DETERMINATION OF THE IN VIVO CARBON DIOXIDE TITRATION CURVE OF ANAESTHETIZED MAN

BY

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SUMMARY

A comparison has been made between the pH changes in the arterial blood of anaesthetized patients exposed to changes of Pco₂ above and below the normal range, and those in the same blood equilibrated with similar changes of Pco₂ in vitro. Changes in the non-respiratory component as represented by standard bicarbonate, were derived from the in vitro equilibrations. There was a linear relationship between log Pao₂ and pH, and between pH and the plasma bicarbonate concentration, over the whole range studied in vivo. In the presence of wide variations of carbon dioxide tension, nitrous oxide anaesthesia of more than 2 hours duration, supplemented with a muscle relaxant and a potent analgesic, did not produce any significant alteration of the non-respiratory component of acid-base balance. Although changes of standard bicarbonate occurred in response to alterations of Pao₂, these changes are not considered to represent true changes of the non-respiratory component. The application of parameters derived from in vitro equilibrations, to the behaviour of arterial blood in vivo is discussed. The mechanisms of extravascular buffering of induced changes of Pco₂ are reviewed, and related to the behaviour of arterial blood in equilibrium with extracellular and intracellular tissue fluids.

The relationship between pH, Pco₂, and the concentration of bicarbonate ion is defined by the Law of Mass Action, commonly expressed in the form of the Henderson-Hasselbalch equation. However, changes of pH and [HCO₃⁻] in response to changes of Pco₂ cannot be inferred from this equation, and must be determined experimentally. These changes may then be graphically represented as carbon dioxide titration or dissociation curves.

Following the report by Shock and Hastings (1935) that the carbon dioxide titration curve of arterial blood in vivo was almost identical with the in vitro curve previously described by Henderson (1928), it has been generally assumed that the relationships derived from the in vitro curve can be applied to the behaviour of arterial blood in vivo (Astrup et al., 1960).

Evidence contradicting this assumption has recently been presented by Siggaard-Andersen (1962a), Cohen, Brackett and Schwartz (1964) and Norman and Linden (1965), in the form of direct comparisons of the in vivo and in vitro carbon dioxide titration curves in dogs. More recently, Brackett, Cohen and Schwartz (1965) have presented similar findings in conscious man. None of these studies has covered the full range of Pao₂ seen during clinical anaesthesia but some have suggested that there is an increasing divergence between the in vivo and in vitro curves as the Pao₂ rises or falls. The reported magnitude of this divergence is sufficient to suggest that parameters such as standard bicarbonate (Jørgensen and Astrup, 1957), and whole blood buffer base (Singer and Hastings, 1948) which are derived from in vitro equilibrations, should not be applied to the response of arterial blood in vivo when the Pao₂ is significantly different from 40 mm Hg (Schwartz and Relman, 1963; Bunker, 1965).

We have been particularly concerned with the evaluation of acid-base disturbances which may arise during anaesthesia. These are commonly quantified in terms of such parameters, although the relationship between the in vivo and in vitro
carbon dioxide titration curves during general anaesthesia has not been satisfactorily determined. We have therefore made a comparative study of the pH changes of arterial blood from anaesthetized patients exposed to changes of carbon dioxide tension, and the same blood equilibrated in vitro with similar changes of $P_{\text{CO}_2}$.

METHODS

This study was carried out on six male and three female patients, aged between 24 and 60, who were undergoing surgery of a minor but lengthy nature. Each patient had agreed to participate in the study, and had been examined by one of us to exclude any condition which might be associated with acid-base disturbances.

All the patients were premedicated with papaveretum 10 mg and Droperidol (dehydrobenzperidol) 10 mg given intramuscularly 1 hour before the start of the study. There was no evidence that this premedication had produced any respiratory or circulatory depression.

Anaesthesia was induced with thiopentone 200–300 mg, and maintained with 70 per cent nitrous oxide and 30 per cent oxygen, except during the period of carbon dioxide inhalation, when the concentration of nitrous oxide was reduced in order to maintain a constant concentration of oxygen in the inspired gases. Muscular relaxation was obtained with tubocurarine 30–45 mg and, following endotracheal intubation, intermittent positive pressure ventilation was maintained with a Manley ventilator (Blease Anaesthetic Equipment). Analgesia was supplemented where necessary with phenoperidine 2 mg initially and 1-mg doses were repeated at hourly intervals.

