

# Trends in Blood Pressure, Osmolality and Electrolytes after Subarachnoid Hemorrhage from Aneurysms

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**ABSTRACT:** Daily trends in blood pressure, osmolality and electrolytes were analyzed in a series of 173 operated aneurysm cases who had subarachnoid hemorrhage (SAH) and were admitted within 4 days of the ictus. High blood pressure was associated with a greater risk of mortality and the development of clinically significant vasospasm (VSP). High osmolality shortly after admission was related to mortality but not VSP. Changes in sodium and potassium had no obvious relationship to mortality or VSP.

**RÉSUMÉ:** Évolution de la pression sanguine, de l'osmolalité et des électrolytes après une hémorragie sous-arachnoïdienne due à un anévrisme L'évolution quotidienne de la pression sanguine, de l'osmolalité et des électrolytes a été analysée dans une série de 173 cas d'anévrismes opérés, qui présentaient une hémorragie sous-arachnoïdienne et qui avaient été hospitalisés en dedans de 4 jours de l'ictus. L'hypertension artérielle était associée à un risque accru de mortalité et de développement d'un vasospasme cliniquement significatif (VSP). Une osmolalité élevée peu après l'admission était reliée à la mortalité, mais non au VSP. Des changements dans les niveaux de sodium et de potassium n'avaient pas de relation évidente avec la mortalité ou le VSP.

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Subarachnoid hemorrhage (SAH) from ruptured aneurysm produces a sudden increase in intracranial pressure, and to maintain cerebral perfusion there is frequently a compensatory increase in systemic blood pressure. The volume of blood escaping the intravascular space must be a major determinant of the degree of rise in intracranial pressure and thus the amount of elevation of systemic blood pressure. The quantity of blood escaping into the subarachnoid space is considered by most observers to be pivotal in the evolution of chronic cerebral vasospasm (VSP). Similarly, chance of mortality is obviously strongly influenced by the volume of hemorrhage. It is not unreasonable therefore to anticipate that blood pressure might be linked not only to the chance of VSP developing but also of death ensuing.

Changes in osmolality and certain electrolyte concentrations have been observed frequently in patients having SAH. Perturbations from normal can be in either direction and reflect both severity of illness as well as iatrogenic influence. There have been few analyses of changes in relation to the exact time of SAH, day of operation, the development of VSP and mortality.

## MATERIALS AND METHODS

### Patient Population

From 1971 to early 1987, 721 patients with subarachnoid hemorrhage from ruptured intracranial aneurysm were seen at the University of Alberta Hospitals or the Royal Alexandra Hospital. Of these, 173 (24%) had daily recordings of vital signs and common biochemical parameters which had been encoded in a data base set up on the Amdahl mainframe computer at the University of Alberta. For the purposes of this review, blood pressure, osmolality, and electrolyte concentrations and their relation to mortality and the development of clinical vasospasm were studied. Patients required 2 or more days of data to be eligible for inclusion in this study. Data had been retrospectively abstracted from the hospital charts, usually as part of previous clinical investigations.

Of these patients 102 (59%) were female and 71 (41%) male. Mean age was 49.2 years with a range of 12 to 81 years. Grade on admission, categorized using the scale of Hunt and Hess was as follows: 42 (24%) grade 1, 51 (30%) grade 2, 33 (19%) grade 3, 36 (21%) grade 4 and 11 (6%) grade 5.

