Potassium Depletion in Severe Heart Disease

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Summary: Exchangeable sodium and potassium, total body water, and sulphate space were measured in 42 patients with severe valvular heart disease who were free of oedema. Compared with normal subjects of the same height, no increase in exchangeable sodium was found but a mean potassium depletion of 27% was shown. This depletion was not related to diuretic therapy, and no relationship between the degree of depletion and post-operative arrhythmias was found. It is concluded that the major cause of the low exchangeable potassium is the reduction in cell mass that occurs in chronic heart disease, and that there is no significant fall in the intracellular potassium concentration.

Introduction

Studies of the electrolytes and body fluids in patients suffering from chronic heart disease have shown that considerable derangement may occur. Fluid retention is often manifested by oedema or by fluid collections in the pleural and peritoneal cavities. Hyponatraemia is frequent, while the exchangeable sodium may be normal or high. In particular, it has been shown that the exchangeable potassium is low in these patients without relation to the plasma levels, which may be normal or high. Since the body potassium is mostly within the cells it is often assumed that the intracellular concentration of potassium must be low, and it has been suggested that osmotic equilibrium across the cell membrane is maintained by the entry of sodium into the cells (Flear, Quinton, Carpenter, Domenet, and Sivyer, 1966). However, wasting is common in patients with severe heart disease and marked cachexia can occur, though the presence of oedema may mask the loss of weight. Under these circumstances a low exchangeable potassium in relation to the normal value expected on the basis of body weight or height may be an indication of a loss of cell mass with little alteration in intracellular potassium concentration.

The present study was undertaken to survey the body fluids and electrolytes in patients with severe long-standing heart disease, and in particular to investigate the incidence and extent of potassium depletion. It has been suggested (Lockey, Longmore, Ross, and Sturridge, 1966) that patients receiving diuretic therapy are more likely to be potassium depleted and would therefore be more liable to postoperative arrhythmias. The relation between potassium depletion and diuretic treatment has been examined, as has the incidence of arrhythmias in the immediate postoperative period.

Methods

Forty-two patients (19 men and 23 women) with severe valvular heart disease were studied (Table I). They agreed to take part in the study after a full explanation of the details of the procedure. Most of them had for several years been treated for heart failure with digitalis and diuretics, and were being prepared for open-heart surgery. The patients were studied after optimal treatment when they were free of oedema, ascites, and pleural effusions, and when their weights had become steady. All but two of the patients receiving diuretics were having potassium supplements. Four had not received diuretics. Some patients showed marked wasting, and the majority had lost some weight. Most, therefore, weighed less than predicted for a person of the same age, sex, and height (Society of Actuaries Build and Blood Pressure Study, 1959). Twenty-eight patients had valve replacement operations within six months after the electrolyte investigation.

