CLINICAL AND BIOCHEMICAL ANALYSIS OF A CASE OF MANIC-DEPRESSIVE PSYCHOSIS SHOWING REGULAR WEEKLY CYCLES.

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THE unfailing regularity of the rhythm of his manic-depressive cycles each week renders the patient in question particularly suitable for investigation, and throws into relief changes which might be less marked if the transition between the phases was more gradual and the periodicity less certain.

Clinical observations continued over a number of months had shown a period of five days of depression, followed by two of mania, and it was decided to undertake parallel clinical and biochemical investigations to ascertain if there existed any metabolic change coincidental with variations in his mental state.

History.—The patient (H. L—) commenced his career as a tradesman, and later became a clergyman. His brother described him as being of a cheerful disposition, and a companionable man who liked to make friends. From an early age he showed an inclination to religious work, and was fond of public speaking.

In 1928, at the age of 51 and after 16 years' successful ministry, he suddenly became depressed, complained continuously of internal trouble, and was obsessed with the idea that he might have a " formation " in the stomach. In this condition he was admitted to hospital in March, 1929, remaining here until March, 1930, and during this time he was continuously depressed. Although still depressed, he was discharged at the request of his relatives and went to live at a country residence, where he remained for a period of nine years in a similar state, although his brother reported that the depression may have been less marked on some days than on others. After that he went to live with his brother elsewhere, and apparently showed no change mentally until April, 1942, when his wife died.

It was shortly after her death that this continuous depression was broken each week by two days of excitement and overactivity. When the change first occurred the days of mania were Tuesday and Wednesday, and gradually shifted until they occurred on Saturday and Sunday. During the manic episodes he was irritable, made himself a nuisance by forcing his company upon his friends and relatives, and squandered his money, e.g., on unnecessary purchases and generous gifts. He attracted attention by his extravagant and bizarre behaviour ; for instance, on one occasion he entered a milliner's shop, kissed the shop assistants, put on a number of ladies' hats, and walked out with them. He also gave cinema tickets with religious texts on them to soldiers. Throughout these periods of mania he was sleepless and noisy. In 1943 he was readmitted to this hospital.

The family history shows that his father's mother died in a mental hospital, and that his twin sister died at the end of two years in a mental hospital at the age of 36.

Clinical.—Since his readmission his weekly cycle has been maintained with almost absolute regularity up to the present, apart from the fact that within the last few weeks the manic phase has been about one day earlier than previously, i.e., whereas before the manic phase began to appear on Saturday morning and to disappear into the melancholic phase on the following evening or on Monday morning, latterly it has begun to show itself on Friday morning and to wane on Sunday morning.

The depressive condition usually starts with a decrease of activity ; he withdraws from the company of the ward, and ceases to speak of his own accord,

although when addressed he will talk readily. At the same time his voice undergoes a change, becoming weaker, more high-pitched and plaintive. He becomes gradually less and less active, and sits or lies about with no desire to occupy himself. Within the next twenty-four hours the depression deepens slowly until it reaches its maximum level. He remains thus for the next four days, until he begins the reascent into the manic phase. During these four days of deep depression he is almost motionless, though never stuporose, has an expression of great unhappiness, never speaks spontaneously, and answers questions with reluctance. When questioned he complains of general debility, of vague pains in the abdomen, or of fatigue. However, he sleeps well at night. During this phase he has to be prompted to empty his bowel and bladder.

The onset of the manic condition is also gradual and takes about twelve hours to reach its height. The first sign of the change is an increase in activity and he nearly always begins to read and write. He answers questions more readily, but his voice is still weak and his expression is worried. In about two to four hours he becomes more active and more talkative. His voice becomes clear and strong. He becomes hyperactive, which takes the form of walking about the ward, talking and arguing with other patients. He becomes boastful, makes complaints, writes numerous letters in great haste, some of which are in verse. After this transition period of ten to twelve hours, the peak of the manic condition is maintained for about twenty hours and during it he is very elated, accessible and amenable to reason, although restless and seeking to attract attention. In the manic state he never sleeps more than one or two hours at night and usually not at all, but is as active throughout the night as during the day.

