Urine concentration in depressive illness

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SUMMARY A total of 132 urine specimens were obtained from 17 depressed patients and 18 controls under conditions of mild water deprivation. Mean values of milliosmoles of solute and millilitres of urine excreted per hour were obtained for each subject. The depressed patients excreted significantly less solute than the control group per unit volume of urine. There was no significant difference between the solute excretion rates of depressed patients and those who had recently recovered from depression—though the trend was towards normality. The significance of these results is discussed in relation to studies on body fluids and electrolytes and the role of ADH and aldosterone in affective disorders.

There is evidence that affective disorders are associated with changes in the size of body fluid compartments and the concentration of electrolytes within them. Coppen and Shaw (1963) using isotope dilution techniques found depressed patients to have significantly raised 'residual sodium'—that is, an increase in the exchangeable sodium in cells and bone. They also found that on recovery total body water and extracellular water increased. Hullin, Bailey, McDonald, Dransfield, and Milne (1967) confirmed the latter finding. Jenner and his colleagues have studied an antidiuretic factor in the urine of a patient with a depressive periodic psychosis and suggested that the water retention is in part produced by vasopressin or a related substance (Goodwin and Jenner, 1967). In the present study we investigated the proportion of solute and solvent in the urine of a series of depressive patients, under standard conditions. We hypothesized that the changes in body water and electrolytes reported in depressive illness should be reflected in changes in urine concentration in such conditions.

SUBJECTS

1. PATIENTS The depressive group consisted of 17 patients (mean age 55 years) admitted to the M.R.C. Clinical Investigation Ward at West Park Hospital, Epsom, suffering from depressive illness. These patients were selected on clinical grounds as having a clear cut depressive illness which had previously responded to electroconvulsive treatment.

2. CONTROLS The control group (mean age 39 years) consisted of eight patients in the same ward who were

not suffering from an affective illness (five were suffering from schizophrenia and three from anxiety neurosis), and 10 members of the medical, nursing, and laboratory staff.

No subject in the investigation had a history of renal disease.

METHODS

1. ASSESSMENT OF DEPRESSION The degree of depression was measured twice weekly by clinical evaluation and by a self-rating questionnaire (Beck, Ward, Mendelson, Mock, and Erbaugh, 1961).

2. URINE CONCENTRATION It is usual to measure urine concentration as a function of the specific gravity or of the osmolality of a 'morning specimen', but Hendry, Harrison and Fletcher (1964) showed that a series of normal subjects investigated in this way showed no correlation between the urine volume and the output of solute per unit time. However, there was a linear and highly correlated relationship between volume and solute output in conditions of mild water deprivation when urine flow was less than 75 ml. per hour. They suggested that in these conditions the urine was formed under the influence of antidiuretic hormone (ADH) and that ADH influence rapidly ceased as the flow rate of 75 ml. per hour was exceeded. Glen, Halliburton, and Macdonald (1969) used this technique to measure urine concentration in patients with angioneurotic and periodic oedema and this is the method we have adopted here.

The subjects were asked to empty their bladder completely after rising in the morning. Approximately one hour later they did so again. The volume of urine passed was noted accurately and an aliquot was collected and deep frozen. The time period between the two emptyings was noted. One cup of tea was allowed the subject during this period. The osmolality of urine specimens was measured in milliosmoles per kilogram of

water on an 'Advanced Osmometer', which operates on the principle of freezing point depression. Values were then derived for each specimen of milliosmoles excreted per hour (y) and millilitres of urine excreted per hour—(x). In view of Hendry's findings, confirmed by Glen and his colleagues, that at urine flow rates of over 75 ml. per hour there was no correlation between urine solute and volume, we excluded all specimens of greater volume than 75 ml. Between two and eight specimens were obtained per subject and the mean urinary osmolality and volume per hour was calculated for each subject.

