CHANGES IN THE BICARBONATE CONCENTRATION OF LUMBAR AND CISTERNAL CEREBROSPINAL FLUID IN MAN FOLLOWING ACUTE HYPOCAPNIA AND HYPERCAPNIA

BY
J. S. PADDLE AND S. J. G. SEMPLE

SUMMARY
Ten patients were studied during air encephalography under general anaesthesia with controlled pulmonary ventilation. Arterial carbon dioxide tension was lowered by over-ventilation, or raised by adding carbon dioxide, and lumbar or cisternal cerebrospinal fluid samples were taken for acid-base analysis. No consistent changes in the bicarbonate concentration of the cerebrospinal fluid were demonstrated. This suggests that changes in the bicarbonate concentration of large cavity cerebrospinal fluid, in response to a change in arterial carbon dioxide tension, may be slower in man than animals.

In all chronic acid-base disturbances in man and animals, changes in the cerebrospinal fluid (c.s.f.) pH are smaller than the corresponding changes in arterial blood (Bradley and Semple, 1962; Pauli, Vorburer and Reubi, 1962; Mitchell and associates, 1965; Fencl, Miller and Pappenheimer, 1966). A rise or fall in the carbon dioxide tension (Pco₂) of the c.s.f. leads to changes in the c.s.f. bicarbonate concentration ([HCO₃⁻]) which tend to limit any alteration in the pH of this fluid. Since c.s.f. contains little protein, these changes are not due to any buffering power of this fluid. The exact mechanism whereby these changes in the [HCO₃⁻] are effected is unknown, but it could be due to active transport of an ion or ions between blood, brain and c.s.f. In animals, changes in the c.s.f. [HCO₃⁻] have been shown to operate within 30 minutes of the onset of a marked alteration in the arterial carbon dioxide tension (PₐCO₂) (Merwarth and Sicker, 1961; Swanson and Rosengren, 1962; Michel, 1964). If a similar mechanism operated in man, then a period of hypocapnia or hypercapnia in an anaesthetized patient might produce a significant change in the [HCO₃⁻] of the c.s.f. (Semple, 1965).

Since the changes in the pH of the c.s.f. may play an important role in the central chemical drive to breathing and small changes in the pH of the c.s.f. profoundly affect pulmonary ventilation (Pappenheimer et al., 1965), then the post-operative level of ventilation might be determined, in part, by the PₐCO₂ at which the patient's ventilation was controlled during anaesthesia. Experiments were performed in anaesthetized subjects to see whether changes in the [HCO₃⁻] of the c.s.f. could be demonstrated during short periods of hypocapnia and hypercapnia.

METHOD
Ten patients for air encephalography under general anaesthesia were studied (table I). They were free of cardiopulmonary disease. Five were passively hyperventilated in order to lower their PₐCO₂ and five were passively ventilated with added carbon dioxide in order to raise their PₐCO₂. The period of controlled ventilation lasted 55–80 minutes. Inspired oxygen concentration was 30 per cent. The patients were divided into three groups: Group 1 (preliminary experiments); Group 2 (hypocapnic); Group 3 (hypercapnic).

Group 1 (preliminary experiments). Two patients were hyperventilated and in two a moderate hypercapnia was induced by ventilating the patients with an added low inspired concentration of carbon dioxide so as to maintain the PₐCO₂ between 50 and 60 mm Hg. Lumbar c.s.f. samples were taken before and at the end of the period of controlled ventilation.

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TABLE I
Details of ten patients submitted to air encephalography under general anaesthesia.