The change in his voice noted above is an unfailing indication of the transition from elation to depression. Towards the end of the manic phase his voice becomes weaker, plaintive, and more highly pitched, and this heralds emotional features premonitory to the descent into depression. It retains these qualities until the end of the melancholic phase and on into the early part of the succeeding ascent, when the timbre and character of his voice improve.

Physical examination.—He is of pyknic type. During the depressed phase his appearance of general physical well-being contrasts sharply with his complaint of fatigue, vague pains all over his body, and widespread discomfort. Whereas during the depressive phase his colour is good and he looks well generally, in the manic phase he looks older, drawn, and sallow.

At no stage, however, has physical examination revealed any specific abnormality. The pulse rate is about 58 in the depression, and changes to about 80 in the manic state, and similarly the blood pressure varies from 100/56 to 150/82. His pupils are somewhat small, but react to light and convergence, and the most exhaustive neurological examination has revealed no abormality. The blood Wassermann is negative.

The urine is free from albumin and sugar, and there is no prostatic enlargement.

Experimental procedure.—Throughout the biochemical examinations lasting seven months, the patient was kept rigidly to a constant mixed diet. This consisted of a daily ration of 4 oz. lean beef, 2 oz. cheese, 1 lb. potatoes, 1 egg, 2 oz. margarine, 1 pint milk with a teaspoonful of cocoa and sugar, 2 apples, 2 oz. rice, 2 oz. cabbage, 8 oz. beetroot, 4 oz. bread, and ½ pint water. The food was weighed and the fluid measured carefully. He was encouraged to take everything offered, and fortunately proved to be very co-operative.

The urine was collected under 5 c.c. of toluene in two twelve-hourly specimens each day, and was stored in the ice chest. At the beginning there was difficulty in getting exact collections owing to his tendency (already mentioned) to suppress his excretory functions, and if left to his own devices in the depressive phase, he would refrain from passing urine for more than thirty hours. Finally, however, he was trained to empty his bladder regularly, so that specimens were usually available for examination.

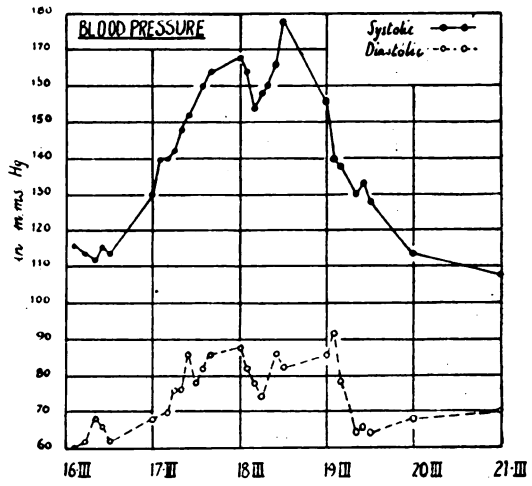
His mental state was recorded daily, and the blood pressure was taken each morning. During the transition periods this procedure gave place to two-hourly recordings of his mental state, blood pressure, pulse and respiration rates, and of his temperature.

