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Mineral Metabolism in Mania

ALEC COPPEN,* M.D., D.P.M.; DAVID MURRAY SHAW,* PH.D., M.B., M.R.C.P.
ANDREW MALLESON,* M.B., M.R.C.P., D.P.M.; ROY COSTAIN,† M.B., D.P.H., D.P.M.

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In a previous paper (Coppen and Shaw, 1963) we showed that depressive illness is associated with a considerable increase in residual sodium (intracellular and a small amount of bone sodium), which returns to normal after recovery. We have now extended these investigations to patients suffering from mania. This paper reports our findings in this condition and also in some of these patients who had recovered from their illness or who had swung from mania into depression. We have also compared these findings with our previous results in depression.

Methods

Twenty-two patients suffering from mania who were admitted to Graylingwell Hospital during a 12-month period were selected for this investigation on the basis of the diagnosis of mania which was made by the consultant psychiatrist in charge of the case and was confirmed by another consultant psychiatrist. Details of age and sex of the patients are shown in Table I. Those patients who were suffering from physical illness, or were over the age of 75, or had taken lithium during the six weeks prior to admission were excluded from the study. One woman who developed diarrhoea and vomiting during the initial illness tests has been rejected from the series. All patients ate a normal ward diet and were up and about the ward and hospital for at least three whole days prior to the initial biochemical test.

The biochemical tests were carried out on the first Friday after admission and were repeated four weeks later if the patient was still in hospital. Height was measured on admission and the weight was recorded on the morning of the tests. Clinical assessments were made at the same time as the biochemical tests, but the results were analysed in different centres and were not compared until the investigations on all patients had been completed.

Two methods of assessment were employed on the first and fifth Tuesday and Friday after admission. One of us (R.C.) assessed each patient for mood, activity, and talk by means of

a nine-point scale for each factor. The second method was to give part of the Hildreth feeling and attitude scales (Hildreth, 1946). As the two feeling scales are the most effective in discriminating between normal and affectively disturbed patients (Fisher, 1949; Campbell, 1957; Shapiro, Campbell, Harris, and Dewsbery, 1958), we used these in the assessment of mood. Each scale consists of 10 statements: the patient was asked to tick the phrases which described his feelings most closely at that particular time. The statements in the feeling scales contain ones which would be chosen by depressed, normal, and elated subjects. Each choice has an empirically determined weight ranging from 0.1 to 9.6.

In feeling scale 1 we found that one of the higher-scoring "manic" responses—"swell"—was not used at all by the patients, probably because it was an Americanism avoided by even the most exuberant patient. This disturbed the balance of the scale, so the results were analysed on feeling scale 2 alone. Patients scoring between approximately plus or minus one standard deviation from the mean for normals (5.90; Campbell, 1957) were regarded as normal. Those scoring below 5.1 were regarded as depressed and those above 6.9 as manic. Manic patients vary rapidly in clinical condition, and therefore the biochemical tests were compared with the Hildreth and clinical assessments performed on the same day. It will be seen that nine patients had changed rapidly after admission and were no longer rated manic on the occasion of their first biochemical tests. The clinical assessment and the classification according to the Hildreth scale showed good agreement but the results were analysed according to their classification on the Hildreth.

The distribution of electrolytes was determined as described previously (Coppen and Shaw, 1963) with the exception that exchangeable sodium was estimated from both urine and a 1 in 3 dilution of plasma. Close agreement was found between these duplicate estimations.

* M.R.C. Neuropsychiatric Research Unit, Carshalton, and West Park Hospital, Epsom, Surrey.

† M.R.C. Clinical Psychiatric Research Unit, Graylingwell Hospital, Chichester, Sussex.

