# An Acid-Base Chart for Arterial Blood with Normal and Pathophysiological Reference Areas

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Siggaard-Andersen, O. An Acid-Base Chart for Arterial Blood with Normal and Pathophysiological Reference Areas, Scand. J. clin. Lab. Invest. 27, 239-245, 1971.

A pH-log (Pco<sub>2</sub>) chart is described, with indications of the normal values for the acid-base status of the blood as well as the values to be expected in different types of acid-base disturbances, including acute and chronic hypercapnia, acute and chronic hypocapnia, acute and chronic base deficit, and chronic base excess. The scales allow conversion of pH to hydrogen ion concentration (10-PH) and conversion of mm Hg to the recommended unit for pressure, kilo pascal. The chart allows estimation of the base excess or deficit of the extracellular fluid as well as the hydrogen carbonate concentration of the plasma. An example of the advantage of plotting the pH and Pco<sub>2</sub> values in the chart is given.

Key-words: Acid-base equilibrium; acidosis; alkalosis; bicarbonate; carbon dioxide; hydrogen ion concentration

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The clinical chemistry laboratory should not only provide accurate and precise determinations of clinical chemical quantities. It should also provide an easily interpretable presentation of the laboratory results. Usually the laboratory supplies reference values (normal values) when reporting the result of a given determination. When more quantities are related in such a way that an integrated interpretation is important, a knowledge of the physiological relationship between the quantities becomes necessary.

New data for the normal physiological and a pathophysiological relationships between the acid-base quantities have been published by several authors, and this new knowledge warrants a method of reporting the acid-base data which is more informative than a mere table of the results. The paper describes a pH-log (Pco<sub>2</sub>) chart suitable for this purpose. (Fig 1.)

## DESCRIPTION OF THE ACID-BASE CHART

1) The various coordinates of the chart

The chart refers to the acid-base status determined in arterial blood or arterialized capillary blood at the temperature of the patient, i.e. usually 37°C.

The pH and the hydrogen ion concentration  $(c_{\rm H}^+)$  of the plasma are both indicated on the abscissa. Hydrogen ion concentration is here calculated simply as  $10^{-p_{\rm H}}$ . If  $10^{-p_{\rm H}}$  is assumed to represent the hydrogen ion activity, and an activity coefficient for hydrogen ions in plasma of 0.8 is taken into account, the values for the hydrogen ion concentration would be a factor of 1.25 higher. The unit for  $c_{\rm H}^+$  is nmol/l (nanomoles per liter =  $10^{-9}$  mol/l). The pH quantity is dimensionless. Several authors have recom-

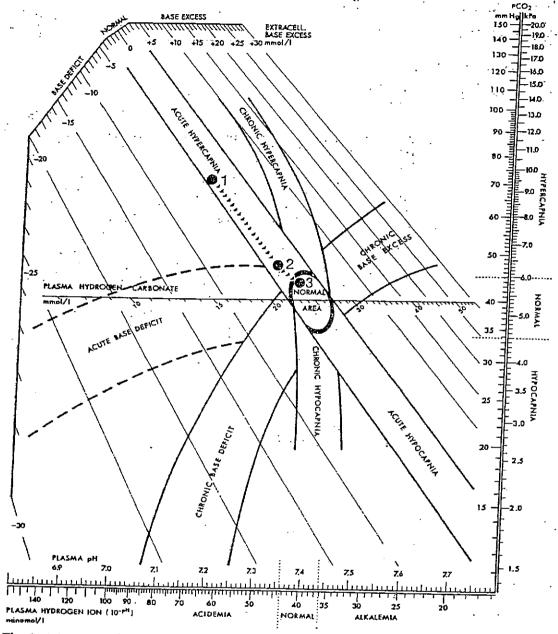


Fig. 1. Acid-base values in a newborn infant plotted in the acid-base chart. The laboratory data referring to points 1, 2 and 3 are given in Table I. The values are indicated by circles the radius of which indicates 2 times the analytical standard deviations. For a description of the coordinates and various areas of the chart, see text. The copyright of the chart has been obtained by Radiometer A/S, Emdrupsvej 72, DK-2400 Copenhagen NV, Denmark.

mended expressing the acidity in terms of hydrogen ion concentration (4, 21), while others prefer the pH concept (7, 14, 36).