RESULTS

The osmolality and volume of each sample for the control group of 18 was found to be significantly correlated and the regression equation $y = 0.39 - x + 11.53$ ($r = 0.537$, $P < 0.05$) was calculated by the method of least squares. An overall evaluation of the degree of depression at the time of passing each specimen was made by combining the clinical and self-rating scales. Eleven patients were either moderately or severely depressed (Beck scores > 17) when their specimens were obtained; the other six patients were only mildly depressed or had recovered.

For each subject a 'predicted' value for y was calculated from the regression equation and the 'observed' value was subtracted from this. The result is called the 'residual F factor' (see Lindegard, 1953). A comparison was made between the various groups using the *t* test (see Table).

TABLE
GROUPS TESTED

Group	Subjects (no.)	Specimens (no.)	Average age of subject (yr)	Average residual F factor (m-osmole/ kg water)
A All depressives	17	73	55	4.59*
B Depressed patients before recovery	11	53	52	5.25*
C Depressed patients after recovery	6	20	59	3.40
D Non-depressive patients	8	33	39	-0.85
E Normal controls	10	26	40	0.69
F All controls	18	59	39	0.01

*Difference from control group F is $P < 0.05$.

The two control groups had similar residual F values and were combined. The depressives differed significantly from the control group ($P < 0.05$). Although there were no significant differences between patients tested when depressed and those tested when well, the latter group's F value tended to be lower—that is, more normal—than the former.

DISCUSSION

Patients suffering from depressive illness concentrate their urine less well—that is, excrete significantly less

solute per unit urine volume—than do normal subjects under similar conditions of mild water deprivation. This difference persists for at least a time after recovery. While no formal renal function studies were done in this preliminary study, there was nothing in the clinical history to suggest renal impairment. Electrolytes account for over half of the urine osmolality and most of the remainder is due to urea. Urea concentration varies widely with dietary composition. The depressive group and one control group (non-depressive patients) had identical diets.

The main hormones controlling water and sodium excretion are ADH and aldosterone. It seems likely that the levels of both are ultimately under hypothalamic control. Our results suggest that this mechanism may be disturbed in people prone to affective disorders. Though overall balance studies (Russell, 1960) showed no significant change in sodium, potassium, or water balance with recovery from depression, the more recent isotope dilution studies do show a redistribution of electrolytes and water within the body. Possibly there is a lessening of sensitivity of the control mechanism so that, though an overall balance is maintained, there is a slower and less effective response to demands made in renal concentration than occurs in non-depressive subjects. The problem is being further investigated.

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REFERENCES

- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., and Erbaugh, J. (1961). An inventory for measuring depression. *Arch. gen. Psychiat.*, **4**, 561-571.
- Coppen, A., and Shaw, D. M. (1963). Mineral metabolism in melancholia. *Brit. med. J.*, **2**, 1439-1444.
- Glen, A. I. M., Halliburton, I. M., and MacDonald, A. C. (1969). The effect of stress and of mild dehydration on renal solute output in angioneurotic and periodic oedema. *J. psychosom. Res.*, **13**, 61-66.
- Goodwin, J. C., and Jenner, F. A. (1967). The cyclical excretion of a sodium thioglycollate-resistant antidiuretic factor by a periodic psychotic. *J. Endocr.*, **38**, xxiv.
- Hendry, E. B., Harrison, I. M., and Fletcher, M. J. (1964). The excretion of water and of solute by the normal urinary system. *Clin. chim. Acta*, **10**, 243-252.
- Hullin, R. P., Bailey, A. D., McDonald, R., Dransfield, G. A., and Milne, H. B. (1967). Variations in body water during recovery from depression. *Brit. J. Psychiat.*, **113**, 573-583.
- Lindegard, B. (1953). Variations in human body-build; a somatometric and x-ray cephalometric investigation in Scandinavian adults. *Acta psychiat. scand.*, Suppl. 86.
- Russell, G. F. M. (1960). Body weight and balance of water, sodium and potassium in depressed patients given electroconvulsive therapy. *Clin. Sci.*, **19**, 327-336.