A list of the estimated and derived values is given below :

Estimated Values										Units
Weight	...	...	...	...	...	...	...	...	...	kg.
Height	...	...	...	...	...	...	...	...	...	cm.
24-hour exchangeable sodium (Na_E)	...	...	...	...	...	...	...	...	...	mEq
Distribution volume of bromine (DBr)	...	...	...	...	...	...	...	...	...	l.
Total body water (T.B.W.)	...	...	...	...	...	...	...	...	...	l.
Concentration of electrolytes in plasma ($[\text{Na}]$, $[\text{K}]$, $[\text{Cl}]$)	...	...	...	...	...	...	...	...	...	mEq/l.
Sodium space	...	...	...	...	...	...	...	...	...	l.
Derived Values										Units
Extracellular water (E.C.W.)	...	...	...	...	...	...	...	...	...	l.
Sodium in extracellular water ($\text{Na}_{E.C.W.}$)	...	...	...	...	...	...	...	...	...	mEq
Residual sodium (Na_R)	...	...	...	...	...	...	...	...	...	mEq
Exchangeable chloride	...	...	...	...	...	...	...	...	...	mEq
Intracellular water (I.C.W.)	...	...	...	...	...	...	...	...	...	l.
Derivation										
	...	...	...	...	...	...	...	...	...	
	...	...	...	...	...	...	...	...	...	
	...	...	...	...	...	...	...	...	...	
	...	...	...	...	...	...	...	...	...	

Fat-free body weight was estimated according to the formula of Pace and Rathbun (1945), which is based on the assumption that it has a water content of 73.2%. Total body fat was then calculated by subtracting fat-free body weight from total body weight.

So far as we know there are no recent British surveys giving the average weight for normal subjects according to age, sex, and height, therefore we compared our patients with data provided by the American Society of Actuaries (*Documenta Geigy*, 1962) for normal Americans. The difference between the expected weight (according to sex, age, and height) and observed weight was calculated for each subject.

In this paper we have compared diagnostic groups consisting of patients of varying age, sex, and body size. The variables we were most concerned to examine—exchangeable sodium, residual sodium, and extracellular water—are correlated with body weight and even more highly correlated with total body water. Moore Olesen, McMurrey, Parker, Ball, and Boyden (1963) have published extensive data on the distribution of sodium and potassium in normal subjects, techniques similar to our own being used, and they give numerous regression equations relating exchangeable sodium and other variables to total body water. We have used these regression equations to analyse our data by employing a procedure proposed by Lindegaard (1953) which has been utilized in a variety of anthropometric and psychosomatic investigations. This technique can be illustrated by considering exchangeable sodium.

Moore *et al.* (1963) give a regression equation which enables the exchangeable sodium of a normal subject to be predicted on the basis of his total body water. We applied this procedure to our patients and calculated the difference between the "observed" and "predicted" values of exchangeable sodium. This difference (the convention of Lindegaard being used) is called: residual F exchangeable sodium (T.B.W.). This was determined for each patient for exchangeable sodium, residual sodium, and extracellular water, which are also highly correlated with total body water. The resulting residuals were then treated as a series of variables and analysed statistically by conventional methods. We have compared the differences between the means of the various groups by using the "t" test. We must emphasize that we have not employed this method to compare our patients with normal subjects but merely as a convenient way of standardizing the data as far as body size is concerned so that we may make meaningful comparisons between patients of different body sizes. However, it will be appreciated that the smaller the residual F for any variable the less does the individual deviate from the normal subjects of Moore *et al.* (1963).

The regression equation for exchangeable sodium on total body water was given by Moore *et al.* in male and female normal subjects between the ages of 20 and 60. The correlation between total body water and exchangeable sodium is 0.94.

$$\text{Na}_E = 68.10 (\text{T.B.W.}) + 253 \text{ mEq}$$

Our estimate of extracellular water is derived slightly differently from that of Moore *et al.*, and therefore we recalculated their extracellular water and residual sodium values and derived new regression equations for these variables on total body water.

These were :

$$\text{Na}_R = 12.83 (\text{T.B.W.}) - 76$$

$$\text{E.C.W.} = 0.380 (\text{T.B.W.}) + 3.58$$

For males and females between 23 and 84 the correlation between the total body water and the residual sodium is 0.68 and between the total body water and the extracellular water is 0.90.