The normal range indicated on the abscissa for pH is 7.36 to 7.44, for  $c_{\rm H}$  + 44 to 36 nmol/l. Any point in the left half of the chart indicates

an increased plasma acidity, which is termed acidemia. Any point in the right half of the chart indicates a decreased plasma acidity, which is termed alkalemia. Re terminology see report of ad hoc committee on acid-base terminology (44).

The carbon dioxide partial pressure (Pco<sub>2</sub>) of the blood, or rather of a gas phase in equilibrium with the blood, is indicated on the ordinate. The units are either conventional mm Hg or kPa (kilo pascal = kilo newton per square meter, the unit recommended for pressure by the International Union of Pure and Applied Chemistry (17)).

The normal range indicated for Pco<sub>2</sub> is 34 to 45 mm Hg or 4.5 to 6.0 kPa.

Any point in the upper half of the chart indicates increased Pco<sub>2</sub>, i.e. hypercapnia. Any point in the lower half of the chart indicates a decreased Pco<sub>2</sub>, i.e. hypocapnia.

The base excess (BE) of the extracellular fluid is indicated on the scale in the upper left corner of the chart. This quantity is defined as the titratable base minus the titratable acid, when titrating the extracellular fluid (Ecf = blood plus interstitial fluid) to an arterial blood plasma pH of 7.40 at a Pco<sub>2</sub> of 40 mm Hg at 37°C (37). The unit employed is mmol/L

Projections to the base excess scale should be made along the slanting lines of the chart. These [base excess lines represent so-called vivo CO2equilibration curves. The slope of the lines has been determined experimentally by several authors by CO2-inhalation or hyperventilation (4, 11, 16, 31, 35, 38). The slope depends on the buffer value of the extracellular fluid (9, 27, 37), which is largely dependent on the hemoglobin concentration of the extracellular fluid (Ecf-Hb) calculated as: (Ecf-Hb) = (Blood-Hb) × (Blood-Volume)/(Ecf-Volume). In the chart the slope corresponds to a hemoglobin concentration of 6.0 g/100 ml (heme conc. = 3.7 mmol/l). Variations in the slope are small and generally without any clinical significance.

The divisions on the scale have been calculated by means of the acid-base nomograms previously published (36).

The normal range indicated for Ecf-BE is -3.0 to +3.0 mmol/l.

Any point in the upper right half of the chart 4-S. J. L. I.

indicates an elevated Ecf-BE, which is termed base excess. Any point in the lower left half of the chart indicates a decreased (negative) Ecf-BE, which is termed base deficit.

The hydrogen carbonate concentration of the plasma is indicated on the scale in the middle of the chart.

Projections to the hydrogen carbonate scale should be made at a minus 45° angle to the scale. This is apparent when rearranging the Henderson-Hasselbalch equation as follows:

 $log (Pco_2) = -pH + pK - log S + log [HCO_3]$ , which indicates that the [HCO\_3]-isopleth's are straight lines with a slope of -1, i.e. -45°. The divisions on the scale refer to plasma of 37°C (units mmol/l) and are calculated from the equation by inserting  $Pco_2 = 40 \text{ mm Hg}$ , pK = 6.10, and S = 0.0306 (mmol/l)/(mm Hg) (36).

### 2) The various areas of the chart

Normal area. This area indicates the acid-base values from normal resting individuals. The values for women and infants tend to fall in the lower left of the area, while normal values for men tend to fall in the upper right of the area. On a vegetable diet the values tend to fall in the right side of the area. On a protein-rich diet the values tend to fall in the left side of the area. The values for the supine body position tend to fall in the upper half of the area, while values for the sitting or standing position tend to fall in the lower half of the area (36).

Acute hypercapnia. This area indicates the values obtained in normal individuals following an acute elevation of the Pco<sub>2</sub> due to CO<sub>2</sub>-inhalation or apnoeic oxygenation (4, 16, 38). An alternative designation of this area is simple acute respiratory acidosis (44).

Any point in this area is characterized by an increased blood Pco<sub>2</sub>, a decreased plasma pH, and a normal Ecf-BE.

Acute hypocapnia. This area indicates the values obtained in normal individuals immediately following hyperventilation (38). With a duration of hyperventilation of more than 10 to 15 min, the values tend to fall in the left side of the area or even outside and to the left of the area (11). This is due to a rapid formation of lactic acid in the liver (3), which causes a base deficit in the

extracellular fluid. An alternative designation of this area is simple acute respiratory alkalosis (44).

Any point in this area is characterized by a decreased blood Pco<sub>2</sub>, an increased plasma pH, and a normal Ecf-BE.

