The predictive value of cerebral anaerobic metabolism with cerebral infarction after head injury

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Cerebral ischemia is a common mechanism of secondary brain injury following severe head injury. The cerebral metabolic rate of oxygen (CMRO2) and of lactate (CMRL), as well as cerebral blood flow (CBF) were measured daily for 5 days after head injury in 44 comatose head-injured patients to determine if metabolic changes could identify the patients who would develop cerebral infarction. Of 41 patients whose CBF remained at levels regarded as adequate to prevent infarction (CBF ≥ 0.2 ml/gm/min), the six who showed a cerebral infarction on computerized tomography (CT) scans exhibited characteristic cerebral metabolic patterns: a CMRO2 of less than 0.6 µmol/gm/min on one or more of the days monitored, and markedly elevated cerebral lactate production (CMRL < -0.06 µmol/gm/min) on Days 1 and/or 2 after injury. Patients who had no areas of infarction on serial CT scans typically had a CMRO2 of 0.6 µmol/gm/min or higher and a low cerebral lactate production. Measurement of CMRO2 and CMRL can be obtained at the bedside and can indicate the presence of an evolving ischemic infarct after head injury.

KEY WORDS □ cerebral metabolism □ head injury □ cerebral ischemia □ cerebral infarction □ cerebral blood flow

The response of the brain to traumatic injury involves several pathological processes, including edema formation, hyperemia, and ischemia. In one autopsy study, 91% of all patients who died of their head injury had histological evidence of ischemic injury.1 Cerebral blood flow (CBF) measurements have been disappointing as a way of prospectively identifying patients who will develop ischemic injury. Global hypoperfusion, defined as a CBF of less than 0.2 ml/gm/min, is uncommon, occurring in less than 15% of all severely head-injured patients.7,21,24 Regional hypoperfusion due to injury, compression, or spasm of a major intracranial artery or hypoperfusion in watershed areas is difficult to demonstrate on CBF studies after head injury. Nevertheless, Overgaard, et al.,23 using a high-resolution intracarotid xenon method to measure regional CBF (rCBF), defined regions where CBF was less than 0.2 ml/gm/min in 14 (61%) of 23 patients with poor neurological outcome, but in only 1.1% of all rCBF measurements performed in patients with a good outcome. The incidence of low rCBF was highest in the first few hours after injury. Most other authors who have used intravenous or inhalational xenon methods to measure rCBF have found the incidence of regional hypoperfusion to be much lower.5,8,10,16,22

Several possible explanations exist for the apparent discrepancy between the low incidence of hypoperfusion demonstrated by CBF measurements and the high incidence of ischemic damage present at autopsy. It is likely that the decreased CBF is transient and occurs at times when CBF is not measured, such as prior to arrival at the hospital. In addition, the CBF may be inhomogeneous, with low-flow areas being obscured by adjacent areas of hyperemia.

In experimental and clinical studies of focal cerebral ischemia, abnormalities of cerebral metabolism persist long after CBF has recovered in tissues that have suffered significant ischemic injury.10,17 and regional cerebral metabolic measurements have provided valuable information regarding the severity of the tissue injury in stroke.1 The purpose of the present study was to determine if two parameters of cerebral metabolism (namely, oxygen consumption and lactate production) could be used to identify the presence of ischemic injury in patients with normal or elevated CBF after a severe head injury.

Clinical Material and Methods

Patient Population and Management

From April 1, 1983, to March 31, 1986, 132 patients were admitted to Ben Taub General Hospital in coma.
(Glasgow Coma Scale (GCS) score ≤ 8) following a closed or penetrating head injury. Fifty-six of this total group had at least one CBF measurement, and 44 had satisfactory sequential measurements of CBF and cerebral metabolism during Days 1 to 5 after injury. Among the major reasons for not obtaining serial measurements of CBF in the remaining patients were that the patient had become moribund or had rapidly improved neurologically. The clinical characteristics of the 44 patients who underwent serial measurement of CBF (Table 1) were similar to those of the total group.

