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## INTERNATIONAL FEDERATION OF CLINICAL CHEMISTRY (IFCC)<sup>1), 2)</sup>

Scientific Division  
Committee on pH, Blood Gases and Electrolytes<sup>3)</sup>

### Approved IFCC Recommendation on Definitions of Quantities and Conventions Related to Blood Gases and pH

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**Summary:** Terminology in blood pH and gas analysis can be confusing, both because more than one name has been used for the same quantity, and because the same name has been used for more than one quantity. In addition, several calculated quantities are commonly used, but in some cases many different algorithms have been published for a single quantity.

This document contains definitions of the most useful quantities in blood pH and gas analysis, and presents algorithms for the most useful calculated quantities. Use of these should lessen confusion among users and should also result in data that are more comparable among laboratories.

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### 1. Introduction

The purpose of this document is to define the most useful quantities in blood pH and gas analysis and to give algorithms for derived quantities. Use of these algorithms, especially for calculations performed within in-

struments, will lead to results that are more comparable among laboratories. The names, units and symbols are intended to be consistent with current IUPAC and IFCC recommendations (1). Many of the recommendations were adopted from the first edition of a closely related document entitled "Tentative Standard for Definitions of Quantities and Conventions Related to Blood pH and Gas Analysis" published by the National Committee for Clinical Laboratory Standards (USA). The second edition of this document has now been published (2) and efforts were made to make these IFCC and NCCLS recommendations internally consistent.

### 2. Selected values used for calculations

Some equations presented in this document require that values appropriate for human blood be selected for certain quantities. Table 1 is a list of these quantities, with units and numerical values that have been adopted. Values were chosen which reflect published experimental data and which are consistent with each other.

### 3. Definition of some measured and derived quantities

#### 3.1 pH

pH is defined (1) as the negative decadic logarithm of the relative molal activity of hydrogen ions. The reference method for blood pH (3) uses a glass electrode sensitive to hydrogen ion and a concentrated KCl bridge solution connected to a reference electrode.

Tab. 1 Selected values used for calculations

Quantity	Symbol	Numerical value <sup>6)</sup>	Unit
Celsius temperature	$\theta$	37,0	°C
Negative hydrogen ion exponent	pH	7,400	
Partial pressure of CO <sub>2</sub>	$p_{CO_2}$	5,33	kPa
Substance concentration of bicarbonate*	$c_{HCO_3^-}$	24,2	mmol · l <sup>-1</sup>
Negative exponent of apparent constant for the CO <sub>2</sub> equilibrium (CO <sub>2</sub> + H <sub>2</sub> O ↔ H <sup>+</sup> + HCO <sub>3</sub> <sup>-</sup> )	$pK'$	6,105	
Concentrational solubility coefficient of CO <sub>2</sub> in plasma	$\alpha_{CO_2}$	0,230	mmol · l <sup>-1</sup> · kPa <sup>-1</sup>
Apparent buffer value of non-bicarbonate buffers in extracellular fluid	$\beta_{ecf}$	14,8	mmol · l <sup>-1</sup>
Concentrational solubility coefficient of O <sub>2</sub> in blood	$\alpha_{O_2}$	0,010	mmol · l <sup>-1</sup> · kPa <sup>-1</sup>
Proton <i>Bohr</i> factor	$\phi_H$	-0,43	
Carbamate <i>Bohr</i> factor	$\phi_C$	0,05	

\* The term "bicarbonate" is used in this document as a synonym for the less-familiar "hydrogen carbonate".

<sup>6)</sup> The decimal sign is a comma.

### 3.2 Partial pressures of carbon dioxide and oxygen

3.2.1 The partial pressure (tension) of a component in a solution is defined as the partial pressure of the component in a hypothetical ideal gas phase in equilibrium with the solution (1). This equilibrium can be attained by tonometry (4).