Chronic hypercapnia. This area indicates the values obtained in patients, children as well as adults, with chronic respiratory insufficiency but with a normal renal function (5, 10, 26, 42). An alternative designation of this area is simple chronic respiratory acidosis.

The renal compensation is not maximal before several days after induction of hypercapnia. In the case of a concomitant potassium depletion, the values tend to fall in the right side or to the right of the indicated area. In this case the renal function cannot be said to be normal, since the potassium depletion enhances the hydrogen ion excretion in the kidneys at a given plasma pH value (24). The area is not extended beyond a Pco<sub>2</sub> of 100 mm Hg because the concomitant fall in blood Po<sub>2</sub> below 40 mm Hg when breathing atmospheric air becomes the limiting factor (26).

Any point in this area is characterized by an increased blood Pco<sub>2</sub>, an elevated Ecf-BE, and a normal or slightly decreased plasma pH.

Chronic hypocapnia. This area indicates the values obtained in normal individuals acclimatized to high altitude (15, 20, 25). An alternative designation of this area is simple chronic respiratory alkalosis (44).

Any point in this area is characterized by a decrease in blood Pco<sub>2</sub>, a decreased Ecf-BE, and a normal or slightly increased plasma pH.

Acute base deficit. This area indicates the values obtained after acute production of non-volatile acid in the organism, i.e. lactic acid in connection with severe anaerobic muscular exercise (8, 33). An acute base deficit may also be produced experimentally by rapid infusion of acid intravenous ly (2, 32). The acidemia stimulates the chemoreceptors to hyperventilation, but in the most acute phase the acidity has not yet increased in the respiratory center or in the spinal fluid, and the respiratory compensation is therefore only partial (2). Acute, in this connection, means of less than 1 hour's duration. An alternative designation of this area is simple acute metabolic acidosis (44).

Any point in this area is characterized by a negative Ecf-BE, a decreased plasma pH, and a normal or slightly decreased Pco<sub>2</sub>.

Chronic base deficit. This area indicates the values obtained in patients with a chronic base deficit but with a normal respiratory function, i.e. chronic renal insufficiency or diabetic acidosis (1, 19, 22, 23, 30, 43), or in normal subjects after ingestion of ammonium chloride (21). Maximal respiratory compensation develops when equilibrium is reached between the different body phases, more specifically between the extracellular fluid, the spinal fluid, and the respiratory center. This lasts 4 to 6 hours after i.v. infusion of acid (2, 31). An alternative designation of this area is simple chronic metabolic acidosis (44).

Any point in this area is characterized by a negative Ecf-BE, a decreased blood Pco<sub>2</sub>, and a decreased plasma pH.

Chronic base excess. This area indicates the values obtained in individuals with a normal respiratory function following administration of hydrogen carbonate (12, 29, 40), or observed in patients, children as well as adults, with a chronic base excess (18, 23). An alternative designation of this area is simple chronic metabolic alkalosis (44).

In case of a concomitant potassium depletion the values tend to fall in the lower part of the area or below the area. In this case the respiratory function cannot be said to be normal, since an increased hydrogen ion concentration is assumed to develop intracellularly in the respiratory center (12).

Any point in this area is characterized by an increased Ecf-BE, an increased plasma pH, and a normal or slightly increased blood Pco<sub>2</sub>.

## APPLICATION OF THE ACID-BASE CHART

When the laboratory data (plasma pH and blood Pco<sub>2</sub>) are plotted in the chart, the acid-base status is readily evaluated with reference to the normal area and the areas of normal physiological compensation. The extracellular base excess and the plasma hydrogen carbonate concentrations may be evaluated by projections to the respective scales.

The expected effects of acid-base therapy may

be evaluated by means of the chart (37), Increasing the alveolar ventilation, voluntarily or artificially, causes the point which represents the acid-base values to slide downwards along the base excess line (the vivo CO<sub>2</sub>-equilibration line). If the alveolar ventilation is doubled, and the blood Pco<sub>2</sub> thereby halved, the new position of the point is easily predicted, and the concomitant rise in plasma pH may be accurately estimated.

The acute effect on the plasma pH of infusion of base may also be evaluated. Rapid infusion of 5 mmol of sodium bicarbonate per liter of extracellular fluid (which corresponds to about 1 mmol per kg body mass) initially causes a rise in the Ecf-BE of 5 mmol/l. The point representing the acid-base values moves from one base excess line to the next base excess line 5 mmol/l higher, the blood Pco<sub>2</sub> remaining virtually constant. As the base is distributed in the whole body, the initial rise in Ecf-BE of 5 mmol/l is about halved (37).

