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Disturbance of Water and Sodium in a Manic-Depressive Illness

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Specific questioning and frequent observation of a 69 year-old woman with cyclic bipolar manic-depressive illness showed that she had disturbances of thirst, appetite, bowel and bladder function and dramatic changes in body weight, in association with different phases of her mental illness. Examination of one manic phase under constant diet and inpatient control showed cardiovascular changes, sodium retention, body weight gain, with raised aldosterone secretion but steady vasopressin. There appears to be a sub-group of manic-depressive patients with evidence of disturbed hypothalamic functions as part of their mental illness, as shown particularly by changes in water and electrolyte metabolism.

Recent interest in the possible role of vasopressin in affective illness (Gold *et al*, 1984) revives the need to examine water and electrolyte metabolism in manic-depressive patients.

The following case was selected for longitudinal study because in an earlier brief hospital admission her weight had suddenly risen in a few days by 3 Kg. during a manic attack, although this rise had been ascribed at that time to the drug therapy. The first study followed her through one manic-depressive cycle to confirm that her fluid balance varied with mental state independently of any drugs; the second examined a later manic attack in more detail under controlled conditions, to establish the nature of the disturbance in water and electrolyte metabolism.

The case

A former physiotherapist married to a doctor who was a keen clinical observer began at age 54 to have recurrent cycles of manic-depressive disorder lasting 45–70 days, as a consequence of which she had numerous hospital admissions and treatments, including ECT for the depressive phase on a number of occasions, and trimipramine, chlorpromazine, lithium carbonate and other drugs. At the times of study this illness had been running for 15–16 years.

The family history was positive: her father and his brother had both suffered recurrent depressions, and their father was said to have been a manic-depressive. The patient's younger sister suffered depressions following the menopause.

The patient herself had had episodes of "losing grip" lasting a week or two at ages 17 and 22, episodes of depression and tearfulness at ages 37, 38 and (puerperally) at 40.

On the physical side she had had appendicectomy at 26, left mastectomy for carcinoma at 54 and cholecystectomy (many small stones) the following year.

Description of the attacks (from husband and patient)

The cycles began with 5–7 days of gastric disturbance, flatulence, occasional epigastric pain, and loose stools. She became uncommunicative; began to feel depressed in mood, slowed down in thought and movement, had difficulty making up her mind, could not remember how to perform simple kitchen tasks or even to wash herself. These depressive phases slowly waxed and waned over about 3–4 weeks.

They were followed at once by hypomanic phases, each heralded by a sudden desire, continuing for two weeks, to eat chocolate or honey. She became constipated, was awake and active all night or at least until 3 a.m., became thirsty (up to 3 L. per day) and developed some urinary urgency and occasional incontinence. She was busy, talkative, sociable, unpredictable, an overspender, generous, broke things easily, was emotional, sexually alive, and felt happy. This phase waxed and waned over 3 weeks and was then followed by about three weeks of normality before the mood cycle started round again: cycle length about 70 days, noted, when in hospital, from age 62 at latest.

Study I

The patient was admitted for observation over seven weeks of a complete mood cycle. She was just two weeks into a depressive episode, with slowed movement and laboured speech, monotonous and without spontaneity, mostly about the hopelessness of her condition. She had been taking lithium carbonate ('Priadel') 1200 mg each night, and diazepam 5 mg at night and thrice daily for a long time, and it was decided to hold these constant through the whole admission rather than complicate the phenomena in the limited available time by introducing a withdrawal and wash-out period. The plasma lithium at 9 a.m. on many occasions from April 1 until mid-May was always 1.0 or 1.1 mmol/L., but on May 13 was 0.9, on May 15 0.6 mmol/L. (hypomanic phase ending, weight dropping) then returned to the 1.0 level, rising on June 3–20 to 1.5 mmol/L– at a time of great weight loss, before settling again to 1.0 mmol/L.