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-operative $P_{aCO_2}$ (mm Hg)</th>
<th>Duration of controlled ventilation (min)</th>
<th>$P_{aCO_2}$ at time of initial c.s.f. sample (mm Hg)</th>
<th>$P_{aCO_2}$ during controlled ventilation (mm Hg)</th>
<th>Cerebrospinal fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td></td>
<td>(1)</td>
<td>(2)</td>
<td>Initial [HCO$_3$] (m.equiv/l)</td>
</tr>
<tr>
<td>1. Preliminary experiments</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lumbar</td>
</tr>
<tr>
<td>Hypocapnic</td>
<td>1 Not done</td>
<td>55</td>
<td>44.0</td>
<td>(1) 21.2</td>
<td>20.4</td>
</tr>
<tr>
<td></td>
<td>2 Not done</td>
<td>68</td>
<td>47.5</td>
<td>(1) 31.4</td>
<td>24.1</td>
</tr>
<tr>
<td></td>
<td>3 Not done</td>
<td>65</td>
<td>59.6</td>
<td>(1) 50.1</td>
<td>23.8</td>
</tr>
<tr>
<td></td>
<td>4 Not done</td>
<td>80</td>
<td>55.8</td>
<td>(1) 57.6</td>
<td>23.0</td>
</tr>
<tr>
<td>2. Hypocapnic</td>
<td>5 39.6</td>
<td>70</td>
<td>44.7</td>
<td>(1) 25.5</td>
<td>20.8</td>
</tr>
<tr>
<td></td>
<td>6 39.1</td>
<td>65</td>
<td>54.8</td>
<td>(1) 27.5</td>
<td>20.1</td>
</tr>
<tr>
<td></td>
<td>7 43.3</td>
<td>67</td>
<td>40.4</td>
<td>(1) 20.6</td>
<td>26.2</td>
</tr>
<tr>
<td>3. Hypercapnic</td>
<td>8 36.8</td>
<td>65</td>
<td>49.1</td>
<td>(1) 64.5</td>
<td>19.5</td>
</tr>
<tr>
<td></td>
<td>9 48.7*</td>
<td>72</td>
<td>50.1</td>
<td>(1) 73.7</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>10 45.1</td>
<td>67</td>
<td>47.0</td>
<td>(1) 69.6</td>
<td>24.5</td>
</tr>
</tbody>
</table>

* Femoral venous sample.

In all three groups patients were breathing spontaneously for about 45 minutes following the induction of anaesthesia until the onset of controlled ventilation. Pulmonary ventilation during this time was variable and periods of hypoventilation or hyperventilation were unavoidable. It is possible that the resultant hypercapnia or hypocapnia before the experiments started may have altered the c.s.f. [HCO$_3$] both in cisternal and lumbar regions. These four preliminary experiments were performed to determine whether changes in the [HCO$_3$] would occur in lumbar c.s.f. following controlled periods of hypercapnia and hypocapnia lasting up to 80 minutes.

The results showed minimal changes in the lumbar c.s.f. [HCO$_3$] and therefore it is unlikely that this would have changed during the period of spontaneous breathing following induction. Since the lumbar and cisternal [HCO$_3$] are the same in the steady state (Bradley and Semple, 1962), these findings enabled the first lumbar c.s.f. sample in Groups 2 and 3 to be adopted as representative of the lumbar and cisternal c.s.f. [HCO$_3$] levels existing before anaesthesia began. In some of the experiments in Groups 2 and 3, the control sample of c.s.f. was taken from the lumbar region and its [HCO$_3$] compared with the cisternal fluid taken after a period of controlled ventilation.

Group 2 (hypocapnic). In one patient a lumbar c.s.f. sample was taken before and an cisternal c.s.f. sample at the end of the period of hyperventilation and in two patients cisternal samples were taken before and at the end of the period of hyperventilation.

Group 3 (hypercapnic). In these three patients lumbar c.s.f. samples were taken before the period of induced hypercapnia and cisternal samples at the end of this period.

Analytical method.
Arterial samples were taken during the anaesthetic into heparinized glass syringes and stored in ice water until analysis, 3–6 hours later, for
CHANGES IN BICARBONATE CONCENTRATION OF C.S.F.

Pco₂ by a Severinghaus electrode. Corrections (Bradley, Stupfel and Severinghaus, 1956) were made for differences between measured body and water bath temperature. Lumbar or cisternal c.s.f. samples were taken before and at the end of the period of controlled ventilation which lasted from 55 to 80 minutes. The technique of c.s.f. collection consisted of attaching a three-way plastic tap to a lumbar puncture needle after lumbar puncture had been performed, and in cisternal punctures the plastic tap was connected to the cisternal needle by a short length of butyl rubber tubing. A 2 ml glass syringe was filled with 1 ml of saline and this was flushed through the side arm of the three-way tap, followed by several flushes of c.s.f. to ensure a bubble-free sample. Two 2.5 ml samples were taken consecutively, capped, and stored in ice water. No samples were visibly contaminated with blood or bubbles. pH and Pco₂ were measured 4-6 hours later. pH was measured at 37.5 °C on a Radiometer capillary electrode allowing repeated flushes of distilled water between samples or buffers, and ensuring that no bubbles of air were permitted to contaminate the samples. Pco₂ was measured on a Severinghaus electrode at 37.5 °C. Readings were corrected for differences between measured and body temperature (Mitchell, Herbert and Carman, 1965) and deriving pH values for c.s.f. from the nomogram and formula of Alexander, Gelfand and Lambertsen (1961).