3.2.2 Standards for  $p_{\text{CO}_2}$  and  $p_{\text{O}_2}$  are prepared from a dry gas mixture of accurately known composition which is then humidified. The partial pressure of gas (G) in the standard is then given by

$$p_G = x_G \cdot (p - p_{\text{H}_2\text{O}}) \quad (\text{Eq. 1})$$

where  $x_G$  is the mol fraction of gas in the dry gas mixture,  $p$  is the ambient pressure and  $p_{\text{H}_2\text{O}}$  is the vapor pressure of water at the equilibrium temperature. If it is necessary to calculate the mol fraction of  $\text{O}_2$  and  $\text{CO}_2$ , gas non-idealities should be taken into account.  $p_{\text{H}_2\text{O}}$  at  $37,0^\circ\text{C}$  is 6,275 kPa.

### 3.3 Substance concentrations of dissolved carbon dioxide and oxygen

Substance concentrations of dissolved carbon dioxide and oxygen are directly proportional to their respective partial pressures.

$$c_G = \alpha_G \cdot p_G \quad (\text{Eq. 2})$$

The proportionality factor  $\alpha$  is called the concentrational solubility coefficient<sup>7)</sup>. Values for  $\alpha_{\text{O}_2}$  in blood and  $\alpha_{\text{CO}_2}$  in plasma at  $37,0^\circ\text{C}$  are given in table 1. The value for  $\text{CO}_2$  was quoted in l. c. (5) as being derived from experimental data (6, 7), as was the value for  $\text{O}_2$  (8–10).

### 3.4 Substance concentrations of total carbon dioxide and of bicarbonate ion

3.4.1 Carbon dioxide participates in several chemical equilibria in plasma and exists in several forms including dissolved  $\text{CO}_2$ ,  $\text{H}_2\text{CO}_3$ ,  $\text{HCO}_3^-$ ,  $\text{CO}_3^{2-}$ , protein carbamates and ion pairs such as  $\text{NaHCO}_3$ ,  $\text{CaHCO}_3^+$  and  $\text{NaCO}_3^-$  (11). The sum of the substance concentrations of each of these species is defined as the substance concentration of total carbon dioxide,  $c_{\text{tCO}_2}$ .

3.4.2 Total carbon dioxide can be measured directly using serum or plasma obtained by anaerobic separation (12, 13). Separation at ambient temperature is acceptable

for most purposes. Total  $\text{CO}_2$  can also be measured in whole blood, and the corresponding concentration in plasma can be accurately calculated (14).

3.4.3 Substance concentration of bicarbonate ion is calculated from total carbon dioxide using equation 3.

$$c_{\text{HCO}_3^-} = c_{\text{tCO}_2} - c_{\text{CO}_2} \quad (\text{Eq. 3})$$

This "bicarbonate" actually includes all  $\text{CO}_2$  species except dissolved  $\text{CO}_2$  and  $\text{H}_2\text{CO}_3$  (5, 15).

3.4.4 Blood gas analyzers calculate substance concentration of bicarbonate from the following form of the Henderson-Hasselbalch equation<sup>8)</sup>, which gives results consistent with equation 3.

$$\lg c_{\text{HCO}_3^-} = \text{pH} - \text{pK}' + \lg p_{\text{CO}_2} + \lg \alpha_{\text{CO}_2} \quad (\text{Eq. 4})$$

Note: Changes in bicarbonate concentration calculated with equation 4 are actually proportional to changes in bicarbonate activity. The calculated bicarbonate concentration is analogous in this regard to a sodium concentration measured in undiluted plasma with an ion-selective electrode (16).

3.4.5 Blood gas analyzers calculate substance concentration of total carbon dioxide from equation 5, which is obtained from equations 2, 3 and 4.

$$c_{\text{tCO}_2} = \alpha_{\text{CO}_2} \cdot p_{\text{CO}_2} \cdot (1 + 10^{\text{pH} - \text{pK}'}) \quad (\text{Eq. 5})$$

