example, if alveoli are well perfused with blood but inadequately ventilated with air).
- Intact brain stem (explained below).

Ventilation is continuously regulated, principally by respiratory centers located in the brain stem. These respond to the amount of CO_2 in arterial blood (i.e. the pCO_2(a)), detected by closely associated chemoreceptor cells. By their neural connection to the chest musculature involved in breathing, these respiratory centres increase the rate and depth of breathing, and thereby increase alveolar ventilation, if pCO_2 is rising and reduce alveolar ventilation if pCO_2(a) is falling.

By this means sufficient CO_2 is eliminated in expired air to maintain pCO_2(a) within narrow normal limits.

Inappropriately reduced ventilation (hypoventilation) leads to inadequate pulmonary gas exchange, evident on blood gas analysis as increased pCO_2 and decreased pO_2(a).

Hyperventilation (overbreathing) is always associated with decreased pCO_2(a) but not necessarily, as might be supposed, increased pO_2(a).

Blood transport of oxygen - two ABG parameters (pO_2(a) and sO_2)

Partial pressure of oxygen in arterial blood (pO_2(a)) is not the only parameter measured during ABG that reflects blood oxygenation; the other is oxygen saturation (sO_2).

As is the convention with pO_2 (see Box 1), the symbol for sO_2 of specifically arterial blood includes the suffix "a" so the ABG parameter of oxygen saturation is sO_2(a).

To understand the difference and relationship between pO_2(a) and sO_2(a), we must examine how oxygen is transported in blood.

Oxygen is poorly soluble in blood and the small amount of oxygen that can be transported simply dissolved in blood (~3.0 mL of oxygen per litre of blood) is quite inadequate to satisfy tissue demand for oxygen.

The oxygen-carrying protein, hemoglobin, contained

in the cells of blood (specifically the red cells or erythrocytes) provides an additional, far more effective, means of transporting oxygen, and increases the oxygen-carrying capacity of blood from ~3.0 to ~200 mL oxygen per litre.

In fact only 1-2 % of the oxygen transported in blood is dissolved in the aqueous phase of blood; this is the portion that is measured by the pO_2(a).

The remaining 98-99 % is transported in erythrocytes bound to hemoglobin.

Each erythrocyte contains 250-300 million hemoglobin molecules and each hemoglobin molecule can bind a maximum of four oxygen molecules.

The product of the reversible binding of oxygen by hemoglobin is called oxyhemoglobin; the term deoxyhemoglobin is used to describe hemoglobin that has no oxygen bound to it.

The oxygen delivery function of hemoglobin, i.e. its ability to "pick up" oxygen in the lungs and "release" it in the microvasculature of tissue cells, is made possible by a reversible conformational change in the quaternary structure (shape) of the hemoglobin molecule that alters its affinity for oxygen. In the deoxy state hemoglobin has low affinity for oxygen and in the oxy state it has high affinity for oxygen.

A number of environmental factors in blood determine the hemoglobin state (deoxy or oxy) and thereby the relative affinity for oxygen.

The most significant of these is the pO_2. Hemoglobin present in blood with relatively high pO_2 has much greater affinity for oxygen than hemoglobin present in blood with relatively low pO_2. The oxygen dissociation curve (ODC) describes this relationship graphically (Fig. 1).

The percentage of total hemoglobin saturated with oxygen (i.e. oxygen saturation, sO_2) is the measure of hemoglobin affinity in this graph.

It is clear from the graph that at the high pO_2 that prevails in the blood exposed to alveolar air in the lung (~13 kPa), hemoglobin is almost 100 % saturated with oxygen; nearly all of the available oxygen-binding sites on the totality of hemoglobin molecules are occupied with oxygen.

By contrast in the milieu of the tissues where pO_2 is much lower, hemoglobin affinity for oxygen is also much lower and oxygen is released from hemoglobin to the tissues.

The hemoglobin in venous blood leaving the tissues consequently has less oxygen bound to it and this is reflected in the much lower sO_2 of venous blood (sO_2(v) ~70 %) compared to that of arterial blood (sO_2(a) >95 %).

