THE UREA CLEARANCE TEST IN PSYCHOTICS.

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IN the routine examination of the urine of patients admitted to this hospital one is struck by the frequency of albuminuria. For example, 27·4% of 667 consecutive female admissions had a trace of albumin in the urine (i.e., a faint cloud appeared when the heat test was applied), while 37·2% had more marked albuminuria (i.e., the urine showed a thick cloud when the heat test was applied); only 35·4% were entirely free from albuminuria. Of 517 consecutive male admissions 20% had a trace of albumin in the urine, 19·5% more marked albuminuria, and 60·5% were free from albuminuria. B. H. Shaw (1) at Stafford found even higher percentages in his 250 admissions in 1935.

Though the factors causing albuminuria are many, such as chronic nephritis, alcoholism, toxic states, febrile states and endocrine dysfunction, these figures were so striking that it seemed worth while to examine the renal efficiency of a group of patients.

Shaw examined the renal function of 44 patients suffering from various types of mental disorder by Rosenberg's modification of Volhard's method. By this method the urine is collected for 24 hours in separate portions under certain standard conditions. The adopted normal criteria are that the specific gravity should reach 1027 in at least one of the specimens, and the total volume in 24 hours should not exceed 750 c.c. He found defective concentration in 34% of the cases examined, and polyuria in many cases, especially in the manic-depressive and melancholic groups.

The chief function of the renal tissue is to eliminate solid substances from the blood in aqueous solution. An important characteristic of the normal kidney is its power of eliminating the required quantity of solids regardless, within wide limits, of the amount of water available for their solution. In most cases of renal disorder, especially in the stage of compensation, examination of the nitrogenous constituents of either urine or blood does not yield any valuable information regarding the degree of functional impairment. The introduction of simultaneous analyses of blood urea and urinary urea by Grehaut in 1904 constituted a great advance in the study of renal efficiency. Then followed Ambard's famous coefficient, now largely given up, but of importance as the first attempt to express mathematically renal functional

capacity. The blood-urea clearance determination constitutes the most sensitive method at present available for the estimation of the degree of functional renal damage.

Eleven cases of epilepsy and 34 cases of melancholia have been examined by the method of Addis modified by Van Slyke (2, 3). This method is intended to measure the renal efficiency in terms of the number of cubic centimetres of blood cleared of urea by the urine per minute; in other words, the volume of blood which contains the same amount of urea as is excreted per minute in the urine.

Procedure Employed.

After a light breakfast from which tea, coffee and other diuretics are excluded the bladder is emptied and the urine passed is discarded. The urine is then collected for the next two consecutive hours, separately. During the second hour a small sample of blood is taken (0·5 c.c.) from the median basilic vein and oxalated. The following estimations are carried out without delay:

Urine, 1st hour: Volume, urea content.
Urine, 2nd hour: Volume, urea content.
Blood: Urea content.

The method of analysis employed was a micro-technique using the Conway unit and Conway micro-burette (4), which we have found to give highly satisfactory results. It may be briefly described as follows:

The unit is like a little saucer covered with a ground-glass lid and has an inner compartment. 1 c.c. of standard acid (0·00667 N.) is put in the inner compartment, and 0·2 c.c. blood with 1 c.c. water and 0·05 c.c. of a buffer solution (consisting of 6·9% dihydrogen sodium phosphate and 17·9% disodium hydrogen phosphate) are put in the outer compartment, along with one half of a 25-mgrm. tablet of urease Dunning, suitably ground, and the cover placed in position. The reagents in the outer compartment are mixed by gently rocking the unit. This is placed in the 37° C. incubator for 15 minutes. Then 1 c.c. saturated potassium carbonate solution is added to the outer compartment and mixed with the other reagents by rocking the unit. After a further hour's incubation the acid in the inner compartment is titrated against 0·00267 N. sodium hydroxide. The urea plus ammonia content of the urine is estimated by the same method, using 0·2 c.c. of a 1 : 50 dilution of urine. The ammonia content is simultaneously estimated, using 0·2 c.c. of a 1 : 4 dilution without, of course, urease. The urea content is obtained by subtraction.

The volume of blood completely cleared of urea =

$$\frac{\text{Urea content of urine}}{\text{Urea content of blood}} \times \text{volume of urine per minute.}$$

When the volume of urine excreted exceeds 2 c.c. per minute, the clearance

TABLE I.

