Effects of anoxia on cerebral metabolism and electrolytes in man

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The oxygen tension (pO₂) of brain tissue obeys the law of supply and demand. Supply is influenced by arterial oxygen content, cerebral blood flow, and cerebral blood pH (by the Bohr effect), and demand depends solely on the functional state of brain metabolism. If the oxygen tension of the blood is reduced (for example, by anoxic anoxia of nitrogen inhalation), presumably a value will be reached below which capillary pO₂ is insufficient to maintain oxygen diffusion into brain tissue; functional impairment with signs of cerebral anoxia will result. Such thresholds for oxygen tension have been determined for brain preparations; below these cerebral oxygen consumption became decreased and thresholds for cerebral venous pO₂—at which electroencephalographic slowing and decreased cerebral metabolism occurred—have also been estimated in animals by several investigators.¹⁻⁵ There is as yet no comparable data available in man except a few determinations of the levels of oxygen saturation in the internal jugular vein at which loss of consciousness occurred during nitrogen breathing and postural hypotension.⁹

It has been reported in animals that when tissue or capillary venous pO₂ fell below threshold during induced anoxia the extracellular sodium ions of the brain decreased and there was an increase of extracellular potassium. This ionic change was said to correlate with electroencephalographic slowing.⁵,⁷,⁸ Such data support the notion that anoxic symptoms and signs are due to failure of the mechanism for active sodium transport in brain, which is apparently dependent on cerebral energy metabolism.

The present study reports for the first time in man similar observations concerning the threshold for cerebral venous oxygen tension below which electroencephalographic slowing appeared with accompanying changes of cerebral metabolism and sodium and potassium ions during brief nitrogen inhalation.

CASE MATERIAL AND METHODS

The subjects studied were 19 volunteer patients between the ages of 18 and 81. (Each subject volunteered for these metabolic studies after the procedures, including the nature of jugular venous puncture, were explained to them and their families. Written permission for jugular puncture and the procedure was obtained from each subject. The arterial and venous punctures are the same as those used for the nitrous oxide method for measuring cerebral blood flow.) Twelve patients were admitted to the study because of cerebrovascular disease with stenosis or occlusion of cerebral vessels confirmed by arteriography. Three were admitted because of epilepsy and the rest had miscellaneous neurological complaints without cerebrovascular disease. None had serious cardiac or pulmonary disorders. The present study was combined with therapeutic tests, which will be reported subsequently, to evaluate the effects of certain changes in cerebral circulation and metabolism.

Continuous measurements of oxygen tension (pO₂), oxygen saturation (sO₂), carbon dioxide tension (pCO₂), pH, sodium ionic activity

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(Na\textsuperscript{+}), and potassium ionic activity (K\textsuperscript{+}) in the internal jugular or arterial blood or both during brief hypoxemia induced by nitrogen inhalation were made on all subjects. Details for continuous recording of cerebral blood flow and metabolism have been reported elsewhere.\textsuperscript{5,7,9,10} One-half hour before the study, 100 mg. of heparin, 100 mg. of meperidine hydrochloride (Demerol\textsuperscript{®}), and 0.4 mg. of atropine were given intramuscularly to each subject. Under local anesthesia, with 1 or 2% procaine hydrochloride, arterial and venous catheterizations were performed percutaneously. The catheter from the brachial or femoral artery was connected to a Statham strain gauge (Model P 23 D6) for recording arterial blood pressure. The cerebral venous catheter was placed in the right internal jugular vein for determining cerebral metabolic changes. In 2 patients simultaneous recordings were made from both internal jugular veins so that they could be compared. In 3 patients simultaneous recordings of arterial blood were made for arteriovenous comparison. Arterial values will be indicated by the prefix “a” and jugular venous values by the prefix “j.” (We have avoided complex symbols such as \textit{PjvCO}_{2} and used the simpler forms such as \textit{JpCO}_{2}.)