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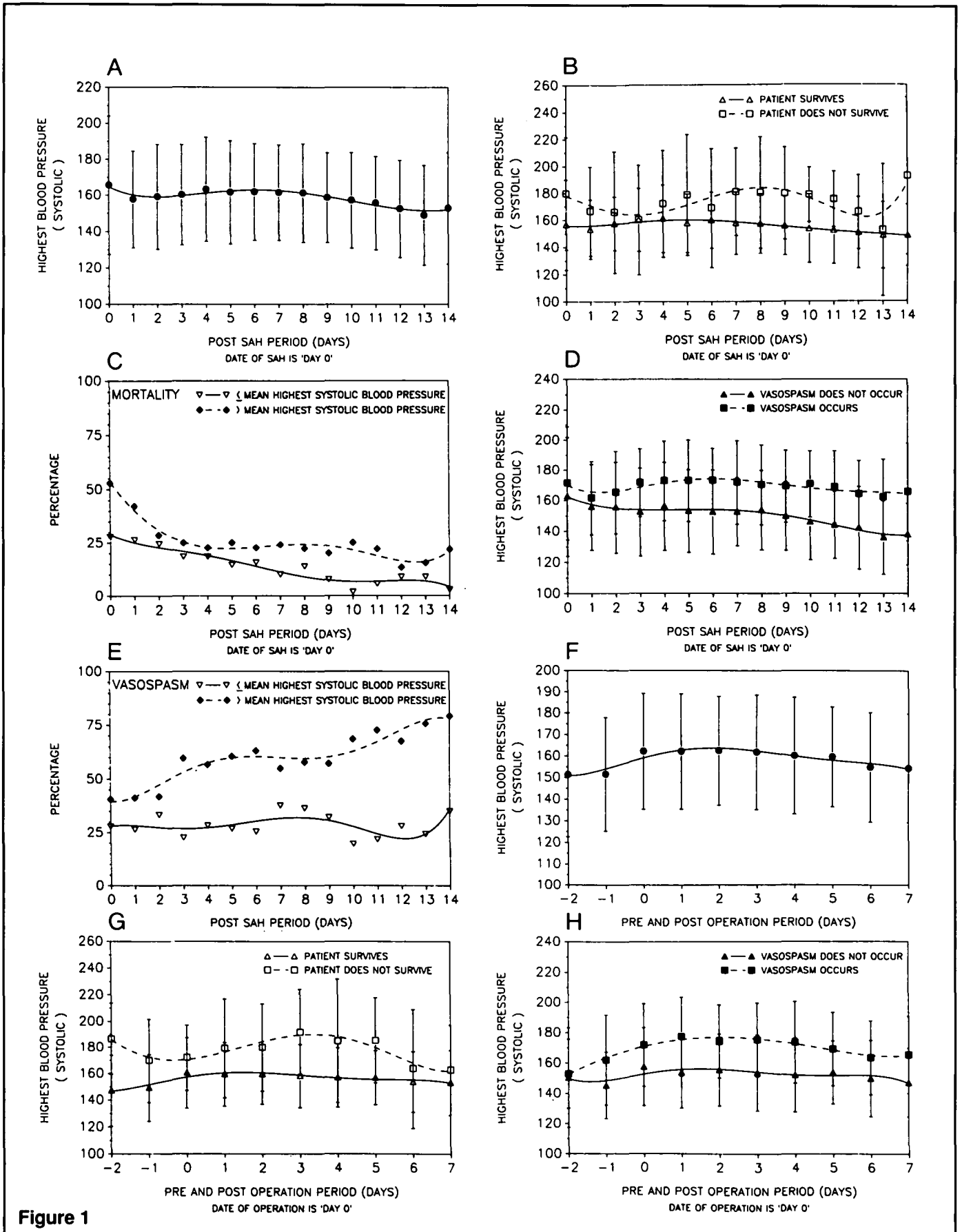


Figure 1

The day of subarachnoid hemorrhage was defined as day 0. The first 2 weeks following SAH were studied as this period encompasses the peak time for vasospasm.<sup>1</sup> Mortality was based on deaths in hospital, occurring in 56 (32%) of patients leaving 117 (68%) survivors. Vasospasm was defined as a delayed neurologic deterioration occurring more than 4 days after subarachnoid hemorrhage associated with angiographic vasospasm.

### Statistical Methods

Information from the data base was edited for analysis by the SPSS statistical package on the University of Alberta computer. Not every patient had complete data for each of the first 14 days post SAH. This meant that the N value for each of the day by day analyses often differed from the study population total of 173. Comparisons between groups were performed both with t-tests and the Kruskal-Wallis one-way analysis of variance. Both tests were performed for each comparison to provide a form of internal verification of results. There was complete agreement in every instance. The level of significance was taken as  $p < 0.05$ .

