intake in 24 hours was 900 calories, and the majority of intakes were much lower than this. The mean daily rise of serum urea in this group remained unchanged throughout the duration of their illness, contrasting with the reductions obtained in the 12 patients studied while receiving the prepared diets.

It is possible that the improvement could be due merely to the provision of a higher intake of calories, but, nevertheless, it is apparent that the inclusion of some protein into the diet had no adverse effect, nor did it increase overall nitrogen catabolism. We believe that provision of exogenous protein may well be a vital factor in the survival of those cases of acute renal failure of surgical aetiology, and of those cases in which repeated haemodialysis may be required before recovery of renal function occurs.

Appendix

	Protein g.	Sodium mg.	Potassium mg.	Calories
½ pt. (300 ml.) milk daily ..	9.0	144.0	460.0	190
Breakfast:				
½ oz. (7.5 g.) oatmeal ..	0.85	2.4	26.0	28
1 „ (30 „) lactose ..				112
1 „ (30 „) cream ..	0.4	7.6	22.0	130
100 ml. water ..				
Dinner:				
1 oz. (30 g.) white fish ..	5.1	34.0	79.0	26
½ „ (15 „) butter ..		30.0	2.0	112
½ „ (15 „) potatoes ..	0.25	6.0	47.0	10
1 „ (30 „) vegetables ..		6.4	31.0	6
Tea:				
1 oz. (30 g.) bread ..	2.2	147.0	30.0	69
½ „ (7.5 „) butter ..		15.0	1.0	56
½ „ (15 „) tomato ..	0.1	0.4	41.0	2
Supper:				
½ oz. (15 g.) chicken ..	3.7	13.9	54.0	26
3 „ (90 ml.) milk ..	2.7	42.6	138.0	57
50 ml. water ..				
½ oz. (7.5 g.) cornflour ..		3.6	4.2	25
½ „ (7.5 „) butter ..		15.0	1.0	56
½ „ (7.5 „) cream ..	0.1	1.9	5.5	32
½ „ (7.5 „) “casilan” ..	6.3			24
3 oz. (90 ml.) milk ..	2.7	42.6	138.0	57
1 egg ..	6.8	74.8	78.0	92
1 oz. (30 g.) cream ..	0.4	7.6	22.0	130
1 „ (30 „) lactose ..				112
(Total liquids, 630 ml.) ..	40.6	594.8	1,179.7	1,352

Summary

Twelve patients with acute oliguric renal failure have been treated with specially prepared diets providing essential calorie requirements and varying amounts of first-class protein.

The advantages of this regime are seen in the reduction of the daily rise in serum urea in renal failure, with decreased body protein catabolism resulting from the provision of essential amino-acids for protein synthesis. The survival of patients with prolonged oliguria and frequent haemodialysis may depend upon adequate protein-calorie replacement, especially in those with burns, trauma, or surgical complications.

We wish to acknowledge the generous assistance of Mr. G. M. Widdowson for the repeated biochemical estimations and the continuous help of the sisters and nursing staff of the General Hospital in the care of these patients. We also acknowledge a full-time grant to L.J.L. from the Endowment Fund, United Birmingham Hospitals.

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TOTAL EXCHANGEABLE SODIUM IN DEPRESSIVE ILLNESS

BY

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Recent reports have suggested that there are changes in sodium metabolism during affective illnesses. Coppen (1960) reported a decrease in the rate of entry of ^{24}Na from blood into C.S.F. in a group of 31 depressed patients; this returned to normal with clinical recovery. Gibbons (1960) estimated the total exchangeable sodium with ^{24}Na on two occasions in 24 patients suffering from a depressive illness and found a mean decrease of exchangeable sodium of about 10% after recovery. Russell (1960) studied overall sodium metabolism in depressive illness by means of extremely careful sodium-balance measurements and failed to find any evidence of sodium retention during the depressive phase. Less carefully controlled studies, not employing true balance techniques, have given variable findings during affective illnesses. Schottstaedt, Grace, and Wolff (1956) reported sodium and water retention in normal subjects during periods of transient depression, and the converse was recorded by Ström-Olsen and Weil-Malherbe (1958) in mania. Crammer (1957) recorded large gains in weight associated with water and sodium retention in cyclical psychosis. Trolle (1945), however, could find no consistent change in the pattern of sodium and water excretion in patients recovering from a depressive illness.

These contradictory reports have left the position of sodium metabolism in affective disorders uncertain, and it was decided to initiate further investigations into this problem, starting with a study of total exchangeable sodium.

The measurement of total exchangeable sodium with the long-life isotope ^{22}Na was used to pursue this problem further. This method combined the advantages of a sodium-balance technique in enabling day-to-day variations of sodium balance to be estimated together with the ease of administration and accuracy of an isotope-dilution method. In addition, even though depressed patients are frequently disturbed or agitated, the technique employed allowed daily estimations of total exchangeable sodium to be made while requiring the minimum co-operation from the patient.

