Effect of Short-Term Hyperventilation on Cerebral Blood Flow Autoregulation in Patients With Acute Bacterial Meningitis

Kirsten Møller, MD; Peter Skinhøj, MD, Professor, DrMedSci; Gitte Moos Knudsen, MD, Professor, DrMedSci; Fin Stolze Larsen, MD, PhD, DrMedSci

Background and Purpose—Cerebral blood flow (CBF) autoregulation is impaired in patients with acute bacterial meningitis: this may be caused by cerebral arteriolar dilatation. We tested the hypothesis that CBF autoregulation is recovered by acute mechanical hyperventilation in 9 adult patients with acute bacterial meningitis.

Methods—Norepinephrine was infused to increase mean arterial pressure (MAP) 30 mm Hg from baseline. Relative changes in CBF were concomitantly recorded by transcranial Doppler ultrasonography of the middle cerebral artery, measuring mean flow velocity (Vmean), and by measurement of arterial to jugular oxygen content difference (a-v DO2). The slope of the regression line between MAP and Vmean was calculated. Measurements were performed during normoventilation and repeated after 30 minutes of mechanical hyperventilation.

Results—At normoventilation (median Pa CO2 4.4 kPa, range 3.5 to 4.9), MAP was increased from 68 mm Hg (60 to 101) to 109 mm Hg (95 to 126). Vmean increased with MAP from 48 cm/s (30 to 61) to 65 cm/s (33 to 86) (P<0.01), and a-v DO2 decreased from 2.2 mmol/L (1.0 to 2.7) to 1.4 mmol/L (0.8 to 1.8) (P<0.05). During hyperventilation (Pa CO2 3.5 kPa, range 3.3 to 4.1), MAP was increased from 76 mm Hg (58 to 92) to 109 mm Hg (95 to 121). Vmean increased from 45 cm/s (29 to 55) to 53 cm/s (33 to 78) (P<0.01), and a-v DO2 decreased from 2.5 mmol/L (1.8 to 3.0) to 1.8 mmol/L (1.2 to 2.4) (P<0.05). Four patients recovered autoregulation completely during hyperventilation. The slope of the autoregulation curve decreased during hyperventilation compared with normoventilation (P<0.05).

Conclusions—CBF autoregulation is partially recovered during short-term mechanical hyperventilation in patients with acute bacterial meningitis, indicating that cerebral arteriolar dilation in part accounts for the regulatory impairment of CBF in these patients. (Stroke. 2000;31:1116-1122.)

Key Words: autoregulation ■ cerebral blood flow ■ cerebral blood flow velocity ■ meningitis ■ ultrasonography, Doppler, transcranial

In patients with acute bacterial meningitis, elevated intracranial pressure (ICP) appears to be related to cerebral edema.1,2 In addition, changes in global and regional cerebral blood flow (CBF) have been reported in acute bacterial meningitis.3,4 The nature of these CBF fluctuations and the pathophysiological importance for the development of cerebral edema and intracranial hypertension are not fully understood. However, it may be reasonable to assume that meningeval inflammation, with the release of a variety of factors, including oxygen free radicals,5 cerebral interstitial acidosis,6 and nitric oxide,7 results in cerebral arteriolar dilation. Such a decrease in cerebrovascular tone would tend to increase cerebral blood volume and subsequently ICP.

Arteriolar dilation also may be expected to affect the normal relation between perfusion pressure and CBF, that is, autoregulation may be disturbed.8 It has previously been shown that CBF autoregulation is impaired in patients with acute bacterial meningitis9,10 and in the rabbit model of meningitis.11

If cerebral arteriolar dilation is responsible for the impairment of autoregulation in patients with acute bacterial meningitis, acute hyperventilation may be hypothesized not only to mediate vasoconstriction8,12,13 but to restore autoregulation. This study was conducted to investigate the acute effect of mechanical hyperventilation on CBF autoregulation in patients with acute bacterial meningitis. Cerebral perfusion was monitored by transcranial Doppler (TCD) and by measuring cerebral oxygen extraction.

Subjects and Methods

Patients
Mechanically ventilated adult patients with acute bacterial meningitis were consecutively evaluated for entry into the study. Acute bacterial meningitis was defined by the presence of a neutrophil pleocytosis (>10×10⁶ leukocytes/L) in cerebrospinal fluid. Patients were included if the diagnosis was made by lumbar puncture in conjunction with clinical symptoms and signs consistent with meningitis. Patients with previous history of head trauma, intracranial surgery, or neurological disease were excluded.