In the period when biochemical investigations were being carried out he was

confined to bed. During this time he suffered no acute illness, and no drugs were administered. Biochemical estimations of certain constituents of the blood and urine were made daily for three weeks, and those which showed variations corresponding with changes in his mental condition were chosen for daily assay over a longer period. The estimations on the urine were conducted on each twelve-hourly sample, and also on the twenty-four hourly sample prepared by mixing aliquot parts of the two twelve-hourly ones. This procedure provided a check in duplicate. The methods employed in this investigation were: Chlorides, Volhard-Arnold method, Hawk's *Physiological Chemistry*, 1938, p. 768; total nitrogen, Kjeldahl, Hawk's *Physiological Chemistry*, 1938, p. 701; ammonia and urea, Van Slyke, D. D., and Cullen, G. E., *J. Biol. Chem.*, 1916, **24**, 117; calcium, Shohl, A. T., and Pedley, F. G., *J. Biol. Chem.*, 1922, **50**, 537; phosphates, Fiske, C. H., and Subbarow, Y., *J. Biol. Chem.*, 1925, **66**, 375; total phosphorus, Berenblum, I., and Chain, E., *Biochem. J.*, 1938, **32**, 295; sodium, *J. Assoc. Off. Agric. Chem.*, 1942, **25**, 429; creatinine, Folin, O., and Wu, H., *J. Biol. Chem.*, 1919, **38**, 81. The methods employed for blood investigations were: Non-protein nitrogen, Koch-McMeekin, *J. Amer. Chem. Soc.*, 1923, **46**, 2066; urea, Harrison, *Chemical Methods in Clinical Medicine*, 1937, p. 80; sugar, Harrison, *Chemical Methods in Clinical Medicine*, 1937, p. 144; chlorides, *Spec. Rep. Ser. M.R.C.*, No. 187, 1933; calcium, Clark, E. P., and Collip, J. B., *J. Biol. Chem.*, 1921, **63**, 461; phosphorus, Berenblum, I., and Chain, E., *Biochem. J.*, 1938, **32**, 295; creatine, Hawk's *Physiological Chemistry*, 1938, p. 426.

Blood Pressure, Pulse and Respiration Rates, and Body Weight.

The blood pressure and pulse rate showed pronounced variations, and it can be seen from a representative three-week period in Graph 4 below that these changes were related to the two phases. In the depression the blood-pressure readings were usually between 100/60 and 110/70 mm. Hg. During the manic phases the values rose to between 140/78 and 150/84, though systolic pressures up to 180 and over were occasionally observed. As a rule, the rise in the blood pressure seemed to be proportionate to the degree of activity and elation.



GRAPH 1.

The respiratory rate varied from 16 per minute in his depression to 20 per minute in his mania.

During the depression he gradually gained two or three pounds in weight, but the increase was lost again during mania.

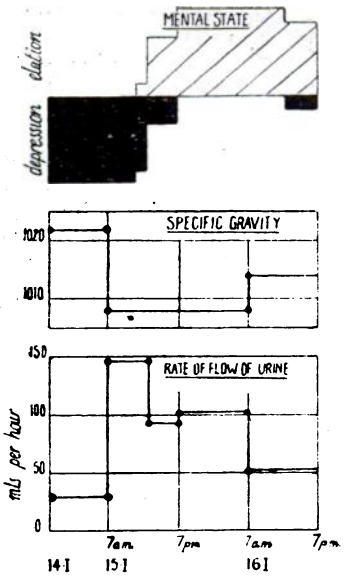
Basal metabolism.—The basal metabolism was estimated each day for three weeks, and on the days of mania the deviations from normal were about plus 30 per cent. These high results can be accounted for mainly by his restlessness and

overactivity. During depression, when co-operation was difficult, the values were minus 10 to minus 15 per cent.

Biochemical Investigation of the Urine.

(A) *Cyclic Biochemical Fluctuations Associated with the Mental Periods.*

1. ***Output of urine.***—As previously mentioned, the patient was kept on a constant diet and fluid intake. The daily total fluid contained in both food and drinks was 1,640 c.c. His weekly renal excretion was between 6,640 and 8,652 c.c. An average taken from nine weekly cycles showed a weekly output of 7,470 c.c. This was not excreted in equal amounts each day, but, as seen from the graph below, there was a striking difference in output in the depressive as compared with the manic state. Whereas the daily output in the former was about 780 c.c., in the latter for the first twenty-four hours it was almost always over 2,000 c.c. Taking an average of nine weeks, the output in the two days of mania amounted to 3,348 c.c., as against 3,894 c.c. for the five days of depression. Thus 44·8 per cent. of the entire weekly



GRAPH 2.