No attempt was made to control the patient's food intake, except that she ate only the official ward meals provided. Her fluid intake was measured as far as possible, and her urine was collected as a series of 24-hour specimens, which were analysed for creatinine (and for Na, K, Ca, Mg) by autoanalyser or absorption spectrometry. Daily urinary creatinine measurement is often a rough constant at about 20 mg/kg body-weight of a patient, and in this woman (weight about 56 kg.) was very often 0.9–1.1 g per day, but at other times between 0.7 and 1.4 g due either to errors in timing consecutive urine specimens or to fluctuations in renal blood flow.

During the manic phase urine samples were taken on several occasions for aldosterone and vasopressin radioimmunoassay. very kindly carried out by Dr. J. D. H. Slater and his colleagues at the Middlesex Hospital (Jowett *et al*, 1973).

Plasma samples were taken at intervals for packed cell volume by carefully standardised haematocrit, as a measure of blood hydration, and for plasma Na and K and serum albumin by standard methods.

The patient was weighed daily befor 8 a.m. in her nightdress, standardised as described by Crammer (1957, 1983).

Results

Figure 1 shows a depressive episode which began March 14 and ended about April 21, or after five weeks. The hypomanic phase began May 1, and ended about May 14 (two weeks), to be followed by a slow onset of depression from about May 22. Thus the complete cycle appeared to be March 14 to May 22, or 69 days long, which agreed with previous reports in this patient. The daily body weight was far from steady (unlike that of a normal person) and showed at least four changes greater than the maximum gain per day (250 g) expected from forced feeding, or maximum loss per day (500 g) from complete starvation without extra sweating (Crammer, 1983):

Phase 1: April 9–17, weight rises from 53 to 57 kg, or average 500 g per day while depression lessens: fluid retention.

Phase 2: April 18–20, weight falls 57 to 55 kg, a loss of 1.5 kg in two days: fluid loss.

Phase 3: May 2–15 weight rises steadily 54.5 kg to 59 kg, 350 g per day: fluid retention. While hypomanic, this was accompanied by complaint of thirst, high fluid intake, and a 24-hour urine output of 5 litres.

Phase 4: May 15–24, weight falls 59 to 56.5 kg then levels off at 57 kg for a week.

Phase 5: May 29 to June 1, fall from 57 to 54 kg at a time of mounting depression.

Weight gain due to fluid retention is accompanied usually by sodium retention (maintaining osmolarity), and weight loss due to extracellular fluid loss is accompanied by a loss of sodium in urine. Table I shows the results of daily urine analyses in the different phases, with mean daily excretion in each phase. The values must be considered with caution, since food intake, which was not regulated, can alter these values. However the main changes are consistent within the phases and the results are suggestive.

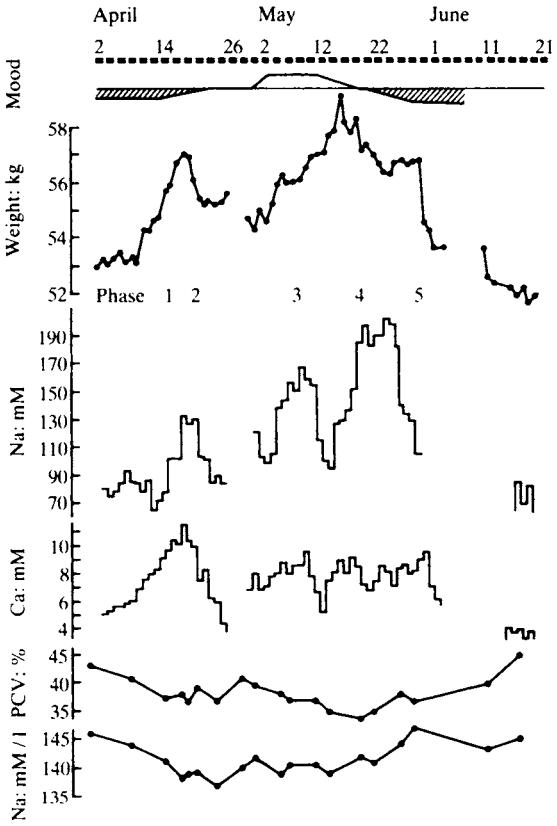

FIG. 1 Changes in body weight, urinary sodium and calcium, and in plasma haematocrit (packed cell volume) and sodium between 2 April and 21 June (Study I). Below the dashed line at the top representing days is an indication of mood state, shaded areas below the horizontal line representing depressive episodes, clear enclosed area above manic phase. Note particularly that while body weight rises constantly during manic phase (phases 3–4), daily urinary sodium loss shows two stages, marked at first, but with a very striking drop during the last 5 days of the manic phase suggesting marked sodium retention at this time.