TABLE I.—*Clinical Data*

Case No.	Age	Height (cm.)	Weight (kg.)	Predicted Weight (kg.)	% Weight Deviation	Diagnosis	Treatment	Duration Diuretics (Years)
				Male Patients				
1	61	156	54·5	60·5	−10%	M.V.D.	D.F.K.	>5
2	60	167	54·5	68·0	−20%	M.V.D.	D.F.K.	1–2
3	31	159	46·5	61·5	−24%	M.V.D. T.I.	D.T.K.	2–5
4	56	172	64·0	74·0	−12%	A.V.D.	E.F.K.	>5
5	49	174	74·5	75·0	0	A.V.D.	D.E.S.	1–2
6	39	170	63·5	69·5	−8%	A.V.D.	D.T.K.	1–2
7	47	170	72·5	71·5	+2%	M.V.D. T.I.	Nil	Nil
8	34	168	67·5	68·0	0%	M.V.D.	D.	Nil
9	44	168	58·0	69·0	−16%	M.V.D. A.V.D.	D.F.K.	1–2
10	56	168	65·5	69·5	−6%	M.V.D. T.I.	D.F.K.	>5
11	62	165	65·5	66·5	−1%	A.V.D.	D.	Nil
12	44	170	55·5	71·5	−22%	M.V.D.	D.F.K.	<1
13	48	170	63·5	71·5	−11%	M.V.D.	D.T.K.	2–5
14	37	187	65·5	83·7	−22%	M.V.D.	D.T.K.	>5
15	50	174	57·7	75·0	−23%	A.V.D.	D.E.S.K.	<1
16	55	168	72·8	70·0	+4%	A.V.D. M.V.D.	D.F.K.	1–2
17	20	183	62·3	73·5	−15%	A.V.D.	D.F.K.	>5
18	53	182	79·5	79·5	0	M.V.D.	D.F.E.K.	2–5
19	61	159	53·1	62·5	−15%	A.V.D.	D.F.K.	2–5
Mean					−10%			
				Female Patients				
20	59	158	59·5	60·0	−1%	M.V.D.	D.F.K.	2–5
21	58	155	35·5	58·6	−39%	M.V.D.	D.F.K.	2–5
22	61	160	44·5	62·1	−28%	M.V.D.	D.F.K.	2–5
23	61	160	54·0	62·4	−12%	M.V.D. T.I.	D.F.K.	>5
24	54	158	44·3	60·0	−26%	M.V.D. T.I.	D.F.K.S.	1–2
25	64	158	43·5	60·5	−28%	M.V.D.	D.T.K.	
26	44	161	62·0	61·0	+2%	M.V.D.	D.F.K.	2–5
27	48	157	64·0	58·5	+9%	M.V.D. T.I.	D.T.K.	>5
28	27	145	42·5	46·0	−7%	M.V.D. T.I.	D.F.K.S.	>5
29	37	153	42·4	52·7	−20%	M.V.D. T.I.	D.F.S.	>5
30	45	163	59·1	58·1	+2%	M.V.D.	D.F.K.	1–2
31	27	160	51·0	53·7	−5%	M.V.D.	D.T.K.	1–2
32	24	162	48·1	53·1	−9%	M.V.D.	D.F.K.	2–5
33	55	157	49·0	60·0	−18%	M.V.D.	D.F.K.	2–5
34	50	152	55·3	57·0	−3%	A.V.D.	D.F.K.	<1
35	60	161	48·2	63·0	−23%	M.V.D.	D.T.K.	<1
36	41	168	67·7	64·5	+5%	M.V.D.	D.	Nil
37	27	166	52·7	57·4	−8%	M.V.D.	D.F.K.	1–2
38	24	156	56·0	50·0	+12%	A.V.D.	D.T.K.	1–2
39	38	154	41·0	54·0	−24%	M.V.D.	D.F.K.	2–5
40	63	159	60·5	61·7	−2%	A.V.D.	D.F.K.	1–2
41	49	162	74·5	62·0	+20%	M.V.D.	D.T.K.	2–5
42	57	164	57·0	65·0	−12%	M.V.D.	D.F.K.	1–2
Mean					−9%			

M.V.D. = Mitral valve disease. A.V.D. = Aortic valve disease. T.I. = Tricuspid incompetence. D = Digitalis. F = Frusemide. T = Thiazide. E = Ethacrynic acid. S = Spironolactone. K = Potassium.

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Measurements of plasma sodium and potassium, exchangeable sodium, exchangeable potassium, total body water, and sulphate space were made, the sulphate space being used as an index of extracellular fluid volume. All measurements were completed within four days. Plasma sodium and potassium were measured by flame photometry.

Exchangeable sodium was determined from the dilution of 30 μCi of ^{24}Na given by intravenous injection (Miller and Wilson, 1953). During the 24 hours allowed for equilibration all urine was collected for measurement of the amount of the dose excreted. The calculation was based on plasma samples taken at 24 hours. In six patients a second sample was taken at 26 hours. The mean percentage deviation from the mean of the two samples was only 1·5%.

Exchangeable potassium was measured with ^{42}K; 100 μCi was injected intravenously and the excretion of ^{42}K was measured in the urine collected for the following 24 hours. The calculation was based on the mean of the urine samples taken at 24 and 26 hours. During the day of measurement potassium supplements were omitted.