### 3.5 Base excess of extracellular fluid

Base excess of extracellular fluid  $c_{\text{BE}}(\text{ecf})$ , is a measure of the non-respiratory component of acid-base imbalance in a patient<sup>9)</sup>. Of the several quantities proposed for this purpose, base excess of extracellular fluid has the best combination of general acceptance and theoretical and experimental validity.  $c_{\text{BE}}(\text{ecf})$  is defined as the substance concentration of base determined by titrating a model of extracellular fluid to a pH of 7,40 with  $p_{\text{CO}_2} = 5,33$  kPa at  $37,0^\circ\text{C}$ . Such a model may be obtained by diluting one volume of blood with two volumes of its own plasma. It is more common, however, to calculate  $c_{\text{BE}}(\text{ecf})$  from the relationship

$$c_{\text{BE}}(\text{ecf}) = c_{\text{HCO}_3^-} - c_{\text{HCO}_3^*} + \beta_{\text{ecf}}(\text{pH} - \text{pH}^*) \quad (\text{Eq. 6})$$

where the quantities with superscript \* have selected numerical values, given in table 1, and  $\beta_{\text{ecf}}$  is the buffer value of non-bicarbonate buffers in extracellular fluid, discussed in section 4.2.

<sup>8)</sup>  $\lg$  denotes the decadic logarithm of the numerical value of a quantity.

<sup>9)</sup> The term "extracellular base excess" is preferred over "in vivo base excess", because the latter does not refer to a true in vivo measurement. Hence, distinguishing in vivo and in vitro is inappropriate.

ecf = extracellular fluid

<sup>7)</sup> The concentrational solubility coefficient is not to be confused with the volumic (Bunsen) solubility coefficient, which is sometimes also symbolized as  $\alpha$ , but expressed as the volume of dissolved gas divided by volume of solution and by partial pressure of gas in atmosphere.

*Note:* Base excess of whole blood and of plasma may be defined analogously. Both vary slightly and in opposite directions in acute, uncompensated respiratory disturbances, whereas base excess of extracellular fluid remains constant (o. c. (17), p. 117). The latter quantity therefore is more useful as an index of the non-respiratory component of an acid-base imbalance than the former two.

### 3.6 Substance concentration of total oxygen

3.6.1 Molecular oxygen exists in two forms in blood, that associated with haemoglobin and that dissolved in blood but not associated with any other species. The sum of the substance concentrations of these two forms is defined as the substance concentration of total oxygen.

$$c_{\text{tO}_2} = c_{\text{O}_2\text{Hb}} + \alpha_{\text{O}_2} \cdot p_{\text{O}_2} \quad (\text{Eq. 7})$$

$c_{\text{O}_2\text{Hb}}$  is commonly measured spectrophotometrically. If  $p_{\text{O}_2}$  is also measured, then  $c_{\text{tO}_2}$  may be calculated from equation 7.  $c_{\text{O}_2\text{Hb}}$  should be expressed as substance concentration of the oxyhaemoglobin monomer.

3.6.2 Substance concentration of total oxygen is also commonly called oxygen content, but the latter term is to be discouraged because it is not consistent with current recommendations of the IFCC Committee on Quantities and Units. The term "content" should be reserved for quantities divided by mass.

### 3.7 Oxyhaemoglobin fraction

(Substance fraction of oxyhaemoglobin)

The amount of oxyhaemoglobin divided by the amount of total haemoglobin is called the substance fraction of oxyhaemoglobin<sup>10</sup>). Total haemoglobin comprises functional haemoglobins, and dyshaemoglobins. Functional haemoglobins are those forms of haemoglobin capable of physiological oxygen transport, i. e. oxyhaemoglobin and deoxyhaemoglobin. Dyshaemoglobins are forms of haemoglobin not capable of physiological oxygen transport, e. g. carboxyhaemoglobin, methaemoglobin and sulfhaemoglobin. The reference method for total haemoglobin is the cyanmethaemoglobin method (18). Oxyhaemoglobin fraction is commonly measured spectrophotometrically (19) and is symbolized  $F_{\text{O}_2\text{Hb}}$ .

### 3.8 Oxygen saturation

3.8.1 This quantity<sup>11</sup>) is defined as the amount of oxyhaemoglobin divided by the amount of functional haemoglobin; it is symbolized  $s_{\text{O}_2}$ . In the theoretical case where no dyshaemoglobins are present, oxygen saturation is numerically equal to oxyhaemoglobin fraction; in practice, oxygen saturation is always the larger.