During a 30-minute control period, the monitoring and measuring devices were set up and calibrated, and the minute volume of ventilation was regulated to produce a steady end-tidal carbon dioxide tension ($P_{\text{CO}_2}$) between 35 and 40 mm Hg, measured with a Hartmann and Braun URA.4 rapid infrared analyzer sampling continuously from the endotracheal tube. Rapid adjustment of the $P_{\text{CO}_2}$ could then be made at any stage during the study, by alteration of the minute volume of ventilation, or by adding carbon dioxide to the inspired gases.

Following the control period, the effects of hypercapnia followed by hyperventilation were studied in five patients, the effects of hyperventilation alone in three patients, and the effects of hypercapnia alone in one patient. In the first group of five patients, the minute volume was kept constant at the level established during the control period, and carbon dioxide was added to the inspired gases so that a $P_{\text{CO}_2}$ of about 75 mm Hg was attained as rapidly as possible and maintained for periods between 40 and 60 minutes. After this period of hypercapnia, the minute volume was increased to 14 l./min and the administration of carbon dioxide discontinued. Hyperventilation was then maintained for a further period of 40 to 60 minutes, following which the ventilation was readjusted to the control level. In the other group of patients, in whom only the effects of hypercapnia or hyperventilation alone were studied, the return to the control level followed a period of 1 hour at an elevated or reduced $P_{\text{CO}_2}$, and was allowed to occur gradually over a period of 1 hour.

Finger blood flow was qualitatively measured with a photoelectric device (Videograph Phase II, Medical and Industrial Equipment), and monitored simultaneously with the e.c.g. on an oscilloscope.

An indwelling Teflon cannula (Becton Dickinson & Co, Rutherford, N.J.) was inserted percutaneously into a radial artery (Barr, 1961), and continuous pressure measurements were made with an Elema-Schonander EMT.34 pressure transducer.

Samples of blood (3 ml) were withdrawn from the artery into heparinized glass syringes at 10-minute intervals throughout the study, additional samples being taken 5 minutes after the changes of carbon dioxide tension. The following measurements were carried out immediately on these samples.

$pH$ was measured anaerobically at 37°C in a capillary microelectrode (Type AME.1b, Radiometer Corp., Copenhagen).

Measurements of $P_{\text{CO}_2}$ were made by the microequilibration technique described by Siggaard-Andersen et al. (1960), and as a check, the $P_{\text{CO}_2}$ was also measured with a carbon dioxide sensitive electrode as described by Severinghaus and Bradley (1958). The technique, and accuracy of these measurements in this laboratory have been described by Kelman, Coleman and Nunn (1966).
Measurements of $P_{O_2}$ were made with a macro-cathode oxygen electrode (Beckman Instruments Inc., Palo Alto, Calif., U.S.A.).

The nasopharyngeal temperature was measured continuously with a thermocouple, and corrections described by Rosenthal (1948) and Nunn, and colleagues (1965) were applied to the pH, $P_{CO_2}$, and $P_{O_2}$ values when there was a difference between the temperature of the patient and that of the measuring electrode.

The haemoglobin concentration was measured by the alkaline-haematin method on samples taken at the beginning and end of each study, and haematocrit determinations were carried out on each sample using a microhaematocrit centrifuge (Hawksley & Son Ltd.).

The lactic acid concentration in arterial blood was determined in four patients in the first group, by the enzymic method described by Lundholm, Mohme-Lundholm and Vamos (1963), using a kit supplied by Biochemica "Boehringer", Mannheim. Measurements were made at 366 nanometers in an Unicam SP.500 spectrophotometer, on samples taken before, during and after the changes of $P_{CO_2}$.

Calculations.

In order to determine the slope of the overall in vivo carbon dioxide titration line, regression coefficients ($\Delta \log P_{CO_2}/\Delta \text{pH}$) were calculated from all the measured values for pH and $P_{CO_2}$ from each patient. Regression coefficients were also calculated from the values obtained during hypercapnia and hyperventilation separately.

The slope of the whole blood in vitro line ($\Delta \log P_{CO_2}/\Delta \text{pH}$) for each patient was taken as the mean of all the equilibration lines on each blood sample by the Astrup technique. The slope of the in vitro line for each sample was checked at the time of measurement, and repeated if there was a difference of slope between consecutive samples of more than $\pm 0.05$ (equivalent to a difference in haemoglobin concentration of $\pm 1.75 \text{ gm/100 ml}$). The slope of the in vitro line for separated plasma was determined by carbon dioxide equilibration of centrifuged plasma from the pooled blood samples from each patient (Siggaard-Andersen, 1964).