output was voided by the kidneys in the two days of mania. The specific gravity was also determined daily, and was found to vary indirectly with the volume. It was observed that the rate of flow of the urine markedly increased at about the time of the transition from depression to mania, and the time of the collection was accordingly altered to isolate a pure specimen of this " transition " urine. Eventually such specimens were obtained. On January 15, 1944, at 7 a.m. the patient was in typical deep depression, which continued until 11.30 a.m., at which time he began to show signs of change-over to the manic state. At 7 a.m. he passed 385 c.c. of urine of specific gravity 1022, this being the first time he had micturated for twelve hours, and representing a rate of renal excretion of 32 c.c. per hour. Seven and a half hours later, at 2.30 p.m., he again passed urine, and by this time he had been in the ascending mental state for three hours. On this latter occasion he passed 1,200 c.c. of urine, with a specific gravity of 1008, which would give a rate of renal excretion of 150 c.c. per hour, assuming that the flow had been at an even rate from 7 a.m. However, another possibility exists, i.e., the increase in flow was simultaneous with the first signs of the change-over in his mental state at 11.30 a.m., in which case, supposing that the rate of flow up to 11.30 a.m. was maintained at approximately 32 c.c. per average of the earlier specimen, the rate

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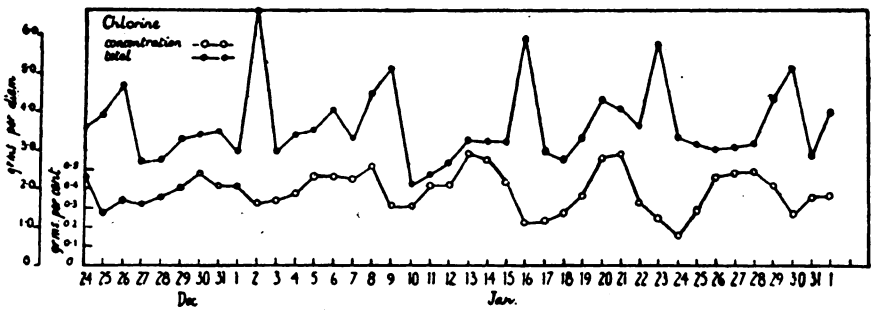
of flow subsequent to 11.30 a.m. must have been 350 c.c. per hour. The rate of flow after 2.30 p.m., however, fell to 98 c.c. per hour, and even at the peak of mania it never rose above 102 c.c. per hour.

Again at 7 a.m. on December 24, 1943, it was recorded that the patient for the previous 12 hours had been excreting urine at an average rate of 26 c.c. per hour. At noon he exhibited the first signs of the change-over to mania, and also passed 500 c.c. of urine, which represents an average rate of renal excretion of 100 c.c. per hour. The mania was only fully developed by 4.30 p.m. In this instance it is clear that the diuresis started whilst the patient was still depressed. It is also interesting to note that the blood pressure in this case was 108/64 mm. Hg at 9.15 a.m., and rose to 136/78 mm. Hg by 4.45 p.m. These facts, together with the consideration that the fluid must have first been mobilized from the tissues into the bloodstream before being excreted by the kidneys, shows that the diuresis preceded the first discernible signs of mania (see Graph 2).

2. *Chlorides.*—The patient was on a diet of constant chloride content, and the amount excreted in the urine was estimated each day for ten weeks. With one exception, the concentration of chloride in the urine was maintained at a fairly constant level from day to day, so that in the depressive state the chloride excretion was relatively low, and rose to a maximum with the increased urine output in the mania. The total weekly renal excretion of chloride varied only slightly from week to week, and in the two days of increased urinary output the chlorides passed



GRAPH 3.

out were about 15·6 gm. (expressed as sodium chloride), which represents about 33·8 per cent. of the weekly total of 46·7 gm. sodium chloride. The daily amount of chloride excreted during the depression was between 5–6 gm., whilst during mania the value was 8–10 gm. It can also be seen in Graph 4 that the lowest valuef or the chlorides always occurred in the twenty-four hours in which the patient changed from the manic to the depressive state.

The small amount excreted on these occasions was about 4 gm. In contrast to this constant low weight of chloride, the volume of urine in which it was contained varied considerably. For example (see Graph 3), on January 24, 1944, there was a relatively large volume of 1,480 c.c., which was 700 c.c. in excess of the average for the depression. Hence this urine had a very low chloride concentration, i.e., under ·2 gm. NaCl per cent. On the other hand, the specimen passed on March 6, 1944, had a volume of 715 c.c., which resulted in a much higher concentration of chloride, i.e., 1·58 gm. NaCl per cent. From this it seems that after the mania the body conserves its chlorides. The need for this appears to be great, for irrespective of the volume of water passed, the chloride output invariably remains at the constant low level of about 4 gm. NaCl.

