communicating artery aneurysm. Hyponatraemia following subarachnoid haemorrhage from an aneurysm of the right internal carotid artery was described by Goldberg and Handler (1960). The post-mortem finding of a slight compression necrosis of the pituitary, secondary to the aneurysm, and of a mild arteriolonephrosclerosis puts this case in a different category to the three cases of hyponatraemia following aneurysmal rupture reported by Joynt *et al.* (1965). All three of their hyponatraemic patients had multiple aneurysms, with an anterior communicating artery aneurysm present in each case.

The biochemical picture of the patient following a spontaneous subarachnoid haemorrhage is incomplete. In primary cerebral haemorrhage a raised blood urea level, sometimes accompanied by an increase in cholesterol and/or blood sugar, has been reported, while the sodium and potassium levels have been lowered with chloride and bicarbonate levels varying widely in either direction. Severe disturbances of sodium metabolism have been reported following aneurysmal rupture, especially in association with anterior communicating artery aneurysms. There is a lack of information on the incidence of these abnormalities and the time sequence in which they arise or the effect of operative interference. Part II which follows describes the incidence of biochemical abnormality in 134 patients with recent spontaneous subarachnoid haemorrhage on admission to hospital. Subsequent articles will deal with the pattern of metabolic response in both conservatively and surgically treated cases.

Part II The patient on admission

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To help to assess the patient on arrival at the neurosurgical centre, we obtained a blood sample from all patients admitted with a diagnosis of recent subarachnoid haemorrhage. All specimens were take soon after arrival in the ward and before any food, drink, or intravenous fluid had been given or other investigations performed.

CASE MATERIAL

All patients came from a referring hospital where a lumbar puncture had confirmed the presence of blood in the cerebrospinal fluid. At first we were particularly interested in patients too ill to look after their own fluid intake and studied all patients admitted within seven days of a spontaneous subarachnoid haemorrhage, who were either in coma or very drowsy. Subsequently all cases of recent spontaneous subarachnoid haemorrhage were included. In this way 79 alert patients (41 men and 38 women) and 55 comatose cases (28 men and 27 women) were sampled. The patients referred to as 'comatose' were either in coma or too drowsy to be responsive to thirst. The day of the haemorrhage is referred to as 'day 0'.

Bilateral carotid angiography, according to our usual scheme (McKissock, Walsh, and Richardson, 1960), was carried out in all but three cases. Where carotid examination was negative, vertebral angiography was done two days later, except in the cases of one 64-year-old woman and a 68-year-old man, each presenting with a non coma-producing subarachnoid haemorrhage who were not subjected to vertebral angiography on account of their age. Of the three patients not examined angiographically, one died before investigation and the diagnosis was obtained at necropsy. In a further case the diagnosis of intracerebral haemorrhage was accepted on the basis of clinical signs and ultrasonography, and in the last case the diagnosis of pontine haemorrhage was assumed from ventriculography. Table I gives details of the lesions found; six cases with bilateral aneurysms are included among the named aneurysms.

TABLE I

SOURCE OF HAEMORRHAGE

Source of Haemorrhage	*No. of Cases*
Anterior communicating artery aneurysm	24
Middle cerebral artery aneurysm	15
Posterior communicating artery aneurysm	20
Multiple aneurysms, with source of haemorrhage not known	8
Angioma	10
Primary intracerebral haemorrhage	29
No abnormality demonstrated on angiography	28
Total	134

LABORATORY METHODS

Blood was taken into E.D.T.A. for determination of the sedimentation rate and packed cell volume (Wintrobe method) and haemoglobin as oxyhaemoglobin (Dacie, 1956).

Heparinized plasma was used for determinations of sodium and potassium (EEL flame photometer), chloride (Schales, 1953), bicarbonate by titration (Varley, 1962a), urea (Varley, 1962b), total protein (King and Wootton, 1956), glutamic-oxaloacetic transaminase (Varley, 1962c). Plasma osmolality was measured by depression of freezing point using an osmometer.[1] Blood sugar was

[1]Advanced Instruments Inc., model H.

determined on a sample taken into fluoride by the method given by Varley (1962) but using Nelson's arseno-molybdate reagent.

