ELECTROLYTE CHANGES IN PATIENTS WITH SUBARACHNOID HAEMORRHAGE

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SUMMARY

1. After spontaneous subarachnoid haemorrhage in man there is an acute rise in arterial blood pressure. Sodium balance studies were carried out on sixty-four patients with this syndrome and marked sodium retention was found to occur which did not appear to be correlated with a low glomerular filtration rate nor with any consistent change in aldosterone excretion.

2. Effective renal plasma flow was measured by p-aminohippurate clearance in twenty-four patients and renal blood flow calculated from the haematocrit. Renal blood flow was found to be significantly depressed during the first week of the illness. The possibility that the sodium retention was due to changes in proximal tubular reabsorption secondary to alterations in intrarenal pressure is discussed.

3. No change in potassium balance was found despite the frequent occurrence of hypokalaemia. The depression of plasma potassium was closely related to the degree of respiratory alkalosis. Since respiratory alkalosis has been shown in animals to occasion a shift of potassium from the extracellular fluid into the cells, it is postulated that a similar change occurs after subarachnoid haemorrhage in man.

Key words: subarachnoid haemorrhage, electrolytes, sodium balance, potassium balance.

It is well established that in a number of diseases of the central nervous system including subarachnoid haemorrhage, changes in plasma and urinary sodium occur. In a recent review of the literature (Matthews, 1965) it was pointed out that in nearly all instances the exact intake of sodium by the patients was not known, so that reports of disturbed sodium metabolism were of limited value.

After spontaneous subarachnoid haemorrhage in man there is, in addition to a low urinary sodium, an acute rise in arterial blood pressure. This rise is greatest at the initial stages and in the uncomplicated case gradually subsides over a period of days as recovery ensues. As
opposed to patients with intracerebral haemorrhage, patients with subarachnoid haemorrhage are not basically hypertensive. This acute rise in pressure was first described by McCordock (1923) and has since been confirmed by Richardson & Hyland (1941), Pluvinage (1949) and Hamby (1952). The initial rise in blood pressure is probably due to a primary fall in cerebral blood flow (James, 1968). At the same time an increase in ventilation occurs, due either to the depression in cerebral blood flow as suggested by James (1968) or possibly to changes in cerebrospinal fluid pH as suggested by Froman & Crampton Smith (1967). Since changes in arterial blood pressure (Selkurt, 1951; Langston, Guyton & Gillespie, 1959) and in ventilation (MacFarlane, Robinson, Howard & Kinne, 1958) are known to cause changes in sodium handling by the kidney, both directly and through changes in aldosterone secretion, the following study was undertaken. In this investigation sodium intake was controlled.

**METHODS**

The investigation was carried out on sixty-four patients suffering from acute spontaneous subarachnoid haemorrhage admitted to the Department of Neurological Surgery and Neurology, Addenbrookes Hospital, Cambridge. Permission for the study was obtained in all cases either from the patient or from the next of kin.

In most instances the study was commenced on the second or third day of the illness but on a few occasions it was possible to start the collections within a few hours of the catastrophe. This investigation in the main confines itself to those patients who made a steady recovery, although five patients are included separately who had a second subarachnoid haemorrhage while under study. Some patients were treated by surgery from about the tenth day and were excluded from the investigation. Some distortion of the results given below is therefore inevitable due to the fact that the most ill patients (i.e. those not suitable for surgery) stayed in the study longer. This source of error did not operate before the tenth day and affected all measurements equally.

*Arterial blood pressure measurements*

Sphygmomanometer recordings were taken either by the author or by senior nursing staff at 4 hourly intervals. The following blood pressures were considered. (1) The baseline pressure of the patient. This was obtained after full recovery some 6 weeks after the haemorrhage and was the mean of the resting pressures of the patient taken on 3 consecutive days. (2) The daily highest recorded mean arterial blood pressure.

Blood pressure rises were expressed as percentage increase over the normal baseline mean arterial pressure for that patient.

*Sodium and potassium balance*

*Intake.* A special diet containing 40 mEq of sodium and 40–50 mEq of potassium per day was given to all conscious patients. Also each patient received 4 g of NaCl (70 mEq of sodium) in capsule form/24 h. Equivalent amounts of sodium and potassium were given to unconscious patients and allowances were also made for extraneous sources of sodium in some patients, i.e. the saline given at the time of a carotid angiogram. In this way all patients received over 100 mEq of sodium and approx. 40–50 mEq of potassium/day. Fluid was in no way restricted and, indeed, care was taken to ensure that the patients did not become dehydrated.
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Output. Urine collections (24 h) were made from 10 a.m. to 10 a.m. Since the values were averaged over 2-day periods an occasional error in urine collection could be ‘corrected’ for by substituting a single 24 h collection value for an averaged one; loss of sodium in sweat and faeces was ignored.