Furthermore, during the depression the amount of chloride excreted and its concentration were higher in the daytime, and this holds true for the normal individual. In the mania, however, when he was sleepless and alert throughout the twenty-four hours, the amount of chloride and the concentration at which it was excreted were higher at night.

3. *Sodium and potassium.*—The amount of sodium excreted daily showed similar variations to that of the chlorides (see Graph 4), which points to a loss of the chief extracellular electrolyte of the body fluid.

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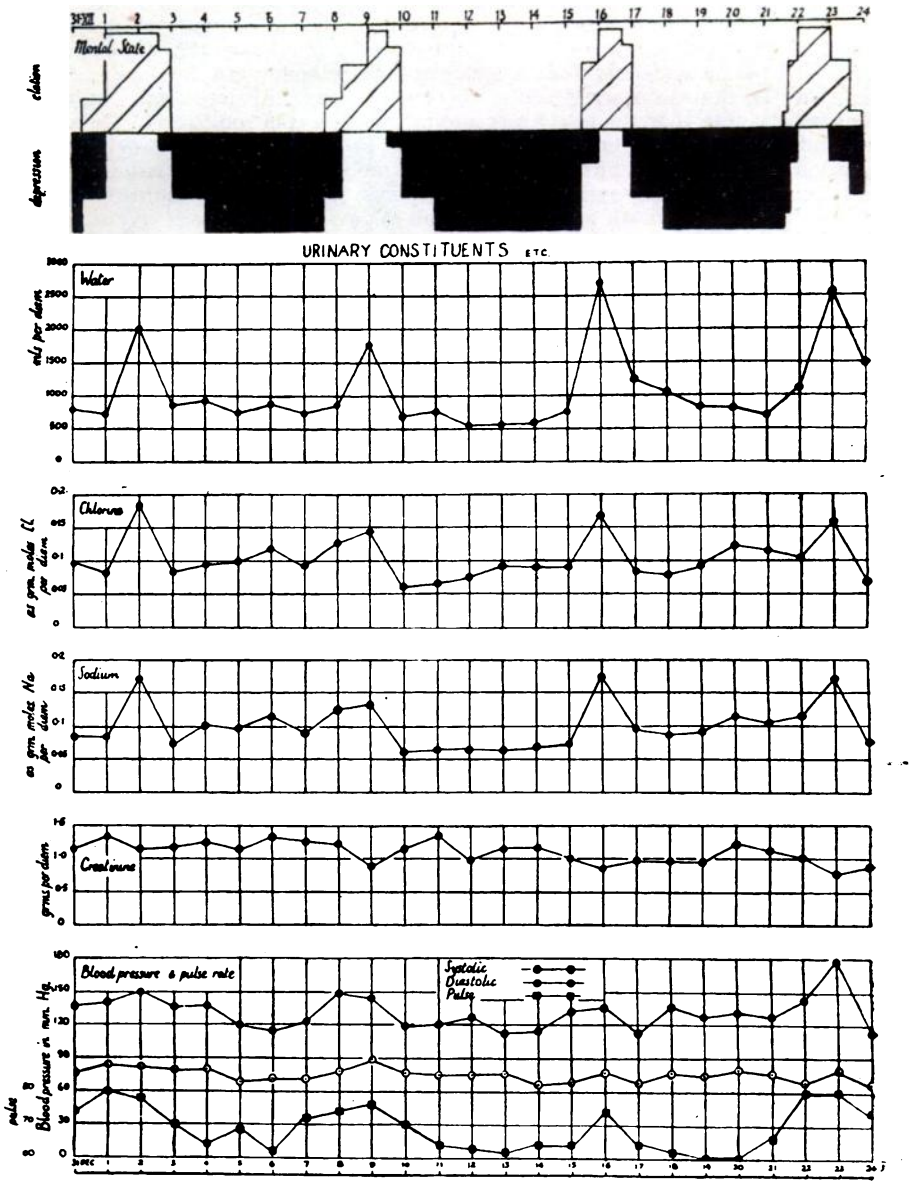
The potassium, however, was independent of the water and chloride passed, and was unrelated to the metabolic fluctuations described previously.

