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Correspondence

TIME, THYROID AND PSYCHOSIS

DEAR SIR,

Having just seen the September 1978 issue of the British Journal of Psychiatry, I am prompted to comment upon the two articles which address that time-honoured problem of defining the relationship between thyroid function and psychopathology (1, 2).

In sampling the serum levels of thyroid hormones with a sophisticated assay, Dr McLarty and colleagues (1) provide us with reassuring data that the prevalence of gross abnormality of thyroid function in a psychiatric population is no greater than that in the population at large. This is valuable information, and it is pleasing to know that the situation has improved since Dr Asher's observations on Myxoedematous Madness! (3). However, as the authors point out, the study was designed to measure the point prevalence of gross thyroid *pathology*. Each individual in the population sampled was studied only once and presumably the blood was taken at different phases in their respective illnesses. We can thus draw few conclusions about the *physiology* of the brain-thyroid axis in relation to any *one* category of psychiatric disease. Hence, the report that a significant difference was found between the serum levels of tri-iodothyronine and thyroxine in males with dementia compared to those with schizophrenia or affective disorder needs further study if we are to understand the implications of this statistical association. The perspective of time must be introduced, and the functioning of the brain-thyroid axis monitored at various points in the course of the illness. Thyroid function is known to be in constant flux changing with season (4), environmental challenge (5) and psychological turmoil (6). Without knowing, for example, the period of time that an individual had been in hospital prior to the blood sample for the thyroid indices being taken in the demented group as compared to those with affective and schizophrenic illness, it is difficult to come to a meaningful conclusion about the differences found between the groups. And yet, defining the *dynamics* of thyroid function in such disorders compared to a normal matched population of controls is potentially fruitful in the development of adjunctive therapeutic strategies. I suspect that we must begin to assume the perspective of both pathologist *and* physiologist in considering such issues.

The research construct underlying Dr Checkley's paper (2) is essentially one that attempts to incorporate these perspectives. Unfortunately, it is probably impossible to clarify the influence of the brain-thyroid axis upon the course of manic-depressive psychosis using retrospective data alone. While Dr Checkley offers such a caveat, he nevertheless concludes from the global data available to him that 'thyrotoxicosis has had little if any effect upon the course of the manic-depressive illnesses which have been studied'. I believe such a conclusion to be unwarranted, as the details of the time relationship between variations in physiology and behaviour are crucial in answering the question posed, and the retrospective nature of the study does not allow for a detailed analysis of such a relationship.

There is much to suggest that a prospective study would be profitable. The interaction of thyroid hormone and catecholamines has been known for many years. They have the same amino acid parent—tyrosine—and there is now increasing evidence to suggest that the thyroid hormones act as modulators of adrenergic receptor function (7). As the level of thyroid hormone available to the cell rises, receptor function appears to be predominantly of the beta type, and available catecholamines produce a greater response as measured by the behaviour of the receiving cell. If such a modulation occurs in the central nervous system, then further research into the interrelationship between the course of manic depressive illness and thyroid metabolism could be very fruitful. With manic depressive illness being a periodic disorder, for example, it is conceivable that an hyperthyroid state occurring during depression would be therapeutic, whereas the same state occurring as the switch into mania began would heighten the manic episode and therefore clinically be seen to increase psychopathology. Hence, the same physiological change could have opposite behavioural effects depending upon the phase of the underlying manic-depressive illness (8, 9). Again, placing our observations within a specific time frame becomes crucial, and it is virtually impossible to do this in retrospect.

As Dr Checkley points out, a further stimulus to a continued effort to evaluate this interrelationship comes from the established knowledge that lithium, one of the most effective anti-manic agents, does have a very marked anti-thyroid effect.

We have recently begun to study in a prospective longitudinal design an individual who has both rapidly cycling manic-depressive illness and also severe hypothyroidism when on lithium carbonate. The initial evidence suggests that the thyroid hormones may be capable of playing an important physiological role in the modulation of affective illness, a rising level of thyroid hormone available to the cell being adaptive and therapeutic during depression but maladaptive and capable of inducing mania when bipolar illness is also present.

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SWEAT LITHIUM IN MANIC-DEPRESSION

DEAR SIR,

Miller *et al* in their letter (*Journal*, November 1978, **133**, 477–8) present interesting data on the concentration of lithium in pilocarpine-stimulated sweat, and go on to suggest that in hot weather some patients may need extra lithium. In most patients, however, due to a concomitant 10-20 fold loss of sodium in sweat, there will be a reduction in renal excretion of lithium with a resultant net gain.

Measurement of electrolyte losses via skin over 24-hour periods is a cumbersome procedure. It was carried out in a 53-year-old female who was receiving a diet containing 95 mEq sodium and 80 mEq potassium, and on a daily dose of lithium carbonate 500 mgm t.d.s. (40 mEq) her serum lithium level was 1.0 mEq/L. During the 1st 3 days of the study, while she was on bed rest at a room temperature of 21–23°C (70–74°F), her daily skin losses were: sodium 0.80, 0.72 and 1.12 mEq; potassium 0.43, 0.50 and 0.70 mEq; and lithium 0.06, 0.06 and 0.07 mEq respectively. On the 4th and 5th day, the room temperature was raised to 30–35°C (86–95°F) while she was still on bed rest, the losses were: sodium 31.44 and 16.68 mEq; potassium 6.13 and 7.76 mEq; and lithium 1.43 and 1.22 mEq respectively (Saran and Russell, 1976). Thus, the amount of lithium lost via skin in hot environment was still too small to make any impact on the daily dose. In contrast, there was a marked loss of sodium.

As Miller *et al* point out, their data is not directly applicable to a clinical situation, but if one were to indulge in a theoretical exercise a patient with a serum lithium level of 1.0 mEq/L would have to lose about 3 litres of fluid as sweat per day to lose 6.9 mEq lithium (equivalent to about 250 mgm lithium carbonate), and this 3 litres of sweat would probably contain 200 mEq sodium (an estimate, as Miller *et al* do not provide figures for sodium concentration). A reduction in renal excretion of sodium by 200 mEq is likely to reduce renal lithium excretion by 50 per cent(Thomsen and Schou, 1968), which depending upon the daily dose of lithium will be in the range of 15–20 mEq. In this hypothetical patient, if sodium and lithium intake remain unchanged, lithium will accumulate at the rate of 8–13 mEq/day.

To summarize, in conditions which lead to excessive sweating there is a large sodium loss, which must be taken into account and either the dose of lithium reduced or the patient advised to increase his sodium intake.

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