Influence of Raised Plasma Osmolality on Clinical Outcome After Acute Stroke

Ajay Bhalla, MRCP; Suki Sankaralingam, MSc; Ruth Dundas, MSc; R. Swaminathan, FRCPath; Charles D.A. Wolfe, MD; Anthony G. Rudd, FRCP

Background and Purpose—Abnormal physiological parameters after acute stroke may induce early neurological deterioration. Studies of the effect of dehydration on stroke outcome are limited. We examined the association of raised plasma osmolality on stroke outcome at 3 months and the change of plasma osmolality with hydration during the first week after stroke.

Methods—Acute stroke patients had their plasma osmolality measured at admission and at days 1, 3, and 7. Maximum plasma osmolality and the area under curve (AUC) were also calculated during the first week. Patients were stratified according to how they were hydrated: orally, intravenously, or both. Outcome included survival at 3 months after stroke. Logistic regression was performed to examine the association between raised plasma osmolality (>296 mOsm/kg) and survival, adjusting for stroke severity. Linear regression was performed to examine the pattern of plasma osmolality across hydration groups.

Results—One hundred sixty-seven patients were included. Mean admission (300 mOsm/kg, SD 11.4), maximum (308.1 mOsm/kg, SD 17.1), and AUC (298.3 mOsm/kg, SD 11.7) plasma osmolality were significantly higher in those who died compared with survivors (293.1 mOsm/kg [SD 8.2], 297.7 mOsm/kg [SD 8.7], and 291.7 mOsm/kg [SD 8.1], respectively; P<0.0001). Admission plasma osmolality >296 mOsm/kg was significantly associated with mortality (OR 2.4, 95% CI 1.0 to 5.9). In patients hydrated intravenously, there was no significant fall in plasma osmolality compared with patients hydrated orally (P=0.68).

Conclusions—Raised plasma osmolality on admission is associated with stroke mortality, after correcting for case mix. Correction of dehydration after stroke requires a more systematic approach. Trials are required to determine whether correcting dehydration after stroke improves outcome. (Stroke. 2000;31:2043-2048.)

Key Words: stroke outcome • cerebrovascular disorders • medical management

There is evidence that organized management in stroke units improves survival and reduces dependency.1 The precise factors that influence this benefit are unknown and remain under investigation. One particular theme that has emerged from stroke unit trials is that there appear to be differences in the way acute physiology (such as temperature, blood pressure, and hydration) are managed between these units and nonstroke units.2 How this improves survival is unclear, but parenteral fluids may have reduced the occurrence of dehydration and maintained systemic blood pressure after acute stroke.3,4 Studies of electrolyte imbalance after stroke are not extensive, and it remains unclear whether initial hydration status influences mortality or functional recovery.5,6 Plasma osmolality may be a more useful marker of hydration status compared with conventional biochemical measurements such as plasma sodium or urea.7 The aim of this study was to measure the effect of dehydration status of acute stroke patients on outcome and to examine the pattern of change of plasma osmolality with hydration.

Subjects and Methods

All patients with a clinical diagnosis of stroke (WHO criteria8), admitted to St Thomas’ Hospital from November 1, 1998, to November 1, 1999, were identified prospectively. Patients with subarachnoid hemorrhage were excluded. The criterion for inclusion for the study was that stroke onset could be accurately determined and that blood samples were taken within 24 hours of stroke onset. Informed written consent was obtained from the patients, their caregivers, or both. The study was approved by the Guy’s and St Thomas’ Hospital Ethical Committee.

Information collected at initial assessment included the following: (1) sociodemographic characteristics (age, sex, and Barthel Index score prior to stroke).9 (2) Case severity (clinical state at the time of admission to hospital included level of consciousness [Glasgow Coma scale] and the presence of dysphagia, dysphasia, and incontinence). (3) Comorbidity (a history of hypertension, myocardial infarction, diabetes mellitus, atrial fibrillation, and previous cerebro-
vascular disease was identified through hospital and general practitioner records; use of diuretics prior to admission was also recorded.