Glomerular filtration rate
Glomerular filtration rates (GFR) were measured daily by the clearance of creatinine. Blood for plasma creatinine was taken at 24 h intervals. The calculated glomerular filtration rates were averaged over 2-day periods.

Aldosterone excretion rates
Aldosterone excretion rates were measured in seven patients by the method of Brooks (1960).

Renal blood flow
Renal blood flow was calculated from the clearance of infused PAH (sodium p-aminohippurate) and the haematocrit in twelve patients during the first and second weeks of the illness. These results were compared with the results of seven patients who volunteered to act as controls. These control hospital patients all had cerebral aneurysms but had not sustained a recent subarachnoid haemorrhage.

Blood was also taken at 2-day intervals for determination of plasma sodium and potassium concentrations. In twenty-five patients arterial blood was taken for arterial $P_{CO_2}$ at 4 day intervals, either on days 1, 5, 9 and 13 or on days 3, 7, 11 and 15. Sodium and potassium determinations were carried out with an Eppendorf flame photometer. $Pa_{CO_2}$ was measured by a microAstrup technique, creatinine and PAH determinations by autoanalyser.

RESULTS

Arterial blood pressure
The greatest increases in arterial blood pressure occurred immediately after the haemorrhage and this pressure rise then gradually subsided over a period of days (Table 1).

Sodium balance
Over the first week or so severe sodium retention occurred despite a lack of significant change in plasma sodium concentration. Sodium excretion then gradually increased as recovery ensued (Table 1). Five patients were being studied when they sustained a second subarachnoid haemorrhage. These patients had been on a constant sodium intake for at least a week before the second haemorrhage. Fig. 1 shows the sudden fall in sodium excretion that occurred. An acute rise in arterial blood pressure was found in these patients, which subsided as the excretion of sodium once more increased.

Potassium balance
The initial plasma potassium concentration was low (Table 1). There was, however, no evidence of increased urinary excretion at this time.

Aldosterone excretion
There was no correlation between aldosterone excretion and plasma potassium in the seven
Table 1. Changes with time after subarachnoid haemorrhage of mean arterial pressure increase, daily sodium excretion, daily potassium excretion, daily urine volume, glomerular filtration rate, plasma potassium concentration and PaCO₂. Means ± SEM are shown. Arithmetic means of pH values are shown.

<table>
<thead>
<tr>
<th>Day</th>
<th>Mean arterial pressure (% increase)</th>
<th>Daily sodium excretion (mEq)</th>
<th>Daily potassium excretion (mEq)</th>
<th>Daily urine volume (ml)</th>
<th>GFR (ml/min)</th>
<th>Plasma potassium (mEq/l)</th>
<th>Plasma sodium (mEq/l)</th>
<th>PaCO₂ (mmHg)</th>
<th>Arterial pH</th>
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<tr>
<td>1-2</td>
<td>32 ± 6 (n = 60)</td>
<td>33 ± 7 (n = 64)</td>
<td>35 ± 6 (n = 61)</td>
<td>73 ± 7 (n = 64)</td>
<td>1100 ± 43</td>
<td>12 ± 4</td>
<td>138 ± 10</td>
<td>28 ± 2</td>
<td>7.46 ± 0.15</td>
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<td>26 ± 2 (n = 64)</td>
<td>36 ± 5 (n = 64)</td>
<td>43 ± 4 (n = 64)</td>
<td>87 ± 4 (n = 64)</td>
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<td>28 ± 2</td>
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<td>40 ± 3 (n = 64)</td>
<td>46 ± 2 (n = 64)</td>
<td>98 ± 3 (n = 64)</td>
<td>1100 ± 43</td>
<td>3 ± 1</td>
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<td>43 ± 3 (n = 64)</td>
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<td>1100 ± 43</td>
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<td>7.46 ± 0.15</td>
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<td>1100 ± 43</td>
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<td>20 ± 3 (n = 64)</td>
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</tr>
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<td>1100 ± 43</td>
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<td>7.46 ± 0.15</td>
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<td>23-24</td>
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<td>1100 ± 43</td>
<td>3 ± 1</td>
<td>138 ± 10</td>
<td>28 ± 2</td>
<td>7.46 ± 0.15</td>
</tr>
</tbody>
</table>

Arithmetic means of pH values are shown.
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patients studied (Table 2). Neither was there any correlation between aldosterone excretion and sodium excretion. In fact despite the low urinary sodium excretion, urinary aldosterone values were also low in the patients studied. Mean daily excretion was $2.7 \pm 0.24 \mu g$ (SE)/24 h (normal range of aldosterone excretion for the laboratory 0–16 $\mu g$/day).