All patients were managed by a protocol that included early intubation, prompt evacuation of hematomas, continuous monitoring of intracranial pressure, and treatment of pressures greater than 20 mm Hg. Medications included phenytoin, dexamethasone, and antibiotics in cases of penetrating injuries. Intracranial hypertension was treated sequentially with hyperventilation (pCO2 25 to 30 mm Hg), drainage of cerebrospinal fluid, mannitol, and finally barbiturates. The CBF values are reported uncorrected for pCO2. Mean CBF in a normal adult population at a normal pCO2 is 0.5 ml/gm/min.14

Cerebral Blood Flow

Cerebral blood flow was measured at least once daily for 3 to 5 days after injury by the Kety-Schmidt technique, using N2O as the indicator. In total, 128 individual CBF measurements were obtained. A No. 18 Teflon catheter was inserted percutaneously into the internal jugular vein and positioned so that the tip was in the jugular bulb. The catheter was placed on the side of the most severe injury, as judged by the computerized tomography (CT) scan, or on the right side if the injury was diffuse. The position of the catheter tip was confirmed by x-ray film. A No. 20 catheter was placed in the radial artery. Ten percent N2O was introduced into the patient’s inspired gases in a stepwise fashion, and 10 timed samples of arterial and jugular venous blood were anaerobically collected during the first 15 minutes of N2O saturation. The N2O concentration was measured in the blood samples on an infrared N2O analyzer using an extraction system modified from that described by Swedlow and Lewis.30 The coefficient of variation for repeated N2O measurements was 0.8%. The CBF was calculated from curves fit to the measured N2O concentrations and integrated to 15 minutes (CBF-15) and to infinity (CBF-infinity).12 The coefficient of variation of repeated CBF measurements was 3%. Because CO2 testing was not performed in all patients, the CBF data collected while patients were in barbiturate coma for intractable intracranial hypertension were excluded from the analysis because of the reduction in cerebral metabolism induced by the barbiturates.

Cerebral Metabolism

Arterial and jugular venous blood samples were obtained simultaneously with the measurement of CBF for determination of blood gases, oxygen saturation, hemoglobin, and lactate concentration. The blood gases were measured on a Corning 165/2 blood gas analyzer and the hemoglobin and oxygen saturation on an IL-282 co-oximeter. The blood samples for lactate concentration were deproteinized immediately after drawing by adding 2 ml of blood to 4 ml of perchloric acid, and the centrifuged supernatants were then refrigerated until they were analyzed by the enzymatic method.18 The coefficient of variation of repeated measurements of lactate by this method was 0.5%. When jugular venous lactate levels were elevated, pyruvate concentration was also measured by the enzymatic method.14 The cerebral metabolic rates of oxygen (CMRO2) and lactate (CMRL) were calculated by multiplying the CBF-15 by the arterial-jugular venous difference of oxygen and lactate, respectively. By this convention, CMRO2 is a positive number since there is always a net consumption of oxygen by the brain. Mean CMRO2 in a normal adult population is 1.5 μmol/gm/min.14 The CMRL can be a positive or a negative number, depending on whether there is a net uptake or excretion of lactate by the brain. Normally, there is a small but measurable cerebral lactate production (mean CMRL ~0.023 μmol/gm/min). Elevated production of lactate by the brain is indicated by a more negative CMRL.

### TABLE 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CBF ≥ 20 ml/gm/min</th>
<th>CBF &lt; 0.2 ml/gm/min</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>no. of cases</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>age (yrs)</td>
<td>35 ± 12</td>
<td>33 ± 10</td>
</tr>
<tr>
<td>sex (M:F)</td>
<td>4:2</td>
<td>24:3</td>
</tr>
<tr>
<td>type of injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DBI</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>SDH</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>EDH</td>
<td>1</td>
<td>8</td>
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<td>10</td>
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<td></td>
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<tr>
<td>GR/MD</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>SD/PVS</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>dead</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

* Abbreviations: CBF = cerebral blood flow; DBI = diffuse brain injury; SDH = subdural hematoma; EDH = epidural hematoma; ICH = intracerebral hematoma; GSW = gunshot wound; GCS = Glasgow Coma Scale; GR = good recovery; MD = moderate disability; SD = severe disability; PVS = persistent vegetative state. For a definition of groups see text.

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* Infrared N2O analyzer manufactured by Vital Signs, Inc., East Rutherford, New Jersey.
† Blood gas analyzer manufactured by Corning Medical Instruments, Medfield, Massachusetts.
‡ Co-oximeter manufactured by Instrumentation Laboratory, Lexington, Massachusetts.

C. S. Robertson, et al.
Anaerobic metabolism with stroke in head injury

Computerized Tomography Appearance

Nonenhanced cranial CT scans were obtained as clinically indicated. Generally, CT was performed on admission, postoperatively, and several times during the first 3 to 6 weeks after injury. Based on the CT scans, the patients were categorized into three groups by a neurosurgeon who was blinded to the CBF data. Group 1 patients exhibited low-attenuation areas on CT, which suggested an infarction. The criteria for distinguishing an infarction from edema were the restriction of a hypodense area to the distribution of an arterial territory with distinct margins, and persistence of the hypodense area after the acute phase of injury. In Group 2 patients, the scans showed low-attenuation areas in the immediate vicinity of hematomas or contusions. Group 3 patients exhibited no areas of low attenuation on CT.