Methods
CBF was monitored by transcranial Doppler ultrasonography (TCD). Mean flow velocity (Vmean) was used as an index of CBF. Measurements were performed during normoventilation and repeated after 30 minutes of mechanical hyperventilation. The slope of the regression line between MAP and Vmean was calculated. Measurements were performed during normoventilation and repeated after 30 minutes of mechanical hyperventilation.

Results
At normoventilation, MAP was increased from 68 mm Hg (60 to 101) to 109 mm Hg (95 to 126). Vmean increased with MAP from 48 cm/s (30 to 61) to 65 cm/s (33 to 86) (P<0.01), and a-v DO2 decreased from 2.2 mmol/L (1.0 to 2.7) to 1.4 mmol/L (0.8 to 1.8) (P<0.05). During hyperventilation, MAP was increased from 76 mm Hg (58 to 92) to 109 mm Hg (95 to 121). Vmean increased from 45 cm/s (29 to 55) to 53 cm/s (33 to 78) (P<0.01), and a-v DO2 decreased from 2.5 mmol/L (1.8 to 3.0) to 1.8 mmol/L (1.2 to 2.4) (P<0.05). Four patients recovered autoregulation completely during hyperventilation. The slope of the autoregulation curve decreased during hyperventilation compared with normoventilation (P<0.05).

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Autoregulation Studies

In all patients, the autoregulation study was performed within 48 hours after diagnostic lumbar puncture. One observer (K.M.) carried out all studies. The study consisted of 2 autoregulation measurements. The order of the autoregulation measurements was not randomized. The normoventilation measurement was performed at baseline ventilator settings. Since it was considered ethically unacceptable to increase the PaCO₂ to normal levels, given the usual therapeutic regimen of these patients in the Department of Infectious Diseases, the “normoventilation” measurement was thus in general performed at slight hyperventilation. The hyperventilation measurement was carried out shortly after the normoventilation measurement after 30 minutes of hyperventilation to achieve a steady-state decrease in PaCO₂ of 1 kPa. The position of the patients was unaltered during both measurements. Similarly, the position of the TCD probe was unaltered in all patients but one, in whom accidental dislocation occurred and was corrected. After the autoregulation study, ventilator settings were returned to baseline settings. No patient exhibited clinical signs of increased ICP such as seizures or papillary abnormalities during the autoregulation study.

Autoregulation measurements were carried out during an infusion of norepinephrine (0.03 to 0.30 μg·kg⁻¹·min⁻¹), leading to a gradual increase in MAP of 30 mm Hg from baseline. MAP, TCD parameters, and blood gas parameters were concomitantly recorded. Where possible, ≥5 simultaneous measurements of MAP, TCD parameters, and blood gas parameters were performed during each autoregulation measurement.

Transcranial Doppler Ultrasonography

Unilateral TCD of the middle cerebral artery was performed with a 2-MHz pulsed probe placed over the temporal window and secured by a headband. Measured parameters included systolic, diastolic, and mean flow velocities (V₀, V₉₀, and Vmean [in cm/s]), respectively. Calculated parameters included Gosling’s pulsatility index (PI), defined as (V₀−V₉₀)/Vmean. Assumingly an unchanged caliber of the middle cerebral artery, V₀ will change in proportion with CBF. Thus, Vmean may be used to measure relative changes in CBF.

Arterial and Jugular Vein Blood Gas Analysis

Blood samples for blood gas analysis were drawn simultaneously from the radial artery catheter and the retrograde jugular vein catheter. Blood gases were measured on an ABL 605 and OSM 3 (Radiometer). Blood hemoglobin content (Hb, in mmol/L) was measured by standard methods.
Arterial oxygen content ($CaO_2$) (in mmol/L) was calculated as:

$$CaO_2 = 0.96 \times Hb \times SaO_2 + 0.01 \times PaO_2$$

where $SaO_2$ denotes arterial oxygen saturation (measured as a fraction of 1) and $PaO_2$ denotes arterial oxygen tension (in kPa).