Experimental procedure.

Premedication consisted of atropine 0.6 mg given intramuscularly. Anaesthesia was induced with thiopentone 2½ per cent, 200–250 mg, and a cuffed armedour endotracheal tube was inserted after injection of suxamethonium 75 mg and spraying of the larynx with 4 per cent lignocaine solution. The patient was then allowed to breathe spontaneously a mixture of oxygen, nitrous oxide and either halothane (through a Fluotec*) or trichloroethylene (through a Boyle bottle). A Secunden thermometer† temperature probe was placed in the upper oesophagus or pharynx and an arterial cannula inserted into the brachial artery. The patient was then sat up and positioned appropriately for the air encephalogram. Lumbar or cisternal puncture was performed and c.s.f. samples were collected. Gallamine 60–80 mg was given and ventilation was controlled using a Beaver ventilator, a supplemented nitrous oxide/oxygen mixture being used to maintain anaesthesia. Carbon dioxide was added in the hypercapnic experiments. Increments of gallamine, halothane or trichloroethylene were given if indicated. Pulsar rate and blood pressure were recorded. Arterial sampling, for which permission was obtained, was as follows: a sample was taken immediately before induction in five patients; during the period of controlled ventilation at least two arterial samples were taken, at 22 and 42 minutes (mean) after the onset of the period of controlled ventilation. At the completion of the period of controlled ventilation, lumbar or cisternal c.s.f. samples and an arterial sample were taken. Following this, air was injected into the subarachnoid space and the air encephalogram commenced.

RESULTS

These are shown in table I.

Group 1 (preliminary experiments). In the hypercapnic experiments, patients nos. 3 and 4, there was a slight fall in the lumbar c.s.f. [HCO₃⁻] of 0.5 and 0.6 m-equiv/l. and in the hypocapnic experiments, patients nos. 1 and 2, a fall of 0.4 m-equiv/l. and a rise of 0.7 m-equiv/l. in the lumbar [HCO₃⁻] occurred respectively.

Group 2 (hypocapnic). In patient no. 7 a fall in the [HCO₃⁻] of 1.6 m-equiv/l. occurred, but in the other two (nos. 5 and 6) there was a rise in the [HCO₃⁻] of 0.3 and 0.7 m-equiv/l.

Group 3 (hypercapnic). In patients nos. 8 and 10 a rise in the [HCO₃⁻] of 1.7 and 1.1 m-equiv/l. occurred but in the third (no. 9) there was a fall in the [HCO₃⁻] of 0.3 m-equiv/l.

In the preliminary experiments (Group 1) there was no consistent change in the [HCO₃⁻] of the lumbar c.s.f. whether the patients were hypocapnic or hypercapnic, nor were any consistent changes in the [HCO₃⁻] demonstrated in Group 2 (hypocapnic) or Group 3 (hypercapnic).

DISCUSSION

No consistent change in the c.s.f. [HCO₃⁻] was observed after hypocapnia or hypercapnia. This

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was true whether the final cisternal [HCO₃⁻] was compared with a control sample taken from the lumbar region or the cisterna magna. It was likely that the [HCO₃⁻] of the lumbar c.s.f. was little different from the [HCO₃⁻] throughout the c.s.f. before the induction of anaesthesia, whereas it was possible that the [HCO₃⁻] of cisternal c.s.f. may have changed during the induction of anaesthesia and positioning of the patient when some degree of hypercapnia was present. However, in Group 1 (preliminary experiments) we were able to find only minimal changes in the [HCO₃⁻] of lumbar c.s.f. as a result of either hypercapnia or hypocapnia. This implied that the [HCO₃⁻] of the initial lumbar c.s.f. samples was probably unaffected by the period of hypercapnia arising during the induction of anaesthesia and positioning of the patient.

Although we were unable to detect any consistent change in the [HCO₃⁻] this does not imply that hypocapnia and hypercapnia were without effect on the c.s.f. composition. Our failure to show any change may have been due in part to the unavoidable limitations of the experimental design.

Firstly, there may have been a change in the [HCO₃⁻] of the extracellular fluid and c.s.f. close to the medullary chemosensitive region which was not reflected in either the lumbar or cisternal samples.

Secondly, a small change in the c.s.f. [HCO₃⁻] may not have been detected because of errors of pH measurement on c.s.f. which is a poorly buffered fluid.