Statistical Analysis

All data are expressed as means ± standard deviations. The data from patients in the different groups were compared by a t-test, and p values less than 0.05 are indicated in Table 2. The arterial lactate concentration and CMRL were examined by linear regression analysis.

Results

Patients Without Global Hypoperfusion

In 41 of the 44 patients, CBF values were always greater than 0.2 ml/gm/min. The clinical characteristics of these patients, categorized by CT scan group into which they fell, are given in Table 1. Six patients (15%) developed areas of low density on serial CT scans which were characteristic of cerebral infarction (Group 1). The location of the infarctions was typical of that described at autopsy in patients who die of their head injury.11 Two patients had infarctions in the distribution of the posterior cerebral artery due to mesial temporal herniation secondary to extracerebral hematomas or diffuse swelling (Fig. 1). Infarctions

![Fig. 1. Computerized tomography scans showing changes in a Group 1 patient who developed an infarction. Left: On admission to the hospital the patient had a large epidural hematoma. Right: A scan obtained on the 1st day after evacuation of the hematoma showing the development of a cerebral infarction in the distribution of the right posterior cerebral artery.]

### TABLE 2

Cerebral blood flow and metabolic parameters in 41 patients without hypoperfusion

<table>
<thead>
<tr>
<th>Parameter*</th>
<th>Group No.</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
<th>Day 5</th>
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<tr>
<td>PaO₂ (mm Hg)</td>
<td>1</td>
<td>26 ± 1</td>
<td>29 ± 3</td>
<td>35 ± 3</td>
<td>31 ± 3</td>
<td>30 ± 3</td>
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<td>CBF (ml/gm/min)</td>
<td>1</td>
<td>0.402 ± 0.136</td>
<td>0.557 ± 0.247</td>
<td>0.510 ± 0.309</td>
<td>0.588 ± 0.258</td>
<td>0.541 ± 0.164</td>
</tr>
<tr>
<td>CBF (ml/gm/min)</td>
<td>2</td>
<td>0.449 ± 0.170</td>
<td>0.428 ± 0.177</td>
<td>0.445 ± 0.210</td>
<td>0.422 ± 0.158</td>
<td>0.409 ± 0.113</td>
</tr>
<tr>
<td>CBF (ml/gm/min)</td>
<td>3</td>
<td>0.568 ± 0.260</td>
<td>0.479 ± 0.179</td>
<td>0.463 ± 0.124</td>
<td>0.432 ± 0.231</td>
<td>0.386 ± 0.062</td>
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<tr>
<td>PaO₂ (mm Hg)</td>
<td>1</td>
<td>34 ± 8</td>
<td>34 ± 5</td>
<td>37 ± 5</td>
<td>41 ± 6</td>
<td>45 ± 13</td>
</tr>
<tr>
<td>CBF (ml/gm/min)</td>
<td>2</td>
<td>32 ± 6</td>
<td>33 ± 5</td>
<td>34 ± 5</td>
<td>35 ± 7</td>
<td>36 ± 7</td>
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<tr>
<td>CBF (ml/gm/min)</td>
<td>3</td>
<td>39 ± 7</td>
<td>36 ± 8</td>
<td>34 ± 5</td>
<td>38 ± 9</td>
<td>32 ± 4</td>
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<tr>
<td>AVDO₂ (µmol/ml)</td>
<td>1</td>
<td>1.76 ± 0.95</td>
<td>1.30 ± 0.62</td>
<td>1.36 ± 0.32</td>
<td>1.30 ± 0.44</td>
<td>1.18 ± 0.99</td>
</tr>
<tr>
<td>AVDO₂ (µmol/ml)</td>
<td>2</td>
<td>2.36 ± 0.95</td>
<td>2.02 ± 0.67</td>
<td>1.87 ± 0.57</td>
<td>1.98 ± 0.77</td>
<td>1.81 ± 0.65</td>
</tr>
<tr>
<td>AVDO₂ (µmol/ml)</td>
<td>3</td>
<td>2.24 ± 0.76</td>
<td>2.15 ± 0.54</td>
<td>2.00 ± 0.58</td>
<td>1.89 ± 1.05</td>
<td>2.09 ± 0.39</td>
</tr>
<tr>
<td>CMRO₂ (µmol/gm/min)</td>
<td>1</td>
<td>0.64 ± 0.15</td>
<td>0.64 ± 0.13</td>
<td>0.63 ± 0.22</td>
<td>0.68 ± 0.08</td>
<td>0.56 ± 0.35</td>
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<tr>
<td>CMRO₂ (µmol/gm/min)</td>
<td>2</td>
<td>1.00 ± 0.32</td>
<td>0.79 ± 0.25</td>
<td>0.77 ± 0.24</td>
<td>0.79 ± 0.27</td>
<td>0.70 ± 0.11</td>
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<tr>
<td>CMRO₂ (µmol/gm/min)</td>
<td>3</td>
<td>1.14 ± 0.36†</td>
<td>1.00 ± 0.33</td>
<td>0.89 ± 0.23</td>
<td>0.77 ± 0.56</td>
<td>0.80 ± 0.02</td>
</tr>
<tr>
<td>CMRL (µmol/gm/min)</td>
<td>1</td>
<td>-0.106 ± 0.069</td>
<td>-0.203 ± 0.196</td>
<td>-0.063 ± 0.053</td>
<td>-0.074 ± 0.096</td>
<td>-0.067 ± 0.018</td>
</tr>
<tr>
<td>CMRL (µmol/gm/min)</td>
<td>2</td>
<td>-0.047 ± 0.052</td>
<td>-0.045 ± 0.043†</td>
<td>-0.047 ± 0.067†</td>
<td>-0.019 ± 0.024</td>
<td>-0.032 ± 0.020</td>
</tr>
<tr>
<td>CMRL (µmol/gm/min)</td>
<td>3</td>
<td>+0.025 ± 0.032‡</td>
<td>-0.017 ± 0.026‡</td>
<td>-0.001 ± 0.027†</td>
<td>-0.005 ± 0.033</td>
<td>-0.002 ± 0.021</td>
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</tbody>
</table>