RESULTS

In presenting the results we have made a primary division into comatose and alert groups; in our experience conscious level is the most important single prognostic factor in all cases of subarachnoid haemorrhage. Figure 1 shows the incidence of abnormal results in relation to conscious level and the range of normal levels employed is given in Table II. The figures quoted for electrolytes, urea, and fasting blood sugar are those given by Wootton and King (1953) as containing 98% of normals. This rather wide range was used to exclude borderline

TABLE II

NORMAL RANGES

Sodium		133-152 mEq./l.
Potassium		3·5-5·6 mEq./l.
Bicarbonate		24-31 mEq./l.
Chloride		99-108 mEq./l.
Urea		12-47 mg. per 100 ml.
Sugar (fasting)		70-110 mg. per 100 ml.
Total protein		6-7·5 g. per 100 ml.
SGOT		5-40 units per ml.
Plasma osmolality		280-300 mOs per litre
Haemoglobin	Males	92-120% (100% = 14·6 g.)
	Females	79-110%
Haematocrit	Males	40-50%
	Females	35-45%

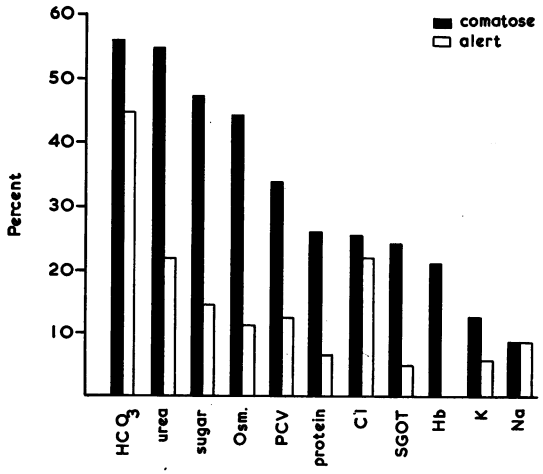

FIG. 1. *Percentage incidence of abnormal results.*

results. The remaining figures are those for our own laboratory and conform to the usually accepted standards with the exception that our upper limits for plasma protein, haemoglobin, and packed cell volume are a little lower.

BLOOD UREA Blood urea, estimated in all cases, was above 47 mg. per 100 ml. in 22·5% of alert patients and in 56·3% of those in coma. The 38 alert women (average age 52·2 years) had a mean blood urea of

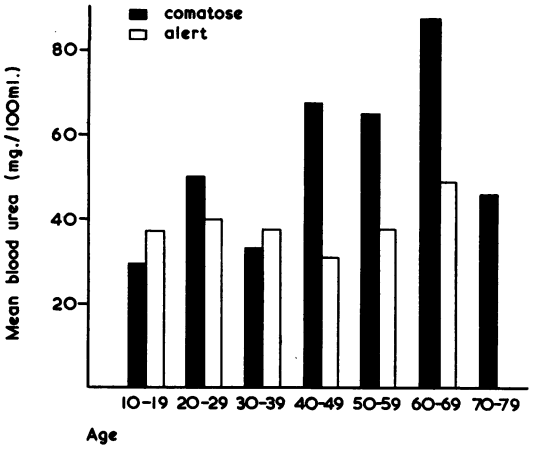

FIG. 2. *Mean blood urea in relation to age and conscious level.*

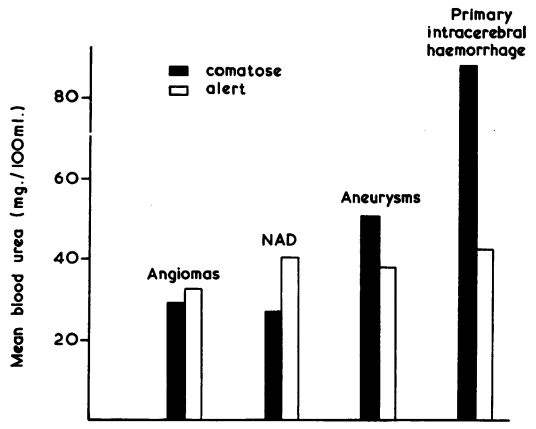

FIG. 3. *Mean blood urea in relation to lesion and conscious level.*

43 mg. per 100 ml. and in the 41 alert men (average age 45·4 years) it was 38 mg. per 100 ml. For 27 comatose women (average age 53·0 years) the mean urea level was 51 mg. per 100 ml. and for 28 comatose men (average age 50·4 years) it was 78 mg. per 100 ml. In none of the other substances estimated was there a marked sex difference.