Values for standard bicarbonate and base excess were derived from the revised curve nomogram described by Siggaard-Andersen (1962b); values for plasma bicarbonate were also derived from the same diagram.

RESULTS

The range of pH measured during this study was 7.120 to 7.666, and the corresponding range of $P_{CO_2}$ was 84.0 to 15.7 mm Hg. The range of $P_{O_2}$ was 89.0 to 135.0 mm Hg, although in most of the patients, the $P_{O_2}$ remained within the range 120 to 135 mm Hg.

Table I shows details of measurements of $P_{CO_2}$ and pH, together with derived values for standard bicarbonate and actual plasma bicarbonate concentrations for each patient. There was no significant difference between the standard bicarbonate values of the initial and final control period ($0.2 < P < 0.3$), although the values during hypercapnia and hyperventilation were significantly different from those of the control periods ($P < 0.005$ and $P < 0.001$ respectively).

Table II shows details of the relationships between the slopes ($\Delta \log P_{CO_2}/\Delta \text{pH}$) of the in vitro lines for plasma and whole blood, and the in vivo lines for the arterial blood of the patient. The relationships of the mean slopes expressed as $\Delta [\text{HCO}_3^-]/\Delta \text{pH}$ are also given in figure 1.

The mean value for the slope of the in vitro line for separated plasma ($-1.202, \text{SD 0.114}$) corresponded to a haemoglobin concentration of 0.5 gm/100 ml when plotted on the revised Siggaard-Andersen curve nomogram.

The mean value for the slope of the in vitro lines for whole blood ($-1.599, \text{SD 0.067}$) when plotted on the same nomogram corresponded to a haemoglobin concentration of 16 gm/100 ml, which accorded well with the mean measured haemoglobin values of 15.4 gm/100 ml.

There was a linear relationship between log $P_{CO_2}$ and pH over the whole range studied in vivo, although the slope of this line (mean $-1.451$, SD 0.129) differed from that of the in vitro line for whole blood in each patient. The relationship between the slope of the in vivo line and that of the in vitro line was relatively constant in each patient, having a mean ratio of 0.91:1 (SD 0.05). The difference between the slopes of the two lines is statistically highly significant ($P < 0.005$).

Figure 2 shows a representative log $P_{CO_2}/\text{pH}$ plot for one typical patient who was subjected to both hypercapnia and hyperventilation. The line...
### Table I
Details of measurements on individual patients.
Quoted values for pH, $P_{a\text{CO}_2}$, standard bicarbonate ($St\text{HCO}_3$), and actual plasma bicarbonate ($[\text{HCO}_3^-]$) refer to mean values during each phase.

<table>
<thead>
<tr>
<th>No.</th>
<th>Control</th>
<th>Hypercapnia</th>
<th>Hyperventilation</th>
<th>Final Control</th>
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<td>pH</td>
<td>$P_{a\text{CO}_2}$</td>
<td>$St\text{HCO}_3$</td>
<td>pH</td>
</tr>
<tr>
<td></td>
<td>(mm Hg)</td>
<td>(m.equiv/l.)</td>
<td>(m.equiv/l.)</td>
<td>(mm Hg)</td>
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<td>40.1</td>
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<tr>
<td>2</td>
<td>7.38</td>
<td>41.2</td>
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<td>7.36</td>
<td>43.9</td>
<td>23.1</td>
<td>7.55</td>
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<td>7.36</td>
<td>45.5</td>
<td>23.8</td>
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</tr>
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<td>5</td>
<td>7.45</td>
<td>34.5</td>
<td>24.5</td>
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</tr>
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<td>6</td>
<td>7.44</td>
<td>31.2</td>
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<td>40.9</td>
<td>24.3</td>
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<td>8</td>
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<td>24.0</td>
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<td>9</td>
<td>7.38</td>
<td>35.8</td>
<td>21.2</td>
<td>7.13</td>
</tr>
<tr>
<td>Mean</td>
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<td>38.4</td>
<td>23.5</td>
<td>7.20</td>
</tr>
<tr>
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<td>±0.44</td>
<td>±1.08</td>
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</tbody>
</table>

### Table II
Details of the slopes ($\Delta \log P_{a\text{CO}_2}/\Delta \text{pH}$) of the carbon dioxide titration lines.

