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Acute lithium poisoning

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LITHIUM was first discovered in 1818 by Arfvedson (1818) as an impurity in Swedish iron ore and, since then, traces of this element have been found widely distributed in salt beds and in vegetable and mineral matter. Although very much less soluble in water the compounds of lithium are like those of potassium in being depressant both to the myocardium and to the central nervous system.

Therapeutically, lithium carbonate and, more especially, effervescent lithium citrate, enjoyed a vogue towards the end of the last century for the treatment of chronic gout and rheumatism, until clinical trials showed the inefficacy of this regime. Then, just before the Second World War, lithium chloride was advocated as a salt substitute for those patients requiring a low-sodium diet, but this form of therapy was later abandoned following reports of severe lithium poisoning, some of the cases ending fatally. (Corcoran, Taylor & Page, 1949; Hanlon *et al.*, 1949; Stern, 1949).

The use of lithium salts in psychiatry began with the observation by Cade (1949) that they acted as sedatives on guinea pigs. Subsequently a number of reports (Baastrup, 1964; Baastrup & Schou, 1967; Glesinger, 1954; Hartigan, 1963; Noack & Trautner, 1951; Schou *et al.*, 1954; Schou, 1968) testified to the value of lithium in the treatment of certain psychoses and, over the last 2 years, this form of therapy has been widely practised in the management of affective disorders, though the benefits prophylactically have come under severe criticism (Blackwell & Shepherd, 1968; Saran, 1969).

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Lithium poisoning occurs when the element accumulates in the body as a result of intake exceeding excretion by the kidneys. At therapeutic serum levels there is often nausea, vomiting, diarrhoea, abdominal discomfort, lethargy, muscular weakness, sleepiness and tremor of the hands. Severe acute intoxication is characterized by ataxia, impairment of consciousness leading to coma and epileptiform fits. The latter may appear spontaneously, or on stimulation, and last a few seconds to half-a-minute. The eyes are wide open and there is hyperextension of the arms and legs, with gasping and grunting. The muscle tone is increased and the deep reflexes are brisk. (Schou, 1968). The EEG shows a decrease of alpha activity and the simultaneous appearance of theta and paroxysmal delta activity, mostly in the frontal region. Occasionally fast activity (beta) and sharp waves have been noted. (Mayfield & Brown, 1966.) When this stage appears the serum lithium level is usually over 2 mEq/l. However, in certain susceptible individuals severe side-effects have been noted at much lower levels. All these changes are reversible. In spite of the widespread use of lithium very few cases of acute over-dosage with suicidal intent have been reported. We present below such a case which presented a most unusual clinical picture.

Case report

Miss R.D., aged 45, was a woman of above-average intelligence, possessing an honours degree in English and being a librarian by profession. From 1943 onwards she had been the victim of a depressive illness, having been in hospital on seven occasions

and treated as an outpatient for the rest of the time. On 12 October 1967 she was admitted to Cane Hill Hospital, Coulsdon with a 6-week history of severe depression and within a few days she started to improve spontaneously. By 3 November she was symptom-free. Nevertheless, because of her record of recurrent severe attacks she was put on lithium carbonate 250 mg three times a day (20 mEq per day) as a prophylactic. On 13 November 1967 at 14.00 hours she suffered a transient loss of consciousness. On examination the blood pressure was 120/70 mmHg and she was noted to be jerking her arms and legs. Over the next 3 hr her blood pressure fell to 90/40 and her pulse went up to 100/min. She was now confused, unable to recognize the nursing staff and was disorientated in time and place. Jerking had increased in all four limbs, being more severe on the right than on the left and there was twitching of the right angle of the mouth. The movements of the arms and legs were characterized by clonic movements at the knee and elbow joints, with extension of the wrists and dorsiflexion of both feet. Her eyes were wide open, with deviation to the right, and the pupils were dilated. Status epilepticus was diagnosed and she was given intravenously 0.25 g of thiopentone sodium. Within minutes of this injection the patient was much calmer, although the jerking of the arms and legs was unaffected. She then admitted to having taken 5.5 g of lithium carbonate (146 mEq) the same morning. The Poisons Reference Service at Guy's Hospital was contacted and, on the advice of Dr Roy Goulding, the patient was given an intravenous infusion of 1000 ml of 1/6th molar lactate. Within 15 min of the start of the drip the convulsions decreased in both intensity and frequency and disappeared altogether in 30 min. Laboratory tests later revealed that, before setting up the intravenous infusion, the serum levels were lithium 3.2 mEq/l, sodium 140 mEq/l and potassium 4.3 mEq/l. Subsequent recovery was uneventful.