When weight fell in phases 4 and 5 the daily urine loss of sodium was of the order of 160–180 mmol; when weight rose in phase 1 the loss was only 80 mmol. If dietary sodium was about 150 mmol per day, these are the urine values to be expected with the recorded weight changes. In phase 3, however, the situation was more complex, with a big weight *gain* yet a daily sodium loss of nearly 140 mmol, about the same as in the weight loss of phase 2. However at this time the patient complained of thirst and certainly

TABLE I

Daily urinary cation excretion in different phases (all values in mMol per 24 hours)

		Sodium	Potassium	Calcium	Magnesium
Phase 1					
Depression declining	Apr. 9	65	50	6.5	8.6
Weight rising	10	85	56	8.2	9.2
	11	89	55	8.5	8.5
(8 days)	12	70	48	7.7	7.3
	13	40	26	8.7	7.5
	14	109	54	11.9	11.4
	15	85	38	8.9	9.0
	16	114	61	11.0	8.6
8-day total (and daily mean)		657 (82)	388 (46)	71.4 (8.9)	70.1 (8.7)
Phase 2					
Weight falling	Apr. 18	176	83	12.8	10.3
(2 days)	19	106	52	7.6	6.1
2-day total (mean)		282 (141)	135 (67)	20.4 (10.2)	16.4 (8.2)
Phase 3					
Hypomanic	May 2	110	50	7.2	7.6
Weight rising	3	128	56	6.4	8.4
	4	186	74	10.5	9.3
(13 days)	5	125	65	7.8	9.4
	6	165	71	8.8	9.4
	7	172	89	8.2	9.7
	8	173	98	9.5	11.8
	9	140	85	8.8	10.5
	10	160	83	11.3	12.2
	11	57	27	3.9	5.7
	12	96	36	5.4	6.6
	13	145	64	7.1	7.6
	14	152	71	11.2	12.5
13 day total (mean)		1809 (139)	869 (67)	106.0 (8.1)	120.7 (9.3)
Phase 4					
'Normal'	May 15	99	37	6.4	5.1
Weight falling	16	173	61	9.7	9.4
	17	184	72	9.2	10.4
(9 days)	18	207	56	9.4	9.4
	19	210	68	7.8	8.7
	20	146	46	5.2	5.8
	21	222	59	8.4	9.0
	22	213	59	9.6	8.4
	23	187	59	8.4	7.2
9-day total (mean)		1641 (182)	517 (57)	74.1 (8.2)	73.4 (8.1)
Phase 5					
Depression increasing	May 29	162	57	12.0	7.9
weight falling	30	177	63	10.2	6.3
(3 days)	31	144	53	7.4	5.3
3-day total (mean)		483 (161)	173 (57)	29.6 (9.9)	19.5 (6.6)

See text for discussion of values.

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drank more: Table II shows urine output of 4.0 to 5.4L during manic phase in May, but only 1.5 to 2.5L in the following depression. She may have eaten more too because the potassium excretion rose to a daily 67 mmol on average, certainly at its highest in this phase, yet the Na:K ratio remained steady through phases 1, 2, 3 at 1.8, 2.1, 2.0 respectively (but rose to 3.2 during the sodium and weight loss of phase 4).