The blood to be measured was pumped at a constant rate by a Sigma motor from the pertinent catheter and was brought into contact with the sensitive surfaces of the pO\textsubscript{2}, pCO\textsubscript{2}, and glass electrodes for pH, Na\textsuperscript{+}, and K\textsuperscript{+} ions which were contained in a cuvette maintained at body temperature. Both arterial and cerebral venous blood were then returned to the systemic circulation through catheters inserted into the median cubital vein. The pO\textsubscript{2} of the blood was measured with a polarographic electrode which permits accurate, stable recording. The output was amplified by a Beckman physiological gas analyzer and recorded on 1 channel of a Grass Model 7 polygraph. The pCO\textsubscript{2} of the blood was recorded with modified Stow\textsuperscript{11} electrodes, which have been improved in response time and stability. Oxygen saturation was recorded with a reflection oximeter.

A small Beckman pH electrode was used for pH recording. Blood sodium was recorded with NAS\textsubscript{11-18} glass e-trodes,\textsuperscript{7,12} which are highly selective for sodium ions in much the same way as a glass pH electrode is highly selective for hydrogen ions. Blood potassium was recorded in combination with sodium by a Beckman cation electrode. The cation electrode is sensitive to both sodium and potassium ions, but comparison with changes in sodium (described above) permits estimation of the change in potassium. Changes in potassium were expressed in terms of millivolts because of technical difficulty with absolute calibration. Radiometer pH meters were used for the pCO\textsubscript{2}, pH, Na\textsuperscript{+}, and Na\textsuperscript{+} + K\textsuperscript{+} electrodes. Reference electrodes for all the glass electrodes made contact with the blood by means of an agar bridge placed adjacent to the electrodes in the cuvette. Any artificial bioelectric potentials were eliminated by this means. Flow artifacts were minimized by pumping the blood at a constant rate past the electrode. Cerebral venous flow was recorded by intermittently heating a thermistor placed in the left internal jugular vein. The area under the thermal curve is inversely proportional to the velocity of internal jugular flow.\textsuperscript{13} The electrodes were calibrated before and after each study. Apparatus was sterilized by ethylene oxide (Ben Venue sterilizer) and circulating benzalkonium chloride (Zephiran\textsuperscript{®}).

The electroencephalogram was recorded from 8 standard scalp positions by means of a Grass 8 channel electroencephalogram, and the electrocardiogram was recorded with a Cambridge electrocardiograph. Expired carbon dioxide tension (pECO\textsubscript{2}) was recorded with a Beckman Spinco infrared gas analyzer. Nasopharyngeal pressure was recorded by means of a strain gauge as an indicator of respiration.

The nitrogen gas was breathed through a face mask until electroencephalographic slowing appeared, when room air was immediately substituted. Electroencephalographic slowing in all patients consisted of the appearance of delta waves or diffuse theta rhythms. This pattern corresponds to the first and second stages of electroencephalographic abnormality during nitrogen inhalation according to the classification of Gastaut.\textsuperscript{14} This change will now be called “electroencephalographic slowing” for convenience. Cerebral changes of cerebral venous blood were correlated with the electroencephalographic change from the continuous records. Values from right internal jugular blood were regarded as repre-
sentative of average cerebral venous blood in this study and were used for statistical analysis. This assumption was later justified since simultaneous changes in gases and electrolytes from right and left internal jugular blood were found to be identical in terms of both absolute values and quantitative changes (Fig. 1).

RESULTS

General observations. Figure 1 is a typical record of changes in JPO₂, JpCO₂, JpH, JNa⁺, JNa⁺ + K⁺, and internal jugular blood flow in a 61-year-old patient with occlusion of the left middle cerebral artery. Nitrogen inhalation produced decreases in JpO₂, JpCO₂, and JNa⁺ and increases in JpH and JNa⁺ + K⁺. Electroencephalographic slowing appeared when JpO₂ decreased to 19.1 mm. Hg. Jugular flow increased by 6%. Expired carbon dioxide tension decreased because of hyperventilation.

Figure 2 illustrates similar changes recorded from both internal jugular veins during nitrogen inhalation in a 52-year-old patient with right middle cerebral occlusion.