To find out if the volume of total body water is normal in these patients we used a procedure suggested by Nicholson and Zilva (1964). They showed that total body water per kg. of body weight had a linear relationship with leanness index ($\text{height}^2/\text{weight}$). Using the regression equation for total body

TABLE I.—Age, Sex, Body Composition and Distribution of Sodium

Diagnosis	Case No.	Age (years)	Sex	Weight (kg.)	Body Fat (kg.)	Fat-free Body wt. (kg.)	Height (cm.)	Total Body Water (l.)	Extra-cellular Water (l.)	Intra-cellular Water (l.)	Na_E (mEq)	Na_R (mEq)	Cl_E (mEq)	Plasma Electrolyte Concentrations (mEq/l.)			Drugs
														Na	K	Cl	
Manic phase (n = 13)	1	47	F	71.7	26.3	45.4	148.6	33.2	14.7	18.5	2,920	860	1,770	140	5.0	108	H
	2	22	F	49.9	8.2	41.7	161.3	30.5	12.4	18.1	2,650	840	1,400	146	4.6	106	C
	3	28	M	72.1	9.4	62.7	171.5	45.9	21.4	24.5	3,570	570	2,670	140	5.0	112	C
	4	48	F	71.2	18.2	53.0	166.4	38.8	15.7	23.1	2,530	300	1,860	142	4.5	107	C
	5	73	M	75.3	18.3	57.0	177.8	41.7	21.2	20.5	3,560	720	2,680	134	5.1	114	C
	6	46	F	89.8	35.3	54.5	162.6	39.9	18.3	21.6	3,960	1,320	2,350	144	4.3	116	H
	7	40	M	94.8	23.4	71.4	172.7	52.3	21.4	30.9	4,140	1,080	2,740	143	4.5	115	C
	8	54	F	58.1	15.3	42.8	174.0	31.3	12.7	18.6	3,100	1,300	1,470	142	4.7	104	I
	9	61	F	66.2	12.0	54.2	146.1	39.7	15.3	24.4	3,540	1,400	1,770	140	4.7	104	H T
	10	48	M	79.4	22.7	56.7	184.2	41.5	17.9	23.6	3,480	760	2,290	152	4.2	115	H T
	11	56	M	79.4	25.2	54.2	168.9	39.7	20.8	18.9	3,550	600	2,550	142	4.5	111	H
	12	57	F	50.6	18.6	32.0	152.4	23.4	9.5	13.9	1,860	570	1,080	136	3.5	102	H O
	13	30	M	104.8	34.0	70.8	182.9	51.8	22.3	29.5	3,620	680	—	132	4.4	—	Nil
Depressed phase (n = 9)	8	54	F	59.9	20.3	39.6	174.0	29.0	12.5	16.5	2,090	210	1,490	150	4.7	107	I
	14	49	F	69.2	30.1	39.1	166.4	28.6	14.0	14.6	2,410	410	1,640	143	4.4	105	C, C + E.C.T.*
	15	63	M	66.9	18.3	48.6	162.6	35.6	12.4	23.2	2,360	590	1,550	143	4.3	112	H O
	16	33	F	59.0	15.0	44.0	162.6	32.2	14.5	17.7	2,310	290	1,740	139	5.1	108	C + E.C.T.
	17	56	F	95.7	37.1	58.6	165.7	42.9	18.2	24.7	3,500	950	2,080	140	4.0	103	C H
	18	33	M	79.8	18.7	61.1	173.4	44.7	15.7	29.0	3,210	850	1,900	150	4.1	110	C
	12	57	F	48.1	17.4	30.7	152.4	22.5	10.8	11.7	1,790	310	1,250	137	3.5	104	E.C.T.
	19	44	F	62.6	23.5	39.1	153.7	28.6	14.0	14.6	2,100	210	1,610	135	4.2	104	Nil
	20	39	M	87.8	19.6	68.2	184.2	49.9	19.9	30.0	3,440	810	2,280	132	4.9	103	C C*
	3	28	M	72.1	6.5	65.6	171.5	48.0	16.0	32.0	3,100	840	1,960	141	4.9	110	C
Normal (n = 10)	17	56	F	93.9	37.6	56.3	165.7	41.2	19.2	22.0	3,430	680	2,360	143	4.1	111	C
	21	66	F	65.9	19.2	46.7	157.5	34.2	16.1	18.1	2,640	370	1,990	141	4.0	111	H H*
	22	45	F	58.7	13.6	45.1	163.8	33.0	15.0	18.0	2,350	340	1,750	134	4.6	105	Nil*
	19	44	F	61.7	23.7	38.0	153.7	27.8	13.5	14.3	1,970	120	1,590	137	3.9	106	E.C.T.
	16	33	F	73.0	24.1	48.9	166.4	35.4	13.4	17.0	2,210	350	1,640	139	4.5	107	C H
	4	48	F	90.7	40.2	50.5	162.6	37.0	16.2	20.8	2,760	330	2,140	134	4.3	112	C
	6	46	F	69.7	24.4	45.3	146.1	33.3	14.8	18.5	2,520	300	1,800	150	4.4	—	H
	9	61	F	69.9	24.4	45.5	146.1	33.3	14.8	18.5	2,520	300	1,800	150	4.3	109	C H
	15	63	M	67.6	19.6	48.0	162.6	35.1	13.2	21.9	2,450	710	—	132	4.5	—	H O
	15	63	M	67.6	19.6	48.0	162.6	35.1	13.2	21.9	2,450	710	—	132	4.5	—	H O