The complexity of the manic phase was further emphasised by the plasma measurements (bottom of Fig. 1). In spite of thirst and climbing body weight the plasma sodium was about 137 mmol/L, having fallen from 146 mmol/L in depression and climbing back to that value about May 28 as depression reappeared. The packed cell volume also fell to its lowest as manic phase ended. In other words during phase 3 the plasma was more hydrated, the osmotically active sodium lower than at any other time, yet this was the time of thirst and greater fluid intake. One explanation could be a small inappropriate secretion of antidiuretic hormone at this time, and the incomplete figures available for Table II show the urine osmolality low yet the antidiuretic hormone well maintained. During the depressive phases, when the plasma sodium was higher, and water formed a smaller fraction of whole blood, the patient experienced no thirst. It was necessary to re-examine these phenomena under better control in a later manic phase.

Study II

The purpose was to re-examine the manic phase (phase 3) under better controlled conditions, and confirm the findings.

The patient was re-admitted the following January towards the end of a depressive phase and placed on a constant diet of known composition for 16 days. The first five were settling-in days: manic phase began on the sixth day (January 18). Mineral and fluid balance, with some relevant hormonal measurements, and clinical observation of mental state, body temperature, blood pressure, etc. were carried out daily, essentially as before. Since Study I her husband had noted three manic phases, each associated with restless nights, marked thirst, a degree of urinary incontinence, and a weight gain (on bathroom scales) of about 6 kg.

Diet

A dietician (Miss P. T. Carden) from the nearby general hospital (King's) very kindly prepared a diet adequate in calories and liked by the patient, in which *the same quantities of the same foods were eaten each day*, and the daily mineral intake calculated with the help of tables (McCance and Widdowson 1960). The diet allowed 50 g salt-free bread, 30 g salt-free butter, 400 g milk, 100 g orange squash, and otherwise distilled water, 40 g lamb and 30 g chicken breast, oatmeal, 50 g potato, and other vegetables and tinned fruit, jelly, Nescafe, and so on, to give a varied menu in the 24 hours. Care was taken to cut all meat from the same joint, and to use a single baking of bread, etc., to aim for uniformity of analysis. The calculated mineral intake was sodium 34 mM, potassium 56 mM, calcium 19.4 mM and magnesium 4 mM. The 24-hour urine content of these ions on the fourth and fifth pre-manic days, which may be taken as the basal starting state, was Na 36, K 42, Ca 1.13 and Mg 1.8 mM: since it is known that in man virtually all the day's sodium intake and four-fifths of the potassium are normally excreted in the 24-hour urine, these values agree well with the calculated values for the diet. It had been intended to have a higher daily sodium intake than this by supplementing with a known weight of oral sodium chloride, but this was omitted in error. However, the results are still interpretable, although the effect was probably to reduce the degree of sodium retention and of weight gain (as in another patient, Crammer 1959*b*).

Fluid intake was free, but always measured, and in fact was roughly constant at 1.5–1.75 litres daily, until with the onset of thirst on the seventh manic day it rose above 2.0 L. (see Fig. 2). The patient had her own bedroom, stayed in the ward under nursing supervision the whole time, and only had access to water and toilet facilities under observation. All urine was collected as a sequence of 24-hour urine specimens. She continued to receive her

TABLE II

Urinary aldosterone and vasopressin in Study I

Date	*Mental State*	*Volume/24 hrs.*	*Osmolality*	*Aldosterone*	*Arginine Vasopressin*
2 May	Hypomanic	4500 ml	149 mOsm.	6.6μg	111 pg/min
3	"	4000 ml	179 mOsm.	6.3 μg	156 pg/min
14	End of manic	5440 ml	180 mOsm.	6.1 μg	214 pg/min
15	"	4600 ml	108 mOsm.	2.0 μg	90 pg/min
1 June	Depression	1580 ml	311 mOsm.	5.6 μg	176 pg/min
2	"	2400 ml	298 mOsm.	8.9 μg	278 pg/min
17	"	2550 ml	490 mOsm.	-	164 pg/min
18	"	1520 ml	370 mOsm.	-	174 pg/min