In previous experiments in our laboratory (Bradley and Semple, 1962) there was a mean difference of 0.002 (SD 0.005) in the pH measurement of 39 duplicate c.s.f. samples and on tonometry with standard gases the c.s.f.-gas difference was +0.7 (SD 1.0) mm Hg. Changes in pH after storage in ice water up to 5 hours were less than the error of measurement. It is unlikely, therefore, that the time lag of 4–6 hours before processing of samples would have affected the [HCO₃⁻]. However, if an error of 0.005 in pH units and 1 mm Hg in Pco₂ were assumed, this could result in a maximum error of 1.9 m-equiv [HCO₃⁻]. The changes in c.s.f. [HCO₃⁻] which we have observed in our experiments are smaller than the error of the measurement and are therefore of no significance.

Changes in the [HCO₃⁻] of the c.s.f. have been demonstrated in man (Severinghaus et al., 1963) following an alteration in the PaO₂. They found a fall in the lumbar c.s.f. [HCO₃⁻] of 4.3 m-equiv/l. within 1–2 days of prolonged hyperventilation at

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of expts.</th>
<th>Period of observation (min)</th>
<th>Arterial blood</th>
<th>Cerebrospinal fluid</th>
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<tr>
<td>Hypocapnic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kazemi, Shannon and Carvallo-Gil (1967)</td>
<td>Dog</td>
<td>5</td>
<td>−19</td>
<td>−19</td>
</tr>
<tr>
<td>Merwarth and Sicker (1961)</td>
<td>Dog</td>
<td>6</td>
<td>−30</td>
<td>−30</td>
</tr>
<tr>
<td>Present experiments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Mean</td>
<td>Man</td>
<td>3</td>
<td>−23</td>
<td>−17</td>
</tr>
<tr>
<td>(2) Range</td>
<td>Man</td>
<td>70, 60, 60</td>
<td>−21, −27, −20</td>
<td>−14, −21, −16</td>
</tr>
<tr>
<td>Hypercapnic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kazemi, Shannon and Carvallo-Gil (1967)</td>
<td>Dog</td>
<td>5</td>
<td>+50</td>
<td>+47</td>
</tr>
<tr>
<td>Swanson and Rosengren (1962)</td>
<td>Cat</td>
<td>7</td>
<td>+42</td>
<td>+35</td>
</tr>
<tr>
<td>Merwarth and Sicker (1961)</td>
<td>Dog</td>
<td>6</td>
<td>+42</td>
<td>+41</td>
</tr>
<tr>
<td>Present experiments</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>(1) Mean</td>
<td>Man</td>
<td>3</td>
<td>+30</td>
<td>+23</td>
</tr>
<tr>
<td>(2) Range</td>
<td>Man</td>
<td>72, 67, 65</td>
<td>+31, +28, +32</td>
<td>+17, +22, +31</td>
</tr>
</tbody>
</table>
ences. This comparison suggests that changes in the \( [\text{HCO}_3^-] \) of large cavity c.s.f. in animals due in measurement could account for these differ-
experiments. It is, therefore, unlikely that errors in \([\text{HCO}_3^-]\) are considerably greater in the animal
perhaps, unlikely. In hypocapnia, the changes in
2
from 5.7 to as little as 1.7 m.equiv/1. in the three
2
were similar but the changes
2
ment in our experiments could have obscured a
2
capnia, since the changes in c.s.f. \([\text{HCO}_3^-]\) range
2
than in our experiments (table II). In hyper-
2
hence the \( \text{Pco}_2 \) changes in the \( \text{Pa}_2 \)
2
sarily the same as cisternal fluid. However, the
2
Pco in and hence the \( \text{Pco}_2 \) of the c.s.f. were so large in our experiments compared
with the difference between the \( \text{Pco}_2 \) of lumbar
and cisternal c.s.f. that no great error will result
from using the \( \text{Pco}_2 \) of lumbar c.s.f. as repre-
sentative of the cisternal c.s.f. In four experiments
we compared the \( \text{Pco}_2 \) of cisternal c.s.f. with
2
and found it to be +0.4, +3.7, −4.8 and −2.8 mm Hg, with intervals of up to 7 minutes between samples.