<table>
<thead>
<tr>
<th>No.</th>
<th>Separated plasma in vitro</th>
<th>Whole blood in vitro</th>
<th>Arterial blood in vivo</th>
<th>In vivo Arterial blood in vivo hypercapnia</th>
<th>Arterial blood in vivo hyperventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-1.444</td>
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<td>0.898</td>
<td>-1.456</td>
</tr>
<tr>
<td>2</td>
<td>-1.282</td>
<td>-1.681</td>
<td>-1.655</td>
<td>0.985</td>
<td>-1.655</td>
</tr>
<tr>
<td>3</td>
<td>-1.176</td>
<td>-1.636</td>
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</tr>
<tr>
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<td>-1.544</td>
<td>-1.448</td>
<td>0.938</td>
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</tr>
<tr>
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<td>-1.549</td>
<td>-1.472</td>
<td>0.950</td>
<td>-1.425</td>
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<td>-1.306</td>
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<td>-1.281</td>
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<td>-1.569</td>
<td>-1.435</td>
<td>0.915</td>
<td>-1.465</td>
</tr>
<tr>
<td>8</td>
<td>-1.167</td>
<td>-1.605</td>
<td>-1.470</td>
<td>0.916</td>
<td>-1.356</td>
</tr>
<tr>
<td>9</td>
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<td>-1.627</td>
<td>-1.322</td>
<td>0.810</td>
<td>-1.322</td>
</tr>
<tr>
<td>Mean</td>
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<td>-1.599</td>
<td>-1.451</td>
<td>0.907</td>
<td>-1.371</td>
</tr>
<tr>
<td>SD</td>
<td>±0.114</td>
<td>±0.067</td>
<td>±0.129</td>
<td>±0.051</td>
<td>±0.092</td>
</tr>
</tbody>
</table>

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which represents the rise from the control level to the level of maximal hypercapnia follows a different course to that of the in vitro line. The lines which represent the fall of $P_{a}O_2$ during hyperventilation and the rise of $P_{a}O_2$ during the return to the control level are coincident, although the slopes of these lines are also different from that of the in vitro line.

Figure 3 shows representative plots from two separate patients, one of whom was subjected to hypercapnia followed by a gradual return to the control level, while the other was hyperventilated prior to a gradual return to the control level. The difference between the slopes of the in vivo response to hypercapnia and hyperventilation was not significant ($0.2 < P < 0.3$).

There was no change in the haemoglobin concentration in any patient during the course of each study, and there were no significant changes of haematocrit values throughout the changes of $P_{a}O_2$.

In three patients, there were no significant changes in the lactic acid concentrations during the changes of $P_{a}O_2$, and in the fourth patient there was an increase from 0.3 mM/litre to 1.2 mM/litre during the phase of hyperventilation only. No changes were seen during the period of hypercapnia.
Fig. 2
Relationship between in vivo and in vitro carbon dioxide titration lines in a typical patient exposed to hypercapnia and hyperventilation consecutively.

Fig. 3
Relationship between in vivo and in vitro carbon dioxide titration lines in two separate patients, exposed to hypercapnia and hyperventilation respectively.
DISCUSSION

Some idea of the carbon dioxide titration curve during anaesthesia in man during hyperventilation can be made from data collected in the studies by Robinson (1960), Papadopoulos and Keats (1959), and more recently by Millar and Marshall (1965).

Our analysis of Robinson's data showed a series of log \( \frac{P_{a102}}{\text{pH}} \) lines having a mean slope of -1.28. Assuming that the patients had normal haemoglobin values, this slope would be indicative of an apparent metabolic alkalosis during hyperventilation. Papadopoulos and Keats (1959) also reported their findings as indicative of a metabolic acidosis arising during hyperventilation, although this only occurred after a period of more than 1 hour. Their control values, and those of samples measured up to 1 hour, lie on an in vivo line having a mean slope of -1.58 for twenty subjects. This is unlikely to represent a metabolic acidosis unless their subjects had a mean haemoglobin concentration of more than 16 gm/100 ml. The findings of Millar and Marshall (1965) are difficult to interpret owing to the wide scatter of values, calculated from their data, for the slope of consecutive in vitro lines in the same patient.