![FIG. 1. Urine sodium excretion in five patients before and after a second subarachnoid haemorrhage (SAH 2). Each point represents the mean urine sodium over a single day period. The bars represent $\pm$ SEM.](image)

**TABLE 2. Relationship between aldosterone excretion and sodium excretion, potassium excretion and plasma potassium concentration**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Day</th>
<th>Urine volume (ml)</th>
<th>Sodium excretion (mEq/day)</th>
<th>Potassium excretion (mEq/day)</th>
<th>Plasma potassium (mEq)</th>
<th>Aldosterone excretion ($\mu g$/day)</th>
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</thead>
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<tr>
<td>12</td>
<td>5</td>
<td>1240</td>
<td>92</td>
<td>23</td>
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<tr>
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<td>6</td>
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<td>1062</td>
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<td>33</td>
<td>3.2</td>
<td>7.5</td>
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<tr>
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<td>2</td>
<td>1010</td>
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<td>58</td>
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<tr>
<td>48</td>
<td>8</td>
<td>1080</td>
<td>119</td>
<td>57</td>
<td>—</td>
<td>3.8</td>
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<tr>
<td>53</td>
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<td>600</td>
<td>56</td>
<td>47</td>
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<td>3.7</td>
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<td>2</td>
<td>830</td>
<td>60</td>
<td>19</td>
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<td>820</td>
<td>35</td>
<td>18</td>
<td>—</td>
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<tr>
<td>55</td>
<td>14</td>
<td>950</td>
<td>41</td>
<td>19</td>
<td>—</td>
<td>1.2</td>
</tr>
<tr>
<td>55</td>
<td>15</td>
<td>1180</td>
<td>57</td>
<td>26</td>
<td>4.1</td>
<td>1.2</td>
</tr>
</tbody>
</table>
Glomerular filtration rate

The changes in glomerular filtration rate after spontaneous subarachnoid haemorrhage were found to be variable. However, the mean glomerular filtration rate over the first 10 days, calculated over 2-day periods, did not fall below 68 ml/min (Table 1).

Renal blood flow

The mean renal blood flow of the seven control patients was 1280±138(SE) ml/min. The mean renal blood flow of twelve subarachnoid haemorrhage patients studied during the first week was 660±128 ml/min; and during the second week 800±120 ml/min. Comparisons of the renal blood flow measurements of the first and second weeks with those of the control group show that both were significantly different from control values.

![Fig. 2. Relationship between plasma potassium (mEq/l) and Pa,co2 (mmHg), at 1 week for twenty-five patients. The correlation coefficient (r) = +0·72 (n = 25). P for the significance of r<0.001.](image)

First week: difference in means = 620 ml/min; \( t = 8.9; \ P<0.001 \). Second week: difference in means = 480 ml/min; \( t = 7.3; \ P<0.001 \).

These results also show a significant difference between the first and second week measurements. Difference in means (between first and second weeks) = 140 ml/min; \( t = 2.28; \ P<0.05 \).

There was no correlation between the changes in renal blood flow and those in blood pressure. If renal blood flow is plotted against percentage change in mean arterial pressure, the correlation coefficient is \( -0.02 \). Nevertheless, since the blood pressure was greatest when renal blood flow was lowest, considerable renal arteriolar vasoconstriction must have occurred at that time.

Changes in Pa,co2 and the relationship between Pa,co2 and plasma potassium

The mean \( Pa,co2 \) was at first found to be low but gradually returned to normal. At the same time as the \( Pa,co2 \) was low, arterial pH was high. Thus a low mean plasma potassium was
found to be associated with a low mean $P_{a,CO_2}$ and a high mean arterial pH. If these relationships were further investigated by comparing individual values, one from each patient taken arbitrarily as near as 1 week from the ictus as was possible, similar correlations were found (Fig. 2). Thus when $P_{a,CO_2}$ (mmHg) was plotted against plasma potassium concentration (mEq/l) the correlation coefficient ($r$) was 0.72, the $P$ value for the significance of $r$ where $n = 25$ (1 observation/patient) was $<0.001$. A significant negative correlation was obtained when arterial pH was plotted against plasma potassium concentration (mEq/l). The $P$ value for the significance of $r$ was $<0.001$.