## RESULTS

### Blood Pressure

The highest systolic blood pressure of each patient was recorded daily. The highest mean systolic blood pressure was on the day of SAH. In this group of patients it was about 163 torr. It fell on day 1 post-SAH then rose gradually until beginning to fall again after day 8 (Figure 1A). The blood pressure was higher on every day except day 3 post-SAH for patients who ultimately died than for survivors (Figure 1B). Differences between survivors and non-survivors were statistically significant days 0, 1 and 7-11. The blood pressure in fatal cases showed considerable variation over time. It was high initially (180 torr), falling by day 2 and then showed a secondary rise starting day 3. This elevation peaked about day 7 and fell after day 11. The pressures for those who survived were much more stable. Mean pressure on day 0 was 158 torr with subsequent days ranging from 150 to 162 torr.

When all cases were categorized on each day by whether they were above or below the mean pressure for that day, the mortality rate was always higher for those with the highest blood pressures. This difference was most marked on day 0 and day 1 and was greater again between days 6 and 11 (Figure 1C).

Figure 1D depicts blood pressure for patient groups categorized by the development of clinical vasospasm. Initially there

is little difference between groups but beginning day 3 and continuing to day 14 there are significantly higher pressures in the vasospasm group. This difference in pressure progressively increases over time. It is interesting to note that the increase in blood pressure occurs before the onset of clinical vasospasm. A striking difference in the incidence of vasospasm is seen when cases on each day are categorized by whether they were above or below the mean highest systolic blood pressure for the group for that day (Figure 1E). Again after day 3 the low blood pressure cases were half as likely to develop VSP as the high blood pressure cases.

Operation to clip the aneurysm was carried out in a variable temporal relationship to the day of hemorrhage. In later years it has been the policy at University of Alberta to operate early after SAH, particularly in good grade patients. Operation itself did not appear to cause any discernible shift in the mean highest systolic blood pressure (Figure 1F). The adverse effect of higher blood pressure on both mortality and incidence of VSP were still seen when times are calculated in relation to day of operation (Figure 1G, 1H).

Similar analyses were carried out using mean highest diastolic blood pressures. Trends were similar although slightly less marked than with systolic blood pressure.

### Osmolality

The initial mean osmolality on day 0 was 295 mOsm/L (Fig. 2A). It fell gradually to a nadir around 280 mOsm/L on day 8 post-SAH, remaining relatively stable thereafter. Figure 2B categorizes patients into survivors and non-survivors. Those who died had higher osmolalities throughout the first 14 days post-SAH. This difference was statistically significant on days 0-4, 6, 7, 10, and 11. Figure 2C depicts mortality for those whose osmolality fell above or below the mean for that particular day. The difference in mortality is most marked in the first 3 days post-SAH with patients in the "hyperosmolar" group having a mortality rate 2-3 times that of the "hypoosmolar" group.

Osmolality had no discernible effect upon the development of clinical vasospasm (Figure 2D). Plotted in relation to day of operation there remained a trend to higher osmolality for patients who died and no appreciable difference between patients developing clinical vasospasm and those who did not.

### Electrolytes

Mean serum sodium on day 0 was 137 mmol/L, rising to 141 mmol/L on day 2 post-SAH, falling to a nadir of 136 mmol/L on day 8 and remaining relatively stable thereafter. There was a

Figure 1 — Relationship of the means of the highest systolic blood pressures to time, mortality and vasospasm.

- A. Mean of highest systolic blood pressures plotted against day from subarachnoid hemorrhage (day of bleed is day 0).
- B. The means of highest systolic blood pressures for the group of patients who survived compared to those who ultimately died.
- C. The patients on each day were categorized into those whose highest systolic blood pressures were above or below the mean highest systolic blood pressure on that day and the mortality rate for each group was calculated.
- D. The patients were categorized by whether or not they developed vasospasm at some point in their hospitalization and the mean highest systolic blood pressures were calculated for each group on each day.
- E. The patients were categorized on each day by whether their highest systolic blood pressures were above or below the mean for all patients. The percentage who developed vasospasm was then calculated for each group.
- F. The means for highest systolic blood pressure were calculated by day in relation to the day of operation (day 0) for aneurysmal clipping instead of in relation to day of subarachnoid hemorrhage.
- G. The patients were categorized into survivors or non-survivors and the mean highest systolic blood pressure for each group was calculated in relation to the day of operation. The non-survivors continued to show higher mean systolic blood pressures.
- H. The patients were categorized into those who did or did not develop evidence of vasospasm at some time and the mean highest systolic blood pressures for each group were calculated in relation to the day of operation.