In hypocapnia, changes in the \( \text{Pa}_2 \) in animals
were similar to those in our experiments whereas
the changes in hypercapnia were a third greater
than in our experiments (table II). In hyper-
capnia, since the changes in c.s.f. \([\text{HCO}_3^-]\) range
from 5.7 to as little as 1.7 m.equiv/l. in the three
animal experiments, any errors in \( \text{pH} \) measure-
ment in our experiments could have obscured a
change in the c.s.f. \([\text{HCO}_3^-]\), although this is,
perhaps, unlikely. In hypcapnia, the changes in
arterial and c.s.f. \( \text{Pco}_2 \) are similar but the changes
in \([\text{HCO}_3^-]\) are considerably greater in the animal
experiments. It is, therefore, unlikely that errors in measurement could account for these differ-
ences. This comparison suggests that changes in the \([\text{HCO}_3^-]\) of large cavity c.s.f. in animals due
to changes in \( \text{Pco}_2 \) are faster than in man.

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REFERENCES

Alexander, S. C., Gelfand, R., and Lamberts, C. J.
(1961). The \( \text{pK} \) of carbonic acid in cerebrospinal

parison of certain acid-base characteristics of
arterial blood, jugular venous blood and cerebro-
spinal fluid in man, and the effect on them of
some acute and chronic acid-base disturbances.
\textit{J. Physiol. (Lond.)}, 160, 381.

Effect of temperature on \( \text{Pco}_2 \) and \( \text{Po}_2 \) of blood

Fencel, V., Miller, T. B., and Pappenheimer, J. R.
(1966). Studies on the respiratory response to
disturbances of acid-base balance, with deductions
concerning the ionic composition of cerebral inter-
stitial fluid. \textit{Amer. J. Physiol.}, 210, 459.

Gilbert, R. G. B., Brindle, G. F., and Galindo, A.
(1966). \textit{Anaesthesia for Neurosurgery}, p. 43. Lon-
don: Churchill.

Kazemi, H., Shannon, D. C., and Carvallo-Gil, E.
(1967). Brain CO\(_2\) buffering capacity in respiratory

changes in blood and cerebrospinal fluid during

Michel, C. C. (1964). C.S.F. \([\text{HCO}_3^-]\) during respira-
tory acid-base disturbances. \textit{J. Physiol. (Lond.)},
170, 66P.

Mitchell, R. A., Carman, C. T., Severinghaus, J. W.,
Richardson, B. W., Singer, M. M., and Snider, S.
(1965). Stability of cerebrospinal fluid \( \text{pH} \) in
chronic acid-base disturbances in blood. \textit{J. appl.
Physiol.}, 20, 443.

(1965). Acid-base constants and temperature co-
efficients for cerebrospinal fluid. \textit{J. appl. Physiol.},
20, 27.

Pappenheimer, J. A., Fencel, V., Heisey, C. R., and
Held, D. (1965). Role of cerebral fluids in control
of respiration as studied in unanesthetized goats.
\textit{Amer. J. Physiol.}, 208, 436.

Chronic derangements of cerebrospinal fluid acid-

Semple, S. J. G. (1965). Respiration and the cerebro-
spinal fluid. \textit{Brit. J. Anaesth.}, 37, 262.

Severinghaus, J. W., Mitchell, R. A., Richardson,
control at high altitude suggesting active transport
regulation of C.S.F. \( \text{pH} \). \textit{J. appl. Physiol.}, 18,
1155.

Swanson, A. G., and Rosengren, H. (1962). Cerebro-
spinal fluid buffering during acute experimental
MODIFICATIONS DE LA CONCENTRATION DE BICARBONATE DANS LE LIQUIDE CEREBROSPINAL LOMBAIRE ET CISTERNAL CHEZ L'HOMME, APRES HYPOCAPNIE ET HYPERCAPNIE AIGUES

SOMMAIRE
Dix patients ont été étudiés au cours d'une encéphalographie à air, sous anesthésie générale avec ventilation pulmonaire contrôlée. La pression artérielle de gaz carbonique se réduisit sous l'hyperventilation, ou fut augmentée par l'addition de gaz carbonique; des échantillons de liquide cérébrospinal lombaire ou cisternal ont été prélevés pour analyse acide-base. Aucune modification consistante de la concentration de bicarbonate dans le l.c.s. n'a été démontrée. Ceci suggère que les modifications de la concentration de bicarbonate dans le liquide cérébrospinal des grandes cavités, en réaction à l'altération de la pression artérielle de gaz carbonique, se manifestent plus lentement chez l'homme que chez les animaux.

VERÄNDERUNGEN IN DER BICARBONAT-KONZENTRATION DER LUMBALEN UND ZISTERNALEN ZEREBROSPINALFLÜSSIGKEIT BEIM MENSCHEN NACH EINER AKUTEN HYPOKAPNIE UND HYPERKAPNIE

ZUSAMMENFASSUNG