Figure 3 shows correlated cerebral arteriovenous differences during nitrogen breathing. Simultaneous records of pCO₂, sO₂, pH, Na⁺, and Na⁺ + K⁺ were recorded from both arterial blood (designated by prefix “a”) and jugular venous blood (designated by prefix “J”). JpO₂, JsO₂, apO₂, and asO₂ all decreased during nitrogen inhalation. However, it should be noted that the decrease in pO₂ of the cerebral venous blood was less than that of the arterial blood. Arterial carbon dioxide tension decreased and apH increased due to the hyperventilation resulting from hypoxia. It should be noted in this case that JN⁺ decreased by 1.7 mEq. per liter while arterial Na⁺ increased by about 1 mEq. per liter, compatible with a loss,
or flux, of sodium ion from cerebral blood into brain tissue. In contrast, cerebral venous content of potassium increased compatible with a release, or flux, of potassium from brain tissue into cerebral venous blood, since \( \text{Na}^+ + K^+ \) increased while \( \text{Na}^+ + K^+ \) decreased. Arterial blood pressure decreased slightly after an initial slight elevation during anoxia.

Figure 4 correlates cerebral venous flow with alterations in cerebral venous gases and electrolytes during anoxia. In this case cerebral venous flow increased almost one and one-half times during nitrogen breathing. The increase in jugular blood flow induced by nitrogen inhalation shows that the effect of decreased blood and tissue p\( \text{CO}_2 \) on cerebral vessels is to increase cerebral blood flow despite a remarkable decrease in cerebral p\( \text{CO}_2 \) (as indicated by the Jp\( \text{CO}_2 \) record), which would tend to constrict cerebral vessels.

The results obtained in 19 patients are summarized in Table 1. Maximum changes in gases and pH were obtained from records during the control period and at maximum alteration during nitrogen inhalation. These results will be discussed under separate headings.

Effects of 100% \( \text{N}_2 \) inhalation on internal jugular p\( \text{O}_2 \), p\( \text{CO}_2 \), and pH. The mean steady state value for Jp\( \text{O}_2 \) in 19 patients was 30.64 ± 3.72 mm. Hg. When 100% nitrogen was inhaled, there was a mean decrease to 16.76 ± 3.29 mm. Hg. The decrease was statistically significant (\( p < 0.01 \)). Jugular venous carbon dioxide tension decreased in all 18 patients
Thresholds for electroencephalographic slowing. Threshold values for \( \text{JpO}_2 \), \( \text{JpCO}_2 \), and \( \text{JpH} \) were obtained at the moment when electroencephalographic slowing appeared. The values are listed in the right 3 columns of Table 1. The mean threshold value for \( \text{JpO}_2 \) was 18.95 ± 2.55 mm. Hg. The mean value for \( \text{JpCO}_2 \) was 44.28 ± 5.74 mm. Hg. The mean value for \( \text{JpH} \) was 7.309 ± 0.075 in pH units. All these thresholds are plotted in Figure 5 with mean values as double circles and standard deviations as longitudinal lines. The threshold values for \( \text{JpO}_2 \) cluster in a narrow area whereas those for \( \text{JpCO}_2 \) and \( \text{JpH} \) are widely scattered. It is apparent that the value for \( \text{JpO}_2 \) is the relevant factor responsible for electroencephalographic slowing.

Effects of 100% \( \text{N}_2 \) inhalation on arterial \( \text{pO}_2 \), \( \text{pCO}_2 \), and \( \text{pH} \). Mean changes in arterial blood were as follows: \( \text{apO}_2 \) decreased from 79.6 ± 10.3 mm. Hg to 24.2 ± 2.5 mm. Hg; \( \text{apCO}_2 \) decreased from 38.4 ± 4.1 mm. Hg to 28.4 ± 1.0 mm. Hg; and arterial \( \text{pH} \) increased from 7.305 ± 0.019 to 7.410 ± 0.040 units.