Total body water was measured by sampling blood at one and a half and two hours after an oral dose of 500 μCi of tritiated water. The patients were fasted for 12 hours before the dose. The separated plasma was freeze-dried in a Thunberg tube and the plasma distilled to dryness by evacuation. Tritium activity in aliquots of the two samples was measured in a liquid scintillation counter and the total body water was taken as the mean of the two results.

The sulphate space was determined by a modification of the method of Savoie and Jungers (1965). Thirty microcuries of ^{35}S was given intravenously at the same time as the ^{24}Na. Four heparinized blood samples were taken at hourly intervals. The radiosulphate was separated from the plasma proteins by passing the plasma samples through a scintillating anion exchange resin (Tracer Lab. No. SRC.1). ^{35}S activity was measured in a liquid scintillation counter. The counts were plotted on semi-log paper and extrapolated to zero time. Corrections were then applied for plasma water content, Donnan equilibrium, and entry of radiosulphate into red cells. The plasma water was taken as 93% and the Donnan factor for sulphate between plasma water and interstitial fluid as 0·95:1. The theoretical factor is the square of that for univalent anions and would be 0·90. The experimental factor, however, is 0·95 (Swan, Feinstein, and Madisso, 1956), presumably because of the protein binding of sulphate. The correction for entry of sulphate into red cells was obtained from the Donnan factor of 0·4 (Swan *et al.*, 1956), a haematocrit reading of 45%, a 1:5 ratio between plasma volume and interstitial fluid volume, and a water content of red cells of 65% (Beilin, Knight, Munro-Faure, and Anderson, 1966). It is calculated that 4% of the sulphate enters red cells. The final correction was calculated to be:

$$SO_4 \text{ space} = 0{\cdot}87 \times \text{observed } SO_4 \text{ space.}$$

Extracellular sodium was calculated by multiplying the corrected sulphate space by the overall extracellular fluid sodium concentration. The latter was derived from the plasma concentration by applying corrections for plasma water content and for the Donnan equilibrium between plasma and interstitial fluid, and was calculated to be plasma concentration $\times 1{\cdot}02$. The residual sodium is the difference between exchangeable and extracellular sodium. The cation space was calculated by dividing the total cation ($Na^e + K^e$) by the total extracellular cation concentration (Na+K) in mEq/litre of water.

Difficulties arise in relating values for Na^e and K^e to the normal. Commonly the individual results are expressed as mEq/kg. body weight and compared with a normal range, or the mean expressed in this way is related to the normal mean value. Results have also been related to expected normal values derived from regressions on body weight. When results are expressed in terms of body weight in oedematous patients, however, interpretation is difficult. The exchangeable potassium will appear artificially low because the weight of the patients is increased by the accumulation of fluid. Sodium, on the other hand, being principally an extracellular ion, varies in proportion to any excess of body fluid, so that an increase may be masked if exchangeable sodium is related to body weight. The objection to using weight as the reference standard is not removed when previously oedematous patients have become oedema-free, because an excess of extracellular fluid may still be present. There is often loss of fat and lean tissue in patients with heart disease, which will tend to offset the increase in weight due to fluid retention, but clearly the respective importance of these two factors will vary considerably from patient to patient.

We therefore considered that the use of any index involving body weight was not valid in interpreting the data for Na^e and K^e in our patients. We have not used lean body mass, as calculation of this index is based on the assumption of a constant water content of lean tissue. Instead we have expressed the results on terms of height as a measure of body size that is unaffected by wasting or oedema. There is, of course, variation in body weight between individuals of the same sex and height, but these variations are likely to be less in patients with severe heart disease, because obesity is uncommon.

The predicted value for each patient was calculated from the regression $\log_e Na^e$ (or K^e) on $\log_e$ height derived from normal subjects by Flear *et al.* (1966). The percentage deviation of Na^e and K^e from the predicted value was then obtained.

In order to provide a graphic presentation of the data and to remove for clarity the logarithmic relationship, the results shown in Figs. 1 and 2 are compared with a normal range derived from publications in which body height was recorded (Crooks, Bluhm, and Muldowney, 1959; MacGillivray, Buchanan, and Billewicz, 1960).