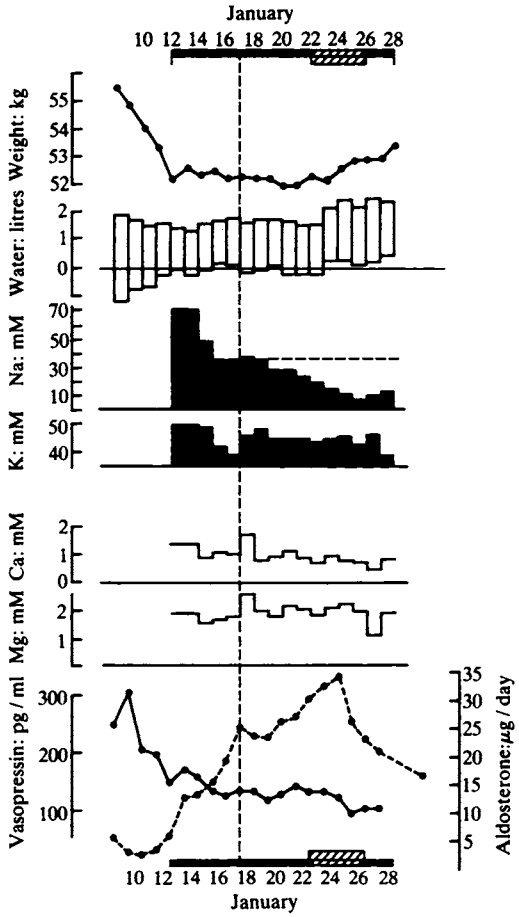

FIG. 2 End of depression, start of manic phase indicated by vertical dotted line. Constantly daily sodium intake 13–28 January, indicated by the dark horizontal line: the shaded rectangle indicates the four days when lithium doses were omitted.

Water intake shown by the top of each plain rectangle, urine output by the bottom: where this is below baseline there is net fluid loss, where above baseline net fluid retention (from January 24).

Sodium excretion is steady for four days, and retention (below horizontal dotted line) begins on January 20.

Aldosterone (dashes in lowest figure) rises anew from January 21 to January 24; vasopressin (continuous) fairly level January 12–28.

usual drugs, nitrazepam 5 mg at night, and 800 mg lithium carbonate (Priadel) every morning, except on the four days shown below.

Blood pressure

At 09.30 each day she had always been lying supine for at least 30 minutes, when I took her pulse and blood pressure, and a blood sample. She then got up, walked about for half an hour, and then sat down, erect, for a repeat of pulse, blood pressure and venesection.

Laboratory

Na, K, Ca, Mg were measured by atomic absorption spectrometry; creatinine, and plasma concentrations of urea, urate, albumin, bilirubin, cholesterol, phosphate and chloride by autoanalyser; packed cell volume by haematocrit; plasma osmolality by freezing point determination; aldosterone, antidiuretic hormone, and plasma renin were kindly measured by Dr J. D. P. Slater and his staff at the Middlesex Hospital.

Results

(a) *Clinical*: On first four days (January 9–12), she was at first slowed, with inability to concentrate, concerned about her bowels, slightly nauseated, not thirsty, but improving to the end of this period. On January 13 she started her special diet, and continued to develop some spontaneity; on January 15 and 16 she was free of depression, more active and normal. Normal stools were passed on January 11 (126 g) and 12 (176 g) and also on January 15. A further stool was passed on the night of January 16, and two further stools on January 17, and these last three were all much softer and came with some urgency. Thereafter she was constipated, with small stools on January 20 and January 28 only.

On January 18, the manic phase began, but at first it was extremely mild. However, by January 22 she was sleeping less (drop from 8 to 5 hours), had become talkative, with some urge to speak, and not always to the point. By January 25 she was very talkative, thoughtless, restless, and joyful, and was complaining somewhat of thirst, as in previous cycles. She longed to smoke a pipe, and eat chocolate.

(b) *Cardiovascular*: The resting pulse was very steady from day to day at 47.6 per min average on the five pre-manic days, and 50 per min from January 18–29 (manic phase) (Table III). But when the effect of exercise and posture was examined there was a striking difference between pre-manic and manic. In the first (six) days the pulse was always quickened after exercise by 3–9 beats/min., but on January 18 and thereafter it was always *slowed* by a similar amount, an abnormal response.