Figure 2 shows the mean urea concentration in relation to age and conscious level. In the alert patients age had little effect on the blood urea, a mean urea concentration of 38 g. per 100 ml. in the 10 to 19-year-old group increasing to 50 mg. at 60 to 69 years. In the comatose patients the mean urea concentration rose from 30 mg. per 100 ml. in the youngest group to 90 mg. in the sixth decade. Figure 3 shows the mean blood urea concentration in relation to the source of haemorrhage. The mean values for the different sites of aneurysm were very similar.

PLASMA OSMOLALITY This was measured in 126 cases (48 comatose and 78 alert). Forty-five per cent of comatose patients and 12% of those alert on admission had results outside the limits of 280 to 300 mOs per litre. Figure 4 shows the mean and range of

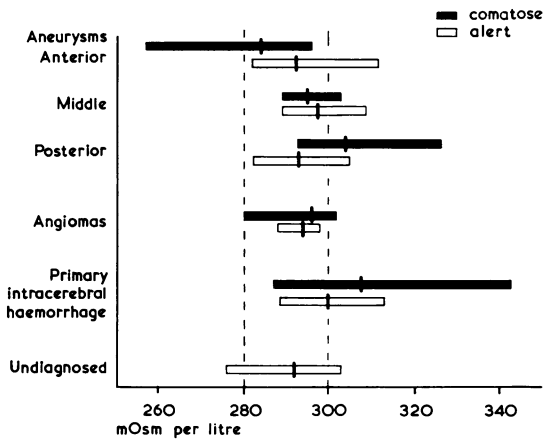

FIG. 4. *Mean and range of plasma osmolality in relation to lesion and conscious level.*

plasma osmolality for each of the diagnostic groups. The greatest disturbance was found among the patients with primary intracerebral haemorrhage where 15 of 28 determinations were above 300 mOs per litre; correcting these 15 for excess of urea and sugar still leaves nine results above 300. As shown in Table III, plasma osmolality rose with the duration of the coma.

TABLE III

PLASMA OSMOLALITY IN RELATION TO DURATION OF COMA

Day	*No. of Cases*	*Mean Osmolality (mOs/l.)*	*Range*
0	11	296	279-307
1	18	299	280-326
2	10	306	276-333
3	3	317	307-343
4	2	288 and 303	
5	2	310 and 326	

TOTAL PLASMA PROTEIN This was determined in 37 comatose and 45 alert cases. Twenty-seven per cent. of the comatose patients and 7% of those alert had a protein concentration above 7·5 g. per 100 ml. The mean for the comatose group was 7·15 g. per 100 ml. (range 6·1 to 9·05) and the alert cases had a mean plasma protein concentration of 6·65 g. per 100 ml. (range 5·85 to 8·2).

PACKED CELL VOLUME Packed cell volume, measured in 133 patients, was increased in 35% of comatose and 13% of alert cases.

HAEMOGLOBIN Haemoglobin was determined for 133 cases and was above the upper limit of normal in 22% of the comatose patients. No alert patient had a raised haemoglobin concentration.

TABLE IV

MEAN PACKED CELL VOLUME AND HAEMOGLOBIN

Sex	*Conscious Level*	*P.C.V. (%)*		*Hb (%)*	
		Mean	*Range*	*Mean*	*Range*
Females	Alert	43	32-48	93	70-110
	Comatose	46	37-59	100	81-124
Males	Alert	45	41-50	104	88-115
	Comatose	47	40-55	108	93-125

SODIUM Sodium levels were determined in 133 cases. No patient had, on admission, a plasma sodium level above normal. A normal sodium concentration was found in the 10 patients with angiomas and all of the 15 patients who had bled from a middle cerebral artery aneurysm; 12 cases had an abnormally low plasma sodium concentration: four patients with sodium concentrations of 124, 130, 130, and 132 mEq./l. had suffered a coma-producing subarachnoid haemorrhage from an anterior communicating aneurysm 48 hours before admission and three of these were still in coma. Three patients (one comatose and two alert) with posterior communicating aneurysms had plasma sodium concentrations of 130, 132, and 130 mEq./l. on days 1, 2, and 2 respectively. One comatose man was admitted with a plasma sodium concentration of 129 mEq./l. on day 2 after a primary intracerebral haemorrhage and the remaining four hyponatraemic cases occurred in the group of patients for whom no source of the subarachnoid haemorrhage was found.

POTASSIUM Potassium was determined in 133 cases with 10 abnormal results. The only raised value, 5·8 mEq./l., was in an alert woman of 65 with a primary intracerebral haemorrhage. Low values (3·2 to 3·4 mEq.K/l.) were found in four patients with posterior communicating aneurysms, two with

primary intracerebral haemorrhage, and in one case each of anterior communicating, middle cerebral, and multiple aneurysm.