Results

The data for body composition and the predicted values for men and women are given in Table II. For convenience the predicted weights and percentage variation from this weight have been included with the clinical data in Table I.

Body Weight.—Fourteen of the 19 men (74%) and 17 of the 23 women (74%) were below the average weight for their age, sex, and height. There was a mean weight deficit of 10% in the men and 9% in the women.

Sodium.—Five of the patients had serum sodium levels below 130 mEq/l. The range was 124–140 mEq/l., with a mean of 134 mEq/l. for both men and women. Exchangeable sodium levels are shown in relation to body height in Fig. 1. The values are within the normal range, and in particular there is no tendency for the Na^e to be high. Comparison of the indi-

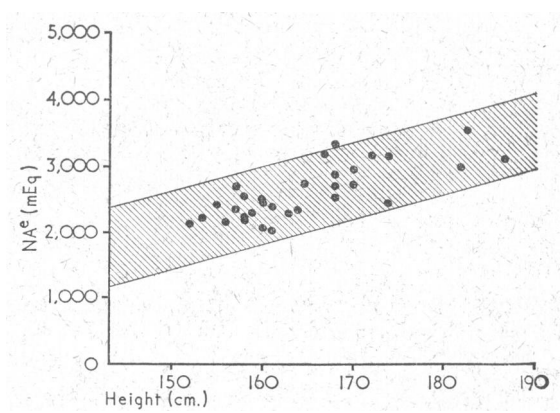

FIG. 1.—Exchangeable sodium in relation to body height. Stippled area indicates normal range.