As an example of the application of the chart, the acid-base values in a newborn infant are shown in Table I and in Fig. 1. The infant cried immediately at birth, but thereafter became increasingly cyanotic. Tracheal suction revealed considerable amounts of aspirated fluid, and a chest X-ray film revealed a picture consistent with aspiration of amniotic fluid. The infant was placed in an incubator and treated with oxygen. Capillary blood was drawn, and the acid-base parameters and the oxygen saturation were measured by methods previously published (36).

Table I. Laboratory data on capillary blood from a newborn infant, & S.-A., born at 14:00 on 14 January 1970, mass 4630 g, aspirated amniotic fluid at birth

| Time (h:min)                   | 14:45     | 17:30          | 22:00 |
|--------------------------------|-----------|----------------|-------|
| Plasma pH                      | 7.18      | 7.33           | 7.37  |
| Blood Pco <sub>2</sub> (mm Hg) | 70        | 47             | 43    |
| Blood base excess (mmol/l)     | -6.6      | -2.0           | -0.9  |
| Blood standard bicarbonate     | <b>;</b>  |                |       |
| (mmol/l)                       | 18.0      | 22.8           | 23.9  |
| Extracellular base excess      |           |                |       |
| (mmol/l)                       | <b>-2</b> | <del>-</del> 1 | 0     |
| Blood heme concentration       |           |                |       |
| (mmol/l)                       | 13.0      | 11.2           | 11.8  |
| Blood oxygen saturation        |           |                |       |
| (fraction)                     | 0.73      | 0.98           | 0.94  |
|                                |           |                |       |

The first measurement 45 min after birth revealed amhypercapnia and an acidemia. The calculated whole blood base excess and the standard bicarbonate both indicated a base deficit in the blood (reference range for blood-BE = -3.0 to +3.0 mmol/l, for standard bicarbonate = 22.5 to 26.5 mmol/l). When the pH and Pco<sub>2</sub> values are plotted in the chart, however, the point falls within the area of acute hypercapnia, and the estimated base excess of the extracellular fluid is within the normal range. The base deficit measured in the blood is due to a redistribution of base (HCO s) between the blood and the poorly buffered interstital fluid caused by the hypercapnia (9, 34). Plotting the pH and Pco, values in the chart obviates the erroneous conclusion that a base deficit is present in the whole extracellular fluid. The next determinations 3h 30 min after birth and again 8 h after birth indicated an improvement of the respiration and a movement of the point representing the acid-base values into the normal area.

#### DISCUSSION

Graphical representation of the acid-base parameters has been advocated by several authors, and many different combinations of coordinates have been proposed (6, 13, 28, 30, 39, 41, 45).

The pH-log (Pco<sub>2</sub>) nomogram has been utilized for a number of years for calculation of the acid-base parameters in the laboratory (36). One advantage of this coordinate system is that the base excess isopleth's (the CO<sub>2</sub>-equilibration curves) for plasma and blood, as well as the whole organism, are practically straight lines (36). Another advantage is that the abscissa and the ordinate indicate the two acid-base parameters that are most easily measured.

A major disadvantage of the chart, when following the acid-base values in a patient, is that time is not indicated, and that the rate of changes is not easily visualized. Therefore a table of the data with indications of time (and comments on therapy, etc.) should follow the chart. A case-history diagram for recording the acid-base values with time as abscissa has previously been published (19, 34). The case-history diagram, however, gives no information concerning the

the various acid-base disturbances.

The laboratory report with the data plotted on the chart should not be considered an acid-base diagnosis in the clinical sense. The acid-base status represented by point 1 (Fig. 1) may be due to an acute respiratory acidosis, but the values might also be due to a chronic respiratory acidosis complicated by an acute metabolic acidosis. The laboratory data alone only allow the conclusion that the pH and Pco2 values fall within the area of acute hypercapnia. The clinical acid-base diagnosis requires a knowledge or assumption concerning how the values arrived at the present location i.e. a knowledge of the path the point followed, and or a knowledge or assumption concerning the acid-base balance (intake, production and excretion of titratable acid or base).