* Figures given are means of tests on two occasions.

H = Haloperidol. C = Chlorpromazine. I = Imipramine. T = Trifluoperazine. O = Orphenadrine. E.C.T. = Electric convulsion therapy.

water per kg. and leanness index, we were able to work out the residual F for total body water per kg. (leanness index).

Comparisons of our biochemical data have been made between five groups of patients:

Manic patients—manic phase.—These included all patients in the present series who were rated as manic when tested.

Manic patients—depressed phase.—These were those patients in the present series who, though considered manic on admission to the series, were at the time of testing rated as depressed.

Manic patients—recovered.

Depressed patients—depressed phase.—These were 23 patients in our previous series who were suffering from severe depression when tested on admission.

Depressed patients—recovered.—These were the same patients retested after recovery.

Results

The electrolyte data are given in detail in Table I divided into diagnostic groups according to the Hildreth scale. Most subjects were tested twice and three patients appeared to be manic on both occasions. In these three subjects only the estimations associated with the higher Hildreth rating were used. When a patient was rated as normal or depressed on two occasions the mean values of the two tests have been used, so that a patient appears only once in each group.

Table II gives the means of F values (T.B.W.) for E.C.W., and exchangeable sodium and residual sodium, and the ratios of I.C.W. to E.C.W. Table III lists the significance of differences between the means.

As residual F for E.C.W. (T.B.W.) is a minus quantity it suggests that the observed values of E.C.W. were somewhat less than would be expected on the basis of the total body water. There was little difference between the groups. The means of the ratios of I.C.W./E.C.W. were also remarkably constant, and the plasma concentrations of sodium, potassium, and chloride were similar in the affectively disturbed and normal groups. In Table IV are the means of residual F for total body water per kg. (leanness index), which show that the total body water in these patients is similar to that of normal people of their height and weight.

In mania there is a marked deviation from normal in the figure for residual sodium, which is 426 mEq in excess of the predicted value for normal subjects. Patients suffering from depressive illness and during the depressed phase following mania have residual sodium values 179 mEq and 143 mEq in excess of normal respectively. Both manic and depressed patients approach the normal value after recovery. In mania the average residual sodium F value is significantly greater than in all other groups, and in patients suffering from depressive illness it was significantly greater when they were ill than when they were well. These changes are illustrated by alterations in the ratio

of $\text{Na}_{\text{E.C.W.}}$ to Na_{R} . Manic and depressed patients' ratios differ from those of recovered patients. Again, patients in mania show the greatest change and have the smallest mean ratio of 3.4. The depressed patients have the next smallest of 4.3. The observed values for exchangeable sodium are higher than normal in mania and in depression. The other groups, in spite of their increased residual sodium, have normal or smaller than normal values of exchangeable sodium.

There are marked differences in body composition in the patients in the present series who were admitted in a state of mania compared with the patients in the previous paper who were admitted in a depressive illness (Table V). Apart from being slightly taller, the manic patients are considerably heavier, largely because of an increase in total body fat. The deviation of body weight from that expected for their age, sex, and height was in opposite directions in mania and depression. Manic patients were significantly heavier than expected, and depressed patients were under their expected weight.

TABLE IV.—Means of Leanness Index and Residual F T.B.W./Wt. (Leanness Index) in Manic Subjects

Affective State	*Leanness Index	*Residual F T.B.W./Wt. (Leanness Index) (ml./kg.)
Manic phase	0.065	+6.0
Depressed phase	0.068	-42.2
Normal phase	0.060	+0.2

* There are no significant differences between these means.