* CBF = cerebral blood flow (normal 0.50 ml/gm/min); PaO₂ = jugular venous O₂ (normal 36 mm Hg); AVDO₂ = arteriovenous oxygen difference (normal 3.0 µmol/ml); CMRO₂ = cerebral metabolic rate of oxygen (normal 1.50 µmol/gm/min); CMRL = cerebral metabolic rate of lactate (normal -0.023 µmol/gm/min).
† Significantly different from Group 1 patients (p < 0.05).

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FIG. 2. Cerebral metabolic rate of lactate (CMRL) on Days 1 and 2 after injury in 41 patients without hypoperfusion characterized by computerized tomography scan. For a definition of groups see text. The dashed line marks a CMRL of -0.06 µmol/gm/min.

Involving the middle cerebral artery (two patients) and anterior cerebral artery territories (one patient) developed following evacuation of intracerebral hematomas. One patient developed infarction of an entire cerebral and cerebellar hemisphere after removal of a large subdural hematoma.

On later CT scans 27 patients (66%) showed low-density areas in the region of previous intracerebral hematomas or contusions (Group 2). This was a heterogeneous group with the low-density areas resulting from edema and/or infarction, but the difference could not be distinguished with certainty on the basis of the CT scan. The area of tissue involvement was, in general, smaller than in Group 1 patients and corresponded to the region of intracerebral hematoma or contusion noted on earlier scans rather than to the arterial distribution as in Group 1.

Eight (20%) of the patients had CT scans of normal density (Group 3). It was assumed that the patients in this group were the least likely to have had significant ischemic injury, and therefore could serve as comatose but nonischemic control subjects.

In addition to a separation on the basis of the three CT criteria, the patients also exhibited differences in the type of injury sustained and the neurological outcome. Those who had no ischemia (Group 3) had almost exclusively diffuse brain injuries, while in most of those who developed cerebral infarctions (Group 1) hematomas were the etiology of injury. The neurological outcome of the six Group 1 patients (who developed major cerebral infarctions) was poor: there were four deaths and two patients survived with severe disability.

Table 2 compares the CBF and metabolic parameters of the three groups during Days 1 to 5 after injury. The PaCO₂ was not significantly different among the groups; the mean PaCO₂ for all measurements was 30 ± 2 mm Hg. The CBF also was not significantly different among the three groups of patients on any day studied.