4. *Creatinine.*—The creatinine output (see Graph 4) was usually between 900



GRAPH 4.

and 1,000 mgm. each day, and showed a regular drop on the first day of his excessive urinary output. The amount excreted on these days was about 600 mgm., which was a deviation from his usual output by about 300 mgm. Special care was taken to ensure that the total volume of urine was collected, and it was certain that these low values could in no way be attributed to incomplete collection. This fall,

TABLE I.—*Showing the Total Daily Amounts of Various Constituents Excreted in the Urine.*

Date.	Total nitrogen in gms.	Total calcium in mgms.	Total acidity, c.c's. N/10NaOH.	Total phosphates in mgms. P.
2.iii.44	—	316	—	857
3.iii.44	—	—	—	—
4.iii.44	—	**276**	—	**702**
5.iii.44	—	**299**	—	**737**
6.iii.44	—	292	—	790
7.iii.44	11·8	353	—	881
8.iii.44	9·5	352	355	691
9.iii.44	10·2	308	338	—
10.iii.44	9·4	308	412	680
11.iii.44	**10·5**	**284**	**381**	**545**
12.iii.44	**11·0**	**267**	**356**	**587**
13.iii.44	10·5	244	363	702
14.iii.44	9·8	320	420	306
15.iii.44	9·7	129	369	761
16.iii.44	10·7	243	277	609
17.iii.44	10·3	291	450	650
18.iii.44	**10·8**	**209**	**348**	**586**
19.iii.44	**11·0**	**192**	**357**	**691**
20.iii.44	9·8	192	339	720
21.iii.44	9·7	202	402	580

TABLE II.—*Showing the Daily Values of the Blood Pressure and Pulse and Respiration.*

Date.	Blood pressure. Diastolic, mm. Hg.	Blood pressure. Systolic, mm. Hg.	Pulse, per minute.	Respirations, per minute.
31.xii.43	74	138	74	20
1.i.44	**84**	**140**	**80**	**20**
2.i.44	**82**	**150**	**78**	**20**
3.i.44	78	136	70	18
4.i.44	80	138	64	20
5.i.44	68	120	69	18
6.i.44	72	114	62	18
7.i.44	72	122	72	18
8.i.44	**78**	**148**	**74**	**20**
9.i.44	**86**	**144**	**76**	**20**
10.i.44	76	118	70	20
11.i.44	74	120	64	18
12.i.44	74	126	63	18
13.i.44	74	112	62	18
14.i.44	66	114	64	18
15.i.44	**68**	**132**	**64**	**20**
16.i.44	**78**	**136**	**74**	**20**
17.i.44	68	114	64	18
18.i.44	78	136	62	18
19.i.44	74	128	61	16
20.i.44	80	132	61	18
21.i.44	74	128	66	18
22.i.44	**68**	**144**	**80**	**20**
23.i.44	**80**	**180**	**80**	**20**
24.i.44	66	114	74	20

moreover, was peculiar to creatinine, and was not exhibited by any other urinary constituent.

(B) *Urinary Constituents showing No Variation in Relation to the Mental Cycle.*

These results are given in the appended tables. They show all the substances estimated during cycles of different periods. It is seen that the values for pH

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TABLE III.—*Showing the Concentration of Various Constituents in the Blood Each Day.*