Jugular venous oxygen content ($C_{jv}O_2$) was similarly calculated as:

$$C_{jv}O_2 = 0.96 \times Hb \times S_{jv}O_2 + 0.01 \times P_{jv}O_2$$

The arterial to jugular oxygen content difference (a-v $DO_2$) was calculated as:

$$a-v \, DO_2 = CaO_2 - C_{jv}O_2$$

Assuming an unchanged metabolic rate of oxygen ($CMRO_2$), a-v $DO_2$ changes in inverse proportion to $CBF$, since, according to the Fick principle, $CMRO_2 = CBF \times (CaO_2 - C_{jv}O_2) = CBF \times (a-v \, DO_2)$. Thus, an increase in $CBF$ will elicit a proportional decrease in a-v $DO_2$, which may be used to estimate relative changes in global $CBF$.\textsuperscript{16,17}

**Statistical Analysis and Criteria for Evaluation of Autoregulation**

All results are presented as medians and ranges. A value of $P<0.05$ was considered statistically significant.

Because data could not be assumed to be normally distributed, as evaluated by calculation of Shapiro-Francia W', nonparametric statistical analysis was performed. Wilcoxon’s test for paired data was used for comparison of $MAP$, a-v $DO_2$, $V_{mean}$, PI, and $Paco_2$ at initial and maximum levels of $MAP$ and at normoventilation and hyperventilation. This method was also used for comparison between slopes of autoregulation regression lines at normoventilation and hyperventilation.

For evaluation of autoregulation in each patient, $MAP$ was plotted against $V_{mean}$. A computer program was used to search for a possible lower limit of autoregulation. This program has previously been validated for this purpose.\textsuperscript{18} The program fits a linear regression line for $MAP$ below the lower limit of autoregulation and a horizontal line above the lower limit by the least sum of squares method, comparing the result with that of fitting a single linear regression line to the data. The slope of the autoregulation curve was calculated as the slope of the single linear regression line, that is, the relative increase in $V_{mean}$ in percent divided by the increase in $MAP$. In the case of preserved autoregulation with identification of a lower limit of autoregulation (defined below), the slope was calculated for the regression line fitting only those points with $MAP$ values exceeding the lower limit.

Preservation of $CBF$ autoregulation was assessed by predefined criteria.\textsuperscript{16} Since the coefficient of variation during measurements of $V_{mean}$ is ~9%,\textsuperscript{19} autoregulation was classified as preserved (1) if the slope of the single linear regression line was $≤0.33\%/mm\,Hg$ (ie, $V_{mean}$ increased $≤10\%$ per increase in $MAP$ of 30 mm Hg), or (2) in the case of identification of a physiologically acceptable lower limit, if it was determined with a standard error of $<25\%$, and the $MAP$ interval used exceeded the $MAP$ value of the lower limit by $≥10\,mm\,Hg$, and the sum of squares for 2 lines was less than the sum of squares for 1 single regression line. Conversely, autoregulation was classified as impaired if no lower limit of autoregulation was identified and the slope of the single linear regression line increased $>0.33\%/mm\,Hg$, that is, if $V_{mean}$ increased $>10\%$ per increase in $MAP$ of 30 mm Hg.

To evaluate how well changes in $V_{mean}$ reflected changes in global $CBF$, the correlation between $V_{mean}$ and a-v $DO_2$ was examined. If both parameters are a reflection of global $CBF$, $V_{mean}$ will change in inverse proportion to a-v $DO_2$. These parameters are not direct measures of $CBF$, but relative changes may be assumed to reflect equal changes in global $CBF$. Hence, Spearman’s $\rho$ was calculated for the correlation between relative changes in $V_{mean}$ and 1/(a-v $DO_2$).

**Results**

**Clinical Outcome**

Seven patients survived and were extubated after a median of 7 (3 to 12) days. Three patients had mild neurological...
In 8 patients, the increase in $V_{\text{mean}}$ exceeded 10% per 30–mm Hg increase in MAP, and no lower limit of autoregulation was identified. Thus, autoregulation was impaired in these 8 patients at normoventilation. In the remaining patient (patient 8), as the slope of the regression line was $<0.33\%$ per mm Hg (0.24% per mm Hg), autoregulation was preserved at normoventilation; however, the a-v $D_O_2$ did decrease from 2.5 to 1.8 mmol/L from baseline to peak values of MAP (during norepinephrine infusion) in this patient.

During hyperventilation, $P_{\text{aco}_2}$ decreased in all patients to 3.5 kPa (3.3 to 4.1) ($P<0.01$). There was a slight but statistically significant change in $P_{\text{aco}_2}$ of $+0.20$ kPa ($−0.15$ to $+0.67$) from the lowest to the highest value of MAP during norepinephrine infusion at hyperventilation ($P<0.05$) (data not shown).