TABLE II.—*Data for Body Composition*

Case No.	Serum Na (mEq/l.)	Serum K (mEq/l.)	Na^e (mEq)	Predicted Na^e	% from Predicted	K^e (mEq)	Predicted K^e	% from Predicted	T.B.W. (litres)	T.B.W. % Weight	E.C.F. (litres)	E.C.F. % Weight	Cation Space (litres)	E.C.F. Na (mEq)	Residual Na (mEq)
							Male Patients								
1	135	4·1	2,140	2,380	−10	1,600	2,540	−37	29·3	53·8			26·2		
2	135	3·9	3,140	2,680	+17	1,740	2,980	−42	32·6	59·8	16·7	30·6	34·1	2,300	840
3	130	4·3	2,240	2,470	−9	1,520	2,660	−43	25·3	54·3	12·6	27·1	27·4	1,690	550
4	132	4·8	3,110	2,820	+11	1,990	3,180	−37	34·0	53·1	19·0	29·6	36·2	2,580	530
5	129	4·7	3,100	2,870	+8	2,050	3,260	−37	38·9	52·2			37·3		
6	132	4·7				2,320	3,100	−25	33·9	53·4	18·9	29·8		2,570	
7	138	4·5	2,950	2,760	+7	2,580	3,100	−17	35·7	49·2	14·3	19·7	37·6	2,030	920
8	132	4·8	2,690	2,700	0	2,160	3,020	−28			15·4	22·8		2,100	590
9	133	4·3	2,500	2,700	−7	2,360	3,020	−22	34·2	59·0	15·8	27·2	34·5	2,160	340
10	137	4·8	3,300	2,700	+22	2,340	3,020	−22	41·8	63·8	18·1	27·6	38·8	2,550	750
11	129	4·0	2,720	2,630	+3	2,100	2,900	−28	34·5	52·6	15·8	24·2	35·2	2,100	620
12	132	3·8	2,710	2,760	−2	2,100	3,100	−32	33·8	61·0	14·0	25·2	34·4	1,900	810
13	135	4·3				2,340	3,100	−25	38·0	59·8	16·1	25·4		2,240	
14	137	4·2	3,080	3,200	−4	2,800	3,780	−26	39·1	59·6	19·6	30·0	40·6	2,760	320
15	131	4·1	2,400	2,870	−16	2,140	3,260	−34	31·5	54·5	17·7	30·6	32·6	2,390	10
16	133	4·1	3,890	2,700	+44	2,920	3,020	−3							
17	138	3·8	3,510	3,100	+13	3,080	3,620	−15							
18	136	4·2	2,960	3,080	−4	2,360	3,580	−34	37·7	47·5			36·9		
19	140	3·9				2,550	2,660	−4	31·3	59·0					
Mean	134	4·3			+5%			−27%		55·8%		26·9%			570
							Female Patients								
20	132	4·4	2,450			1,580	2,290	−31	23·9	40·2	12·0	20·2	28·8	1,630	820
21	134	4·6	2,390			890	2,220	−60	21·9	61·6	15·0	42·2	22·8	2,070	320
22	138	4·3	2,410			1,110	2,340	−52	23·2	52·0	13·9	31·2	24·0	1,970	440
23	137	4·7	2,470			1,930	2,340	−17	29·5	54·6	17·6	31·4	30·0	2,480	−10
24	133	4·5	2,150			1,370	2,290	−40	23·8	53·7	13·9	31·4	24·8	1,900	250
25	132	3·8	2,200			1,240	2,290	−46	22·6	51·9	15·1	34·8	24·6	2,060	140
26	136	4·9	2,330			1,450	2,360	−38	25·9	41·8	17·6	28·4	25·6	2,460	−130
27	137	3·7	2,650			2,190	2,260	−3	32·5	50·8			33·4		
28	132	3·6				1,330	1,960	−32	21·4	50·3	13·1	30·4		1,780	
29	125	5·4	2,200			1,180	2,160	−45	26·7	63·0	14·5	34·2	25·2	1,870	330
30	134	3·7	2,260			1,710	2,420	−29	28·0	47·4	13·2	24·4	28·0	1,820	440
31	134	4·0	2,020			1,500	2,340	−36	24·9	48·8	12·5	24·5	24·8	1,720	300
32	140	3·4				1,800	2,390	−25	24·6	55·2	10·6	22·0		1,530	
33	135	4·1	2,340			1,190	2,260	−47	23·5	48·0	14·5	29·6	24·6	2,020	320
34	139	4·5	2,120			1,720	2,140	−20	24·0	43·4	15·5	28·0	25·9	2,220	−100
35	138	4·3	2,010			1,990	2,360	−16	23·2	48·2	13·8	28·6	27·4	1,960	50
36	129	3·6				2,160	2,540	−15	30·2	44·6					
37	134	3·9				2,080	2,500	−17	28·3	53·7					
38	135	3·7				1,790	2,240	−20	26·3	47·0					
39	134	4·2				1,530	2,180	−30	22·0	53·7					
40	136	4·4				2,550	2,320	+11	29·9	49·4					
41	131	3·7				2,570	2,390	+7	29·3	39·3					
42	124	3·7	2,320			1,750	2,440	−28	24·0	42·0	12·1	21·2		1,550	770
Mean	134	4·1						−27%		49·6		28·9			280

T.B.W. = Total body water. E.C.F. = Extracellular fluid.

vidual measurements with predicted values in the men shows that there is no significant deviation from the normal (Table II). Exchangeable sodium values were not predicted for women, since the correlation coefficient for the regression $\log_e Na^e$ on $\log_e$ height was only 0·15 (Flear *et al.*, 1966).

Potassium.—Serum potassium did not show variation from normal, with a mean of 4·3 mEq/l. in the men and 4·1 mEq/l. in the women. Fig. 2 indicates that the majority of the patients

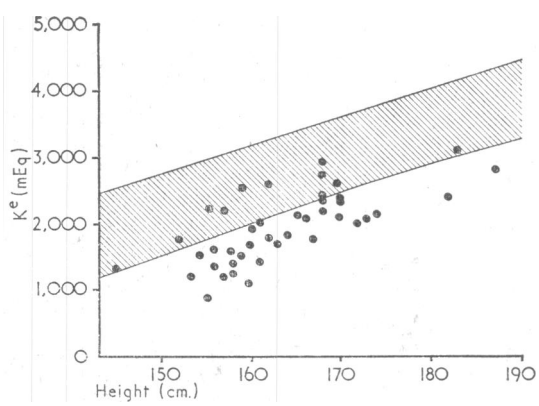

FIG. 2.—Exchangeable potassium in relation to body height. Stippled area indicates normal range

had values for K^e below the normal range. This potassium depletion was confirmed when the measurements were compared with individual predicted values. All the men and all but two of the women had values below predicted. There was a mean depletion of 27% in both the men and the women, in comparison with the expected value for normal subjects of the same height. In Fig. 3 the relation between the potassium depletion and the weight deficit is shown. K^e as a percentage of predicted has been plotted against the body weight as a percentage of expected weight and a close correlation found ($r = 0·608$).