Date.	Serum chlorides mgm.% $NaCl_2$.	Non-protein nitrogen, mgm.%.	Urea nitrogen, mgm.%.	Alkali reserve, c.c. CO_2%.	Creatine, mgm.%.	Total phosphorus in mgms.% P.	Haemoglobin, Sahli.	Sugar in mgms.%.	Calcium in mgms.% Ca.
11.viii.43	—	—	—	—	—	—	—	76	9·3
12.viii.43	—	—	—	—	—	—	—	101	9·3
13.viii.43	—	—	—	—	—	—	—	75	9·8
14.viii.43	—	—	—	—	—	—	—	**64**	**10·0**
15.viii.43	—	—	—	—	—	—	—	**91**	**10·4**
16.viii.43	—	—	—	—	—	—	—	108	9·8
17.viii.43	—	—	—	—	—	—	—	68	11·1
18.viii.43	—	—	—	—	—	—	—	90	10·9
15.xi.43	359	33·2	14·3	58·4	5·9	36	106	—	—
16.xi.43	342	25·2	14·1	59·4	4·1	28	100	—	—
17.xi.43	352	25·9	13·2	57·4	4·5	29	102	—	—
18.xi.43	360	35·0	13·8	54·2	7·3	—	108	—	—
19.xi.43	358	40·4	15·1	61·3	8·7	40	109	—	—
20.xi.43	**372**	**36·0**	**16·5**	**60·2**	**5·9**	**28**	**105**	—	—
21.xi.43	**360**	**33·7**	**15·7**	**59·5**	**6·1**	**24**	**107**	—	—
22.xi.43	372	33·6	15·9	57	7·1	30	104	—	—
23.xi.43	353	33·2	15·4	61·3	5·1	35	106	—	—
24.xi.43	340	38·8	12·5	56·7	6·2	48	102	—	—
25.xi.43	357	35·0	15·7	61·4	6·8	40	106	—	—
26.xi.43	362	41·6	15·3	—	6·1	36	103	—	—
27.xi.43	**359**	**32·3**	**14·4**	—	**4·6**	**32**	**106**	—	—
28.xi.43	**356**	**30·4**	**13·5**	—	**3·9**	**33**	**105**	—	—
29.xi.43	361	34·8	15·5	—	5·9	24	108	—	—
30.xi.43	362	35·6	16·7	—	5·2	—	106	—	—
1.xii.43	380	29·6	16·0	—	4·5	46	108	—	—
2.xii.43	378	36·1	16·2	—	4·7	33·5	104	—	—
3.xii.43	365	39·6	13·7	—	4·2	40	105	—	—
4.xii.43	**379**	**35·6**	**16·5**	—	**4·2**	**30**	**110**	—	—
5.xii.43	**364**	**33·5**	**12·7**	—	**5·8**	**39**	**107**	—	—

TABLE IV.—*Showing Total Daily Amounts of Various Constituents Excreted in the Urine.*

Date.	Volume in c.c.	Total chlorine in gms.	Total sodium in gms.	Total creatinine in mgms.	Total potassium in gms.	Total nitrogen in gms.	Total urea nitrogen in gms.	Total phosphorus in mgms. P.	Total ammonia in mgms.
31.xii.43	800	3·52	1·98	1,136	1·30	11·1	8·6	644	256
1.i.44	**745**	**2·91**	**1·97**	**1,430**	**0·80**	**8·6**	**6·9**	**655**	**402**
2.i.44	**2,010**	**6·55**	**3·94**	**1,105**	**0·80**	**10·1**	**8·7**	**542**	**361**
3.i.44	850	2·91	1·66	1,173	1·05	9·3	7·9	1,710	331
4.i.44	905	3·40	2·33	1,240	1·21	10·2	8·2	805	398
5.i.44	750	3·52	2·28	1,125	1·3	11·0	9·8	780	405
6.i.44	885	4·12	2·68	1,318	1·06	15·5	13·5	1,000	380
7.i.44	730	3·27	2·06	1,284	0·98	11·6	9·7	674	394
8.i.44	**865**	**4·49**	**2·85**	**1,211**	**1·28**	**12·8**	**11·9**	**860**	**371**
9.i.44	**1,775**	**5·11**	**3·02**	**870**	**0·97**	**9·7**	**9·0**	**462**	**355**
10.i.44	690	2·13	1·40	1,124	1·15	10·4	9·4	729	408
11.i.44	760	2·30	1·47	1,358	0·91	12·3	11·2	808	—
12.i.44	535	2·61	1·44	950	0·51	9·8	8·6	753	—
13.i.44	565	3·27	1·41	1,152	0·75	9·9	9·2	734	—
14.i.44	575	3·21	1·55	1,198	0·74	10·5	9·1	736	—
15.i.44	**740**	**3·21**	**1·75**	**999**	**0·56**	**14·1**	**10·4**	**585**	—
16.i.44	**2,700**	**5·88**	**4·08**	**864**	**1·05**	**17·9**	**11·3**	**742**	—
17.i.44	1,210	2·92	2·19	968	1·06	10·0	7·9	1,110	—
18.i.44	1,050	2·79	2·02	966	0·81	9·2	7·5	1,108	—
19.i.44	805	3·33	2·08	942	0·80	10·0	9·3	578	—
20.i.44	800	4·37	2·64	1,224	0·84	11·8	10·9	380	—
21.i.44	700	4·06	2·38	1,106	1·10	10·6	8·9	788	—
22.i.44	**1,102**	**3·64**	**2·64**	**1,108**	—	**9·0**	**7·9**	**545**	—
23.i.44	**2,569**	**5·71**	**3·91**	**773**	**1·22**	**11·0**	**8·8**	**326**	—
24.i.44	1,480	2·43	1·72	888	1·19	9·8	9·2	—	—