Although pO_2(a) only reflects a tiny proportion (1-2 %) of the oxygen in arterial blood, it is highly significant because it determines the amount of oxygen bound to hemoglobin (the sO_2(a)) and thereby the total amount of oxygen that is contained in arterial blood for delivery to tissues. If pO_2(a) is reduced, then less oxygen can be carried by hemoglobin (i.e. sO_2(a) is reduced) and less oxygen is available to tissues.

Examination of the oxygen dissociation curve (Fig. 1) reveals that a significant decrease in pO_2(a) from 16 kPa to 10 kPa has only slight effect on sO_2(a) and therefore the oxygen-carrying capacity of blood, but there is a sharp fall in sO_2(a) as pO_2(a) falls below 10 kPa. The delivery of oxygen to tissues becomes increasingly compromised as pO_2(a) falls below this level.

Although pO_2(a) only reflects a tiny proportion (1-2 %) of the oxygen in arterial blood, it is highly significant because it determines the amount of oxygen bound to hemoglobin (the sO_2(a)) and thereby the total amount of oxygen that is contained in arterial blood for delivery to tissues. If pO_2(a) is reduced, then less oxygen can be carried by hemoglobin (i.e. sO_2(a) is reduced) and less oxygen is available to tissues.

Examination of the oxygen dissociation curve (Fig. 1) reveals that a significant decrease in pO_2(a) from 16 kPa

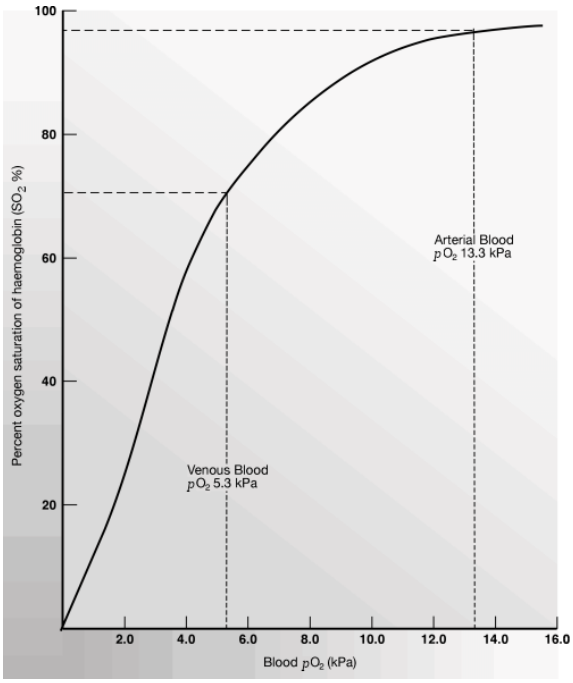


Fig.1: Oxygen dissociation curve. Relationship between the amount of oxygen dissolved in blood (PO2) and the amount of oxygen carried by hemoglobin (SO2).

to 10 kPa has only slight effect on sO_2(a) and therefore the oxygen-carrying capacity of blood, but there is a sharp fall in sO_2(a) as pO_2(a) falls below 10 kPa. The delivery of oxygen to tissues becomes increasingly compromised as pO_2(a) falls below this level.

For optimum oxygenation of tissues:

- Blood must contain an adequate amount of hemoglobin.
- That hemoglobin must be >95 % saturated with oxygen in arterial blood (sO_2(a) >95 %).
- To achieve sO_2 (a) >95 %, pO_2 (a) must be >10.6 kPa (80 mmHg).
- Maintenance of pO_2(a) above 10.6 kPa depends on the factors required for effective pulmonary gas exchange (see above).

Acid-base balance: the maintenance of normal blood pH

In this section we turn the attention away from the ABG parameters that reflect blood oxygenation (pO_2(a), sO_2(a)) to those that reflect acid-base balance. They are: pH, pCO_2(a), bicarbonate concentration (HCO_3^-) and base excess. pCO_2(a) has already been introduced in the discussion of pulmonary gas exchange, and its inclusion here reflects the central role that the lungs play in the maintenance of blood pH.