The different areas are not defined with mathematical accuracy, and the areas published by different authors vary considerably. Many different factors influence the acid-base values of the blood. The normal area, for example, is dependent on age and sex, on the composition of the diet, body position, altitude, etc., and the slope of the vivo CO2-equilibration curves is dependent on the buffer value of the extracellular fluid. For these reasons the areas should not be interpreted as more than reference areas or indications of the acid-base values to be expected in certain types of acid-base disturbances.

### ACKNOWLEDGEMENT

The author wishes to thank Messrs. Radiometer, 72 Emdrupvej, DK-2400 Copenhagen NV, for printing the chart on special log-paper and thus making it available.

#### REFERENCES

- 1. Albert, M. S., Dell, R. B. & Winters, R. W. Quantitative displacement of acid-base equilibrium in metabolic acidosis, Ann. intern, Med. 66, 312, 1957.
- 2. Asch, M. J., Dell, R. B., Williams, G. S., Cohen, M. & Winters, R. W. Time course for development of respiratory compensation in metabolic acidosis. J. Lab. clin. Med. 73, 610,

- degree of normal physiological compensation of 3. Berry, M. N. & Scheuer, J. Splanchnic lactic acid metabolism in hyperventilation, metabolicalkalosis and shock. Metabolism 16, 537, 1967.
  - 4. Brackett, N. C., Jr., Cohen, J. J. & Schwartz, W. B. Carbon dioxide titration curve of normal man: effect of increasing degrees of acute hypercapnia on acid-base equilibrium. New Engl. J. Med. 272, 6, 1965.
  - 5. Brackett, N. C., Jr., Wingo, C. F., Muren, O. & Solano, J. T. Acid-base response to chronic hypercapnia in man. New Engl. J. Med. 280, 124, 1969,
  - 6. Davenport, H. W. The ABC of Acid-Base-Chemistry. 5. ed., revised, Univ. of Chicago Press, Chicago 1969.
  - 7. Davis, R. P. Logland: a Gibbsian view of acid-base balance. Amer. J. Med. 42, 159, 1967.
  - 8. DeLanne, R., Barnes, J. R., Bronha, L. & Massart, F. Changes in acid-base balance and blood gases during muscular activity and recovery. J. appl. Physiol. 14, 328, 1959
  - 9. Dell, R. B. & Winters, R. W. A model for the in vivo CO2 equilibration curve. Amer. J. Physiol. 219, 37, 1970.
  - 10. Engel, K., Dell, R. B., Rahill, W. J., Denning, C. R. & Winters, R. W. Quantitative displacement of acid-base equilibrium in chronic respiratory acidosis. J. appl. Physiol. 24, 288,
  - 11. Engel, K., Kildeberg, P. & Winters, R. W. Quantitative displacement of blood acid-base status in acute hypocapnia. Scand. J. clin. Lab. Invest. 23, 5, 1969.
  - 12. Goldring, R. M., Cannon, P. J., Heinemann, H. O. & Fishman, A. P. Respiratory adjustment to chronic metabolic alkalosis in man. J. clin. Invest. 47, 188, 1968.
  - 13. Guerisoli, J. M. p. 261 in Equilibrio Acido Base. Fundamentos, Fisiologia, Laboratorio. G. F. Fernandez, Buenos Aires, 1970.
  - 14. Hills, A. G. & Reid, E. L. pH defended is it defensible? Ami. intern. Med. 65, 1150, 1966.
  - 15. Hurtado, A. & Aste-Salazar, H. Arterial blood gases and acid-base balance at sea level and at high altitude, J. appl. Physiol. 1, 304, 1948.
  - 16. Ichiyanagi, K., Masuko, K., Nishisaka, N., Matsuki, M., Horikawa, H. & Watanabe, R. Acid-base balance of arterial plasma during exogenous and endogenous hypercapnia in man. Resp. Physiol. 7, 310, 1968.
  - 17. Manual of symbols and terminology for physicochemical quantities and units. Pure & appl. Chem. 21, 1, 1970.
  - 18. Kildeberg, P. Respiratory compensation in metabolic alkalosis. Acta med. scand. 174, 515,
  - 19, Kildeberg, P. p. 228 in Clinical Acid-Base Physiology. Studies in Neonates, Infants and Young Children. Munksgaard, Copenhagen and Williams & Wilkins, Baltimore, 1968.