CHLORIDE Chloride, estimated in all patients, was below normal in 25 patients (16 aneurysms, six undiagnosed, and three primary intracerebral haemorrhages), six of whom also had a low plasma sodium level. A raised plasma chloride level was present in eight cases (four with primary intracerebral haemorrhage, two with angiomas, one middle cerebral aneurysm, and one undiagnosed). In two of the cases with primary intracerebral haemorrhage the raised chloride level was compensating a low plasma bicarbonate level.

PLASMA BICARBONATE This level was low in 35 of the 70 patients in whom the measurement was made (20 of 36 aneurysms, four of four angiomas, seven of 14 primary cerebral haemorrhage, and four of 15 patients with no lesion found). In most instances the deficit was less than 5 mEq./l. though in eight cases (four comatose and four alert) plasma bicarbonate concentrations between 15 and 19 mEq./l. were found. All four alert cases had a normal blood urea, but in three of the four comatose patients urea was raised (63, 147, and 205 mg.).

BLOOD SUGAR Blood sugar was estimated in 109 patients who were considered to be in the fasting state on admission. Increased values were three times as common in comatose patients as in alert, 45% and 15% of cases respectively, and were most commonly encountered with ruptured middle cerebral aneurysms. A more detailed treatment of the blood sugar results is deferred to a later paper.

SERUM GLUTAMIC-OXALACETIC TRANSAMINASE Determinations were made in 56 cases (28 aneurysms, five angiomas, 10 primary intracerebral haemorrhage, and 15 undiagnosed). Six patients, all with aneurysms, had raised transaminase levels. Four of these were in coma and of the other two one had only recently recovered consciousness. The increases were not great, only two being over 140 units.

ERYTHROCYTE SEDIMENTATION RATE The E.S.R. was determined for 113 patients as part of the haematological examination. Raised values were more frequent among the alert than in the comatose cases. Table V gives the proportion of cases, comatose or alert, with a raised E.S.R. in relation to time since ictus.

INCIDENCE OF BIOCHEMICAL ABNORMALITIES The incidence of biochemical abnormalities has been assessed by taking all the results for sodium, potassium, bicarbonate, urea, transaminase, osmolality, and sugar for each of days 0, 1, and 2 in each group and then expressing the number of abnormal results as a percentage of the total number of tests run on the group. As the full range of tests was not always carried out on every patient, the different groups in Table VI are sometimes not strictly comparable; however, the differences in composition are not great enough to swamp the general trend of events.

TABLE V

RAISED E.S.R. IN RELATION TO TIME SINCE ICTUS

Day	*No. of Cases*	*No. Raised*
0	19	5 (26·3%)
1	34	8 (23·5%)
2	28	7 (25%)
3	11	4 (36·3%)
4	8	5 (62·5%)
5	7	3 (42·8%)
6	5	4 (80%)
7	1	0

TABLE VI

PERCENTAGE OF ABNORMAL TESTS

	Day 0	*Day* 1	*Day* 2
All cases	17·6	25·6	29·9
All alert cases	10·4	16·2	21·5
All comatose cases	22·7	49·4	41·5
Aneurysms, alert	10·7	16·2	23·3
Aneurysms, comatose	21·0	45·0	51·4
Primary intracerebral haemorrhage, alert	0	28·4	42·8
Primary intracerebral haemorrhage, comatose	29·6	35·6	39·6
Angiomas, alert	No cases	10	No cases
Angiomas, comatose	16·7	21·4	0 (1 case)
No source of bleeding found, alert	7·7	11·4	16
No source of bleeding found, comatose	14·3	20	No cases

DISCUSSION

Early in our investigations of subarachnoid haemorrhage the importance of the patient's conscious level in relation to prognosis became apparent. The most striking finding in this survey of our patients' biochemical condition on admission has been the influence of conscious level on the incidence of abnormal results. Figure 1 and Table VII show that abnormal results occurred twice, or more, as frequently at the time of admission if at that time the patient was in coma or very drowsy. With the exception of the patients with intracranial angiomas, this was true of all diagnostic groups. In both comatose and alert cases the degree of disturbance increased

with the passage of time over the first few days after the haemorrhage.