The MAP range at hyperventilation was 33 mm Hg (29 to 43). With a MAP increase of 41% (31% to 74%) during norepinephrine infusion, $V_{\text{mean}}$ increased by 18% (2% to 51%) ($P<0.01$) (Figure 1), and a-v $D_O_2$ decreased, corresponding to a relative increase in CBF of 30% (10% to 60%) ($P<0.05$).

The slope of the regression lines decreased during hyperventilation compared with the slope at normoventilation ($P<0.05$). In 4 patients (patients 5, 7, 8, and 9), autoregulation was completely recovered during hyperventilation. In 1 patient (patient 5), the lower limit of autoregulation was identified at 108 mm Hg, and the slope of the regression line above the lower limit was 0. In 3 patients (patients 7, 8, and 9), the slope of the single linear regression line was $<0.33\%$ per mm Hg. In patients 7 and 8, a lower limit of autoregulation appeared to be present at 71 and 89 mm Hg, respectively, but the standard error of the MAP value exceeded 25%. In 3 patients, the slope decreased but autoregulation was not completely recovered; in 2 patients, the slope increased slightly.

At the lowest MAP level, $V_{\text{mean}}$ and a-v $D_O_2$ were not significantly altered at hyperventilation compared with normoventilation, although there was a trend toward decreased $V_{\text{mean}}$ and increased a-v $D_O_2$. However, $V_{\text{mean}}$ and a-v $D_O_2$ were significantly reduced and increased, respectively, at peak MAP values.

Absence of cerebral ischemia both during normoventilation and hyperventilation was indicated by the jugular venous oxygen content. Ischemia would cause a high oxygen extraction and, consequently, a low jugular venous oxygen content. During normoventilation, values of $P_{jvO_2}$ and $S_{jvO_2}$ at the lowest MAP were 4.6 kPa (3.9 to 5.8) and 0.62 (0.56 to 0.83), respectively, and at high MAP 5.4 kPa (4.9 to 6.7) and 0.78 (0.70 to 0.86), respectively. During hyperventilation, $P_{jvO_2}$ and $S_{jvO_2}$ at the lowest MAP were 3.9 kPa (3.4 to 4.4) and 0.60 (0.51 to 0.70) and at high MAP 4.8 kPa (4.0 to 5.3) and 0.70 (0.60 to 0.79). Compared with values measured in healthy subjects ($S_{jvO_2}$ 0.55 to 0.70, calculated as mean±2 SD), these values are within or slightly above normal ranges; one measurement in patient 7 was slightly below the normal range. This indicates that global cerebral oxygen delivery was sufficient to meet cerebral metabolic requirements in the patients both during normoventilation and hyperventilation.
PI (normoventilation, low MAP: 1.5 [1.1 to 1.9], peak MAP: 1.3 [0.8 to 1.9] [for comparison between values at low and peak MAP, P=0.05]; hyperventilation, low MAP: 1.4 [1.1 to 2.5], peak MAP: 1.3 [1.0 to 2.3] [for comparison between values at low and peak MAP, P=0.17]) did not change significantly from normoventilation to hyperventilation. However, at normoventilation, a trend was observed toward a decrease in PI from the low MAP to peak values of MAP.

**Correlation Between Measured Parameters**

During each autoregulation measurement in the individual patient, 6 (2 to 10) simultaneous measurements of MAP and Vmean and 5 (2 to 6) simultaneous measurements of MAP, a-v DO2, and Vmean were performed.

Changes in Vmean were well reflected by inversely proportional changes in a-v DO2, that is, the relation between the 2 parameters was hyperbolic (Figure 3), indicating that changes in Vmean during norepinephrine infusion were a result of true changes in global CBF. There was a statistically significant correlation between relative changes in Vmean and 1/(a-v DO2) for the pooled data for all patients (normoventilation: Spearman’s \( r = 0.92 \), number of measurements \( n = 30 \), \( P < 0.01 \)); the correlation decreased during hyperventilation (\( r = 0.73 \), \( n = 35 \), \( P < 0.01 \)).

**Discussion**

We found that CBF autoregulation was impaired in 8 of 9 patients with acute bacterial meningitis, by use of TCD and the a-v DO2 method to determine relative changes in CBF during manipulation of MAP. This finding is in accordance with previous studies performed in patients in the early phase of acute bacterial meningitis with the use of identical methods as well as the \(^{13}\)Xe clearance technique.