- Lahiri, S. & Milledge, J. S. Acid-base in Sherpa altitude residents and lowlanders at 4880 m. Resp. Physiol. 2, 323, 1967;
- 21. Lennon, E. J. & Lemann, J., Jr. Defense of hydrogen ion concentration in chronic metabolic acidosis: a new evaluation of an old approach. Ann. intern. Med. 65, 265, 1966.
- 22. Möller, B. The hydrogen ion concentration in arterial blood. A clinical study of patients with diabetes and diseases of the kidneys, lungs and heart. Acta med. scand. 165. Suppl. 348, 1, 1959.
- 23. Monti, M. & Rooth, G. Respiratory compensation to metabolic acid-base disturbances. Scand.

  J. clin. Lab. Invest. 26, 381, 1970.
- 24. Murray, J. F. Carbon dioxide retention without acidosis: a common occurrence due to coexisting potassium depletion (abstract). Amer. Rev. resp. Dis. 86, 126, 1962.
- 25. Rahn, H. & Otis, A. B. Man's respiratory response during and after acclimatization to high altitude. Amer. J. Physiol. 157, 445, 1949.
- Refsum, H. E. Acid-base status in patients with chronic hypercapnia and hypoxaemia. Clin. Sci. 27, 407, 1964.
- 27. Refsum, H. E. & Kim, B. M. Relationship between the acid-base changes of arterial plasma during acute changes of the CO<sub>2</sub> tension in vivo and the hemoglobin concentration of the blood. Resp. Physiol. 2, 283, 1967.
- Rispens, P. Significance of Plasma Bicarbonate for the Evaluation of H<sup>\*</sup> Homeostasis. Van Gorcum, Groningen, 1970.
- Rodriquez, B., Mookerjee, B., Harner, R. & Webster, G. In vivo titration of acute alkali infusions in man (abstract). Clin. Res. 14, 369, 1966.
- Rooth, G. p. 80 in Clinical Acid-Base and Electrolyte Balance. Studentlitteratur, Lund, 1970
- 31. Russell, C. D., Roeher, H. D., Illickal, M. M., DeLand, E. C. & Maloney, J. V., Jr. p. 29 in Whole body base excess: acute response to acid-base stress in the dog. The RAND corporation, RM-6203-PR 1970.

Received 24 December 1970

Accepted 23 January 1971

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- 32. Schwartz, W. B., Örning, K. I. & Porter, R. The internal distribution of hydrogen ions with varying degrees of metabolic acidosis. J. clin. Invest. 34, 373, 1957.
- 33. Siggaard-Andersen, J. Unpublished data on the acid-base values in young men following 1000 and 1500 m sprinting.
- 34. Siggaard-Andersen, O. A graphic representation of changes of the acid-base status. Scand. J. clin. Lab. Invest. 12, 311, 1960.
- 35. Siggaard-Andersen, O. Acute experimental acidbase disturbances in dogs. Scand. J. clin. Lab. Invest. 14, Suppl. 66, 1962.
- 36. Siggaard-Andersen, O. The acid-base status of the blood. Scand. J. clin. Lab. Invest.—15, Suppl. 70, 1963, and Munksgaard, Copenhagen, 1967.
- Siggaard-Andersen, O. Therapeutic aspects of acid-base disorders. pp. 99-131 in Evans, F. T. & Gray, T. C. (eds.) Modern Trends in Anaesthesia. Butterworths, Margate, 1966.
- 38. Siggaard-Andersen, O. Unpublished data on CO2 inhalation and hyperventilation in man.
- Stinebaugh, B. J. & Austin, W. H. Acid-base balance: common sense approach. Arch intern. Med. 119, 182, 1967.
- Stone, D. J. Respiration in man during metabolic alkalosis. J. appl. Physiol. 7, 577, 1955.
- Van Slyke, D. D. Acidosis and alkalosis. Bull. N. Y. Acad. Med. 10, 103, 1934.
- 42. Van Ypersele de Strihou. C., Brasseur, L. & DeConinck, J. The carbon dioxide response curve for chronic hypercapnia in man. New Engl. J. Med. 275, 117, 1966.
- Van Ypersele de Strihou, C. & Frans, A. The pattern of respiratory compensation in chronic metabolic acidosis. Arch. int. Physiol. 76, 547, 1968.
- 44. Winters. R. W. Report of ad hoc committee on acid-base terminology. Ann. N. Y. Acad. Sci. 133, 251, 1966.
- Winters, R. W., Engel, K. & Dell, R. B. Acidbase Physiology in Medicine. A Self-Instruction Program. The London Comp., Canada, 1967.