Stroke subtype was determined according to the Bamford Classification.

Every patient had a standardized swallowing assessment within 24 hours of admission by a speech therapist or by experienced nursing staff to ascertain the presence of dysphagia. The swallowing test was not attempted in a number of circumstances in which the patients were drowsy, did not open their eyes to speak, or were drooling. Five milliliters water was given to the patient, while 2 fingers were placed above and below the larynx to feel the swallow reflex. If coughing or choking occurred after 2 minutes or there was an absent swallow, this indicated a failed test. If this procedure was successful, the test was repeated with one-third-filled glass of water, observing for the same signs for a failed test.

Analysis
Blood samples were taken within 24 hours of stroke onset (admission) day 1 and 3 and 7 days after stroke. All patients had plasma osmolality, serum sodium, and urea measured at these time points. Plasma glucose was also measured within 24 hours of stroke onset. Patients were recumbent for at least 30 minutes before samples were taken. Samples were collected in lithium heparinized containers and transferred to the chemical pathology laboratory for further processing within 30 minutes. Plasma samples were frozen at 4°C and then centrifuged. The osmolality of the plasma was determined by the depression of freezing point method (Advanced Micro, Advanced Instruments). Calculated plasma osmolality was estimated by using the equation 2×(sodium+potassium)+glucose+urea. Serial plasma urea and electrolytes were determined by the routine analysis Vitros 950 (Johnson & Johnson).

Whether the patient was hydrated orally, by intravenous fluids, or by both methods was recorded from bedside fluid balance charts during the first week. All staff, apart from the principal investigator (A.B.), were unaware of plasma osmolality results during the first week of admission.

Outcome
Patients were assessed during face-to-face interviews if alive at 3 months after stroke. Outcome assessment included death and dependency at 3 months (Barthel Index of 20, independent; Barthel Index <20, dependent).

Statistical Analysis
Analysis of serial measurements of plasma osmolality during the first week was summarized in 2 ways: by calculating the area under the curve (AUC) and also the maximum value for each patient. Univariate associations of plasma osmolality on admission between survivors and dead patients were analyzed with the Student t test. Multiple logistic regression was undertaken to examine the association between admission plasma osmolality and mortality, adjusting for age, sex, stroke severity, Barthel Index before stroke, plasma glucose, diabetes mellitus! and stroke subtype (classified as cerebral infarction or primary intracerebral hemorrhage). Plasma osmolality was considered as a dichotomous variable: ≥296 mOsm/kg and >296 mOsm/kg, the upper limit of normal being 296 mOsm/kg. Comparison of admission, maximum, AUC, and day 7 plasma osmolality across the 3 hydration groups were analyzed by using linear regression with 95% confidence intervals for differences, adjusting for age, sex, and stroke severity. Linear regression was also used to determine the association between age, serum sodium, serum urea, and plasma osmolality. Samples of 5 patients in each hydration group were selected at random (1 in 5 random sample) and plotted to determine the pattern of plasma osmolality variation. To assess the agreement between measured plasma osmolality and calculated plasma osmolality, the mean difference of both these measures and the standard deviations of these differences were estimated. As the data were normally distributed, we would expect most of the differences to lie within ±2 SD. The limits of agreement were calculated from (1) mean difference minus 2 SD and (2) mean difference plus 2 SD.