Blood pressure showed a 27% increase in resting diastolic pressure with onset of manic phase (see Table III), with a much smaller rise in systolic pressure. As expected, both pressures increased on exercise and change of posture, to about the same extent in pre-manic as in manic phases (normal). The changes in pulse and diastolic pressure occurred at the very start of hypomanic phase, long before there was a noticeable increase in physical activity. They were consistent with the idea that there was a change in central vasomotor control from the start of manic phase, resulting in a change in renal blood flow and an increased sodium retention.

(c) *Sodium and water balance*: Figure 2 and Table IV show what happened. There was little change over baseline until the third manic day (January 20) when sodium began to be

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TABLE III

Standard morning blood pressures before and during manic phase (all values in mmHg)

	Supine		*Erect*		*Postural*
	Sys.	*Dias.*	*Sys.*	*Dias.*	*gain*
Premanic					
Jan. 13	120	62	135	90	
14	110	55	110	60	
15	110	58	132	90	
16	108	68	120	90	
17	100	65	125	98	
Av.	109.6	61.6	124	80.5	+14/+19
Manic					
Jan. 18	115	90	124	100	
19	110	65	130	100	
20	110	65	130	100	
21	130	90	140	100	
22	112	85	120	95	
Av.	115.6	79	129	101	+13/+22
Manic gain	+6	+17	+5	+21	

retained, and this continued for the remaining metabolic days. Water only began to be retained on the seventh day (January 24). The weight gain over 5 days (January 24–29) was only 1.3 kg, the total sodium retention by the 29th of the order of 160 mM, which at an extracellular fluid concentration of 140 mM/L is worth a weight gain of nearly 1.2 kg. The positive fluid balance over the last five days implies retention of about 1.5 L. These values agree quite well. In the hypnomanic phase of Study I, and in the husband's reports they were three times bigger. Here they are probably small because of the rather low sodium in the diet. In an earlier case (Crammer, 1959*b*) varying the daily sodium intake altered the sodium and water retention.

If we look at plasma changes (Table V) the haematocrit dropped with the onset of manic phase, 42% to 39%, a smaller change than noted in Study I, but again pointing to increased hydration of the blood. Plasma sodium showed a tendency again to fall, most noticeable in the last five days, the plasma osmolality likewise, and the plasma albumin and urea also fell in the last four or five days. This was a time when clinically thirst was most in evidence and a *higher* plasma osmolality would have been expected.

In a short-cycle manic-depressive previously studied (Crammer, 1959*b*) while off all drugs, phases of sodium and water retention were observed in step with the mental states, with fall in resting pulse, rise in body weight, and in particular the same fall in PCV and plasma sodium and evidence of increased hydration of the blood as noted here. Jenner *et al*, (1967) also noticed such a change in their case.

Antidiuretic hormone (Fig. 2 and Table V) fell steadily as osmolality fell, and therefore could not be seen to be playing any part in the fluid rentention and thirst of January 24 and after. Paradoxically, at the end of the depression (Phases A and B), plasma osmolality and sodium were quite high (higher than in Study I) but there was no thirst, antidiuretic hormone was not greatly raised, and in fact sodium and water excretion were up, and the body weight falling. There is no evidence here of a role for arginine vasopressin in the pathophysiology of this illness (compare Gold *et al*, 1984). If antidiuretic hormone can come into play it may do so following a much greater degree of sodium retention.

The salt retention took priority in this patient's manic phase, and her aldosterone rose at this time, although already at a high steady level because of the rather low daily sodium intake. No increase in potassium excretion was seen, however. Aldosterone was not raised in Study I, perhaps because dietary sodium was freely available. Plasma renin activity did not show any relevant change. It was higher while the controlled low sodium diet was given, but did not rise in the manic phase, and the effect of posture and exercise remained similar in non-manic and manic conditions.

(d) *Calcium and magnesium:* Urinary magnesium increased in the manic phase, starting on the fourth day (January 21), a change from about 1.75 to 2.10 mM per day, a 20% rise. Calcium remained roughly constant, with a 10% drop only in the last four days, and plasma calcium was constant until this time and then fell slightly.