Of the cerebral metabolic parameters studied, CMRL provided the clearest separation of the three groups of patients early in their hospital course (Fig. 2). In the patients who had no ischemic injury (Group 3), CMRL was consistently close to zero, indicating low cerebral lactate production. As shown in Fig. 3, CMRL was directly related to the arterial lactate concentration in this group of patients (r = 0.51481, p < 0.01). There was a net uptake of lactate by the brain when the arterial lactate level was greater than 1.5 to 2.0 µmol/ml, similar to the uptake demonstrated in experimental studies where the arterial lactate concentration was increased by intravenous infusion of lactate. Figure 4 shows an example of this characteristic normal cerebral lactate metabolism in a Group 3 patient with a diffuse brain injury who developed no areas of infarction on his CT scan.

Group 1 patients, who developed a cerebral infarction on CT scans, had a markedly negative CMRL, especially on Days 1 and 2 after injury. Occasionally, the cerebral lactate production was 10 times greater than the mean CMRL of the Group 3 patients. When cerebral lactate production was elevated, the jugular venous lactate:pyruvate ratio was also increased. As shown in Fig. 3, there was an inverse relationship between the CMRL and arterial lactate concentration (r = -0.34893, p < 0.05), suggesting that the brain's increased anaerobic metabolism contributed to the systemic lactic acidosis. A cerebral lactate production greater than 0.06 µmol/gm/min was characteristic of the patients who developed an infarction. This level of lactate production was not found in any patient in Group 3. Figure 5 shows an example of elevated cerebral lactate production in a Group 1 patient who de-
Anaerobic metabolism with stroke in head injury

Fig. 4. Example of cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO2) and lactate (CMRL) in a Group 3 patient with no ischemic injury.

Fig. 5. Example of cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO2) and lactate (CMRL) in a Group 1 patient who developed an infarction in the distribution of the middle cerebral artery.

Also tended to be lower in the patients who developed an infarction, suggesting that rather than hypoperfusion, which would result in an increased AVDO2, these patients had a markedly inhomogeneous blood flow with a mean CBF in excess of the injured brain's metabolic needs.

Patients With Global Hypoperfusion

Three patients (7%) had a CBF of less than 0.2 ml/gm/min on Day 1 after injury. The metabolic profiles on two of these patients are shown in Fig. 7 as examples of reversible and irreversible global ischemia. The CBF shown in Fig. 7 left is from a patient with an ipsilateral subdural hematoma. The CBF increased from 0.138 to 0.367 ml/gm/min when mechanical hyperventilation was reduced and the pCO2 was allowed to rise from 21 to 31 mm Hg on the 1st postoperative day after evacuation of the hematoma. Accompanying the increased CBF were an increase in CMRO2 from 0.5 to 0.82 μmol/gm/min and a marked decrease in cerebral lactate production from 0.242 to 0.013 μmol/gm/min; these metabolic changes are consistent with reversal of cerebral ischemia due to hypocarbia. The CBF remained normal for the remainder of the time that it was monitored, and the patient eventually recovered with only moderate disability.

The CBF shown in Fig. 7 right is from a patient with a subdural hematoma. The patient had a CBF of 0.12 ml/gm/min, an extremely low CMRO2 of 0.13 μmol/gm/min, and a CMRL of −0.045 μmol/gm/min. An increase in cerebral perfusion pressure from 70 to 120 mm Hg due to dopamine administration raised CBF to 0.177 ml/gm/min. The accompanying modest increase in CMRO2 suggested that the increase in CBF resulted in improved perfusion of areas that were ischemic but, because the CMRO2 remained low and cerebral lactate production was low, extensive irreversible tissue injury.
FIG. 7. Example of cerebral blood flow (CBF) and cerebral metabolic rate of oxygen (CMRO₂) and lactate (CMRL) in a patient with reversible global ischemia due to hyperventilation with hypocarbia (left) and in a patient with global cerebral infarction (right).

was suspected. A CT scan showed that most of the right cerebral hemisphere, which had been compressed by the hematoma, exhibited marked decrease in attenuation. The patient died 2 days later of uncontrolled intracranial hypertension.

In the third patient with a CBF of less than 0.2 ml/gm/min, CT scans showed only marked hydrocephalus, a normal intracranial pressure, and a persistently very low CBF, CMRO₂, and cerebral lactate production. He was presumed to have a severe brain-stem injury, and he died several months after the injury, having remained in a persistently vegetative state.