3.8.2  $s_{\text{O}_2}$  can be measured spectrophotometrically, preferably using multiple wavelengths so that carboxyhaemoglobin and methaemoglobin are accounted for (19).

3.8.3 An estimate of  $s_{\text{O}_2}$  can be obtained from  $p_{\text{O}_2}$ ,  $p_{\text{CO}_2}$ , pH and an empirical equation for the relationship between  $p_{\text{O}_2}$  and  $s_{\text{O}_2}$  (oxygen-haemoglobin equilibrium curve; oxygen dissociation curve). Several equations have been proposed;  $s_{\text{O}_2}$  may be estimated with any of them (8, 20, 21). However, direct measurement of  $s_{\text{O}_2}$  is recommended because in the calculation foetal haemoglobin, glyated haemoglobin, dyshaemoglobin, abnormal haemoglobin and glycerate 2,3-bisphosphate are not taken into account (22).

### 3.9 $p_{50}$

3.9.1  $p_{50}$  is defined as the partial pressure of oxygen in a haemoglobin solution having an oxygen saturation of 50%. For oxygen saturations between 40% and 90%, the relation between  $p_{\text{O}_2}$  and  $s_{\text{O}_2}$  is approximated quite well by the Hill equation (8). Therefore  $p_{50}$  can be obtained from the following:

$$\lg p_{50} = \lg p_{\text{O}_2} - \frac{\lg [s_{\text{O}_2}/(1 - s_{\text{O}_2})]}{n_{\text{Hill}}} \quad (\text{Eq. 8})$$

The value of  $n_{\text{Hill}}$  may be taken as 2,7 (20, 23). The method has been tested (24) and guidelines for the procedure have been given (22).

3.9.2 The standard  $p_{50}(p_{50,\text{std}})$ , is defined as the  $p_{50}$  which would be obtained at the selected values of pH = 7,40 (pH\*),  $p_{\text{CO}_2} = 5,33$  kPa ( $p_{\text{CO}_2}^*$ ) and  $\theta = 37,0$  °C. Provided that actual  $p_{50}$ , pH and  $p_{\text{CO}_2}$  have been measured at 37,0 °C,  $p_{50,\text{std}}$  can be calculated with the following equation.

$$\lg p_{50,\text{std}} = \lg p_{50} + \phi_{\text{H}}(\text{pH}^* - \text{pH}) + \phi_{\text{c}}(\lg p_{\text{CO}_2}^* - \lg p_{\text{CO}_2}) \quad (\text{Eq. 9})$$

$\phi_{\text{H}}$  and  $\phi_{\text{c}}$  are Bohr factors (see section 4.3 and table 1). Experimental data (20) fitted to a mathematical model (8) gives  $p_{50,\text{std}} = 3,56$  kPa. For freshly drawn blood of healthy people, values between 3,12 and 3,89 kPa have been found (24). An abnormal  $p_{50,\text{std}}$  may be caused by one or more of the factors mentioned in the last sentence of 3.8.3.

<sup>10</sup>) Note that fractions and saturations as defined here may be multiplied by 100 and expressed as a percentage.

<sup>11</sup>) Saturation of a component in a system is defined as the amount of component present divided by the amount present in the fully saturated system.

#### 4. Selection of numerical values for calculations

##### 4.1 Apparent equilibrium constant for the reaction of carbon dioxide to bicarbonate ion, $K'$

The apparent equilibrium constant for the reaction of carbon dioxide to bicarbonate ion,  $K'$  is expressed as

$$K' = \frac{a_{m,H^+} \cdot c_{HCO_3^-}}{c_{CO_2}} = \frac{a_{m,H^+} \cdot c_{HCO_3^-}}{\alpha_{CO_2} \cdot p_{CO_2}} \quad (\text{Eq. 10})$$

and the more familiar  $pK'$  is expressed as

$$pK' = -\lg K' = \text{pH} + \lg p_{CO_2} + \lg \alpha_{CO_2} - \lg c_{HCO_3^-} \quad (\text{Eq. 11})$$

where  $c_{HCO_3^-}$  follows from equation 3. The value of 6,105 given in table 1 has been determined in independent experimental studies (5).