Effects of 100% \( \text{N}_2 \) inhalation on arterial and jugular \( \text{Na}^+ \) and \( \text{K}^+ \). Measurements of jugular sodium (\( \text{JNA} \)) were made successfully in 16 patients. In 11 of the 16, \( \text{JNA} \) decreased, in 4 patients it remained unchanged, and in only 1 it was increased. The mean decrease of \( \text{JNA} \) was 0.64 ± 0.79 mEq. per liter. This decrease was statistically significant (\( p < 0.05 \)). Measurements of jugular potassium (\( \text{JNA}^+ + \text{K}^+ \)) were successfully made in 12 patients. There was an increase in 9 patients, no change in 2, and a decrease in 1. The mean increase in jugular potassium was 0.36 ± 0.38 mV, which was statistically significant (\( p < 0.05 \)).

The above data can be summarized by stating that during cerebral anoxic anoxia with electroencephalographic slowing there is a decrease of sodium and an increase of potassium ionic activity of the cerebral venous blood.

Concurrent measurements of arterial sodium and potassium activity were made in 2 patients during the cerebral venous flux described above. Arterial \( \text{Na}^+ \) decreased in one and increased in the other. Venous changes were apparently independent of arterial change.

Factors which may influence \( \text{JpO}_2 \) threshold values. Other factors that might predispose individual subjects to cerebral anoxia were
now evaluated. The distribution of the threshold values for JpO₂ were analyzed to find out if factors such as age, presence of cerebrovascular disease, and the steady state level of JpO₂, JpCO₂, and pH predisposed to anoxic electroencephalographic change and any degree of sodium and potassium flux.

Age. The subjects were divided into 2 groups above and below 35 years of age. In the 12 subjects aged 36 years or older the mean threshold JpO₂ for electroencephalographic change was 19.1 ± 2.7 mm. Hg. It was 18.2 ± 2.4 mm. Hg for the group below 35 years. There was no statistical difference between the 2 groups.

Cerebrovascular disease. The possible influence of cerebral vascular disease was assessed by dividing the subjects into 2 groups, those with and those without known cerebrovascular disease. There were 11 subjects in the group with cerebrovascular disease who had a mean threshold of JpO₂ for electroencephalographic slowing at 18.7 ± 2.8 mm. Hg. In those without cerebrovascular disease the threshold was 19.2 ± 2.3 mm. Hg. No statistical difference was evident between the 2 and no predisposition was found when the types of cerebrovascular disease were analyzed according to type of arteriographic abnormality—cerebral arteriovenous malformation, occlusion or stenosis of major cerebral vessels, or disease of small cerebral vessels.

Cerebral susceptibility to electroencephalographic slowing. The subjects were divided into 2 groups according to the severity of electroencephalographic change—that is, those with theta waves and those with delta waves during anoxia. In the group with theta slowing, the average threshold for JpO₂ was 19.6 ± 3.7 mm. Hg (6 patients). In those with delta slowing, it was 18.6 ± 1.7 mm. Hg (12 patients). There was no statistically significant difference between the 2 groups.

Initial values of JpO₂, JpCO₂, and JpH. It was considered that the threshold of JpO₂ for electroencephalographic slowing might be influenced by the resting metabolic status of the brain as expressed by initial values of JpO₂, JpCO₂, and JpH. Statistical analysis failed, however, to show any correlation between the threshold JpO₂ and steady state values of JpO₂, JpCO₂, and JpH.

Fig. 4. Increase in cerebral blood flow resulting from nitrogen inhalation despite decrease in JpCO₂. Jugular blood flow (JF), measured by the thermovelocity method was increased by about one and one-half times. Record shows that decrease of cerebral capillary pO₂ results in increased cerebral blood flow despite decreased cerebral capillary pCO₂ and increase of cerebral capillary pH.