TABLE V.—Body Composition

Sex	Diagnosis	Height (cm.)	Weight (kg.)	Fat (kg.)	Fat-free Body (kg.)	Deviation from Predicted Weight (kg.)
Male	Mania (9)	175.4	82.3*	21.0*	61.3	+9.4†
	Depression (10)	170.1	67.1	12.2	54.9	-4.3
Female	Mania (13)	160.1	66.8*	22.2*	44.6	+7.3†
	Depression (13)	156.2	56.7	14.2	42.5	-3.3

Except where indicated the means are not significantly different.

* Mania: difference from depression $P < 0.02$.

† Mania (males + females) difference from predicted weight $P < 0.01$.

Discussion

The assessment of mania presents considerable difficulties; the change from mania through a normal phase to depression may occur in a matter of 24 hours. The clinical picture may show some discrepancies in which, for example, the mood is a mixture of elation and fleeting periods of depression, and there may also be outbursts of irritability, anger, and aggressiveness when an attempt is made to curb overactivity. Often it is hard to define the normal phase; a patient who has recklessly spent several thousand pounds or given away his home and livelihood during his period of mania may develop severe guilt feelings and anxiety as soon as he becomes normal. For this reason

TABLE II.—Water and Sodium Distribution

Diagnosis	n	Residual F Factors (Means and Standard Errors)			*I.C.W./E.C.W.	$\text{Na}_{\text{E.C.W.}}/\text{Na}_{\text{R}}$	$\text{Na}_{\text{R}}/\text{Cl}_{\text{R}}$
		*E.C.W. (T.B.W.) (l.)	Na_{R} (T.B.W.) (mEq)	Na_{R} (T.B.W.) (mEq)			
Mania—manic phase	13	-1.28 ± 0.50	+345 ± 101	+426 ± 100	1.31	3.4	1.63
„ —depressed phase	9	-2.16 ± 0.55	-136 ± 55	+143 ± 66	1.41	5.2	1.48
„ —recovered	10	-1.67 ± 0.57	-64 ± 65	+63 ± 53	1.31	6.3	1.38
Depression—depressed phase	23	-1.74 ± 0.23	+51 ± 74	+179 ± 38	1.31	4.3	1.51
„ —recovered	23	-1.35 ± 0.33	-133 ± 61	-17 ± 44	1.31	9.9	1.41

* There is no significant difference between the means of the groups for these variables.

TABLE III.—Significance of the Difference between the Means of the Groups in Table II

	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
1 Mania—manic phase	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2 „ —depressed phase	0.002	—	—	—	0.05	—	—	—	N.S.	—	—	—	N.S.	—	—	—
3 „ —recovered	0.01	N.S.	—	—	0.01	N.S.	—	—	N.S.	N.S.	—	—	N.S.	N.S.	—	—
4 Depression—depressed phase	0.05	N.S.	N.S.	—	0.01	N.S.	N.S.	—	N.S.	N.S.	0.05	—	N.S.	N.S.	0.02	—
5 „ —recovered	0.001	N.S.	N.S.	0.02	0.001	N.S.	N.S.	0.005	0.02	N.S.	N.S.	0.005	0.005	N.S.	N.S.	N.S.
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		$\text{Na}_{\text{E.C.W.}}$				Na_{R}				$\text{Na}_{\text{E.C.W.}}/\text{Na}_{\text{R}}$				$\text{Na}_{\text{R}}/\text{Cl}_{\text{R}}$		

the number of "recovered" patients after a month of treatment was relatively small.

As we consider mania to be primarily an affective disorder we decided to analyse our results on the self-assessment of mood based on the Hildreth feeling 2 scale. Analysis based on the doctors' ratings of mood and the Hildreth scale gave similar biochemical results, but the doctors' ratings of activity and talk did not. It is our opinion that any method of evaluation of mania will inevitably contain misclassifications, particularly in the separation of normal from depressed phases. However, any misclassification should not introduce a bias into the results, and it should be emphasized that both self-ratings and the doctors' ratings were performed entirely independently of the biochemical estimations. In spite of these difficulties the results of the present investigation in comparison with the earlier findings in depression allow some definite conclusions to be drawn about changes in electrolytes in mania.