TABLE IV

Daily urine excretions during metabolic experiment (Study II)
Urine data on constant diet. All values millimol

Diet (same every day) from tables: Na 34.0, K 56, Ca 19.4, Mg 4 mM

State	*Date*	*Volume*	*Creatinine*	Na	K	Mg	Ca	Li
End of Depr. A	9 Jan.	3055 ml	8.6	156	58	3.76	3.79	18.6
	10 Jan.	2600	8.4	166	55	3.46	3.38	18.5
	11 Jan.	2220	8.4	153	51	2.53	2.44	16.7
	12 Jan.	1800	8.3	101	43	2.16	2.23	17.1
Diet, B	13 Jan.	1000	7.3	66	41	1.61	1.26	15.3
	14 Jan.	2010	12.5	76	60	2.29	1.51	17.3
	15 Jan.	1630	9.1	49	49	1.66	0.90	13.0
	16 Jan.	1500	8.4	36	42	1.77	1.13	13.2
	17 Jan.	1555	8.4	36	39	1.83	1.09	13.0
Mania Onset, C_1	18 Jan.	1820	8.7	38	46	2.66	1.78	19.2
	19 Jan.	1730	9.0	36	48	2.08	0.87	13.8
	20 Jan.	1660	8.3	29	45	1.86	1.00	16.1
	21 Jan.	1790	9.0	29	45	2.24	1.20	18.6
	22 Jan.	1640	8.9	25	45	2.14	0.98	18.2
Lithium Stop, C_2	23 Jan.	1620	9.2	21	44	1.94	0.82	11.3
	24 Jan.	1890	9.1	16	45	2.21	1.04	8.9
	25 Jan.	2240	9.0	12	46	2.24	0.90	6.7
	26 Jan.	2040	9.0	9	43	2.08	0.84	4.9
Lithium Resume	27 Jan.	2240	9.0	11	47	1.34	0.56	7.2
	28 Jan.	1940	8.5	12	39	2.02	0.97	10.9

Note the raised magnesium, lithium and calcium on the switch day (Jan. 18).

Thus, the suggestion from Study I of increased urinary magnesium loss in manic phase was confirmed by the metabolic balance study. The onset of manic phase on January 18 was marked by looser stools, before constipation set in, and by high excretions of magnesium and lithium, and to a lesser extent of calcium, just for 24 hours.

The signficance of these changes is uncertain: it would be necessary to confirm their re-occurrence at each manic onset, or in other similar patients, and to examine changes in fecal minerals at the same time to begin to analyse what may be coincidence, an effect of physical exercise, or of changed bowel habit or altered renal function, or have some other explanation.

Discussion

Physical signs and biochemical disturbances in the course of a major psychiatric illness may be purely coincidental, perhaps due to some concomitant physical illness, or quite commonly result from a change in the patient's behaviour (Kety, 1959). In spite of many years of hope and study (Barnes & Francis, 1909; Pighini, 1907; Gjessing, 1976), no biochemical disturbance has been found causal of a major psychosis. There is, however, another but neglected possibility, that changes in the regulation of the body temperature (Nikitopoulou & Crammer, 1976), of pulse and blood pressure, or of urinary secretion may be signs of central nervous disturbance quite as much as are the appearance of hallucinations or of pathological mood.

In the present case, long-standing undoubted bipolar affective disorder has been shown to be accompanied by pathological variations in body weight, due in part to changes in the renal excretion of sodium and in the retention of water, and accompanied by pathological thirst in the manic phase. This phase has also exhibited a change in cardiovascular regulation. These phenomena were all small, and easily overlooked. They have on occasion been reported in other patients before (Klein & Nunn, 1945; von Stockert, 1958; Crammer, 1959b; Jenner *et al*, 1967; Hullin *et al*, 1967, 1977; Allsopp *et al*, 1972), mostly in cases who were drug-free. It

TABLE V
Plasma measurements during metabolic balance (Study II)