DISCUSSION

The threshold pO₂ of cerebral capillary blood for anoxic symptoms. The application of new electronic monitoring devices in the present study has made it possible to determine the threshold value for partial pressure of oxygen in the cerebral venous blood at which electroencephalographic slowing appears dur-
In the dog, Noell\textsuperscript{2} reported depression of cerebral arteriovenous differences for oxygen content when calculated values for cerebral venous PO\textsubscript{2} fell below 19 mm. Hg during anoxic anoxia. This threshold value for JpO\textsubscript{2} was confirmed by the work of Hirsch\textsuperscript{4} who investigated the relationships in the isolated canine head between cerebral metabolic rate for oxygen and the PO\textsubscript{2} of superior sagittal sinus blood. He found that the cerebral metabolic rate decreased whenever cerebral venous PO\textsubscript{2} was lowered below 17 to 19 mm. Hg during ischemic anoxia. Despite the use of different species and different criteria for assessing cerebral dysfunction, results reported in animals support data now recorded in man.

More than thirty years ago, Lennox, Gibbs, and Gibb\textsuperscript{st} reported in a few human studies that loss of consciousness occurred if the oxygen saturation of the jugular venous blood fell below 24%. If it did not fall below 30%, the subject remained conscious. Simultaneous measurements of pH, which were not given by them, would be necessary to calculate the oxygen tension from these measurements of oxygen saturation. Accurate measurement of cerebral capillary PO\textsubscript{2} is of much greater physiological importance than its oxygen saturation since oxygen available to brain tissue is dependent on the plasma PO\textsubscript{2} of the cerebral capillaries and not on the oxygen combined in the erythrocytes as oxyhemoglobin. This is because the release of oxygen from erythrocytes, and hence plasma PO\textsubscript{2}, is greatly influenced by capillary pH due to the Bohr effect. Unfortunately, pH values were not made available from their data, but if one assumes or supposes that their JpH was 7.30, the calculated JpO\textsubscript{2} would be 17 to 20 mm. Hg. If this assumption is permitted, their threshold JpO\textsubscript{2} would also be in agreement with our results.

The causes of decreased cerebral capillary pCO\textsubscript{2} during anoxic anoxia. The decrease in JpCO\textsubscript{2} during nitrogen inhalation is partly due to hyperventilation which decreased the apCO\textsubscript{2}. However, in experiments reported in the monkey, cerebral JpCO\textsubscript{2} decreased during anoxic electroencephalographic slowing despite the fact that apCO\textsubscript{2} and respiration were maintained constant.\textsuperscript{5} In addition the effect of hyperventilation which usually occurs during anoxia in man, the following factors would