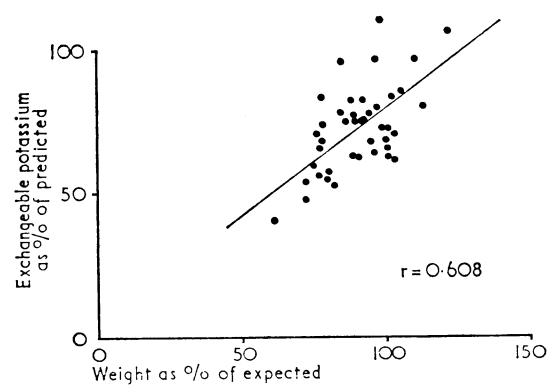

FIG. 3.—Correlation between exchangeable potassium as percentage of predicted and body weight as percentage of predicted, with regression line.

Total Body Water.—When expressed as a percentage of body weight the mean total body water was 55·8% in men and 49·6% in women. There was, therefore, no significant variation from the normal. McMurrey *et al.* (1958) found a mean value of 54·3% in normal men and 48·6% in normal women. Fig. 4 shows that there is close agreement between the total body water and the cation space and provides a check on the accuracy of the measurements.

Extracellular Space.—The sulphate space as a mean percentage of body weight was 26·9% in the men and 28·9% in the women. Normal values obtained by the same method are 21·3% and 17·4% respectively (Savoie and Jungers, 1965).

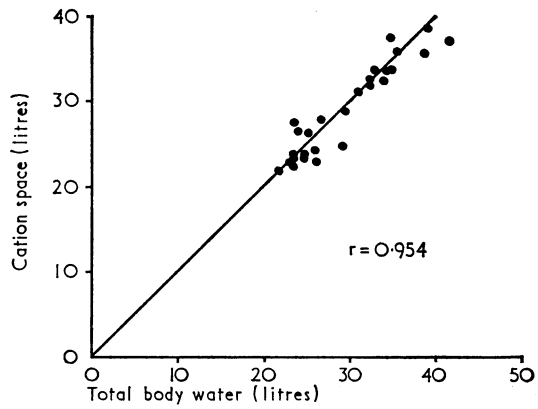

FIG. 4.—Correlation between cation space and total body-water, with line of identity.

Since there is an increase in extracellular fluid volume while the total body water is normal, a reduction in the cell water content is suggested. The mean residual sodium for men was 570 mEq and for women 280 mEq. Fig. 5 shows the relation of extracellular sodium to exchangeable sodium.

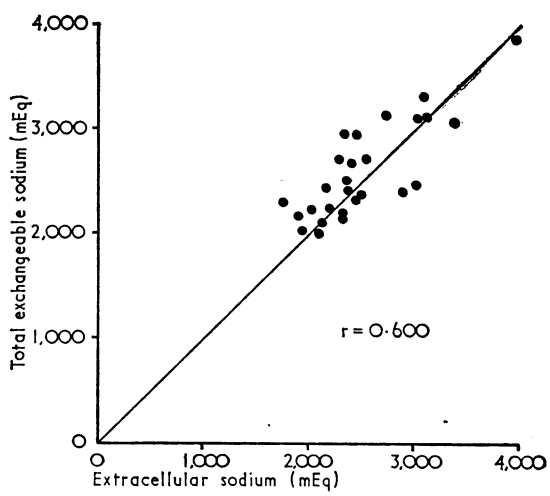

FIG. 5.—Relation between exchangeable sodium and extracellular sodium, with line of identity.