Discussion

Recent experimental studies have shown that, while the conditions necessary for ischemic injury are established during a period of hypoperfusion, much of the actual damage occurs during the reperfusion phase. Clinical, electrophysiological, biochemical, and histological recovery followed hours to days later by neuronal death has been described in several models of temporary central nervous system ischemia.5,15,25,26,33 This has given investigators the hope that ischemic damage can be ameliorated by interrupting the various injury cascades that develop after a period of ischemia. In fact, several agents have been demonstrated to be effective in these experimental models.

Clinical trials of agents that appear to reduce ischemic injury require the identification of patients who may benefit early in the course of their injury, when they are most likely to be helped. Changes may not be seen on CT scans for several days, and clinical changes in neurological examination and intracranial pressure after a head injury are not specific for the development of infarction. It is suggested that the evolution of metabolic changes caused by ischemic injury which may permit treatment of the injury may also provide a way of identifying patients who have suffered an ischemic event.

Global CMRO₂ is typically decreased in patients following a focal cerebral infarction. Regional CMRO₂ studies have shown the changes to be most marked in the infarcted tissue but also to involve surrounding tissue, and even the contralateral cerebral hemisphere. The CMRO₂ values reported in irreversibly injured tissues are generally less than 0.6 µmol/gm/min, a value that approximates the theoretical threshold of energy expenditure necessary for nervous tissue to maintain basal functions and membrane integrity.1,3 However, CMRO₂ is also decreased in patients who are comatose following severe head injury. The reduction of metabolism has been shown to be in proportion to the level of coma.22 Because the decrease of CMRO₂ due to secondary ischemic injury is superimposed on an already globally depressed metabolism secondary to the coma, a considerable overlap in values with patients who do not have ischemic injury would be expected. Nevertheless, although a CMRO₂ of 0.6 µmol/gm/min or more did not eliminate the possibility of ischemia in the present study, a CMRO₂ of less than 0.6 µmol/gm/min occurred almost exclusively in patients with clear ischemic injury (Group 1).

Under circumstances where CMRO₂ is decreased simply because of the lower cerebral energy requirements associated with coma, anaerobic metabolism might be expected to be unchanged or even decreased. This was, in fact, the case in the head-injured patients in the present study who developed no evidence of ischemic injury (Group 3). In contrast, when cerebral energy requirements cannot be met by the aerobic metabolism of glucose, anaerobic metabolism is increased. In experimental models of temporary cerebral
Anaerobic metabolism with stroke in head injury

ischemia, increased cerebral production of lactate occurs both during the period of hypoperfusion, due to the decreased availability of oxygen, and also during the early reperfusion period, even in the presence of adequate oxygen, due to damage to or inhibition of aerobic pathways.\textsuperscript{19,28} Because the increased cerebral lactate production of secondary ischemic injury is superimposed on the low cerebral lactate production associated with coma due to head injury, there is a clearer separation of the group of patients with ischemic injury even when the area of infarction is small and not detectable from the measurement of mean CMRO\textsubscript{2}.

Since the blood samples for CBF and for arteriovenous difference of oxygen and lactate are obtained from only one internal jugular vein, the possibility of overlooking an infarction in the opposite cerebral hemisphere exists. Studies of oxygen and glucose concentration performed on samples drawn simultaneously from both internal jugular veins have demonstrated small differences in normal adults, while marked differences can occur in patients with unilateral lesions.\textsuperscript{9} This did not appear to be a significant problem in the present study, since the infarctions occurred either on the side of the major hematoma or bilaterally in the one patient with a diffuse injury. However, limitation of sampling could result in an inability to identify these characteristic metabolic changes of ischemic injury. For this reason, the jugular venous catheter should be placed on the side more likely to be ischemic.

Some investigators have expressed concern over the validity of CMRL measurements, as the use of arteriovenous difference of lactate to calculate CMRL requires that the lactate in venous blood be in equilibrium with the tissue that it drains.\textsuperscript{2,32} This condition is generally met when calculating CMRO\textsubscript{2}, but lactate may not equilibrate across the blood-brain barrier as rapidly as oxygen. Furthermore, arterial lactate concentration fluctuates with time. However, as the present study shows, the large increase in lactate production by ischemic brain greatly overshadows the fluctuation in the calculated CMRL due to physiological changes in arterial lactate concentration, and changes in the calculated CMRL occur rapidly in circumstances where cerebral ischemia is produced or reversed, as demonstrated in Fig. 7 left. Therefore, as long as the measurements are obtained while the patient is in a steady state, these theoretical concerns appear to be of limited practical significance. Measurements of the cerebral metabolism of oxygen and lactate, which can be easily obtained at the bedside, can indicate the presence of an evolving major ischemic infarct after head injury.

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References


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