No.	Initials, sex, age.	Duration of mental illness.	Physical condition at time of test.	Mental condition at time of test.	Albuminuria at time of test.	Blood urea (mgrm. %).	Urinary urea (grm. %).	Urine volume c.c. per hour.	c.c. blood cleared per minute.	Renal efficiency (%.)
	C. E. H—, female, 53 years	2 years	General debility	Depressed, delusional, hallucinations of hearing and sight, deterioration of personality	Faint trace	40·2	3·29 3·88	27 33	55 62	102 116
2	M. B. R—, female, 50 years	2 ,,	,, ,,	Depressed, delusional, auditory and visual hallucinations, deterioration of personality	,, ,,	20·8	2·00 1·95	37 38	74 75	137 139
3	A. M. W—, female, 43 years	2 ,, recurrent since aged 28 years	,, ,,	Chronic melancholia with deterioration of personality	,, ,,	22·2	1·79 1·46	130 102	175 86	230 158
4	A. J—, female, 52 years	2 years	Fair	Melancholia, visceral delusions, ideas of unworthiness, stereotyped attitude, resistive	Trace	19·4	2·45 3·03	29 31	88 112	163 207
5	E. D. H—, female, 42 years	1½ years	Underweight	Melancholia, perplexed state, retarded thought and action	—	17·0	2·13 2·04	17 23	67 74	124 138
6	A. M—, female, 51 years	1 year	Fair, well nourished	Melancholia, mildly agitated, retarded thought and action, ideas of ruin	—	15·4	2·04 2·34	20 31	76 109	141 202
7	H. M. C—, female, 56 years	1½ years	Undernourished	Involutional melancholia, agitated, apprehensive, difficult with food	Trace	22·6	1·43 1·15	19 57	36 50	67 93
8	M. G—, female, 52 years	1 year	Fair	Melancholia, ideas of contamination, now convalescent	—	32·2	2·37 2·75	34 36	55 66	102 122
9	A. W—, female, 55 years	2 months ; recurrent since aged 50 years	,,	Melancholia, retarded, lack of confidence	—	13·8	0·64 0·77	75 70	52 60	96 111
10	N. F—, female, 60 years	18 years	General debility	Chronic melancholia, stereotypies of speech and gait, delusions of impending burning	—	32·2	2·78 3·23	27 21	58 59	107 109
11	A. G—, female, 43 years	3 years	Fair	Depressed, delusions of persecution, hallucinations of hearing, antagonistic, abusive	Trace	21·0	2·82 2·34	11 17	58 59	107 109

TABLE I—*continued.*

No.	Initials, sex, age.	Duration of mental illness.	Physical condition at time of test.	Mental condition at time of test.	Albuminuria at time of test.	Blood urea (mgrm. %).	Urinary urea (grm. %).	Urine volume c.c. per hour.	c.c. blood cleared per minute.	Renal efficiency (%).
12	B. L—, female, 65 years	1 year	Fair	Convalescent from attack of melancholia	Trace	20·2	1·94 2·01	32 40	70 81	130 150
13	D. M—, female, 54 years	2½ years	General debility	Slowly recovering from profound depression, retarded thought and action	—	25·4	2·42 2·19	30 27	67 58	124 107
14	E. M—, female, 48 years	8 months	Fair	Depressed, retarded, delusions of unworthiness and of causing disease	—	23·8	1·71 1·57	33 43	53 56	98 104
15	J. S. R—, female, 58 years	1 year	General debility	Depressed, agitated, apprehensive, self-absorbed	—	13·0	1·77	33	101	187
16	M. J—, female, 60 years	5 years	Fair	Insomnia, depressed, apprehensive	Trace	20·2	2·04 1·50	21 35	60 50	111 93
17	A. P. M—, female, 60 years	2 ,, recurrent since aged 25 years	General debility	Recovering slowly from long period of depression, lassitude, inactivity	—	25·0	2·79 2·38	19 25	63 61	117 113
18	A. C—, female, 48 years	4 months; recurrent since aged 26 years	Menorrhagia and anæmia	Manic-depressive psychosis; now mildly depressed and retarded	+	16·6	1·70 1·30	21 41	61 65	112 120
19	A. McM—, female, 63 years	4 months; recurrent since aged 33 years	Malnutrition	Agitated melancholia, ideas of sin and impending judgment, hallucinations of hearing, ideas of reference	Faint trace	25·4	1·85 1·66	26 53	48 61	89 113
20	E. B—, female, 48 years	1½ years	Fair	Convalescent from attack of recurrent melancholia with suicidal impulse	—	20·2	1·94 1·47	34 37	72 57	133 106
21	E. E. R—, female, 41 years	1 year	Emaciation	Melancholia, ideas of visceral disease, refusal of food owing to delusions	—	33·8	3·54 2·67	12 17	47 42	87 78
22	I. C. F—, female, 45 years	5 years	Fair	Melancholia with suicidal impulses, affective loss; now convalescent	—	30·2	2·48 2·80	8 20	30 54	56 100

