

people who appeared to have a vested interest in their spouse's disability and who firmly resisted attempts to explore this aspect of the problem. Treating such patients alone seems inappropriate to me now, since a large part of the real problem lies outside them: namely, in the inability of their spouses to acknowledge their role in maintaining the patients' symptoms, and in the spouses' reluctance to undergo therapy in relation to this.

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LITHIUM THERAPY AND OPHTHALMIC GRAVES' DISEASE

DEAR SIR,

We were interested to read Dr Rosser's paper (*Journal*, January 1976, 128, p 61). We have recently had a patient treated with lithium carbonate who developed ophthalmic Graves' disease (Rundle and Wilson, 1945). This condition is characterized by classical exophthalmos and an abnormal hypothalamic-pituitary axis with normal levels of tri-iodothyronine and thyroxine and absence of other signs of hyperthyroidism. In thyroid disorder exophthalmos indicates an auto-immune process and occurs in this condition in classical Graves' disease and occasionally in Hashimoto's disease.

Case history. The patient is 35. His mother and one brother had required thyroidectomy for thyrotoxicosis, and another brother had exophthalmos. His first admission was in 1956 and there have been fifteen further admissions; most of these were for over-activity, over-talkativeness, lack of sleep and grandiose ideas. A diagnosis of manic depressive psychosis was made.

He was first treated with lithium carbonate in March 1967, at which time there was no mention of any abnormality of thyroid status or of abnormality of the eyes. He was noted to have exophthalmos, with a rather prominent thyroid, at admission in May 1968. This admission became necessary 'a few days' after he had ceased to take lithium carbonate; treatment with this was immediately restarted. No further mention of his thyroid state occurs in the notes until 1973. During the intervening period he received lithium therapy except for periods of two months and of one month during 1968. In 1973, during a further admission following his discontinuing all medication including lithium, his protein-bound iodine level was recorded as 9.2 $\mu\text{g}/100\text{ ml}$ and he

was noted to have moderate exophthalmos. A physician's opinion at that time was that he was euthyroid and that his mildly raised protein-bound iodine was a reflection of over-activity, although this level in most laboratories would be taken to indicate hyperthyroidism. After this he was not treated with lithium until June 1975. In March 1976 his eye signs became more prominent; there was some enlargement of the thyroid, but no other signs of thyrotoxicosis. He was over-active, aggressive, talkative and grandiose at this time, but had been on lithium continuously for nine months. Levels of tri-iodothyronine and thyroxine were within the normal range. However, there was a reduced response of thyroid-stimulating hormone (TSH) to thyrotrophin-releasing hormone (TRH). Values of TSH before, 20 minutes after and 60 minutes after intravenous injection of TRH were recorded as <0.5, 2.8 and 1.6 milliunits per litre. This was despite the known effect of lithium in enhancing the release of TSH after TRH injection and indicates an abnormal hypothalamic-pituitary axis: hence a diagnosis of ophthalmic Graves' disease was made (Hall *et al.*, 1970).

Discussion. This case is of interest taken alongside those of Rosser. We infer that eye signs did not occur in her cases. Nevertheless, in this case there may have been an element of the rebound phenomenon she suggests in the episodes of 1968 and 1973 occurring after self-withdrawal from lithium therapy. This explanation would not account for the exacerbation in March 1976. The case certainly indicates that a 'forme fruste' of hyperthyroidism may occur despite lithium therapy. It may be that this was Graves' disease in a predisposed subject in which the known effects of lithium were successful in minimizing the output of tri-iodothyronine and thyroxine. It is also conceivable that lithium withdrawal may have stimulated an auto-immune process, and it would certainly be of interest to look at antithyroid antibodies in patients on lithium therapy. Added circumspection might be advisable in the lithium therapy of patients with a marked family history of thyroid disorder.

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