Relation Between Diuretics and Potassium Depletion.—The patients have been separated into groups according to duration of diuretic therapy. Table III shows that there is no relation between the duration of diuretic therapy and the amount of potassium depletion; the four patients who had not received diuretics had a mean depletion of 22%.

TABLE III.—*Duration of Diuretic Therapy in Relation to Potassium Depletion*

Duration of Diuretics									
Nil		<1 Year		1–2 Years		2–5 Years		>5 Years	
Case No.	% K Depletion	Case No.	% K Depletion	Case No.	% K Depletion	Case No.	% K Depletion	Case No.	% K Depletion
7	17	12	32	2	42	3	43	1	37
8	28	15	34	5	37	13	25	4	37
11	28	34	20	6	25	19	4	10	22
36	15	35	16	9	22	20	31	14	26
				16	3	21	60	17	15
				24	40	22	52	23	17
				30	29	25	46	26	38
				31	36	27	3	28	32
				37	17	32	25	29	45
				38	20	33	47		
				40	+11	39	30		
				42	28	41	+7		
Mean	22%		26%		25%		30%		30%

Potassium and Postoperative Arrhythmias.—Table IV shows the arrhythmias occurring in the first 48 hours post-operatively in the 28 patients who had valve replacement operations. Episodes of nodal rhythm were common in the immediate postoperative period and have not been recorded, nor has atrial fibrillation, since most of the patients were in atrial fibrillation preoperatively. Ventricular arrhythmias were seen in six of the patients and the mean potassium depletion in these was 26%, similar to the overall mean.

TABLE IV.—*Postoperative Arrhythmias and Potassium Depletion*

Case No.	Operation	Arrhythmias	% K Depletion
1	M.V.R.	Died. Asystole on table	37
2	M.V.R.	Ventricular ectopics	42
3	M.V.R.	Nil	43
5	A.V.R.	Nil	37
6	A.V.R.	Nil	25
7	M.V.R.	Ventricular ectopics and one run of V.T.	17
8	M.V.R.	Nil	28
9	M.V.R. A.V.R.	Nil	22
12	M.V.R.	Nil	32
13	M.V.R.	Nil	25
14	M.V.R.	Runs of V.T. followed by frequent ectopics	26
15	A.V.R.	Nil	34
16	M.V.R. A.V.R.	Ventricular ectopics	3
17	A.V.R.	Nil	15
18	M.V.R.	Nil	31
20	M.V.R.	Nil	52
22	M.V.R.	Nil	40
24	M.V.R.	Nil	38
26	M.V.R.	Nil	3
27	M.V.R.	Nil	30
28	M.V.R.	Died on table. Asystole→V.F.	45
29	M.V.R.	Bradycardia	29
30	M.V.R.	Frequent ventricular ectopics	25
32	M.V.R.	Died. Inadequate circulation	47
33	A.V.R.	Nil	20
34	M.V.R.	Nil	16
35	M.V.R.	Nil	17
37	M.V.R.	Nil	34

M.V.R. = Mitral valve replacement. A.V.R. = Aortic valve replacement. V.T. = Ventricular tachycardia. V.F. = Ventricular fibrillation.

Discussion

Studies on patients with heart failure who are oedematous have shown high levels of exchangeable sodium even when expressed as mEq/kg. body weight (Farber and Soberman, 1956; Birkenfeld, Liebman, O'Meara, and Edelman, 1958). When oedema-free patients have been studied the results have been somewhat conflicting. Carrol, Gotterer, and Altshuler (1965) found an increase in exchangeable sodium, whereas Oleson (1966) found the level to be insignificantly higher than in control groups, and Lockey *et al.* (1966) found only one patient to have a level at the upper limit of the normal range. The variation in findings may well be a reflection of the difficulty in assessment when excess fluid has been removed, and it has repeatedly been shown that exchangeable sodium falls with loss of oedema (Aikawa and Fitz, 1955; Flear *et al.*, 1966; Oleson, 1964). The findings reported here support the view that exchangeable sodium is not raised in oedema-free patients.