##### 4.2 Apparent buffer value of non-bicarbonate buffers in extracellular fluid, $\beta_{ecf}$

4.2.1 This quantity is defined as

$$\beta_{ecf} = - \left( \frac{\partial c_{HCO_3^-}}{\partial \text{pH}} \right) \quad (\text{Eq. 12})$$

$\beta_{ecf}$  has been measured experimentally in healthy people (17, 25, 26) by varying  $p_{CO_2}$ , allowing equilibration with the extracellular fluid and then measuring pH and bicarbonate concentration. Extracellular fluid as used here includes interstitial fluid, lymph, plasma and fluid in erythrocytes and other formed elements in blood. Theoretical calculations have also been made with various physiological models (27–29).

4.2.2 The value given in table 1 is from o. c. (17) (p. 116). It is recognized that  $\beta_{ecf}$  is not constant, but is a function of plasma protein, phosphate, blood haemoglobin concentration, blood volume and interstitial fluid volume (27). However, variations in  $\beta_{ecf}$  are small and generally without clinical significance (17).

##### 4.3 Bohr factors

The proton Bohr factor,  $\phi_H$ , is defined as

$$\phi_H = \left( \frac{\partial \lg p_{O_2}}{\partial \text{pH}} \right)_{s_{O_2}, p_{CO_2}, T} \quad (\text{Eq. 13})$$

and the carbamate Bohr factor,  $\phi_C$ , is defined as

$$\phi_C = \left( \frac{\partial \lg p_{O_2}}{\partial \lg p_{CO_2}} \right)_{s_{O_2}, \text{pH}, T} \quad (\text{Eq. 14})$$

The values given in table 1 are from l. c. (23). It is assumed that the other factors influencing haemoglobin-oxygen affinity, mentioned in section 3.8.3, are also kept constant.

#### 5. Temperature coefficients

5.1 Because pH,  $p_{CO_2}$  and  $p_{O_2}$  are all temperature-dependent quantities, they are often adjusted to the actual body temperature of the patient. This adjusts for changes in vitro when blood is drawn from a patient at body temperature and then analyzed at 37,0 °C. Attention has been focused on the fact that measurements adjusted to some temperature other than 37,0 °C are of limited usefulness because of the unresolved question of what values are most beneficial at these other temperatures. Therefore, some prefer not to use temperature adjustments, but to measure at 37,0 °C and interpret the results with reference values for 37,0 °C. If temperature adjustments are made, both the temperature-adjusted value and the value at 37,0 °C should be reported, using unambiguous symbols.

5.2 Measurements sometimes need to be made at temperatures other than 37,0 °C and it may then be desired to adjust the values to 37,0 °C to facilitate interpretation. The following relationships have been determined experimentally for whole blood (8, 30–33) and may be used for such adjustments,

$$\frac{\Delta \text{pH}}{\Delta T} = -0,015 \text{ K}^{-1} \quad (\text{Eq. 15})$$

$$\frac{\Delta \lg p_{CO_2}}{\Delta T} = 0,021 \text{ K}^{-1} \quad (\text{Eq. 16})$$

$$\frac{\Delta \lg p_{O_2}}{\Delta T} = 0,018 - 0,013 \tanh [4,37 \lg (p_{O_2}/19,2 \text{ kPa})] \text{K}^{-1} \quad (\text{Eq. 17})$$

where  $\tanh$  denotes the hyperbolic tangent;  $\Delta T$  is the difference between two temperatures and has the unit K. The  $p_{O_2}$  to be inserted in equation 17 is the value at 37,0 °C; thus, when  $p_{O_2}$  has been measured at another temperature, an iterative procedure must be followed to reach the value at 37,0 °C. For a discussion of the effect of temperature on pH and  $p_{CO_2}$  see o. c. (17) (p. 88–89).

Each of the relations above is only an approximation and the temperature coefficients are actually complex functions of several variables including pH, protein concentration, haemoglobin concentration and other quantities.