The constancy of the ratio of I.C.W./E.C.W. and the residual F for E.C.W. (T.B.W.) show that the partition of water between extracellular water and intracellular water remains the same in spite of changes in the clinical state and in residual sodium. The F values for extracellular water show that the volume of extracellular water is consistently low in all groups, whether affectively disturbed or normal. We do not know the significance of this. The volume of total body water also showed little variation. In the series of depressed patients there was a significant rise of 1.2 litres with recovery. In the other groups where paired comparisons were impossible the F values for total body water per kg. based on leanness index depart little from that of normal subjects of their weight and height. If all the data are taken into consideration it appears that total body water varies very little between clinical groups, and that the differences that do exist are very small compared with the alterations in sodium.

Residual sodium is greatly increased in mania, and this change is in the same direction as in depression but is more extreme. This is illustrated in the Chart, where all the patients in the present and previous investigation are combined into

Residual F Na* (T.B.W.) in patients grouped according to their mood at the time of testing, including individuals in the present series and those described in our previous investigation.

three groups—normal, depressed, and manic—and their mean residual sodium values are compared. The rise in residual sodium with affective illness is also illustrated by the ratio of sodium in the extracellular water to residual sodium, which is decreased in both mania and depression. The ratio of exchangeable sodium to exchangeable chloride is also significantly increased in mania and depression, and this further illustrates the increase in residual sodium, because chloride is mainly extracellular and there is no alteration in the concentration of sodium or chloride in the extracellular water. It also suggests that if sodium has entered the cells there has not been a concomitant shift in chloride.

There is some difference between the F values for exchangeable sodium—for example, sodium in the extracellular water

plus residual sodium—and for residual sodium. However, this discrepancy is for the most part explained if it is borne in mind that the F values are derived from regression equations based on the total body water. The observed values of the extracellular water are rather less than would be expected for the patients' total body water, and therefore as sodium is predominantly an extracellular ion (concentration 140 mEq/l.) their low extracellular water produces an exchangeable sodium rather less than expected. Though the patients' intracellular water is consequently 1–2 l. larger, this would not be expected to produce much alteration in the predicted value of residual sodium, as intracellular sodium concentration is low.

Residual sodium includes both intracellular and bone sodium, and we have already discussed the difficulties of discriminating between changes in these two compartments (Coppen and Shaw, 1963). We have also discussed the paucity of information about possible causes of this change in sodium, which include the actions of adrenocortical steroids such as cortisol and aldosterone, as well as the posterior pituitary hormones (Coppen and Shaw, 1963).

What conclusions can we draw about these changes in sodium in depression and mania? Firstly, are these changes causal to or one of the secondary manifestations of this condition? To answer this with certainty would involve observing the clinical effects of reducing residual sodium, and it is most difficult to do this. However, a recent investigation of the effects of lithium therapy on the electrolyte distribution suggests that changes in sodium may be of great aetiological importance in affective disorders. Lithium carbonate, administered in therapeutic dosage, was found to alter greatly the distribution of sodium, probably by its action on sodium transport across the cell membrane (Coppen, Malleon, and Shaw, 1965). There is good evidence that lithium salts are effective in the treatment of mania (Maggs, 1963), and it is tempting to relate their therapeutic effects to the actions of lithium on sodium distribution.

In mania there are similar but more extreme changes in sodium distribution than in depression, and we were unable to differentiate them apart from this quantitative difference. Manic patients who subsequently became depressed showed changes very similar to those in patients with a depressive illness, and recovered manic patients were similar to patients who had recovered from depression and to normal subjects. If the changes in sodium distribution are related in any way to the onset of mania, then it is possible that the differences between mania and depression are due to the observed quantitative dissimilarities or to other biochemical factors. Mania and depression often occur in rapid alternation, and it is not intrinsically improbable that the underlying biochemical causes are similar.

There were highly significant differences in body composition between manic-depressive patients and patients suffering from a depressive illness without a history of mania. Manic-depressive patients had very considerably increased body fat compared with depressives and with normal American subjects of the same height, age, and sex. Depressive patients, on the other hand, were slightly below the weight of normal American subjects. We cannot say whether this increase in body fat is the consequence of manic illness or is related to the patient's normal personality and other constitutional factors. Normally it would take several months of excessive eating to gain 8.2 kg. of body fat. There is evidence (Lindegaard, 1956; Bagge, 1963) that body fat is correlated with the personality factor of submissibility (similar to extraversion), and it is possible that manic-depressives and depressive patients have different previous personalities. To-day mania is a relatively uncommon condition: out of the last 200 patients admitted to this unit suffering from depression only 5% had had a history of mania. Almost all the manic patients in the present series had a history of depression, and, indeed, over 50% had a depressive episode during the present study. Severe depressions to-day

are often diagnosed as manic-depressive psychosis, but our conclusion is that this is a rather uncommon condition, perhaps occurring in patients with a special constitution and previous personality.