TABLE I—*continued.*

No.	Initials, sex, age.	Duration of mental illness.	Physical condition at time of test.	Mental condition at time of test.	Albuminuria at time of test.	Blood urea (mgrm. %).	Urinary urea (grm. %).	Urine volume c.c. per hour.	c.c. blood cleared per minute.	Renal efficiency (%).
23	C. E. M—, female, 64 years	1 year; recurrent since aged 51 years	General debility	Profound depression, ideas of unworthiness and impending disaster, desire for death, stereotyped attitude, silent and resistive	Faint trace	34·6	1·13 1·55	9 15	13 22	24 41
24	W. G. L—, male, 66 years	2½ years	Underweight	Melancholia, hypochondriacal delusions, deterioration of personality	,, ,,	32·8	1·08 2·38	33 16	24 37	45 68
25	G. S. T—, male, 58 years	5 ,,	Well-nourished	Chronic melancholia, slight retardation, ideas of unworthiness and physical weakness, mannerisms of gait	—	20·8	1·82 1·54	80 72	101 81	187 150
26	J. F—, male, 65 years	10 ,,	Fair	Chronic melancholia, slight agitation, ideas of unreality	Faint trace	32·6	2·24 2·65	118 137	135 185	250 247
27	G. A. S—, male, 68 years	6 months	,,	Melancholia, ideas of unworthiness and ruin, ideas of reference, egocentric, retarded	—	27·4	1·76 1·67	38 40	51 50	95 93
28	A. F—, male, 68 years	2 years	Underweight	Agitated melancholia, fear of impending disaster, ideas of physical weakness, stereotypy of utterance	—	28·0	1·85 1·98	79 47	76 63	141 117
29	D. A—, male, 65 years	2 ,,	Fair	Melancholia, ideas of ruin, lack of confidence, stereotyped utterance	—	20·0	1·59	79	87	162
30	P. G—, male, 44 years	2½ ,,	General debility, flabby, headaches	Melancholia, inertia, vague fears	—	27·0	2·16	63	82	152
31	A. P—, male, 66 years	3½ ,,	Mild diabetes	Agitated melancholia, ideas of reference, suspicious and indecisive	Trace	23·4	1·28 1·59	70 61	59 54	109 100
32	T. B—, male, 45 years	1 year	Renal glycosuria	Melancholia, ideas of unworthiness, despair, self-absorbed	—	20·4	1·63 1·95	177 84	163 78	220 144
33	R. C. H—, male, 51 years	18 years	Fair	Chronic melancholia, mild enfeeblement	—	33·8	2·38 2·46	26 34	46 55	85 102

TABLE I—*continued.*

No.	Initials, sex. age.	Duration of mental illness.	Physical condition at time of test.	Mental condition at time of test.	Albuminuria at time of test.	Blood urea (mgrm. %).	Urinary urea (grm. %).	Urine volume c.c. per hour.	c.c. blood cleared per minute.	Renal efficiency (%).
34	H. D—, male, 62 years	5 years	Fair	Melancholia, self-absorbed, hypochondriacal ideas	—	27·0	2·14 2·89	16 30	41 76	76 141
35	M. G—, female, 43 years	40 ,,	Epilepsy	Epileptic amentia	+	11·8	1·59 1·27	26 53	89 101	165 187
36	C. H—, female, 38 years	27 ,,	,,	,, dementia	—	17·0	0·82 0·79	76 96	54 59	100 109
37	I. M. L—, female, 54 years	51 ,,	Epilepsy, vasomotor disorders	,, ,,	—	23·0	1·24 0·83	55 74	52 40	96 74
38	C. G. J— female, 35 years	12 ,,	Epilepsy	,, psychosis	+ ; hyaline casts	25·0	1·24 1·80	22 39	30 58	55 107
39	R. H—, male, 28 years	13 ,,	,,	Epileptic psychosis with profound mental enfeeblement	—	20·6	1·37 1·15	68 80	70 64	131 119
40	J. L—, male, 39 years	23 ,,	Epilepsy, varicose veins, rather corpulent	Epileptic personality with minor degree of mental enfeeblement	—	21·8	1·62 1·51	65 49	77 62	141 115
41	F. K—, male, 28 years	15 ,,	Epilepsy (severe)	Epileptic psychosis with mental enfeeblement	—	28·6	2·32 2·87	37 55	61 96	113 178
42	R. O. D—, male, 46 years	21 ,,	Epilepsy (following head injury)	Epileptic personality	—	23·0	2·23 2·92	68 51	103 117	191 217
43	F. W. H—, male, 40 years	28 ,,	Fair, epilepsy	,, dementia	—	19·0	0·79 0·90	57 60	40 47	74 87
44	A. P. P—, male, 44 years	32 ,,	,, ,,	,, personality	—	21·8	1·15 1·38	57 63	51 65	94 120
45	H. J. T—, male, 42 years	25 ,,	Epilepsy (scarlatinal nephritis, age 13 years)	,, dementia	Faint trace	18·6	0·96 0·63	63 77	53 38	98 70