Results
One hundred eighty-four consecutive patients with a diagnosis of stroke (WHO criteria) were admitted to St Thomas’ Hospital, of whom 5 with a diagnosis of subarachnoid hemorrhage were excluded and 12 were admitted 24 hours after stroke onset. One hundred sixty-seven patients were therefore eligible for the study. Demographic and clinical data are shown in Table 1. The mean plasma osmolality on admission was 295.2 mOsm/kg (SD 9.8, range 274 to 340 mOsm/kg). The mean serum sodium was 140.1 mmol/L (SD 2.9, range 131 to 148 mmol/L). The mean serum urea was 7.1 (SD 3.5, range 1.7 to 29.1 mmol/L). Fifty-five (33%) patients were hyperglycemic on admission (glucose >7 mmol/L). Thirty-nine patients (26%) had stress hyperglycemia (glucose >7 mmol/L in nondiabetics) on admission. Diabetic patients had significantly raised plasma osmolality (300 mOsm/kg) compared with nondiabetic patients (294 mOsm/kg; 95% CI

Table 1. Demographic and Case Mix Data of Stroke Patients at Admission

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, y</td>
<td>73.2±12.2</td>
</tr>
<tr>
<td>Male, n</td>
<td>80 (48)</td>
</tr>
<tr>
<td>Barthel index before stroke</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>20 (12)</td>
</tr>
<tr>
<td>20</td>
<td>147 (88)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>81 (49)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>17 (10)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>20 (12)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>17 (10)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>26 (16)</td>
</tr>
<tr>
<td>Severity</td>
<td></td>
</tr>
<tr>
<td>Dysphagia</td>
<td>68 (41)</td>
</tr>
<tr>
<td>Dysphasia</td>
<td>88 (53)</td>
</tr>
<tr>
<td>Glasgow Coma Scale &lt;13</td>
<td>40 (24)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>85 (51)</td>
</tr>
<tr>
<td>Stroke subtype</td>
<td></td>
</tr>
<tr>
<td>TACS</td>
<td>31 (19)</td>
</tr>
<tr>
<td>PACS</td>
<td>56 (33)</td>
</tr>
<tr>
<td>PCOS</td>
<td>14 (8)</td>
</tr>
<tr>
<td>LACS</td>
<td>48 (29)</td>
</tr>
<tr>
<td>PICH</td>
<td>16 (10)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

TACS indicates total anterior circulatory stroke; PACS, partial anterior circulatory stroke; PCOS, posterior circulatory stroke; LACS, lacunar circulatory stroke; and PICH, primary intracerebral hemorrhage.
Patients (50) who died than in those who survived. In patients who were taking a diuretic before admission (295.5 mOsm/kg) had the same osmolality as 123 patients who were not taking diuretics (295.1 mOsm/kg; 95% CI 2.8 to 2.9, P=0.8). There was no significant association with the use of diuretics before admission and raised plasma osmolality (P=0.68). Similarly, there were no differences in (AUC) plasma osmolality in 30 patients (292.2 mOsm/kg) who continued diuretic therapy in the first week after stroke compared with 125 patients (293.5 mOsm/kg) who did not (95% CI 2.9 to 4.7, P=0.64). Serum sodium was significantly associated with plasma osmolality (coefficient=1.7 per mmol/L increase in serum sodium, 95% CI 1.2 to 2.1; P<0.001). Serum urea was significantly associated with plasma osmolality (coefficient=1.4 per mmol/L increase in serum urea, 95% CI 1.1 to 1.8; P<0.001). Age was also significantly associated with plasma osmolality (coefficient=0.15 per year increase in age, 95% CI 0.03 to 0.27; P=0.02). There was no difference in plasma osmolality levels between patients with cerebral infarction (295.4 mOsm/kg, SD 10) and primary intracerebral hemorrhage (292.5 mOsm/kg; 95% CI 1.8 to 7.6, P=0.23).

Outcome

One hundred seventeen patients (70.1%) were still alive at 3 months after their stroke. Eleven (6.6%) died within 1 week of admission to hospital. Mean admission and maximum and AUC plasma osmolality were all significantly higher in those who died than in those who survived. In patients who survived, 52 (44.4%) achieved a Barthel Index score of 20 3 months after their stroke. Only mean admission plasma osmolality was significantly higher in patients who were dependent after their stroke (Table 2). There was no significant difference in survivors between those who used diuretics before admission and those who did not (P=0.4).