![Diagram](image_url)
<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Blood source</th>
<th>( pO_2 ) before, after</th>
<th>( pCO_2 ) before, after</th>
<th>( pH ) before, after</th>
<th>Na(^+) mEq/L</th>
<th>Na(^+)+K(^+) mV.</th>
<th>Threshold values</th>
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<td>1. 66 M</td>
<td>66</td>
<td>M</td>
<td>Right carotid stenosis</td>
<td>R.J.</td>
<td>30.0-22.8</td>
<td>36.0-33.0</td>
<td>7.335-7.395</td>
<td>+0.6</td>
<td>+1.2</td>
<td>24.1 33.0</td>
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<td>M</td>
<td>Left vertebral stenosis</td>
<td>R.J.</td>
<td>25.2-21.0</td>
<td>49.0-40.3</td>
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<td>+0.15</td>
<td>22.6 45.0</td>
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<td>3. 61 M</td>
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<td>M</td>
<td>Left middle cerebral artery occlusion</td>
<td>R.J.</td>
<td>29.7-18.9</td>
<td>57.0-52.8</td>
<td>7.195-7.210</td>
<td>0</td>
<td>0</td>
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<td>41</td>
<td>F</td>
<td>Gross obesity</td>
<td>R.J.</td>
<td>32.0-20.0</td>
<td>51.7-48.0</td>
<td>7.195-7.210</td>
<td>-2.0</td>
<td>+0.15</td>
<td>19.1 47.5</td>
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<td>M</td>
<td>Left middle cerebral artery disease</td>
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<td>48.4-32.3</td>
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<td>+1.0</td>
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<td>6. 18 M</td>
<td>18</td>
<td>M</td>
<td>Epilepsy</td>
<td>R.J.</td>
<td>35.3-13.3</td>
<td>56.3-50.8</td>
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<td>7. 81 F</td>
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<td>F</td>
<td>Generalized arteriolosclerosis</td>
<td>R.J.</td>
<td>28.0-12.0</td>
<td>50.8-44.3</td>
<td>7.345-7.400</td>
<td>0</td>
<td>+</td>
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<td>8. 47 F</td>
<td>47</td>
<td>F</td>
<td>Takayasu syndrome</td>
<td>R.J.</td>
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<td>43.0-38.0</td>
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<td>F</td>
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<td>R.J.</td>
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<td>36</td>
<td>F</td>
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<td>R.J.</td>
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<td>F</td>
<td>Convulsive disorder, arteriovenous malformation</td>
<td>R.J.</td>
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<td>12. 61 F</td>
<td>61</td>
<td>F</td>
<td>Bilateral carotid stenosis</td>
<td>Right posterior cerebral artery occlusion</td>
<td>R.J.</td>
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<td>46.0-38.7</td>
<td>7.375-7.430</td>
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<td>+1.0</td>
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<td>13. 81 M</td>
<td>81</td>
<td>M</td>
<td>Left middle cerebral artery occlusion</td>
<td>R.J.</td>
<td>26.2-15.2</td>
<td>37.2-33.7</td>
<td>7.345-7.390</td>
<td>-1.0</td>
<td>+0.2</td>
<td>19.0 35.0</td>
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<td>14. 52 M</td>
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<td>M</td>
<td>Right middle cerebral artery occlusion</td>
<td>R.J.</td>
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<td>43.5-38.0</td>
<td>7.340-7.390</td>
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<td>M</td>
<td>Left internal carotid occlusion</td>
<td>R.J.</td>
<td>41.0-17.6</td>
<td>56.2-47.8</td>
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<td>F</td>
<td>Hypertensive cerebral arteriolospathy</td>
<td>R.J.</td>
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<td>53.8-52.2</td>
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<td>M</td>
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<td>R.J.</td>
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<td>51.7-43.0</td>
<td>7.210-7.277</td>
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<td>27</td>
<td>F</td>
<td>Posttraumatic epilepsy</td>
<td>R.J.</td>
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<td>52.6-48.9</td>
<td>7.280-7.303</td>
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<td>Giant cell arteritis</td>
<td>R.J.</td>
<td>26.6-13.5</td>
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<td>7.280-7.303</td>
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<td>+0.5</td>
<td>15.5 48.9</td>
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</table>

Threshold values for electroencephalographic slowing are listed in the 3 columns at extreme right. In the columns of Na\(^+\) and Na\(^+\)+K\(^+\), figures indicate changes from control values. Signs of plus and minus without figures indicates the direction of the change when absolute values were not available. R.J. = Right jugular venous blood. L.J. = Left jugular venous blood. A. = Arterial blood. 0 = No change.
contribute to the decrease in cerebral venous pCO₂: [1] decreased CO₂ production by anoxic brain since aerobic metabolism becomes depressed, [2] increased removal of cerebral tissue CO₂ by increased cerebral blood flow since there is a direct vasodilator effect of reduced pO₂ on the smooth muscles of cerebral arterioles, and [3] increased transformation of CO₂ dissolved in the plasma to combined CO₂, which occurs when hemoglobin falls.