## 6. References

1. Siggaard-Andersen O, Durst RA, Maas AHJ. Approved IUPAC/IFCC recommendation (1984) on physico-chemical quantities and units in clinical chemistry with special emphasis on activity and activity coefficients. *J Clin Chem Clin Biochem* 1987; 25:369–91; *Ann Biol Clin* 1987; 45:89–109.
2. National Committee for Clinical Laboratory Standards. Definitions of quantities and conventions related to blood pH and gas analysis. 2nd ed. Tentative standard. Document C12-T2, NCCLS, 771 East Lancaster Avenue: Villanova, PA 19085, 1991.
3. Maas AHJ, Weisberg HF, Burnett RW, Müller-Plathe O, Wimberley P, Zijlstra WG, et al. Approved IFCC methods. Reference method (1986) for pH measurement in blood. *Clin Chim Acta* 1987; 165:97–109; *Labmedica* 1987; 3:33–7; *J Clin Chem Clin Biochem* 1987; 25:281–9.
4. Burnett RW, Covington AK, Maas AHJ, Müller-Plathe O, Weisberg HF, Wimberley PD, et al. IFCC method (1988) for tonometry of blood: reference materials for  $p_{\text{CO}_2}$  and  $p_{\text{O}_2}$ . *Clin Chim Acta* 1989; 185:S17–S24; *J Clin Chem Clin Biochem* 1989; 27:403–8; *Ann Biol Clin* 1989; 47:373–6; *Biochim Clin* 1989; 13:945–9; *J Biomed Lab Sci* 1989; 2:185–92; *J IFCC* 1989; 1:78–86.
5. Maas AHJ, Rispens P, Siggaard-Anderson O, Zijlstra WG. On the reliability of the Henderson-Hasselbalch equation in routine clinical acid-base chemistry. *Ann Clin Biochem* 1984; 21:26–39.
6. Bartels H, Wrbitsky R. Bestimmung des  $\text{CO}_2$ -Absorptionskoeffizienten zwischen 15 und 38 °C in Wasser und Plasma. *Pflügers Arch* 1960; 271:162–8.
7. Austin WH, Lacombe E, Rand PW, Chatterjee M. Solubility of carbon dioxide in serum from 15–38 °C. *J Appl Physiol* 1963; 18:301–4.
8. Siggaard-Andersen O, Wimberley PD, Göthgen J, Siggaard-Andersen M. A mathematical model of the hemoglobin-oxygen dissociation curve of human blood and of the oxygen partial pressure as a function of temperature. *Clin Chem* 1984; 30:1646–51.
9. Christoforides C, Hedley-White J. Effect of temperature and hemoglobin concentration on solubility of  $\text{O}_2$  in blood. *J Appl Physiol* 1969; 27:592–6.
10. Roughton FJW, Severinghaus JW. Accurate determination of  $\text{O}_2$  dissociation curve of human blood above 98.7% saturation with data on  $\text{O}_2$  solubility in unmodified human blood from 0 to 37.0 °C. *J Appl Physiol* 1973; 35:861–9.
11. Wimberley PD, Siggaard-Andersen O, Fogh-Andersen N, Boink ABTJ. Are sodium bicarbonate and potassium bicarbonate fully dissociated under physiological conditions? *Scand J Clin Lab Invest* 1985; 45:7–10.
12. Van Slyke DD, Neill JM. The determination of gases in blood and other solutions by vacuum extraction and manometric measurement. *J Biol Chem* 1924; 61:523–73.
13. Dijkhuizen P, Fongers TME, Rispens P, Zijlstra WG. A new reference method for the determination of the total  $\text{CO}_2$  concentration in biological fluids. *Clin Chim Acta* 1978; 86:339–47.
14. Rispens P, Zock JP, Zijlstra WG. Quantitative relationships between total  $\text{CO}_2$  concentration in blood and plasma, plasma bicarbonate concentration, plasma pH and carbon dioxide tension between 16–42 °C. In: Durst RA, editor. *Blood pH, gases and electrolytes*. Washington DC: NBS Special Publication 450, 1977:39–45.