In the multiple logistic regression model, plasma osmolality >296 mOsm/kg on admission showed a significant association with stroke mortality at 3 months independent of age, sex, stroke severity, Barthel Index before stroke, and stroke subtype. (Table 3). From the regression equation between measured and calculated plasma osmolality, a measured plasma osmolality >296 mOsm/kg is equated to a calculated plasma of >294 mOsm/kg. After controlling for the identical factors in the logistic regression model, the OR of calculated plasma osmolality >294 mOsm/kg associated with stroke mortality at 3 months was 1.5 (95% CI 0.58 to 3.7, P=0.4). To assess the agreement between measured plasma osmolality and calculated plasma osmolality, the mean differences in both measurements were 0.97 mOsm/kg.

### Table 2. Relationship of Mean Admission, Maximum, and AUC Plasma Osmolality (pOsm) on 3-Month Stroke Mortality and Disability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dead (n=50)</th>
<th>Alive (n=117)</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>pOsm, mOsm/kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>300 (11.4)</td>
<td>293.1 (8.2)</td>
<td>−10 to −3.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Maximum*</td>
<td>308.1 (17.1)</td>
<td>297.7 (8.7)</td>
<td>−14.6 to −6.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AUC*</td>
<td>298.3 (11.7)</td>
<td>291.7 (8.1)</td>
<td>−9.9 to −3.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Barthel &lt;20 (Dependent, n=65)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pOsm, mOsm/kg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission</td>
<td>294.8 (8.0)</td>
<td>290.9 (7.9)</td>
<td>0.9 to 6.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Maximum</td>
<td>299 (9.2)</td>
<td>296.9 (78)</td>
<td>−0.1 to 6.2</td>
<td>0.06</td>
</tr>
<tr>
<td>AUC</td>
<td>292.7 (7.5)</td>
<td>290.4 (8.7)</td>
<td>−0.6 to 5.3</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Values are given as n (SD).
*Eleven patients who did not survive during the first week were excluded from the analysis.

### Table 3. Multiple Logistic Regression Analysis Showing Association Between Plasma Osmolality and Death at 3 Months*

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma osmolality &gt;296 mOsm/kg</td>
<td>2.4</td>
<td>1.0–5.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Glucose†</td>
<td>2.2</td>
<td>0.7–6.7</td>
<td>0.17</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.5</td>
<td>0.33–6.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Age ≥65 y</td>
<td>1.9</td>
<td>0.48–7.26</td>
<td>0.36</td>
</tr>
<tr>
<td>Sex, female</td>
<td>1.14</td>
<td>0.43–2.59</td>
<td>0.91</td>
</tr>
<tr>
<td>Dysphasia</td>
<td>1.5</td>
<td>0.53–4.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>8.7</td>
<td>2.82–26.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Glasgow Coma Scale &lt;13</td>
<td>2.34</td>
<td>0.79–6.93</td>
<td>0.13</td>
</tr>
<tr>
<td>Incontinence</td>
<td>1.52</td>
<td>0.38–6.16</td>
<td>0.6</td>
</tr>
<tr>
<td>Barthel Index &lt;20</td>
<td>2.34</td>
<td>0.65–8.44</td>
<td>0.2</td>
</tr>
<tr>
<td>Primary intracerebral hemorrhage</td>
<td>2.42</td>
<td>0.58–10.1</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, stroke severity, Barthel Index before stroke, plasma glucose, diabetes, and stroke subtype.
†Continuous variable.
Dehydration is a common phenomenon after stroke, particularly in the elderly. In the early phase of stroke, dehydration may be caused by decreased oral intake of water due to disturbed consciousness or dysphagia. Electrolyte disturbances such as hypernatremia or hyponatremia, resulting from the syndrome of inappropriate antidiuretic hormone, can lead to complications such as seizures or death. 