Less information has been available on the effects of hypercapnia in anaesthetized man, though Holaday, Ma and Papper (1957) reported the onset of metabolic acidosis which tended to be proportional to the degree of carbon dioxide retention in patients who were allowed to hyperventilate for long periods.

The data available on anaesthetized animals suggest that there may be a species difference in acid-base response. Shaw and Messer (1932) in a well controlled study, showed a difference between the response of cats and dogs while breathing 10-11 per cent carbon dioxide, although their results during hyperventilation were equivocal. Their results in dogs, however, have been well confirmed by Siggaard-Andersen (1962a), Morris and Millar (1962), Norman and Linden (1965), and Brown and Clancy (1965). Our analysis of their respective data gives a mean value of -1.30 for the slope of their in vivo lines, this being equivalent to a haemoglobin concentration of about 5 gm/100 ml.

Our data are in reasonable agreement with those of Cunningham, Lloyd and Michel (1962) who describe the in vivo responses of conscious man to changes of \( P_{a102} \). Brackett, Cohen and Schwartz (1965) have recently described a direct comparison of the in vivo and in vitro carbon dioxide titration curve in conscious subjects breathing spontaneously in an atmosphere containing an excess of carbon dioxide. A log \( P_{a102} \)/pH line derived from their in vivo data had a mean slope of -1.18, which represents a buffering response of the whole blood in vivo which is weaker than that of separated plasma in vitro, a finding which we are unable to interpret. We were unable to confirm their quoted linear relationship between \( P_{a102} \) and \([H^+]\) (nanomolar concentration) over the entire range that we have studied in vivo, although it was very nearly linear above a \( P_{a102} \) of 40 mm Hg.

It appears, therefore, that although most workers are agreed that the in vivo response of arterial blood to changes of \( P_{a102} \) differs from that of the same blood in vitro, there is no general agreement on the magnitude. Furthermore, Bunker (1965) has drawn attention to the considerable disagreement as to the validity of parameters derived from in vitro measurements when these are applied to the response of the patient as a whole. The difference in the magnitude of this effect under different conditions has prompted us to control certain factors which might influence the acid-base response to changing \( P_{a102} \) during anaesthesia. These factors are:

1. Maintenance of a constant oxygen saturation of arterial blood at a level slightly above the normal value.
2. Maintenance of constant conditions of ventilation during each phase of the study, by automatic ventilation of the lungs, with complete muscular relaxation.
3. Avoidance of the administration of fluid intravenously, such as blood, citrate, or dextrose solutions, in an attempt to prevent extraneous alterations in the non-respiratory component of acid-base equilibrium (Huckabee, 1958).

That these measures have been successful is suggested by the remarkable stability of the in vivo titration line during the course of anaesthesia of more than 2 hours duration. Although the slope of the in vivo line was different from that of the in vitro line, there was little or no shift of the intercept of the former along the isobar representing a \( P_{a102} \), of 40 mm Hg. This was supported by...
the initial and final control values of standard bicarbonate, before and after the changes of Pa\textsubscript{\text{aO}2} (table I), and implied that there had been no true change of the non-respiratory component as a result of the variations of Pa\textsubscript{\text{aO}2}.

It would appear that despite deliberate wide variations of the Pa\textsubscript{\text{aO}2}, the influence of the anaesthetic technique used in this study has been confined to changes in the respiratory component of acid-base equilibrium. The source of non-respiratory changes during anaesthesia cannot thus be related to ventilatory factors.

During hypercapnia there was a mean fall of standard bicarbonate of 2.4 m.equiv/L in response to a mean rise of Pa\textsubscript{\text{aCO}2} of 32.1 mm Hg. During hyperventilation, there was a mean rise of standard bicarbonate of 1.3 m.equiv/L in response to a fall of Pa\textsubscript{\text{aO}2} of 172 mm Hg (table I). It is clear that these changes of standard bicarbonate do not represent true alterations of the non-respiratory component. If standard bicarbonate is required to give an indication of the true non-respiratory state, then allowance should be made for the phenomenon which we have described, and the measured standard bicarbonate may be corrected as follows:

Corrected standard bicarbonate
\[ = \text{Measured standard bicarbonate} + 0.075 (\text{Pa}_{\text{aCO}2} - 40) \]

Alternatively, the base excess may be corrected:

Corrected base excess
\[ = \text{Measured base excess} + 0.0975 (\text{Pa}_{\text{aCO}2} - 40) \]

The assumption is made that base excess = 1.3 (standard bicarbonate - 24), which is only approximately true as the ratio depends upon the actual value of base excess and the haemoglobin concentration (Sigggaard-Andersen, 1964).