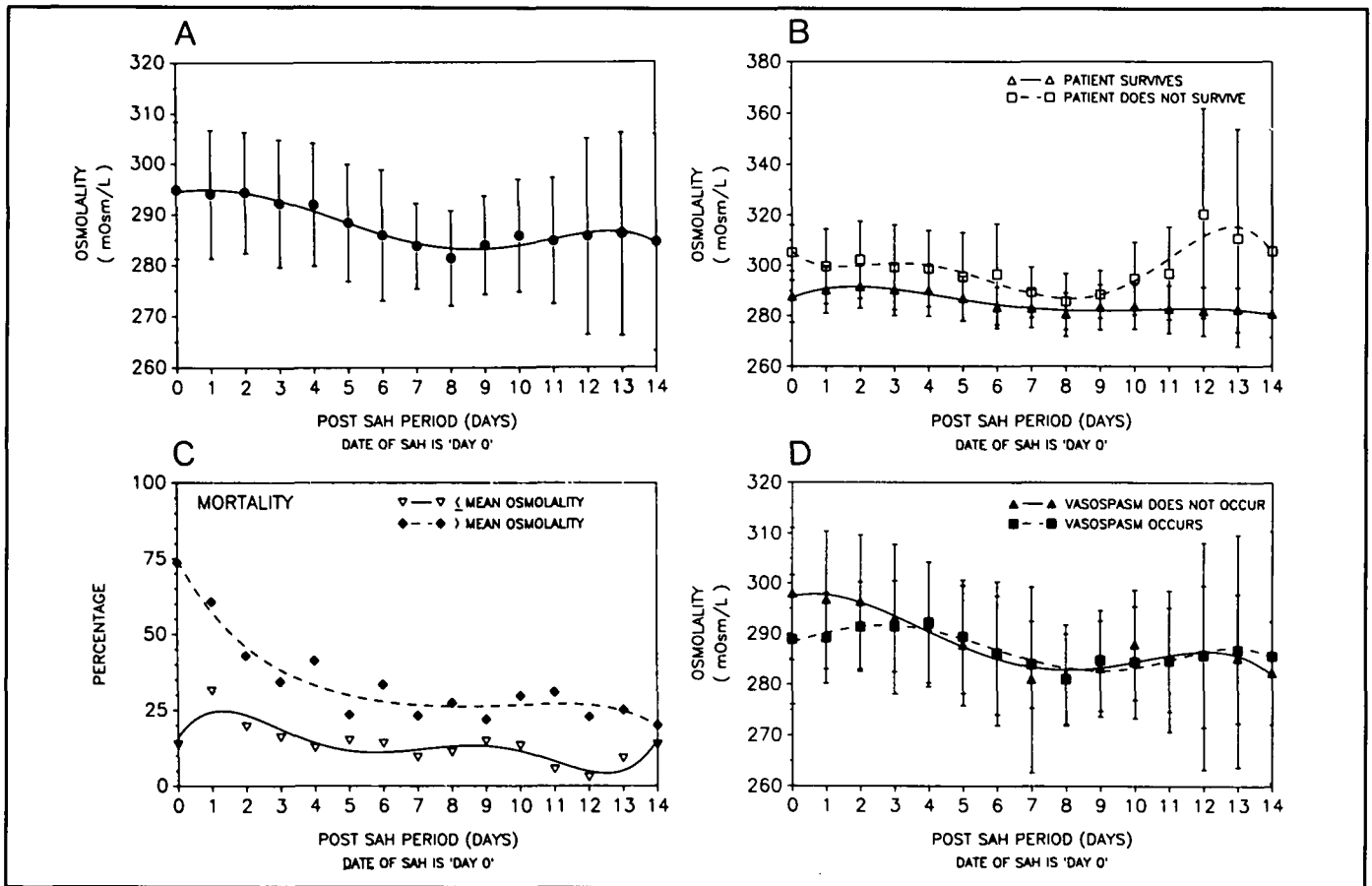


Figure 2 — Relationship of osmolalities to time, mortality and vasospasm.  
 A. Mean of highest osmolality plotted against day from subarachnoid hemorrhage (day of bleed is day 0).  
 B. The means of osmolalities for the group of patients who survived compared to those who ultimately died.  
 C. The patients on each day were categorized into those whose osmolalities were above or below the mean of all osmolalities on that particular day and the percentage of mortality for each group was calculated.  
 D. The patients were classified by whether or not they developed vasospasm at some point in their hospitalization and the mean osmolality of each group was calculated by day post subarachnoid hemorrhage.

minimal trend to higher serum sodiums in the fatal cases but this was not statistically significant. There was no discernible difference in serum sodium in patients developing clinical vasospasm compared to those who did not. Plotted in relation to time of operation, serum sodium mirrors osmolality in demonstrating a small but insignificant elevation on the day of surgery but again showed no significant impact on either mortality or vasospasm.

Initial potassium was 3.6 mmol/L, rising gradually to 4.1 mmol/L by day 14. There was no obvious relation between potassium levels and either mortality or the development of vasospasm. Serum potassium in contrast to sodium tended to be lower around the time of operation but again did not influence mortality or VSP.

### DISCUSSION

The importance of high blood pressure in the immediate phase after SAH has been recognized as having prognostic impact for a poor outcome for some years. Various multivariate analyses of different series of aneurysm cases have found it to be as important or almost as important as neurological grade on

admission.<sup>2-8</sup> In these studies the blood pressure was generally that recorded on admission but the time of admission post-SAH varied widely. Nonetheless the influence of hypertension after SAH was evident in every study.

Ljunggren and associates reported on 219 consecutively treated cases in 1981.<sup>9</sup> Eighteen patients having early surgery had been treated for hypertension prior to their SAH (diastolic pressure > 110 mm Hg on at least 2 occasions). Delayed ischemic deficits developed in 50% of this group compared to only 13% of non-hypertensive cases. Six of 8 hypertensive cases given antihypertensive medication after their SAH developed delayed ischemic deficits.