Dehydration acutely after stroke may worsen the ischemic process, owing to an increase in blood viscosity and a decrease in blood pressure. Studies have shown that hemodilution can affect cerebral blood flow and cerebral hemodynamics by influencing plasma viscosity, but no beneficial effect on stroke outcome has been established.

A significant relationship between raised plasma osmolality and mortality has been shown in long-stay community patients and acutely ill patients, which suggests that dehydration may have influenced survival. Studies involving stroke patients are limited. Joynt et al demonstrated no significant difference in plasma osmolality on admission between stroke patients and control subjects. O’Neill et al, who studied only 15 patients, found no significant differences in plasma osmolality between survivors and dead stroke patients.

In this study, admission mean plasma osmolality in stroke patients showed a wide variation, indicating a large variance in water homeostasis, which implies that some patients were overhydrated and others underhydrated. The upper limit of normal for measured plasma osmolality in this study was 296 mOsm/kg. Previous reports suggest that a plasma osmolality >296 mOsm/kg is considered indicative of a hyperosmolar state. Hypernatremia was evident, with 1 patient having a plasma sodium of 160 mmol/L. Diabetic patients and those with stress hyperglycemia were also prone to raised plasma osmolality.

**Table 4. Relationship of Mean, Maximum, AUC, and Day 7 Plasma Osmolality on Hydration During First Week**

<table>
<thead>
<tr>
<th>Plasma Osmolality, mOsm/kg</th>
<th>Oral (n=70)</th>
<th>Intravenous/Oral (n=39)</th>
<th>Intravenous (n=47)</th>
<th>Unadjusted P*</th>
<th>Adjusted P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>292.4 (8.3)</td>
<td>294.7 (8.8)</td>
<td>299.1 (11.2)</td>
<td>&lt;0.001</td>
<td>0.97</td>
</tr>
<tr>
<td>95% CI for difference from oral</td>
<td>297.3 to 287.5</td>
<td>298.5 to 290.5</td>
<td>300.2 to 296.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>296.6 (8)</td>
<td>298.5 (9.1)</td>
<td>300.8 (16.4)</td>
<td>&lt;0.001</td>
<td>0.25</td>
</tr>
<tr>
<td>95% CI for difference from oral</td>
<td>292.3 to 300.9</td>
<td>301.5 to 297.1</td>
<td>302.6 to 295.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC</td>
<td>291.4 (7.3)</td>
<td>291.1 (8.9)</td>
<td>298 (11.3)</td>
<td>&lt;0.001</td>
<td>0.13</td>
</tr>
<tr>
<td>95% CI for difference from oral</td>
<td>287.1 to 295.2</td>
<td>294.2 to 294.1</td>
<td>294.8 to 297.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 7</td>
<td>291.6 (8.4)</td>
<td>288.7 (26.1)</td>
<td>299.4 (16.8)</td>
<td>0.01</td>
<td>0.16</td>
</tr>
<tr>
<td>95% CI for difference from oral</td>
<td>286.3 to 300.1</td>
<td>284.0 to 294.0</td>
<td>294.2 to 300.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Comparison of plasma osmolality (pOsm) within hydration groups was performed by using linear regression, with oral group as the baseline. Values are given as n (SD).

*Adjusted for age, sex, and stroke severity.

**Discussion**

This is the first study to date to examine the relationship between plasma osmolality and stroke mortality in a cohort of consecutively admitted patients. In this study, we have found an association between raised plasma osmolality during the first week after stroke and mortality and functional outcome.

Dehydration is a common phenomenon after stroke, particularly in the elderly. In the early phase of stroke, dehydration may be caused by decreased oral intake of water due to disturbed consciousness or dysphagia. Electrolyte disturbances such as hypernatremia or hyponatremia, resulting from the syndrome of inappropriate antidiuretic hormone, can lead to complications such as seizures or death. 