15. Maas AHJ, Siggaard-Andersen O, Rispens P, Zijlstra WG. Calculation of the true bicarbonate concentration and concentration of other carbon dioxide species in plasma. In: Maas AHJ, Kofstad J, Siggaard-Andersen O, Kokholm G, editors. *Physiology and methodology of blood gas and pH*. Copenhagen: Radiometer AS 1984; 4:101–18.
16. Maas AHJ, Siggaard-Andersen O, Weisberg HF, Zijlstra WG. Ion-selective electrodes for sodium and potassium: a new problem of what is measured and what should be reported. *Clin Chem* 1985; 31:482–5.
17. Siggaard-Andersen O. *The acid-base status of the blood*. 4th ed. Copenhagen: Munksgaard 1974.
18. International Committee for Standardization in Hematology. Recommendations for reference method for haemoglobinometry in human blood (ICSH standard 1986) and specifications for international haemoglobinocyanide preparation. 3rd ed. *Clin Lab Haemat* 1987; 9:73–9.
19. Zwart A, Buursma A, Van Kampen EJ, Zijlstra WG. Multi-component analysis of hemoglobin derivatives with a reversed-optics spectrophotometer. *Clin Chem* 1984; 30:373–9.
20. Severinghaus JW. Simple accurate equations for human blood  $\text{O}_2$  dissociation computations. *J Appl Physiol: Respir Environ Exercise Physiol* 1979; 46:599–602.
21. Lobdell DD. An invertible simple equation for computation of blood  $\text{O}_2$  dissociation relations. *J Appl Physiol* 1981; 50:971–3.
22. Wimberley PD, Burnett RW, Covington AK, Fogh-Andersen N, Maas AHJ, Müller-Plathe O, et al. Guidelines for routine measurement of blood hemoglobin oxygen affinity. *Scand J Clin Lab Invest* 1990; 203 50 Suppl:227–34.
23. Kwant G, Oeseburg B, Zwart A, Zijlstra WG. Human whole-blood  $\text{O}_2$  affinity: effect of  $\text{CO}_2$ . *J Appl Physiol* 1988; 64:2400–10.
24. Kwant G, Oeseburg B, Zijlstra WG. Reliability of the determination of whole-blood oxygen affinity by means of blood-gas analyzers and multi-wavelength oximeters. *Clin Chem* 1989; 35:773–7.
25. Brackett NC, Cohen JJ, Schwarz SB. The carbon dioxide titration curve of normal man. *N Engl J Med* 1965; 272:6–12.
26. Boening D, Schweigart U, Nutz V, Stegemann J. The in vivo and in vitro  $\text{CO}_2$  equilibrium curves of blood during acute hypercapnia and hypocapnia. I. Experimental investigations. *Pflügers Arch* 1974; 350:201–12.
27. Dell RB, Lee LE, Winters RW. Influence of body composition on the in vivo response to acute hypercapnia. *Pediatr Res* 1971; 5:523–38.
28. Boening D. The in vivo and in vitro  $\text{CO}_2$  equilibration curves of blood during acute hypercapnia and hypocapnia. II. Theoretical considerations. *Pflügers Arch* 1974; 350:213–22.
29. Zock JP, Rispens P, Zijlstra WG. Carbon dioxide loading and the acid-base equilibrium states of the human isolated internal environment. *Proc Kon Ned Akad Wet* 1983; C86:101–20.
30. Zwart A, Kwant G, Oeseburg B, Zijlstra WG. Human whole-blood oxygen affinity: effect of temperature. *J Appl Physiol: Respirat Environ Exercise Physiol* 1984; 57:429–34.
31. Thomas LJ Jr. Algorithms for selected blood acid-base and blood gas calculations. *J Appl Physiol* 1972; 33:154.
32. Greenburg AG, Molder PV. Temperature coefficients for  $p_{\text{CO}_2}$  and pH in whole blood. *Arch Surg* 1965; 91:867.
33. Nunn JF, Bergman NA, Bunatian A, Coleman AJ. Temperature coefficients for  $p_{\text{CO}_2}$  and  $p_{\text{O}_2}$  of blood in vitro. *J Appl Physiol* 1965; 20:23.