<sup>9</sup> In a cooperative study Kassell and Torner<sup>10</sup> found that an admission systolic blood pressure > 170 mm Hg was associated with a 2.9 times greater risk of mortality than an admission pressure < 140 mm Hg. In the same way, a diastolic pressure above 110 mm Hg had a mortality rate 3.4 times that of cases with diastolic pressures < 90 mm Hg.<sup>10</sup> In a review by the same authors of 2,265 aneurysm cases, hypertension was considered a medical "complication" post-SAH and preoperatively in 16% of cases, hypotension in 1%. Postoperatively hypertension was slightly less common and hypotension more common.<sup>11</sup> O'Neill et al.<sup>12</sup> conducted a



prospective study of the effect of post-ictal blood pressure on outcome following surgical treatment of ruptured aneurysms. A significant association was found between the trend for rising diastolic blood pressure levels and the tendency towards a poor outcome. There was a similar trend for systolic blood pressure which did not reach statistical significance. Fewer than 7% of 325 cases were admitted day 0 and only about half were admitted within day 0-3 post-SAH. The outcomes were (unlike previous studies) not merely classified as dead or alive but according to (i) dead, (ii) vegetative, (iii) severe or (iv) moderate disability and (v) good recovery. If the highest systolic blood pressure was > 161 mm Hg within 24 hours of admission the relative percentages in each of the above groups were: 15%, 0%, 16%, 15%, 55%. For those with blood pressures under this value the figures were: 12%, 1%, 7%, 12%, 68%. Patients with blood pressure  $\geq$  160/95 mm Hg were 1.6 times as likely to have a poor outcome as those with lower blood pressures.<sup>12</sup> Initial systolic blood pressure was significantly correlated with 3 month outcome in a prospective study of 188 patients conducted by Disney et al.<sup>13</sup> The blood pressure was categorized as < 141, 141-180 and > 180 torr. Good outcomes occurred in 24%, 17% and 3%; moderate disability in 17%, 15%, 18%; severe disability in 14%, 13%, 13%; vegetative in 8%, 12% and 0%; dead in 38%, 44% and 68%. In other words, cases with an admission systolic blood pressure < 180 mm Hg were 8 times as likely to be normal as those with admission blood pressures over 180 torr. Similarly, cases with high blood pressures were 1.8 times as likely to die. Patients whose maximum systolic blood pressure at any point in their illness was > 180 torr. were significantly less likely to have a good outcome than those whose blood pressure was never above 180 (9% vs. 28% good outcomes). Mortality however was not related to the maximum blood pressure from any point in the hospital stay (46% vs. 47% deaths).<sup>13</sup>

