

### ENDOCRINE POSSIBILITIES IN MANIC DEPRESSIVE ILLNESS

DEAR SIR,

Paschalis *et al* (1) have published results of sweat analyses in persons in the manic phase of manic depression which show that the  $K^+/Na^+$  ratio is too high and that conversely it is too low in depressives. This suggests that aldosterone levels might be too high in mania and too low in depression.

Reinberg *et al* (2) have recently shown (in man) that urinary levels of aldosterone have a very marked circannual rhythm reaching a peak of  $12 \pm 3.2$  in May and a nadir of  $3.5 \pm 2.3 \mu\text{g}/24 \text{ hrs}$  in October. It has long been known that manic attacks are particularly common in early summer (3) which again suggests an association between mania and high levels of aldosterone. Finally it has recently been shown that spironolactone—a specific aldosterone antagonist—is successful against mania (4).

Paschalis' results indicate that a faulty  $K^+/Na^+$  ratio is not the only disorder present in manics; from their figures it is clear that the sweat is far too concentrated i.e. there is fluid retention also. This could be due either to low cortisol levels or to high levels of antidiuretic hormone (ADH). The fact that lithium alleviates mania and suppresses ADH suggests that the latter is the cause. Conversely depressives have very dilute sweat (1) and most drugs which improve depression raise ADH (5). However, one should be careful about jumping to the conclusion that manic/depression is a disorder of ADH because it is difficult to distinguish between the activities of cortisol and of ADH which have a mirror-image relationship to each other e.g. rats with congenital diabetes insipidus can be improved by adrenalectomy, but they can be almost normalized by hypophysectomy (which removes cortisol but leaves aldosterone) (6). Conceivably giving lithium to manics is the exact converse of this last. It has been shown, for instance, in a 48-hr cycling manic-depressive that urinary 17 OCHS levels were low on manic days and high on depressive ones (7). It has also been shown that serum cortisol levels in depressives are high (8); this will cause water losses easily confused with ADH inadequacy. Raising ADH levels may correct this just as adrenalectomizing rats with diabetes insipidus corrects their condition. It need not mean that depressives have low levels of ADH any more than that rats with diabetes insipidus are really suffering from hyperadrenalism. Moreover, it has just been shown that in at least one group of depressives there was no abnormality of ADH levels (9).

Reinberg *et al* have shown that serum cortisol also

has a circannual rhythm, the peak being in February and the nadir in September. So perhaps cortisol-release is stimulated by cold; cold-diuresis suggests that this might be so.

Manic onset correlates better with mean temperature than with day-length (10). This may well be true also of aldosterone which probably rises in summer to offset sodium losses due to heavier sweating. In conditions of sodium shortage aldosterone output is primarily controlled by the renin/angiotensin II system (11) and angiotensin II is thought to inhibit ACTH release. This might explain the apparent inverse relation between aldosterone and cortisol.

Reinberg *et al* have also shown that the circadian rhythms of cortisol and aldosterone mimic the circannual ones. Although the peak times for both hormones vary with season, that of aldosterone always follows that of cortisol by several hours and rarely occurs before noon, so perhaps its rhythm is controlled by the diurnal temperature which rises normally until mid-afternoon. Perhaps the tendency of 48 hr-cycling manic-depressive to switch moods in the early hours is due to the clinical temperature reversal around 2–3 a.m. It even seems possible that the improvement in unipolar depressives as the day wears on might be correlated with the progressive rise in the aldosterone/cortisol ratio.

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#### References

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## Some Books Received

- Psychiatric Medicine Update: Massachusetts General Hospital Reviews for Physicians.** Editor-in-Chief THEO C. MANSCHRECK. New York: Elsevier North-Holland. \$24.95.
- Psychobiology of Essential Hypertension.** By HERBERT WEINER. New York: Elsevier North-Holland. \$14.95 paper, \$26.00 cloth.
- The Symptom Iceberg: A Study of Community Health.** By DAVID RAINSFORD HANNAY. Henley-on-Thames: Routledge & Kegan Paul. £5.95 (paperback).
- I Haven't Had to Go Mad Here: The Psychotic's Journal from Dependence to Autonomy.** By JOSEPH H. BERKE.
- The Four Fundamental Concepts of Psychoanalysis.** By JACQUES LACAN. Harmondsworth, Middlesex: Penguin. £2.95.
- Asian Patients in Hospital and at Home.** By ALIX HENLEY. London: King Edward's Hospital Fund for London. £5.50.
- The Concepts of Illness, Disease and Morbus.** By F. KRÄUPL TAYLOR. Cambridge University Press. £6.50.
- 1979 Year Book of Psychiatry and Applied Mental Health.** Edited by D. X. FREEDMAN, A. J. FRIEDHOFF, L. C. KOLB, R. S. LOURIE, J. C. NEMIAB and JOHN ROMANO. London: TB Medical Publishers. £26.50.
- Psychopathology: Its Causes and Symptoms.** By F. KRÄUPL TAYLOR. Sunbury on Thames, Middlesex: Quartermaine House. £9.50, £5.50 (paperback).
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- Out in Inner Space: A Psychoanalyst Explores the New Therapies.** By STEPHEN A. APPELBAUM. New York: Doubleday. £14.95.
- Short-Term Dynamic Psychotherapy: Evaluation and Technique.** By PETER E. SIFNEOS. New York: Plenum Publishing. \$18.95.
- Cancer, Stress, and Death.** Edited by JEAN TACHÉ, HANS SELYE and STACEY B. DAY. New York: Plenum Publishing. \$22.50.
- Partial Hospitalization: A Current Perspective.** Edited by RAYMOND F. LUBER. New York: Plenum Publishing. \$23.50.
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- Hormones and Aggression. Volume 2.** By PAUL F. BRAIN. Edinburgh: Churchill Livingstone. March 1979. £12.75.
- Psychotherapeutic Processes.** Edited by M. KAPUR, V. N. MURTHY, K. SATHYAVATHI and R. L. KAPUR. Bangalore: National Institute of Mental Health and Neuro Sciences. Proceedings of a Seminar held in 1978.
- Recent Advances in Clinical Psychiatry.** Edited by KENNETH GRANVILLE-GROSSMAN. Edinburgh: Churchill Livingstone. 1979. £15.00.
- Mindsplit: The Psychology of Multiple Personality and the Dissociated Self.** By PETER MCKELLAR. London: J. M. Dent. 1979. £7.95.