Discussion

Severe intoxication from lithium salts can occur in one of three ways:

1. A single large overdose.
2. Cumulative overdose in a patient on lithium treatment.
3. Decreased excretion of lithium in a patient receiving optimal subtoxic therapeutic dosage, due to either reduced sodium or water intake, or to intercurrent illness, especially with reduced urine output (Trautner *et al.*, 1955).

The occurrence of side-effects depends not only on the absolute level of lithium in the serum but also on the steepness of rise of the serum concentration. However, when the serum level falls, or is lowered by haemodialysis, the recovery is not immediate,

indicating that the intracellular lithium level is an important factor, or may indeed be the prime factor that determines the appearance of clinical toxicity.

In animals, the long-term excessive administration of lithium may lead to sodium loss through the kidney and a consequent lowering of the serum sodium. At the terminal stages there is also an associated rise of the serum potassium leading to cardiac arrest (Radomski *et al.*, 1950). In the cases of human intoxication following administration of lithium as salt substitute there was also a reduction in CO₂ combining power (Hanlon *et al.*, 1949; Stern, 1949; Corcoran *et al.*, 1949). However, none of these biochemical disturbances can adequately explain the production of fits. In dogs, Moracci (1931) produced tonic and clonic seizures of corresponding muscles on direct application of lithium salts to the motor cortex. In man EEG changes, such as lowering of frequency and increase of voltage appear with subtoxic doses of lithium (Mayfield & Brown, 1966). These changes become more pronounced with toxic doses.

There is no specific antidote to lithium poisoning. An attempt is usually made to increase the removal of lithium by some means or other. In volunteers Thomsen & Schou (1968) found that potassium chloride and thiazide diuretics did not accelerate lithium excretion, although urea, sodium bicarbonate, sodium lactate, acetazolamide and aminophylline all did so. The remarkable response in our patient to 1/6th molar lactate is not easily explained. It could not have been due to an increased excretion of lithium by the kidney, for the improvement began within 15 min of giving the intravenous infusion. A possible explanation could be that the lactate was responsible for raising the seizure threshold. Yet another hypothesis would be that lactate caused a prompt displacement of lithium from the central nervous system. Finally, it could just have been a coincidence.

As lithium is now widely used in psychiatric practice, especially for depressed patients, the incidence of acute intoxication to this drug is likely to increase. At present the main line of treatment is symptomatic and supportive. Where facilities and time allow, haemodialysis may be performed, although this treatment, when tried, has not been always successful (Hawkins & Dorken, 1969). Whether 1/6th molar lactate intravenously will again be successful remains to be demonstrated.

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Pseudo-Meigs' syndrome associated with a pseudomucinous cystadenoma

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MEIGS' SYNDROME is the association of a benign ovarian tumour of fibrous tissue origin (fibroma, thecoma, granulosa-cell tumour and Brenner tumour) with hydrothorax and ascites, the latter disappearing on removal of the tumour.

The pseudo-Meigs' syndrome includes all other tumours of the ovary, benign or malignant, associated with hydrothorax and ascites, which latter also disappear on removal of the tumour, and is rarely encountered. The association of the condition with a pseudomucinous cystadenoma has been reported in eleven cases (Smith & Boronow, 1967), and a further case is presented.

Case report

M.C. (Hospital No. B.45987), a married nullipara, aged 59 years, was referred to gynaecological out-patients after the routine discovery of an abdominal mass in a psychiatric unit.

There was a long history of recurrent attacks of

depression which had been managed by electroconvulsive therapy. She complained of recent shortness of breath on exertion and stated that there had been some swelling of the abdomen for 2-3 months. The menopause had occurred at the age of 52 and there had been no post-menopausal bleeding. There was no other relevant medical history. Clinical examination showed no abnormality of the cardiovascular system. Examination of the chest revealed slight displacement of the trachea to the right with reduced air entry in the left chest, and dullness at the left base.

Abdominal examination showed the latter to be distended by a cystic swelling arising out of the pelvis, equivalent in height to a 26-week pregnancy. There was shifting dullness in both flanks. Pelvic examination showed no obvious abnormality and there was no nodularity in the Pouch of Douglas. The patient was admitted for investigation.

Investigations: Hb, 14.0 g%, ESR normal, urine