Material and Methods

Serial estimations of total exchangeable sodium were carried out on 14 recently admitted male and female patients. The diagnosis of depression was made on a history of severe and unremitting depression associated with a varying proportion of accompanying symptoms such as guilt, delusions of unworthiness, retardation, suicidal ideas, sleep disturbance, poor appetite, etc. Patients suffering from concomitant physical disease, malnutrition, or dehydration were excluded, and no patient who had taken tranquillizing drugs or who had

had other forms of physical treatment within one month of admission was accepted. No attempt was made to differentiate endogenous, reactive, or involutional depressions. Details of the patients' age, sex, period of testing, treatment, and initial weights are shown in

TABLE I.—Results of Total Exchangeable Sodium Estimations in Depressed Patients

No.	Sex and Age	Total Length of Observation (Days)	Treatment	Initial Weight (kg.)	Mean Exchangeable Sodium (mEq)		
					Period 1	Period 2	Period 3
<i>Patients Who Recovered</i>							
1	F 27	30	E.C.T. × 8	62.0	2,300	2,245	2,205
2	M 54	26	„ × 5	46.3	2,373	2,358	2,127
3	F 75	46	„ × 13	59.4	2,274	2,382	2,061
4	M 58	27	„ × 6	51.3	2,363	2,304	2,209
5	F 41	17	„ × 3	50.8	1,897	1,898	1,992
6	F 52	19	„ × 5	46.3	2,292	2,249	2,105
7	M 57	27	„ × 6	49.2	2,579	2,589	2,778
8	F 40	29	„ × 6	62.8	2,175	2,057	2,069
9	M 36	27	„ × 6	72.6	3,371	3,439	3,538
10	F 72	26	„ × 5	48.1	1,798	1,979	1,924
11	F 31	29	„ × 6	56.2	2,311	2,302	2,319
12	M 35	23	„ × 6	77.8	3,181	3,556	3,420
Mean					2,409	2,446	2,396
<i>Patients Who Did Not Recover</i>							
1	F 73	36	E.C.T. × 3	78.0	2,410	2,385	2,308
2	F 65	29	„ × 6	44.0	1,633	1,634	1,666

Period 1 = Days 6–10 inclusive. Period 2 = Five days in middle of period of observation. Period 3 = Last five days of observation.

Table I. There was little change of weight after treatment, a mean increase for the group of 0.8 kg. being recorded.

The clinical state of the patients was recorded daily on behaviour charts. All the patients were treated with electric-convulsion therapy (E.C.T.). Each treatment was preceded by premedication with 1/100 g. (0.65 mg.) of atropine followed by 0.2 g. of sodium thiopentone and 30 mg. of suxamethonium chloride before the administration of E.C.T. They included one group of 12 who recovered or were substantially improved, and two patients who did not improve with treatment. The ordinary ward diet was given without restriction and patients were encouraged to take part in ward activities.

Radioactive sodium (^{22}Na) was obtained from the Radiochemical Centre, Amersham, and was diluted in carrier NaCl solution to an activity of about $1\mu\text{C./ml.}$ The stock solution was stored in a refrigerator in a tightly sealed "polythene" container and doses were pipetted from it as required. The body counter used is shown in Fig. 1. A rigid chair was fixed to a board and the counter itself was an unshielded sodium iodide (thallium-activated) crystal 5 cm. long by 5 cm. in diameter optically coupled to an 11-stage photomultiplier, the output of which was fed through an amplifier to a scaling unit. The counter and the cathode follower were attached firmly to a mount which swung back to allow access to the chair and which could be accurately replaced in its original position. The arrangement was similar to the standard chair position described by Marinelli (1957). Conventional extra high tension (E.H.T.) and scaling circuits were used. To correct for day-to-day instrumental variation, a ^{22}Na standard, placed in the holder on the right-hand side of the chair, was counted before the apparatus was used on each occasion.

Before ^{22}Na was given, individual differences in the shielding of the counter by the body and variations in

background for the naturally occurring ^{40}K in each subject were determined by measuring the background count with and without the patient in the chair. The correction for each individual was applied to background counts thereafter.

The reproducibility of counting rates was estimated on patients who had been given ^{22}Na on the previous day. The subject was placed in the chair and counted; the procedure was then repeated after leaving the chair.

The coefficient of variation of these readings was 0.67% (Table II). The effect of movement on counting

FIG. 1.—Whole-body counting equipment.