When the Pa\textsubscript{\text{aO}2} does not deviate significantly from the normal limits, it will be seen that the error introduced by the use of derived parameters such as standard bicarbonate is small, and for the purposes of clinical assessment its effect should not be exaggerated.

The explanation of the difference between the response of arterial blood to in vivo and in vitro equilibration with changes of Pa\textsubscript{\text{CO}2} provides ample opportunity for hypothesis. Schwartz and Relman (1963) have drawn attention to the different environment of blood in a tonometer and that in a dynamic equilibrium with other body fluids. Figure I shows the difference between the incremental rise of plasma bicarbonate concentration of whole blood and separated plasma in vitro to carbon dioxide-induced changes of pH. The response of arterial blood in vivo lies between these, suggesting that it equilibrates with a fluid phase having a buffering capacity which is less than that of whole blood but greater than that of plasma.

Due to the efficiency of the lungs as tonometers, the arterial Pa\textsubscript{\text{CO}2} rapidly follows the changes of alveolar Pa\textsubscript{\text{CO}2}, and further equilibration of the blood with the extracellular fluid has been shown to be very rapid (Brown and Clancy, 1965). If blood were in equilibrium only with the extracellular fluid, which has no efficient buffering mechanism against changes of pH induced carbon dioxide we should expect the carbon dioxide titration lines for arterial blood in such equilibrium to have a slope of about -1.30. This value is calculated by assuming a dilution of 5 l. of whole blood containing 15 gm/100 ml of haemoglobin, with about 10 l. of extracellular fluid.

The mean slope which we have found for arterial blood in vivo is -1.45 (table II), and thus must represent equilibration of the whole blood with a fluid phase having a buffering capacity which is higher than that of extracellular fluid alone.

Equilibration would have reached an acute steady-state within the period of 1 hour for which the changes of P\textsubscript{\text{CO}2} were maintained in our study (Giebisch, Berger and Pitts, 1955), and since no measurable deviation from the slope of our in vivo titration line has occurred after the first 5 minutes within this period, we have assumed that intracellular mechanisms must have contributed within these first few minutes to the buffering of the extracellular changes of P\textsubscript{\text{CO}2} and pH. This assumption is given support by the findings of Brown and Clancy (1965), and the reviews of the intracellular acid-base mechanisms by Elkinton (1956) and Robin, Wilson and Bromberg (1961).

Adler, Roy and Relman (1965a, b) have demonstrated the titration lines of muscle cells in response to changes of extracellular P\textsubscript{\text{CO}2} and [HCO\textsubscript{3}-] in vitro. Intracellular pH remains relatively constant when the extracellular P\textsubscript{\text{CO}2} varies between 40 and 70 mm Hg; this means that the
buffering capacity of the cell is very high compared with that of other body fluids. The rise of [HCO₃⁻] within the cell, for the range of Pco₂ change from 40 to 70 mm Hg, is therefore much greater than it is in blood. Since the cell membrane is relatively permeable to bicarbonate ions (Adler, Roy and Relman, 1965a), it is reasonable to assume that there will be a migration of bicarbonate ions from cells into the extracellular fluid in response to a concentration gradient. The rate and extent to which this occurs will influence the corresponding gradient across the capillary membrane, and thus the rate at which bicarbonate ions will migrate out of the blood (Shaw and Messer, 1932); this in turn will influence the slope of the carbon dioxide titration line for arterial blood in vivo.

Such a migration of ions from within the cells during periods of altered carbon dioxide tension has been reviewed by Fenn (1961), and can be predicted by application of the Donnan equilibrium. Experimental confirmation of these ionic shifts was given simultaneously by Elkinton and associates (1955) and Giebisch, Berger and Pitts (1955) who demonstrated an exchange of sodium and other unidentified ions for hydrogen ions across the cell membrane during acutely induced acid-base disturbances.

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REFERENCES


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ETUDE DE LA COURBE DE TITRAGE DU GAZ CARBONIQUE IN VIVO CHEZ L'HOMME ANESTHESIE

SOMMAIRE


BESTIMMUNG DER IN VIVO-KOHLEN- DIOXIDTITRATIONS Kurve BEIM NARKOTISIERTEN MENSCHEN

ZUSAMMENFASSUNG