All biochemical reactions are sensitive to change in pH, so that optimum survival and function of cells require that blood pH is maintained within the narrow range of 7.35-7.45, despite normal cell metabolism being associated with the production of metabolic acids.

Even mild excursion outside the normal range has multiple deleterious effects, and a pH of less than 6.8 or greater than 7.8 is incompatible with life.

The maintenance of normal blood pH is a complex synergy of action involving the chemical buffers present in blood (principally bicarbonate), red blood cells and the function of three organs: the kidneys, lungs and brain stem.

The following discussion assumes an outline understanding of some basic concepts: pH, acids, bases and buffers (see Boxes 2-4 for a reminder).

To understand the maintenance of blood pH and the other ABG parameters used to assess acid-base balance, it is useful to consider the way carbon dioxide (CO_2) is transported in blood from tissue cells to lungs. In the microvasculature of tissues CO_2 diffuses from cells – where it is produced – to blood due to the prevailing pCO_2 gradient (pCO_2 in tissue cells higher than that in blood).

A small amount (~5 %) remains simply dissolved in blood plasma and the cytoplasm of erythrocytes, and a similar amount is carried in erythrocytes bound to hemoglobin that has yielded up its oxygen to tissues, but most (90 %) is hydrated to carbonic acid in erythrocytes by the action of the enzyme carbonic anhydrase. Nearly all (~96 %) of this carbonic acid rapidly dissociates, yielding bicarbonate and hydrogen ions, thus (reaction should be read from left to right):

pH is a logarithmic scale (0 to 14) of acidity/alkalinity. Pure water has a pH of 7 (neutral, i.e. neither acidic nor alkaline). pH above 7is alkaline and pH below 7 is acidic. pH is actually a measure of hydrogen (H) ion concentration and defined as negative log (to the base 10) of the hydrogen ion concentration in moles per litre. thus:

$$pH = -\log_{10}[H^+]$$

where $[H^+]$ = hydrogen ion concentration (mol/l)

From this equation: pH 7.4 = H^+ concentration of 40 nmol/L
pH 7.0 = H^+ concentration of 100 nmol/L
pH 6.0 = H^+ concentation of 1000 nmol/L

From these examples it is evident that:

as pH falls, hydrogen ion increases
also, due to the logarithmic nature of the pH scale, an apparently small change in pH is in fact a large change in hydrogen ion concentration. So, for example, doubling hydrogen ion concentration from 50 to 100 nmol/L is actually only a fall of 0.3 pH units (7.3 to 7.0).

Normal arterial blood pH is 7.35 -7.45 (i.e. $[H^+]$ of 45-35 nmol/L)

Box 2 - A note on pH

An acid is a substance that dissociates in solution to release hydrogen ions. A base accepts hydrogen ions.

For example, hydrochloric acid (HCl) dissociates to hydrogen ions and chlorine ions:

$$HCl \longrightarrow H^+ + Cl^-$$

whereas bicarbonate (HCO_3^-), a base accepts hydrogen ions to form carbonic acid:

$$HCO_3^- + H^+ \rightarrow H_2CO_3$$

Hydrochloric acid is a strong acid, meaning it dissociates easily, yielding many hydrogen ions; it therefore has a low pH.

By contrast, carbonic acid is a weak acid; it dissociates much less easily, yielding fewer hydrogen ions and therefore higher pH than hydrochloric acid.

Box 3 - A note on acids and bases

A chemical buffer is a compound in solution (the conjugate base of a weak acid) that resists change in the pH of the solution when acid is added, by "mopping up" hydrogen ions.

The principal buffer in blood is bicarbonate, which is the conjugate base of the weak acid, carbonic acid. The presence of bicarbonate in blood serves to minimize the change in pH of blood that occurs when acids produced during cell metabolism are released from cells to blood.