TABLE II.—Estimation of Consistency of Repeated Body Activity Measurements

Observation No.	Counting Rate (Counts/100 secs.)	Observation No.	Counting Rate (Counts/100 secs.)
1	29,479	9	29,321
2	29,761	10	29,279
3	29,683	11	29,617
4	29,290	12	29,194
5	29,630	13	29,318
6	29,322	14	29,290
7	29,321	15	29,422
8	29,011		
		Mean	29,396

Coefficient of variation = 0.67%.

rates was also determined. Minor alterations in the position of the hands and legs and lateral movement of the body had negligible effect on counting rates, but the activity recorded rose if the patient's back was not in contact with the back of the chair. Care was taken to avoid this error. Initial counts were of the order of 70,000 with a background of 3,000 counts per 100 seconds, and all counts were made in duplicate or triplicate.

A volume containing 5 to 10 $\mu\text{C.}$ of ^{22}Na was pipetted from the stock solution into a glass container and given

to the patient, together with three rinsings. No measurable activity remained in the container. In preliminary experiments several patients were counted frequently during a period of several hours: it was found that the count rates declined rapidly, but levelled to a plateau after two or three hours. This was presumably due to an initial high concentration of ^{22}Na in the stomach, followed by its distribution throughout the body. Six hours was taken as the time of complete distribution, and all urine passed was collected up to this time. The body count at six hours was measured. On subsequent days the patient was fasted from 7.30 p.m. until 8 a.m., when estimates of body activity were made with the body counter and a spot sample of urine was collected. Where practicable, estimations were made daily on each patient, who thus had from three to six estimations of exchangeable sodium per week.

The urine samples were stored in a refrigerator in tightly stoppered polythene bottles sealed with waterproof adhesive tape. At the end of the investigation the sodium concentration in each sample was estimated in duplicate with an EEL flame photometer. The activities in the urine, and in a suitably diluted stock solution of ^{22}Na , were counted in a conventional well-type scintillation counter. At least 10,000 counts were made on each urine sample and standard.

The exchangeable sodium was calculated from the formula:

$$\text{Total exchangeable sodium} = \frac{\text{Amount of } ^{22}\text{Na in body (counts/100 sec.)} \times \text{sodium content of sample (mEq./ml.)}}{^{22}\text{Na content of sample (counts/100 sec./ml.)}}$$

(Veall and Vetter, 1958). The amount of ^{22}Na in the body at six hours was found by subtracting the activity lost in the urine from the amount given. On subsequent days the fraction of ^{22}Na remaining was calculated from the ratio of body counts on that day to the body counts at 6 hours.

The day-to-day variation in a control subject are shown in Fig. 2. The coefficient of variation for these

FIG. 2.—Total exchangeable sodium measured in a control subject.

readings was 4.8%. This is consistent with the coefficient of variation of the estimation of exchangeable sodium calculated from the standard deviations of the various individual measurements (2.7%), and with the day-to-day variation of total body sodium, which may be as much as 5% (Veall, Fisher, McClure Browne, and Bradley, 1955).

Results

In 14 subjects the means of the values for exchangeable sodium on days 1 and 2, 3 to 5, 6 and 7, 8 to 10, 11 to 13, 14 to 16, were compared (Fig. 3). A mean increase of 7% in the exchangeable sodium was found between the mean of days 1-2 and that of days 6-7 ($P < 0.01$).

FIG. 3.—The equilibration of ^{22}Na is shown by the points on the graph which represent the mean total exchangeable sodium of the group of 14 depressed patients during the initial 16 days.

No significant difference was found between days 6-7 and subsequent days. The sixth day was therefore taken as the first day for complete equilibration of ^{22}Na .

The mean values of the exchangeable sodium of days 6-10 inclusive were compared with those of the last five recorded days and those of the five days in the middle of the period of investigation. No significant difference was found between any one of these mean values in the group of 12 patients who recovered.

The exchangeable sodium measured on the morning in which E.C.T. was administered gives an index of the sodium balance of the previous day. These figures were compared with the exchangeable sodium of the following day; there was no significant difference between them.

Discussion

We have confirmed at a statistically significant level the observation reported by certain other workers (Miller, Munro, Renschler, and Wilson, 1954; Veall *et al.*, 1955) that the exchangeable sodium measured by ^{22}Na increases during the first few days after the administration of the isotope. In our group there was an increase of 7% between the mean of days 1-2 and that of days 6-7, but there was no significant change on subsequent days.