Dehydration acutely after stroke may worsen the ischemic process, leading to complications such as seizures or death.
To assess the agreement between measured plasma osmolality and calculated plasma osmolality, we used a well-validated approach, as suggested by Bland and Altman. The limits of agreement between both of these measures were $-13.12$ mOsm/kg and $15.23$ mOsm/kg. This implied that the calculated plasma osmolality may be $13.12$ mOsm/kg below or $15$ mOsm/kg above the measured plasma osmolality. These values are unacceptable for clinical purposes, and therefore the agreement between both measures is not satisfactory. This is further reinforced by the fact that the corresponding OR for the calculated plasma osmolality ($>294$ mOsm/kg) failed to be significantly associated with stroke mortality at 3 months. The added disadvantage of using calculated plasma osmolality rather than measured plasma osmolality is that one is estimating plasma osmolality from at least 4 variables (sodium, potassium, urea, and glucose), each with its own measurement error which may contribute to the overall measurement error of the calculated plasma osmolality.

From this study, it appeared that stroke patients were initially hydrated appropriately, with patients with high plasma osmolality levels at admission being hydrated intravenously. The explanation of higher maximum and AUC plasma osmolality levels in patients hydrated intravenously throughout the first week may have been explained by differences in stroke severity. Patients who were intravenously hydrated tended to have severe strokes. There is still controversy over whether dysphagia leads to significant dehydration, and therefore these findings cannot be explained by a simple division of intravenously hydrated and orally hydrated groups reflecting poor and good outcome. One may have expected a fall in plasma osmolality from admission to day 7 in individuals hydrated intravenously throughout the first week compared with orally hydrated individuals, assuming that individuals who were receiving intravenous fluids were receiving larger volumes of fluid; however, no significant fall was demonstrated. Measurement of oral fluid intake was not achieved owing to practical difficulty in obtaining accurate volume measurements. These findings are different from those in a study by O’Neill and colleagues, in which significant falls in plasma osmolality were demonstrated in patients who were hydrated intravenously rather than orally.

Fluid balance, particularly in elderly patients, is notoriously haphazard and difficult to manage because the clinical indicators of dehydration can be subtle. A decline in thirst perception is a consequence of aging, and it has been shown that high levels of plasma osmolality can lead to a diminished subjective awareness of thirst. Cortical dysfunction after cerebrovascular disease has also been implicated in causing hypodipsia. When a patient is dysphagic and is thus dependent on intravenous fluids, clinicians have to use clinical and biochemical evidence for dehydration to adequately rehydrate patients. Evidence suggests that independent elderly individuals often drink what is offered to them and then communicate their requests for further replenishment, unlike semidependent individuals, who often go unnoticed.

In this study, we have demonstrated that the present method of hydration with fluids may be inappropriate. Although patients are being hydrated intravenousy, clinicians must be mindful that insufficient fluid replacement may be taking place. Frequent measurement of serum urea and electrolytes as well as plasma osmolality, which gives valuable supportive evidence of water homeostasis, must be considered.

In this study we have demonstrated that high plasma osmolality levels in the acute phase of stroke are associated with excessive mortality rates. This may enable identification of stroke patients who may benefit from fluid replacement in a more systematic fashion. Further work is required to determine the scale of water homeostasis and stroke subtype. Fluid intervention trials are re-
quired to test the hypothesis that plasma osmolality levels after acute stroke are indicators of water balance and that improving plasma osmolality levels in the acute phase will also improve clinical outcome.

Acknowledgments
This study was supported by the Research and Development Cerebrovascular Disease Program, London, and the Stroke Association.

References
Influence of Raised Plasma Osmolality on Clinical Outcome After Acute Stroke
Ajay Bhalla, Suki Sankaralingam, Ruth Dundas, R. Swaminathan, Charles D. A. Wolfe and Anthony G. Rudd

*Stroke*. 2000;31:2043-2048
doi: 10.1161/01.STR.31.9.2043

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/31/9/2043

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/