To illustrate the buffering action of bicarbonate consider a solution of sodium bicarbonate (the buffer) to which a strong acid, in this case hydrochloric acid, is added. The hydrogen ions resulting from strongly dissociating hydrochloric acid are incorporated in to the weak acid, carbonic acid thus:

$$H^+Cl^- + NaHCO_3 \text{ ------> } H_2CO_3 + NaCl$$

hydrochloric acid sodium bicarbonate carbonic acid sodium chloride

The important point is that because the hydrogen ions from hydrochloric acid have been incorporated into a weak acid that does not dissociate as easily, the total number of hydrogen ions in solution, and therefore the pH, does not change as much as would have occurred in the absence of the buffer.

The pH of any buffered solution is governed by the relative concentration of the weak acid and its conjugate base according to the following so-called Henderson-Hasselbalch equation for bicarbonate buffer in blood:

$$pH = 6.1 + \log \frac{[HC0_3]}{[H_2C0_3]}$$ where $[HC0_3]$ = concentration of bicarbonate
$[H_2C0_3]$ = concentration of carbonic acid

From this equation it is possible to derive an important relationship between three ABG parameters: pH, pCO_2(a) and bicarbonate that aids understanding of acid-base balance (see text).

Box 4 - A note on bicarbonate buffer

$$CO_2x + H_2O \xleftarrow{\text{carbonicanhydrase}} H_2CO_3 \longrightarrow HCO_3^- + H^+$$

The potentially dangerous fall in red-cell pH induced by the influx of hydrogen ions is ameliorated by them combining with reduced hemoglobin (hemoglobin, now stripped of its oxygen is acting as a buffer here). Around 65% of the bicarbonate passes from erythrocytes and is transported in blood plasma; the rest remains in the cytoplasm of erythrocytes.

When venous blood arrives in the capillary networks that surround the alveoli in the lungs, the small amount of CO_2 dissolved in blood passes across the alveolar membrane due to the prevailing pCO_2 gradient. This loss of CO_2 from blood reverses the direction of the above equation (should now be read from right to left) reflecting a reversal of the sequence of events that occurred in the microvasculature of the tissues. So, in blood perfusing the alveoli, hemoglobin releases hydrogen ions as it combines with inspired oxygen.

These hydrogen ions are buffered by (combine with)

bicarbonate to form carbonic acid, which dissociates to carbon dioxide (CO_2) and water. The CO_2 diffuses from blood to alveoli. The process is continuously regulated so that the amount of CO_2 being removed from blood at the lungs equals the amount of CO_2 being added to the blood in the tissues.

To summarize, there are four ways in which CO_2 is transported in blood:

- 5 % is transported simply dissolved in plasma and erythrocyte cytoplasm. pCO_2(a) is a measure of this small portion of total CO_2.
- 90 % is transported as bicarbonate (the principal blood buffer) (the concentration of bicarbonate (mmol/L) is calculated during ABG).
- 5 % is transported loosely bound to hemoglobin in red cells.
- <0.1 % is transported as carbonic acid.

References

1. White C, Doherty D, Henderson J et al. Benefits of introducing universal cord blood gas and lactate analysis into an obstetric unit. Australia and New Zealand J of Obstetrics and Gynaecology 2010; 50: 318-28

2. Westgate J, Garibaldi J, Greene K. Umbilical cord blood gas analysis at delivery: a time for quality data. Br J of Obstetrics and Gynaecology 1994; 101: 1054-63

3. Riley R, Johnson J. Collecting and analyzing cord blood gases. Br J of Obstetrics and Gynaecology 1993; 36: 13-23

4. Sykes G, Johnson P, Ashworth F et al. Do apgar scores indicate asphyxia. Lancet 1982; 319: 494-96

5. Low J. Intrapartum fetal asphyxia: definition, diagnosis and classification. Am J Obstet Gynecol 1997; 176: 957-59

6. Omo-Aghoja L. Maternal and fetal acid-base chemistry: A major determinant of outcome. Annals of Medical and Health Sciences Research 2014; 4: 8-17

7. Liston R, Sawchuck D, Young D et al. Intrapartum Fetal Surveillance (Chapter 2) in: SOGC Clinical Practice Guideline No 197. J Obstet Gynecol Canada 2007; 29 (Suppl 4): S25-S44