Cerebral ionic fluxes of sodium and potassium during anoxia in man. It is now widely recognized that glass electrodes can be used successfully in man to demonstrate changes in sodium and potassium ionic activity which in turn may be related to changes in ionic concentration, just as the electric output of a glass pH electrode is used to measure hydrogen ion concentration. The increase of cerebral capillary-venous potassium and decrease of cerebral capillary-venous sodium were found to be statistically significant during cerebral anoxia. These changes appeared to be independent of arterial changes, although in patient No. 18, the electrolyte changes of arterial blood were in the same direction as those of cerebral venous blood but were quantitatively less. As far as patient No. 18 is concerned, the ionic changes could be attributed partly to changes in the brain and, possibly, partly to arterial changes derived from anoxic changes in other organs such as the liver. However, in the instance illustrated in Figure 3, the ionic changes in the arterial blood were in the opposite direction to those in the cerebral venous blood, indicating that the blood perfusing cerebral capillaries loses sodium and gains potassium ions during anoxia with electroencephalographic change. In animal experiments, a decrease of Na⁺ and an increase of K⁺ of the cerebral extracellular fluid were reported during anoxic anoxia, which coincided with similar changes in cerebral venous blood. (Some controversy exists about the size or even the functional existence of the extracellular space of the brain. However, for convenience, the thin layer of fluid between the electrode and brain surface was arbitrarily defined as extracellular fluid.) It was deduced from this that sodium ions were moving into and potassium ions were moving out of brain cells. These ionic changes of cerebral venous blood in animals and man during anoxia are believed to be caused by a sodium influx and potassium efflux across membranes of brain cells presumably because anoxia suppresses aerobic metabolism and the high-energy requirement of the cellular sodium extrusion mechanism (sodium pump) fails to be supplied.

The apparatus used in the present study in man for measurement of ionic changes in cerebral venous blood as well as previous confirmatory measurements reported by us in the monkey eliminates the possibility of contamination from bioelectric direct current potentials derived from the brain, since both sodium electrode and reference electrode made contact only with cerebral venous blood pumped at a constant rate through a cuvette with temperature constant at 37°C. The entire recording system was far removed from the brain and hence from bioelectric direct current potentials of cerebral origin. The data reported here in man, therefore, support our previous results in animals. In man, as in animals, a sodium influx and a potassium efflux relating to cerebral functional impairment and recovery appear also to be demonstrable during anoxia.

Schade reviewed similar experimental data in animals found by others and reported a rapid rise in impedance of the brain during asphyxia, which he assumed to be due to transport of sodium chloride, accompanied by water, into the apical dendrites of cortical neurons. Bakay found that severe hypoxia (asO₂ 26%) with CO₂ accumulation increased the cerebral uptake of Na as well as P in cats, although milder hypoxia (asO₂ 44%) failed to produce similar effects. Plum and his co-workers later confirmed the increased sodium and decreased potassium concentration of a single edematous hemisphere caused by ischemic anoxia in the rat by generally accepted biochemical methods.

CONCLUSIONS

Evidence presented here suggests that during anoxia in man the brain gains sodium and loses potassium. Maintenance of ionic homeostasis by the human brain would, therefore, appear to be dependent or oxidative metabolism similar to findings established in the nerve axon of lower forms. If ionic homeo-
stasis in the human brain fails, due to temporary anoxia, electroencephalographic slowing and functional abnormality result. If oxygen is rapidly restored to the brain, oxidative metabolism and active sodium transport resume with recovery of cerebral function and electroencephalographic activity, provided that irreversible anoxic damage has not occurred. If this conclusion proves to be correct, an explanation is provided for reversible ischemic paralysis and other transient disorders of brain function in man which result from temporary impairment of oxygen delivery to the brain.

SUMMARY

1. Internal jugular blood gases and electrolytes were continuously recorded in 19 patients and correlated with electroencephalograms made during acute anoxemia induced by nitrogen inhalation.

2. Acute anoxemia produced statistically significant decreases in oxygen and carbon dioxide tension but an increase in pH of the cerebral venous blood.

3. Lowered oxygen tension of cerebral blood has a direct vasodilator effect on cerebral arterioles of man, independent of any changes in cerebral blood pCO₂ or pH.

4. When cerebral venous oxygen tension fell below 18.95 ± 2.55 mm. Hg, electroencephalographic slowing regularly appeared regardless of other variables.

5. A decrease in sodium and an increase in potassium ionic activity of the cerebral venous blood were observed in acute anoxemia, independent of arterial changes in these ions. These changes were statistically significant.

6. It was concluded that during temporary anoxia, the brain gains sodium and loses potassium while the reverse occurs during recovery from anoxia and return of cerebral function. Ionic homeostasis and electric activity of the human brain appear to be dependent on oxidative metabolism.

REFERENCES