The present work is in accord with previous observations but demonstrates that the most dramatic significance for mortality of the reactive hypertension is very early after the SAH. It also provides evidence that clinically significant VSP is predicted by systolic hypertension even before patients would have received any therapy designed to artificially increase blood pressure. This study was not designed to address the unknown elements that go into producing an actual blood pressure such as the use of vasoactive drugs, fluid balance, previous hypertensive disease and so on. Just as the early hypertension may be a homeostatic response to overcome the first threat of SAH, that of raised intracranial pressure, so the later hypertension may be a homeostatic defense mechanism responding to cerebral ischemia due to late onset, chronic vasospasm.

Our search for general trends in osmolality and electrolytes which might be associated with mortality and vasospasm was not as revealing as the observations on blood pressure. The possible exception to this would be the apparent raised mortality rate (but not VSP rate) in those cases with the higher osmolalities. One of the earliest systematic analyses of electrolyte abnormalities in aneurysm cases was that of Landolt et al.<sup>14</sup> who noted such disturbances in 44% of 126 cases who were operated and who had good outcomes. The most common observation was a mild reduction in sodium and increase in potassium (26%) without clinical effect. A reduction in sodium of < 130 mOsm/L and potassium increase > 5 mOsm/L occurred in 8%

and was an indicator of a poor prognosis. Takaku et al.<sup>15</sup> studied 1,000 operated and 80 unoperated aneurysm cases. Nine percent showed disturbances such as polyuria, hypernatremia and hyponatremia. The occurrence of these abnormalities worsened the prognosis. The mortality rate was highest (42%) with hypernatremia, and was 15% with hyponatremia. Electrolyte abnormalities were more common between days 3 and 7 post-SAH, 64% of such cases had VSP. Mortality for all operated cases was 6% compared to 23% for 75 patients considered to have significant fluid and electrolyte problems.

SAH occurred in 290 patients reviewed by Doczi and coworkers,<sup>16</sup> with 81% having aneurysms. Five percent were diagnosed as syndrome of inappropriate anti-diuretic hormone secretion on the basis of sodium levels of 118-125 mOsm/L, serum osmolalities 250-270 mOsm/L, urinary osmolalities of 400-1310 mOsm/L and 24 hour urinary sodium excretion of 43-250 mOsm/L. The abnormalities lasted between 3 and 9 days (mean of 6). The abnormality developed an average 8 days after SAH. Nine monkeys had SAH induced by Nelson and colleagues.<sup>17</sup> Hyponatremia developed in 78% and excessive amounts of sodium were excreted in the urine. The natriuresis lasted 4 days. The nadir of mean serum sodium was 126 mOsm/L which occurred on average 5 days post-SAH. Review of current literature suggested that the etiology of the low sodium is secretion of a natriuretic factor such as atrial natriuretic factor so that the early term "cerebral salt wasting syndrome" is justified. In aneurysm cases it is probably advisable to attempt to maintain osmolality in the normal range as well as the electrolytes. If sodium falls to dangerous levels simultaneous administration of saline and a diuretic might be necessary. Blanket use of fluid restriction in the face of falling sodium levels is unwise. The general state of the patient and their hydration must be considered.

The hypertensive, hyperosmolar victim of recent SAH is at special risk from both delayed ischemia from vasospasm as well as other causes of mortality.

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