8. Thornberg E, Thringer K, Odeback A et al. Birth asphyxia: incidence clinical course and outcome in a Swedish population. Acta Paediatr 1995; 72: 231-37

9. Kumar S, Paterson-Brown S. Obstetric aspects of hypoxic ischemic encephalopathy. Early Human Development 2010; 86: 336-44

10. Kurinczuk J, White-Koning M, Badawi N. Epidemiology of neonatal encephalopathy and hypoxic-ischemic encephalopathy. Early Human Development 2010; 86: 329-38

11. Perlman J. Intrapartum hypoxic-ischemic cerebral injury and subsequent cerebral palsy. Pediatrics 1997; 99: 851-59

12. Peliowski-Davidovich A. Hypothermia for newborns with hypoxic ischemic encephalopathy. Paediatric Child Health 2012; 17: 41-43

13. Mokorami P, Wiberg N, Olofsson P. Hidden acidosis: an explanation of acid-base and lactate changes occurring in umbilical cord blood after delayed sampling. Br J of Obstetrics and Gynaecology 2013; 120: 996-1002

14. Lievaart M, de Jong P. Acid-base equilibrium in umbilical cord blood and time of cord clamping. Obstet Gynecol 1984; 63: 44-47

15. Valero J, Desantes D, Perales-Pulchat A. Effect of delayed umbilical cord clamping on blood gas analysis. Eur J Obstet Reprod Biol 2012; 162: 21-23

16. Armstrong L, Stenson B. Effect of delayed sampling on umbilical cord arterial and venous lactate and blood gases in clamped and unclamped vessels. Arch Dis Child Fetal Neonatal Ed 2006; 91: 342-45

17. Duerbeck N, Chaffin D, Seeds J. A practical approach to umbilical artery pH and blood gas determinations. Obstet Gynecol 1992; 79: 959-62

18. Manor M, Blickstein I, Hazan Y et al. Postpartum determi nation of umbilical artery blood gases: effect of time and temperature. Clinical Chemistry 1998; 44: 681-83

19. NCCLS. Procedures for the Collection of Arterial Blood Specimens; Approved Standard – Fourth Edition. NCCLS document H11-A4. Wayne, PA: National Committee for Clinical Laboratory Standards 2004.

20. Thorp J, Dilly G, Yeomans E et al. Umbilical cord blood gas analysis at delivery. Am J Obstet Gynecol 1996; 175: 517-22

21. Armstrong L, Stenson B. Use of umbilical cord blood gas analysis in the assessment of the newborn. Arch Dis Child Fetal Neonatal 2007; Ed 92: 430-34

22. American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Umbilical cord blood gas and acid-base analysis. Obstet Gynecol 2006; 108: 1319-22

23. McDonald S, Middleton P, Dowsell T et al. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. Cochrane Database of Systematic Reviews 2013, Issue 7.

24. Andersson O, Hellstrom-Westas L, Andersson D et al. Effects of delayed compared with early umbilical cord clamping on postpartum hemorrhage and cord blood gas sampling: a randomized trial. Acta Obstet Gynecol Scand 2012; 92: 567-74

25. Di Tommasso M, Seravalli V, Martini I. Blood gas values in clamped and unclamped umbilical cord at birth. Early Human Development 2014; 90: 523-25

26. National Institute for Health and Care Excellence (NICE). Intrapartum care: Care of healthy women and their babies during childbirth. (Clinical guideline 55) 2007

27. Haken N, Carlsson A. Reduced prevalence of metabolic acidosis at birth: an analysis of established STAN usage in the total population of deliveries in a Swedish district hospital. Am J Obstet Gynecol 2010; 202: 546 e1-7

28. Nordstom L. Lactate measurement in scalp and cord arterial blood. Curr Opin Obstet Gynecol 2001; 13: 141-45

29. Westgren M, Divon M, Horal M et al. Routine measurements of umbilical artery lactate levels in prediction of perinatal outcome. Am J Obstet Gynecol 1995; 173: 1416-22