Spontaneous hyperventilation is a characteristic clinical feature of patients with acute bacterial meningitis before coma and intracranial hypertension ensue, and it is possible that the arterial hypocapnia helps maintain a normal cerebral vascular tone and prevents a further rise in ICP in the setting of cytotoxic cerebral edema. The pathogenesis of the impaired CBF autoregulation is unclear, but cerebral interstitial acidosis is present in acute bacterial meningitis and may account for development of cerebral vasodilation. In the present study, we expected CBF autoregulation to be restored during mechanical hyperventilation. Indeed, autoregulation was partially or completely recovered in 6 of the 8 patients in whom CBF autoregulation was absent at normoventilation.

The recovery of autoregulation induced by short-term hyperventilation is suggested to result from alkalization of the interstitial fluid. An alternative explanation for the partial or complete recovery of autoregulation is that a decrease in ICP induced by hyperventilation may have improved cerebral perfusion pressure. If ICP were high during normoventilation, the true perfusion pressure would be markedly lower than MAP, and the autoregulation measurement might then have been performed at perfusion pressures located below the lower limit of autoregulation. With a decrease in ICP during hyperventilation, perfusion pressure would approach MAP, and the resulting autoregulation curve might then be located above the lower limit, causing the slope to decrease in comparison with that obtained at normoventilation. The present data, however, show that during the normoventilation study a-v DO2 was within or below the normal range, indicating that global CBF was adequate or relatively high even at the initial (low) MAP. This would be an unlikely finding in a patient in whom CBF was compromised by a high ICP and whose cerebral perfusion pressure was located below the lower limit of autoregulation.

Recovery of autoregulation during hyperventilation has been described in patients with acute liver failure and in patients with intracerebral tumors or infarction. In patients with head trauma, Cold et al\(^\text{23}\) reported that autoregulation was preserved at a PaCO2 of 4.5 kPa but was lost when the PaCO2 was reduced to 3.0 kPa. In contrast, Newell et al\(^\text{24}\) found an improvement in dynamic cerebral autoregulation as measured by TCD, with a reduction in PaCO2 from 4.9 to 3.7 kPa in head-injured patients.

In this study, although there was a trend toward decreased cerebral perfusion during hyperventilation, as estimated by Vmean and a-v DO2, this decrease was not statistically significant at baseline MAP values. At least 3 different explanations are possible for the apparent paradox that CBF autoregulation was affected during hyperventilation, whereas cerebral perfusion appeared to be unaffected. First, hyperventilation may have mediated a decrease in ICP and hence an increase in cerebral perfusion pressure and CBF. Although ICP may be elevated in acute bacterial meningitis, monitoring of ICP is not routinely performed in patients with acute bacterial meningitis in our department and was not carried out in this study, which precludes further analysis of this possibility.

**TABLE 2. Autoregulation Measurements During Normoventilation and Hyperventilation**

<table>
<thead>
<tr>
<th></th>
<th>Paco2</th>
<th>Baseline MAP</th>
<th>Peak MAP</th>
<th>Vmean at Baseline MAP</th>
<th>Vmean at Peak MAP</th>
<th>a=v Do2 at Baseline MAP</th>
<th>a=v Do2 at Peak MAP</th>
<th>Slope of Autoregulation Regression Line, % per mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normoventilation</td>
<td>4.4</td>
<td>68 (60–101)</td>
<td>109*</td>
<td>48 (30–61)</td>
<td>65*</td>
<td>2.2 (1.0–2.7)</td>
<td>1.4§</td>
<td>1.10 (0.23–1.62)</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>3.5†</td>
<td>76 (58–92)</td>
<td>109†</td>
<td>45 (29–55)</td>
<td>53§</td>
<td>2.5§ (1.8–3.0)</td>
<td>1.8§</td>
<td>0.45§ (0–1.27)</td>
</tr>
</tbody>
</table>

All values are presented as medians and ranges.