Summary

Total body water and the distribution of electrolytes were studied on two occasions in 22 patients admitted to hospital suffering from mania. Their mood on the day of each test was assessed by doctors' rating and part of the Hildreth scale. On the basis of these assessments the patients were divided into three groups: mania, depression, and normal. The results have also been compared with our previous findings in depression.

Total body water and its partition between intracellular water and extracellular water did not change significantly with affective state, but extracellular water was consistently lower than normal in all groups, and this was also found for depressed patients (ill and recovered). Concentrations of sodium, potassium, and chloride in plasma were constant. Residual sodium (intracellular sodium with the addition of a small amount of sodium in bone) was greatly increased in mania. The smaller increment in residual sodium seen in the depressed phase of mania was similar to that found previously in severe depressive illness.

Body fat was greater than normal in mania, and was significantly greater than in the group of depressed subjects.

It was concluded that mania is accompanied by similar electrolyte abnormalities to those seen in depression but that the changes in mania are more extreme. The differences in body fat could be a consequence of the illness or they might indicate that there is a constitutional difference between patients suffering from a manic-depressive and a depressive illness.

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Deafness in Acute Otitis Media

J. F. NEIL,* M.A., B.CHIR., F.R.C.S.ED.; S. H. HARRISON,† M.B., CH.B.

R. D. MORBEY,† M.R.C.S., L.R.C.P., D.OBST.R.C.O.G.; G. A. ROBINSON,† M.B., B.S.

G. M. T. TATE,† B.A., B.M., B.CH.; H. T. TATE,† M.B.E., M.B., CH.B., D.OBST.R.C.O.G., M.M.S.A.

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Acute otitis media in children is a common disease in general practice. Fry (1961) found that 10% of the children in his practice had one or more attacks in any one year, and the Medical Research Council Working Party (1957) reported a yearly incidence of 8%. Though it is known that deafness is found during an attack, there seems to have been very little evidence of the long-term effects on hearing of this common disease until the survey carried out in Liverpool by Lowe, Bamforth, and Pracy (1963). Cases followed up by general practitioners have all been tested by the ability to hear the whispered voice, and this has been shown to be a very inaccurate test (Huizinga, 1958). There have been several series followed up audiometrically, but these have consisted of patients who have been referred to hospital (Young and Simson Hall, 1948; Dixon, 1958; McNeill, 1962). The M.R.C. report states that only 1% of cases of acute otitis media are referred to hospital, so these series must be regarded as highly selected.

In this paper we report an audiometric follow-up of 121 children diagnosed as having had acute otitis media who have been treated at home by their general practitioner.

Method

The series consisted of all children under the age of 11 with acute otitis media seen in two general practices between March 1960 and April 1961. The practices, one of three doctors and

one of two, are in a market town in the Nottinghamshire coal-field. The total practice population at the time was 12,500, and the estimated population of children under 11 was 2,200. In general, housing conditions were good, and the children, coming from all social classes, well cared for.

When a child seen at home or in the surgery by one of the practitioners was found to have acute otitis media a special card was completed (Fig. 1). The definition of acute otitis media we used was that put forward by Fry (1958): "An acute condition with earache and a red drum or with a sudden onset of discharge from the ear, either following earache or arising *de novo* with no previous history of chronic ear disease."

The completed cards were left at the surgery for the otologist to collect, and as soon as practicable he visited the child at home.

All treatment was left to the general practitioner, and the otologist took no part in it unless the child was referred to hospital for his advice in the usual way. His function was to assess the condition, and in some cases to carry out an audiogram during the attack. His findings were recorded on the reverse side of the card.

For children over 5 years of age the follow-up examination was arranged six months or more after the attack, and those

* Consultant E.N.T. Surgeon, Nottingham General Hospital and King's Mill Hospital, Sutton-in-Ashfield, Notts.
† General Practitioner, Mansfield.