	Day	PCV	OSM	(Na)	aVP	(Ca)	PRA recumbent	PRA erect
Phase A	9			250				
	10				300			
	11	39	305	153	207	2.40	1.52	2.26
	12							
B	13	Diet begun						
	14	41	305	152	169	2.43	5.26	6.83
	15	42	304	145	155	2.40	5.39	7.02
	16	42	303	150	138	2.39	5.57	7.07
	17							
Manic Onset C	18			146	138	2.41	5.55	7.20
	19	39	300		136			
	20			144	120	2.36	5.58	7.30
	21							
	22	38	291	145	145	2.40	5.61	
	23	39	296	148	135	2.45	5.57	6.88
C_2	24	(wt. starts upwards)						
	25		291	141	125	2.35	5.56	6.94
	26	39	292	145	98	2.31	5.55	6.90
	27		287	142	107	2.24	5.34	6.93
	28		277	144	107	2.23	5.31	6.90
	29		281	141		2.19	5.27	6.81

Phase A depressed; Phase B start of constant diet; Phase C onset of manic phase.
PCV, packed cell volume %; OSM, osmolality in mOsm/Kg; (Na) (Ca), sodium, calcium concentrations in mM l; aVP, arginine vasopressin in Pg.ml; PRA, plasma renin activity.

seems evident that in some, though perhaps only in a minority, functional psychoses may have physical signs and biochemical signs just like other illnesses. It is least difficult to detect them in repeating periodic illnesses (Crammer, 1959a; Jenner, 1968) but there is no reason to suppose they will be confined to such illness and they need to be sought much more often. We accept the idea that hormonal provocation tests such as the dexamethasone suppression test (Carroll, 1982) or the clonidine-growth hormone test (Checkley *et al*, 1981) may help in diagnostic differentiation, in exploring central nervous dysfunction, and in predicting success in pharmacotherapy. Should we not similarly take advantage for the same purposes of the disturbances in regulation of water and electrolytes which occur naturally in the course of psychiatric illness? They are easy to follow clinically in terms of weighing the patients - and collecting timed blood and urine specimens for simple analyses. Psychiatric diagnoses are based on the grouping of symptoms, and a label such as catatonic schizophrenia or major bipolar affective disorder carries no guarantee of pathophysiological unity. On the other hand cases which have in common a disturbance in cardiovascular regulation, or in body weight may be found to have also a similarity in pharmacological response.

The observations here concentrated on the manic phases. In Study I on free food and water, weight gain appeared as a consequence of thirst and water retention; the blood becoming increasingly hydrated. Some pilot data suggested that vasopressin secretion, (Gold *et al*, 1984) might be playing a role, while aldosterone appeared unimportant. In Study II, which examined the manic onset rather than the manic ending, and which severely limited daily sodium intake, the reverse seemed to be true. Sodium retention came first, before there was any thirst or increase in water intake or in weight, and it seemed possible that aldosterone was involved rather than vasopressin. Hullin's group (Allsopp *et al*, 1972; Hullin *et al*, 1977) have been pioneers in emphasising the importance of aldosterone in these cases. One might speculatively develop a hypothesis that the manic phase may begin with a vascular disturbance, particularly renal and leading to inappropriate aldosterone secretion and sodium retention. At a certain point, the sodium input stimulates thirst and vasopressin secretion, and the resulting dilution of sodium results in a cut-off of thirst and of manic

symptoms and return to the starting point. Thus the manic phase would have different mechanisms predominating at different times in its course.

However this may be, modern renal physiology emphasises the angiotension-renin-aldosterone system in the genesis of thirst, and a cardiac natriuretic hormone, and nervous control of renal function (Ganong and Barbieri, 1982; Seldin and Gebisch, 1985) as factors also to be taken into account. Elucidation of the mechanisms at work in the fluid disturbances of psychiatric cases will require the application of this knowledge and much better and fuller hormonal measurements than those reported here. The purpose of this paper is to draw attention to physical signs—cardiovascular, changes in body water, changes in magnesium excretion—which appear to be part of a psychotic illness. Explanation comes later.

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