Our exchangeable potassium results agree with those of other workers in showing significant depletion (Flear *et al.*, 1966; Lockey *et al.*, 1966). When compared with the predicted values there is a mean depletion of 27% in both men and women. Since nearly all body potassium is confined to the cells, a fall in exchangeable potassium may be due to a fall in the intracellular potassium concentration or a reduction in the body cell mass. The close correlation between cation space and total body water (Fig. 4) confirms that there is osmotic equilibrium between the cells and the extracellular fluid (Oleson, 1967).

The evidence from this study indicates that the low exchangeable potassium is not due to a comparable fall in the intracellular potassium concentration. If it were reduced, osmotic equilibrium would be maintained by an entry of

sodium into the cells. However, no excess of exchangeable sodium has been shown, even though an expanded extracellular fluid volume was found. When exchangeable sodium has been found to be increased (Oleson, 1964), the excess has been wholly accounted for by the increase in extracellular fluid sodium. Calculation of the residual sodium in our patients shows little increase and provides further evidence against the hypothesis that sodium has entered the cells. The methods used are likely to overestimate the residual sodium, since transcellular water, a term introduced to describe water in glandular lumina and cerebrospinal fluid (Edelman, Olney, James, Brooks, and Moore, 1952), appears to be penetrated less by sulphate than by sodium. For example, equilibration of sulphate with the cerebrospinal fluid is slow and incomplete (Richmond and Hastings, 1960), whereas 90% of the cerebrospinal fluid exchanges with ^{24}Na at 24 hours (Miller and Wilson, 1953). The findings therefore indicate that the measured depletion of total exchangeable potassium is mainly a reflection of loss of cell mass. It appears that there is a reduction in the intracellular water, since extracellular fluid volume is increased, while the total body water expressed as a percentage of body weight is normal.

The close correlation between potassium depletion and weight deficit (Fig. 3) indicates the importance of loss of weight in producing this depletion.

Measurements of intracellular electrolyte concentration are difficult, though the problem for potassium is less than for sodium, since the extracellular content is small. Flear, Crampton, and Matthews (1961) found no change in the intracellular potassium content of skeletal muscle in patients with congestive heart failure, using an in-vitro inulin method for the determination of the extracellular space. It is probable, however, that a slight fall in intracellular potassium concentration occurs when there is hyponatraemia, since a fall in the plasma sodium concentration is balanced by a corresponding fall in the concentration of the principal intracellular cation.

If the myocardial cells are affected in the same ways as the rest of the body, a lowered intracellular potassium concentration $[K]_i$ would be expected to lower the membrane potential E, according to the Nernst equation $\left(E \propto \log \frac{[K_i]}{[K_e]}\right)$, where $[K_e]$ is the extracellular potassium concentration, and thus to increase the excitability of the cell and produce arrhythmias. Only 6 of the 28 patients who had operations had ventricular arrhythmias in the immediate postoperative period. There was no relation between the incidence of arrhythmias and the extent of potassium depletion.

Patients with severe heart disease could not be maintained free of oedema without diuretic therapy, and this treatment has in the past been incriminated as the cause of low body potassium (Lockey *et al.*, 1966). The four patients not on diuretic therapy all had low levels of body potassium, though the depletion was slightly less than in those on treatment, probably because their heart disease was less severe; these particular patients had no weight deficiency. Our evidence therefore indicates that diuretic treatment has little direct part in producing potassium depletion.

It seems that the reduction in cell mass is the major factor involved in decreasing the exchangeable potassium, and that no significant fall in intracellular potassium occurs.

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Cardiac Abnormalities in Poisoning with Tricyclic Antidepressants

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Summary: Of 80 consecutive admissions to a general hospital for drug overdose, 10 had taken one or other of the tricyclic antidepressants. All 10 had abnormalities of cardiac conduction as shown by prolonged Q–T_c intervals, and eight had S–T segment and T-wave changes. Five of the 10 patients had arrhythmias and two of these died. Continuous electrocardiographic monitoring is recommended in patients with overdosage of tricyclic antidepressants.

Introduction

The iminodibenzyl derivatives, imipramine and amitriptyline, also known as the tricyclic compounds, may produce alterations in myocardial conduction, cardiac arrhythmias, and death when taken in excessive doses (Connelly and Venables, 1961;

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