![Graph](image)

**Fig. 3.** Relationship between the maximum percentage increase in mean arterial pressure (MAP) (log scale) and urinary sodium excretion (mEq/day). The maximum percentage increase in mean arterial pressure for any single patient is plotted against the lowest urinary sodium excretion in mEq/day, taken within 3 days of this highest pressure measurement. The correlation ($r$) of the log of the maximum % increase in mean arterial blood pressure against urinary sodium excretion is $-0.65$. $P$ for the significance of $r$ ($n = 61$) is $<0.001$.

**Relationship between the rise in blood pressure and the decrease in sodium excretion**

During the investigation it became apparent that those patients who sustained the greatest increases in arterial blood pressure had the greatest decrease in sodium excretion. Because of this the greatest increase in arterial blood pressure was compared with the lowest urinary sodium excretion in the ensuing 3 days. When the pressure rises were expressed as a percentage of the baseline pressure a significant exponential relationship was found (Fig. 3). Essentially the same results were obtained if systolic increase, diastolic increase or mean increase were compared. No correlation was found between potassium excretion and blood pressure rise.

**DISCUSSION**

From these results certain conclusions can be drawn. After subarachnoid haemorrhage in man there is an acute rise in blood pressure; there is at the same time a fall in urinary sodium excretion resulting in sodium retention. This fall in the urinary excretion of sodium cannot be explained by a fall in GFR or by an increase in aldosterone excretion.
Renal blood flow is significantly decreased during the first and second weeks of the illness, the flow during the second week being significantly higher than that of the first week. Since the greatest increases in blood pressure occur when renal blood flow is lowest, this suggests that the renal arteriolar vasoconstriction must at this time be considerable. It must be admitted, however, that the 'effective' rather than actual renal blood flow is being measured under these circumstances. The comparison of mean values in the controls, subjects, patients in the first week and in the second week, depends on the assumption of a constant PAH extraction ratio.

In recent years it has been suggested that changes in renal artery perfusion pressure can alter sodium excretion irrespective of changes in glomerular filtration rate. Selkurt (1951) and Langston et al. (1959) showed in dogs that increasing the mean perfusion pressure to the kidney caused natriuresis. Decreasing renal arteriolar resistance and thereby increasing the effective intrarenal arterial pressure is also associated with an increase in the excretion of sodium (McDonald & De Wardener, 1965; Barraclough & Mills, 1965; Earley & Friedler, 1966), Langston et al. (1959) showed in dogs that raising perfusion pressure caused greater increases in sodium excretion after complete spinal anaesthesia than before.

De Bono & Mills (1965) have shown that proximal tubular reabsorption of sodium is in some way dependent on the balance between systemic arterial pressure and renal arteriolar resistance. Whether this is due to a natriuretic factor or some physical change in the renal vasculature is not yet clear.

Despite the fact that the blood pressure is highest initially and therefore an increase in sodium excretion might have been expected, at this time renal arteriolar resistance is greatest so that a decrease in intrarenal precapillary pressure probably occurs.

In a recent series of experiments on dogs (James & Wise, 1969) where neurogenic hypertension was caused by artificially increasing cerebrospinal fluid pressure, a similar relationship between changes in blood pressure and sodium excretion was found. When the kidney was denervated and renal arteriolar resistance thereby decreased, the previously noted relationship was abolished. In fact there was a tendency for the higher pressure rises to cause an increase in sodium excretion. Also in these experiments there was a dissociation between glomerular filtration rate and sodium excretion. Glomerular filtration rate recovered almost immediately after acute rises in arterial pressure whereas sodium excretion failed to recover for a long period. A similar pattern is seen in the present investigation.

The increase in ventilation which results in a respiratory alkalosis is unlikely to explain the sodium retention, as an increase in ventilation is associated with an increase in sodium excretion rather than a fall (MacFarlane et al., 1958). However, the increase in ventilation may well explain the low values of plasma potassium concentration. Giebisch, Berger & Pitts (1955) have shown in nephrectomized dogs that an increase in ventilation results in a movement of potassium ions into the cells, and were able to establish a linear relation between $Pa_{CO_2}$ and plasma potassium concentration. Since an exactly similar relationship was found in patients with subarachnoid haemorrhage, it is possible that a similar mechanism of shift of potassium ions into the cells explains the low plasma potassium values under these circumstances.

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REFERENCES