Apart from our inability to demonstrate a significant change in sodium excretion after E.C.T., our results are in agreement with those of Russell (1960). It has been shown that sodium-balance studies carried out concurrently with ^{22}Na estimation of exchangeable sodium give essentially similar results (Martin, Walker, and Chapman, 1957). Since equilibration of radioactive sodium is incomplete at 24 hours, estimates of 24-hour exchangeable sodium by ^{24}Na before and after recovery from depression are not comparable to balance studies or to longer-term isotope investigations. For this reason our results are not necessarily inconsistent with those of Gibbons (1960). The differences he reported between patients when depressed and when recovered may be either due to loss of sodium from the body or they are the result of redistribution of sodium between compartments which have different rates of equilibration with the isotope. The present investigation supports the latter hypothesis. The report of a considerable slowing in the movement of sodium from blood to C.S.F. has shown that, at least in this system, transfer rates are abnormal in depression (Coppen, 1960).

Any changes in the size of the slowly equilibrating compartments may be detected by measurements of the 24-hour exchangeable sodium, but they would not necessarily be found in sodium-balance studies or in long-term investigations. Little is known of the nature of these more slowly exchanging compartments, but it is probable that they are related to the large fraction of body sodium (about 40%) contained in bone. Miller *et al.* (1954), using ^{22}Na , found that the counts over the patella remained constant during the initial week when the exchangeable sodium was increasing, even though the specific activity of the plasma was declining. This suggested a continuing exchange of ^{22}Na with bone. There is evidence that the proportion of the exchangeable sodium in bone can be increased or decreased by various factors, including changes in adrenocortical hormones (Nichols and Nichols, 1956). The hormonal changes occurring in depression have not been studied comprehensively, but it is probable that they include considerably increased adrenocortical activity (Persky, Grinker, Hamburg, Sabshin, Korshin, Basowitz, and Chevalier, 1956). However, the discrepancies between the results of the short- and long-term exchangeable sodium experiments can be resolved only by an investigation of changes in the distribution of electrolytes in the body compartments.

Summary

Total exchangeable sodium was measured before and during the period of treatment in 14 patients suffering from a depressive illness, by means of a technique employing the long-life isotope ^{22}Na . Contrary to previous studies, no change in sodium balance was detected in the 12 patients who recovered during the period of investigation.

We thank Mr. J. Vennart, of the Radiological Protection Service, both for his valuable advice and assistance and for lending us some of the equipment used in this investigation. Thanks are also due to Mr. J. Bailey and Mr. D. Arrowsmith for their careful and diligent assistance.

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A pedestrian who uses a zebra crossing in West London is four times safer than a person crossing within fifty yards of it. Compared with tests in 1955 a study made in 1961 shows no decrease in the protection offered to pedestrians. This study also showed that it was safer to cross at a light-controlled junction than at a junction with zebra crossings. (*Road Research 1961*, annual report of Road Research Board, published for Department of Scientific and Industrial Research, H.M.S.O., price 8s. 6d., by post 9s.)

NEEDLE BIOPSY OF THE PARIETAL PLEURA IN PATIENTS WITH PLEURAL EFFUSION

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Since DeFrancis and his associates¹ recorded their first cases of successful biopsy of the parietal pleura with the Vim-Silverman needle in 1955, its diagnostic value has been repeatedly demonstrated.²⁻¹⁷ It has been found to be the single most rewarding diagnostic procedure in our experience at the Philadelphia General Hospital in cases of tuberculous effusion.^{4, 5, 12}

It is the purpose of this paper to review the results of a large series of needle biopsies done in a general hospital, and to study in particular the significance of this procedure in effusions caused by malignancies. Its significance in tuberculosis has been thoroughly evaluated in a previous report.¹²

The present series comprises 185 patients on whom 256 needle biopsies were done by interns and residents of the Philadelphia General Hospital for pleural effusion during a period of 40 months.

Method and Material

The method of biopsy is that which has been described by DeFrancis *et al.*¹ Thoracentesis is done in the usual manner after infiltration of procaine hydrochloride. A 19-gauge needle, attached to a syringe, is inserted while aspirating. When fluid is obtained the progress of the needle is stopped and a haemostat is clamped on the needle at the skin surface. The needle is then withdrawn and the distance between its point and the haemostat is a measure of the depth of the parietal pleura. This distance, minus 5 to 10 mm., is measured from the point of the Vim-Silverman needle and marked with another haemostat. The skin is nicked with a scalpel blade and the biopsy needle inserted to the level of the haemostat. Thus the point of the biopsy needle will lie just outside the parietal pleura. The split needle of the Vim-Silverman needle assembly may then be inserted to its full depth. The other needle is pushed in a centimetre or so while the split needle is held; the entire assembly is then rotated 360 degrees and removed. A small cylinder of tissue is usually found within the split needle.

Several pieces of tissue may be obtained by repeating the procedure through the same skin incision and directing the biopsy needle in slightly different directions. When the biopsy is unsatisfactory it can be repeated.

The patients included in this series were those admitted to the Philadelphia General Hospital from January, 1957, to April, 1960. These patients also often had a thoracentesis with examination of the effusion for tubercle bacilli and for malignant cells by cell block. The latter