Only 16% (six comatose and 15 alert) of patients were normal to all the tests made but multiple abnormal results in any one case were much more common in those in coma. This raises the question as to whether the same event causes the coma and the biochemical disturbance or if the abnormal biochemical findings follow on the coma and are a result of the patient being unable to fend for himself. The results fall into two groups: those in which the findings are fairly similar in both the comatose and the alert patients and those in which there is a marked difference with change in conscious level. In those tests reflecting the patient's state of hydration there was a much larger proportion of abnormal results among the comatose cases and the average concentration of each constituent was always higher in this group. About 40% of comatose cases had some laboratory evidence of dehydration and in many of the patients who had been in coma for several days before reaching us this was sufficiently severe to require immediate correction, though clinical evidence of water deficit was not always evident.

That there are other factors than just water lack operating in comatose cases is shown by their higher incidence of increased blood sugar and transaminase levels. A subarachnoid haemorrhage of sufficient severity to give a continuing state of coma might, indeed, be expected to have a greater effect on the general metabolism.

In contrast to the above results, electrolyte disturbances showed a more nearly equal distribution between the comatose and alert cases and were minimal at this stage of the illness, except for the frequent mildly low bicarbonate concentrations.

A number of metabolic changes seemed to be related to the site of the lesion: for instance, the occurrence of a raised blood sugar level was more common among the patients with middle cerebral artery aneurysms than in those with aneurysms at other sites, and hyponatraemia was found in some cases with anterior communicating or posterior communicating artery aneurysms but never with a middle cerebral artery aneurysm. In this series none of the cases of primary intracerebral haemorrhage had a raised transaminase level though some of those with a ruptured aneurysm did. Discussion of these changes is deferred to later papers.

As summarized in Part I of this paper an increased blood urea concentration in cases with cerebrovascular accidents has been reported by several investigators without any clear indication as to whether the lesion was thrombotic or haemorrhagic, or as to the source of the haermorrhage. In our patients the blood urea level was over 47 mg. per 100 ml. in 37% of the patients with aneurysms and in 65% of the cases of primary intracerebral haemorrhage. No case with an angioma had an increased blood urea level and only small rises were found in the 18% of cases with no lesion demonstrated in which the blood urea levels were outside normal limits. Figure 2 shows that most of the increase in blood urea was in the patients comatose from a primary intracerebral haemorrhage. These are the patients most likely to have had an increased blood urea level before they suffered their stroke. However, their corrected osmolality rose more steeply with the duration of coma than did that of the other groups of cases, indicating that they were not so well able to conserve water and that the increased urea level in these cases is in part a reflection of dehydration.

The primary object of this paper has been to present an account of the type, magnitude, and frequency of the biochemical disturbances in our patients at the time of admission. It also provides the foundation for further investigation of the subsequent changes. The most striking remediable derangement at this stage is dehydration in patients with moderate or gross depression of consciousness. In our experience the whole general condition of the dehydrated patient is worse than in those patients with similar degrees of depressed consciousness whose hydration is normal, in spite of the still widespread notion that such patients should be subjected to fluid restriction. Patients showing evidence of dehydration appear less well able to withstand the various diagnostic procedures that may be needed to define the lesion, and also represent a more difficult surgical problem, both in their response to anaesthesia and in their general post-operative course. With relation to the former they are subject to hypotensive episodes undoubtedly related to hypovolaemia, and post-operatively appear more liable to cerebral swelling and thrombotic episodes both intracranial and peripheral.

While at times rehydration of such patients before any procedure may be followed by a gratifying improvement in their general condition and conscious state, the problem can nevertheless be acute in patients whose lesion makes their surgical management a matter of urgency. This places one in the clinical dilemma of either proceeding in the face of a fluid deficit or taking the undoubted risks of rapid rehydration. The true answer lies in the early management of such cases, which require careful maintenance of an adequate fluid intake in relation to output, bearing in mind that overhydration must also be avoided and at the same time recognizing that there may be large losses from hyperventilation

and pyrexia and particularly from the brisk diuresis consequent on the therapeutic use of urea.

SUMMARY

Biochemical investigation of 134 patients on admission to the neurosurgical department following a recent spontaneous subarachnoid haemorrhage showed some abnormality in 84% of cases.

The incidence and degree of disturbance was greater in the comatose cases than in the alert. The difference between comatose and alert cases was particularly marked in those tests indicating dehydration. Fasting blood sugar and transaminase were also more often abnormal in the patients in coma while electrolyte disturbances were more nearly equal in the two groups.

The severity of the dehydration increased with the time the patient had been comatose before arrival.

It is concluded that the risk of dehydration in the unconscious or very drowsy patient is still not sufficiently recognized.

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