amounts to about 75 c.c. blood per minute. With urine volumes below 2 c.c. per minute the following formula is used :

$$\frac{\text{Urea content of urine}}{\text{Urea content of blood}} \times \sqrt[2]{\text{Volume of urine per minute}},$$

for which the standard is about 54 c.c. blood per minute. Using these figures as standard, the results found were expressed as percentages of the standard. The range normally allowable is from 70% upwards. In interpretation it is also to be remembered that if the urinary urea exceeds 2·5% in any specimen it is improbable that renal damage exists, as such a concentration is unattainable by diseased kidneys.

Results.

The table of results shows two figures for almost every patient, the first being calculated on the excretion during the first hour, and the second on the excretion during the second hour.

Figures for the renal efficiency fell below the standards adopted for normality in only 2 of the 34 melancholic patients and in 1 of the 11 epileptic patients studied.

In 17 of the cases which had a slight albuminuria at the time of the test, 6 had a renal efficiency above 130%.

The results indicate that albuminuria occurring in patients suffering from melancholia or epilepsy is rarely associated with renal deficiency.

The two melancholic cases which showed marked renal impairment have certain features in common, and have a bad prognosis. The following is a more detailed account of these cases.

No. 23. C. M—, female, aged 64. Before breakdown this patient was a bright attractive person who always had plenty of friends. There were no previous mental illnesses. In 1924, when she was 51 years old, she had a vague abdominal condition which was diagnosed as " enteroptosis ", and while complaining of this pain, she quite suddenly became depressed and suicidal. She recovered after a few months' institutional treatment, and had a remission which lasted seven years. She broke down again in 1931, and since then has had four short remissions. Her condition now is one of profound depression with the most devastating ideas of unworthinesss and auditory hallucinations accusing her of evil practices. She is very retarded and answers in short sentences with difficulty. She says she is the cause of untold suffering to others, and that she is about to be burned. She sits in a stereotyped attitude, is resistive and difficult with food, and sleeps badly. She has been in this depressive state for over a year, and the outlook is very unfavourable. Physically she has lost much weight ; the urine contains a trace of albumin, and occasionally a few hyaline casts.

No. 24. G. W. L—, male, aged 66. This patient before his breakdown was a vigorous responsible man of well-balanced mental type. His mental illness seemed to follow directly on a physical illness. In December, 1933, he suffered from erysipelas of the groin, followed by septicæmia, and then by low-grade infective arthritis of hips and spine. Almost immediately after the septicæmia he showed signs of depression with strong suicidal impulses. Since then he has improved a little at times, but always relapsed again. His condition is one of profound

depression with ideas of physical disease and persistent pessimism. He sits in a stereotyped posture, resisting efforts to help him, soils himself occasionally, and has filthy habits. He swears and is abusive when coaxed with food, and when alone sits gibbering his perseverations of physical ruin and hopelessness. He is troubled with insomnia. Physically his condition is poor; he is very much underweight, and his urine contains albumin and occasionally hyaline casts. We consider the prognosis very bad.

I have to thank my assistant, Miss E. Semeonoff, B.Sc., for much technical assistance and valuable advice, and Dr. C. C. Easterbrook, Physician Superintendent, for permission to publish the cases.

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