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A metabolic profile of patients receiving prophylactic lithium therapy

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Previous findings have indicated that lithium might affect bone metabolism due to its similarity to calcium and magnesium (Birch & Jenner, 1973; Birch, 1974). Since this is a potential long-term side effect it was thought essential to screen a large number of patients for any resultant metabolic abnormalities and to use the opportunity to determine other interrelationships.

Ninety patients receiving lithium therapy for recurrent affective disorder were investigated during one of their regular visits to the out-patient clinic during which a sample is routinely taken for lithium estimation. The patient series is essentially that described by Hullin, McDonald & Allsopp (1972). A 'spot' urine sample was taken in addition to a 25 ml blood sample. The patient was interviewed and body weight and height were determined. Lithium, sodium, potassium, magnesium, calcium, phosphate, chloride, urea and creatinine were determined in both serum and urine. Serum alkaline phosphatase was also estimated.

In order to obtain values for the excretion rates and clearance of the estimated parameters, algebraic transformations were carried out on the data and a total of ninety variables was subjected to correlation analysis. Preliminary conclusions may be drawn from the results of the correlation analysis though it is expected that further findings will emerge following more detailed statistical analysis.

There is no evidence of gross abnormality in alkaline earth metal excretion. However, osteoporosis may not be readily detectable by normal clinical chemical techniques (Gallagher, Young & Nordin, 1972). Urine lithium/creatinine ratio is correlated with urine magnesium/creatinine ratio ($P < 0.01$).

Males appear to excrete lithium at a lower rate with respect to creatinine than females though this may be related to lean body mass. Premenopausal females receive a higher dose/body weight than both males and post-menopausal females ($P < 0.05$) and yet maintain a lower serum lithium. Clearance of lithium is negatively correlated with age ($P < 0.05$) in agreement with Schou (1968) though this conflicts with Fyrö, Petterson & Sedvall (1973). There is no correlation between urine lithium/creatinine ratio and urine volume/creatinine ratio indicating that lithium excretion is not apparently controlled by urine excretion rate. The lithium : creatinine clearance ratio in all groups was about 0.17, somewhat lower than that found by Geisler, Schou & Thomsen (1971).

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A selective excitatory effect of lithium on cholinoceptive neurones in the spinal cord and brain of cats and rats: a possible significance in manic-depression

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The administration of lithium salts to manic-depressives causes a marked reduction in the transport of choline into erythrocytes (Lee, Lingsch, Lyle & Martin, 1974). If this action of lithium has any significance for its effectiveness in manic-depression then lithium may have an action similar to that of hemicholinium at central cholinergic synapses. This possibility has been examined at a number of sites in brain and spinal cord, but the results were opposite to those anticipated and revealed what appeared to be a selective excitatory action of lithium on cholinoceptive neurones. This selectivity leads to the tentative suggestion that the effects may be presynaptic and restricted to cholinergic nerve terminals: lithium may have a similar action at the neuromuscular junction (Kelly, 1968; Carmody & Gage, 1973).

The experiments were carried out in cats and rats anaesthetized with pentobarbitone or urethane-pentobarbitone respectively. Lithium was administered microelectrophoretically from 5-barrelled micropipettes containing LiCl. Other barrels contained acetylcholine bromide (ACh), NaCl, hemicholinium and, in a few experiments, sodium glutamate.

The first experiments were carried out upon feline Renshaw cells in the spinal cord because they have an identifiable cholinergic input from motor axon collaterals. Lithium was administered for periods of up to 50 min whilst observing either the background firing rate or the magnitude of the discharge to a submaximal antidromic ventral root volley. On most cells there was a gradual increase in the firing rate or synaptic discharge, with little or no effect in the first 5-10 minutes. The excitation was slowly reversible. Appropriate controls demonstrated that the excitation was not due to the passage of current.

Other spinal interneurones, for which evidence of a cholinergic input is lacking, were not excited by Li or ACh. Hemicholinium depressed the synaptic discharge of Renshaw cells and also caused excitation, as reported previously (Quastel & Curtis, 1965). However, unlike Li, hemicholinium produced a similar excitation of non-cholinoceptive spinal interneurones.

In tests on supraspinal neurones in cats and rats, lithium excited most (about 80%) of all cells excited by ACh in cerebral cortex, thalamus, caudate nucleus, hypothalamus and brain stem but usually failed to excite non-cholinoceptive neurones in the same regions of the CNS. In the hypothalamus, where cells may also be excited by histamine, there was no correlation between histamine-evoked and Li-evoked excitation. There appeared to be a difference between presumed relay neurones and non-relay neurones in the thalamus in that non-relay cells were usually insensitive to Li, although equally sensitive to ACh.

The unique action of Li upon cholinoceptive neurones poses a problem in defining its mode of action but adds a further dimension to the spectrum of central actions of this ion of possible relevance to its use in the treatment of manic-depressives.

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