titratable acidity, calcium, potassium, ammonia, and phosphorus are all within normal limits. There are variations in calcium and phosphorus, but these bear no relation to the mental cycle. The daily values for nitrogen vary between 10 and 11 gm., of which about 90 per cent. are contributed by urea.

Biochemical Investigation of the Blood.

The difficulties associated with repeated venepuncture restricted a long serial examination of the blood. Specimens were examined daily for three consecutive weeks, and from the results obtained only non-protein nitrogen showed any variation in relation to the mental cycle. On the day before the excessive output of urine, the results of this estimation were consistently the highest for the week. The blood sugar, plasma chloride, serum calcium, total phosphates, erythrocytes, haematocrit and haemoglobin were within normal limits, and exhibited no periodic fluctuation.

Summary.

The patient under investigation, at the age of 51, became subject to a state of depression, which lasted for 14 years without complete remission. In 1942, at the age of 65, he developed weekly mental cycles in which he was in a depression for five days, followed by a manic state of two days. At first the mania appeared in the early part of the week, and gradually shifted to the week-end. When this investigation started the mania occurred every Saturday and Sunday, but lately it has appeared on Friday and Saturday. The transition from one phase to the other was characterized by a mixed state, showing both depressive and manic features. This patient belongs to a small group recognized by Kraepelin, which is characterized by the onset of depression in late middle age, changing in old age to a manic depressive cycle.

Closely correlated with his mental cycles are cyclic clinical and metabolic fluctuations. There was a definite rise in the blood pressure, pulse and respiratory rates, during the manic phase, and a corresponding fall during the depression. The basal metabolism estimated for three weeks was found to be plus 30 in the mania and about minus 10 during the depression.

There was a gain of 2 to 3 lb. in weight during the depression, and a corresponding weight loss during the manic phase. There was a regular diminution of creatinine in the twenty-four-hourly urine passed in the period during which the transition from depression to mania occurred, although the urinary volumes on these days were the highest for the week.

The most marked fluctuations found were those in the water, chloride, and sodium output in the urine. The water excretion for the two days of mania amounted to nearly half the weekly total, and the amounts of sodium and chloride were correspondingly high on these two days. There was, therefore, a cyclic metabolic fluctuation, which consisted of a retention of water and salt in the depressive phase, and a release of these in the manic phase. This means that the urinary constituents showing variation were probably derived from the extracellular body fluid.

Furthermore, it appears that a sudden rise in the flow of the urine started when the patient was still in his depression, and was maintained at this high rate during the opening stages of his mania. By the time the patient had reached his most excited state this rate had already decreased. Also, there appeared to be no connection between the excessive output of the urinary constituents and the rise in blood pressure, pulse and respiratory rates during these transitions.

Further investigations on this case are in process, and the results of these will be published later.

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