* P < 0.01 compared with values at baseline MAP.
† P < 0.05 compared with values at baseline MAP.
‡ P < 0.01 compared with normoventilation.
§ P < 0.05 compared with normoventilation.
| Not significant compared with normoventilation. |
Second, cerebrovascular CO₂ reactivity may have been absent or impaired in some of the patients. However, absence of CO₂ reactivity should have been evident at all levels of MAP and not only at low levels. The third possibility is that the number of patients was too small for statistical significance, even though CBF was really reduced at all levels of MAP, that is, a type 2 error occurred. This also may explain why PI remained unchanged throughout the measurements. PI has been suggested to indicate cerebrovascular impedance. Hence, PI would be expected to increase during hyperventilation compared with normoventilation. An increase in PI would also be expected at peak MAP compared with baseline MAP during hyperventilation in the patients who recovered CBF autoregulation during hyperventilation.

With the slight increase in Paco₂ during norepinephrine infusion observed during hyperventilation, the slope of the regression lines would tend to increase slightly. Accordingly, it is likely that an even more pronounced decrease in the slope of the regression lines might have been expected during hyperventilation if the Paco₂ had remained constant. CO₂ reactivity was not calculated, and hence no correction was performed for the observed increase in Paco₂. Despite this, the decrease in the slope of the regression lines from normoventilation to hyperventilation was significant.

The correlation coefficients between relative changes in Vmean and 1/(a-v DO₂) decreased somewhat from normoventilation to hyperventilation. This may be explained by the partial or complete recovery of autoregulation, which decreased the range of variation in both Vmean and a-v DO₂ during hyperventilation compared with normoventilation; accordingly, the correlation coefficient between these 2 parameters will tend to decrease during hyperventilation.

Measuring Vmean by transcranial Doppler provides reliable estimates of relative changes in CBF if the cross-sectional diameter of the insonated artery remains constant during the examination. We used an infusion of norepinephrine to increase MAP in the patients. A constant diameter of the middle cerebral artery during norepinephrine infusion has been reported in healthy volunteers and in patients with neurological diseases as well as in patients with acute liver failure. Changes in the diameter of the insonated artery do not explain the increase in Vmean because a-v DO₂ would then have been expected to remain unchanged despite changes in Vmean. In contrast, Vmean increased and a-v DO₂ decreased with increasing MAP, and there was a good correlation between relative changes in Vmean and 1/a-v DO₂.

Changes in a-v DO₂ will be inversely proportional to changes in CBF only if CMRO₂ remains constant throughout the study period. Constancy of CMRO₂ has been demonstrated during norepinephrine infusion in patients with acute liver failure and is usually present during short study intervals. If the blood-brain barrier is dysfunctional or defective, as is probably the case in acute bacterial meningitis, the cerebrovascular and cerebral metabolic response to norepinephrine may be altered. To our knowledge, no studies have been performed regarding the effect of norepinephrine on cerebral blood flow and metabolism in acute bacterial meningitis. However, an increase in cerebral oxidative metabolism caused by norepinephrine infusion should be unaffected by the Paco₂. Also, the relation between MAP, Vmean, and a-v DO₂ should be unaltered from normocapnia to hypocapnia. Hence, an increase in CMRO₂ does not explain our results.

The study was carried out in patients in the early phase of severe acute bacterial meningitis, necessitating sedation and mechanical ventilation for clinical reasons. Five patients had severe septic shock concurrently with acute bacterial meningitis, and all were sedated, but neither septic shock nor sedation appears to affect the integrity of autoregulation. From a clinical point of view, the recovery of CBF autoregulation during mechanical hyperventilation may protect the brain from fluctuations in perfusion pressure. The stabilization of CBF may be important in patients with acute bacterial meningitis, since vasogenic edema is more likely to result from an increase in perfusion pressure if the blood-brain barrier is disrupted. Unfortunately, the cerebrovascular effects of "prophylactic" hyperventilation will be compensated during long-time hyperventilation. Moreover, hyperventilation may critically reduce blood flow in endangered brain areas if carbon dioxide reactivity is preserved in these areas. Regionally compromised CBF has been reported in patients with acute bacterial meningitis, whereas the CO₂ reactivity in these areas awaits further study.
Although none of our patients had critically low jugular venous oxygen saturation, this may be an important cause for concern in some patients. The potential clinical benefit of a more stable CBF may thus be achieved at the cost of an overall reduction in global CBF during hyperventilation compared with normoventilation. Further studies in patients with acute bacterial meningitis are warranted before general recommendations can be made regarding therapies that reduce CBF, for example, hyperventilation or the administration of vasoactive drugs such as indomethacin. If such therapies are instituted, we suggest that cerebral oxygen consumption should be closely monitored to help avoid cerebral ischemic complications.

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