

# Monitoring lithium levels



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Lithium revolutionised the management of bipolar disorder, but close monitoring of this medication is required.

## BACKGROUND

GPs are increasingly taking responsibility for managing patients with bipolar disorders. This commitment has led to changed management models.

Whereas psychiatrists once managed bipolar disorders, some psychiatrists now practise by making or confirming the diagnosis and referring the patient back to the GP – with or without detailed recommendations – for ongoing management. Thus, many GPs now prescribe and/or monitor their patients' psychotropic medications.

Lithium is one of the front-line psychotropic drugs and is a commonly recommended mood stabiliser for managing bipolar disorder. It can also be useful in augmenting antidepressant medication for unipolar depression.

Lithium was in effect 'discovered' by Melbourne psychiatrist Dr John Cade and remains one of the great Australian

medical discoveries.

The lengthy lag time between that report and lithium's more widespread use reflected both the influence of British cynicism and the need for formalised studies. The health and economic benefits of its use, as well as the impact of lithium to reduce suicide rates, were slowly appreciated.

## LITHIUM TOXICITY

While lithium is a naturally occurring element, was once an additive in some soft drinks and is variably present in water supplies, it is not an innocuous substance.

When practitioners prescribe and monitor a patient receiving lithium, they are accepting a significant responsibility. It has many side-effects – both short-term and long-term – and this column will focus on the issue of lithium toxicity<sup>0r</sup>.

Serum monitoring – after at least five days of a stable dose, and with blood collected 12 hours after the last dose of lithium – seeks to ensure that the lithium level is within a prescribed range. At the broadest level, the range is 0.5-1.5 mmol/L. Some practitioners favour a range of 0.6-0.8 mmol/L.

When sub-therapeutic, lithium is generally ineffective. At higher levels – whether at upper range levels or above – side-effects such as tremor, impaired concentration and tiredness emerge.

Lithium toxicity is marked by a variable set of symptoms, with relatively constant ones being significant tremor, gastrointestinal symptoms, restlessness, impaired concentration and delirium. Lithium toxicity is not a rare

phenomenon: one US monitoring centre received more than 5000 reports in one year. Toxicity can occur as a consequence of deliberate or accidental overdose, progressive renal failure, dehydration during extremely hot weather and from drug-drug interactions.

While lithium toxicity has not been described at low serum levels, a recent case report<sup>1</sup> indicates that a reported low serum level may not negate such a possibility.

## CASE REPORT

A 60-year-old professional man – who had previously been hospitalised with psychotic elevated and depressed mood states – had had his bipolar condition essentially controlled for over 20 years.

In the weeks prior to an urgently requested consultation, he had shown marked memory and other cognitive problems – so distinctive that his wife was concerned about a possible dementia. She had also wondered whether he might be lithium toxic and organised three lithium level tests over a two-week period – all being quantified at 0.4 mmol/L, seemingly discounting the possibility of lithium toxicity.

At clinical assessment, his cognitive impairment was substantive and he was immediately admitted to a general hospital, where an EEG indicated drug toxicity and his lithium medication was ceased. Sixty hours after his last lithium tablet, the hospital's pathology laboratory quantified his lithium level at 1.1 mmol/L. Medical management involved saline perfusion and, after a few days, his

lithium was reintroduced, as his confusion had settled.

## WHY THE FALSELY LOW LEVEL?


The pathology company was contacted (by phone and letter) and asked to explain the anomaly. Despite indicating that they would provide a report, no written response was provided.

There are likely to be two explanations. Firstly, that there is a problem with the lithium assay used by that pathology company. Secondly, that their (and perhaps other) automated assays may be susceptible to the so-called 'Hook phenomenon', where, in some quantitative immunoassays, increasing concentrations produce values that first rise and then fall, so generating spuriously low results.

As there are currently no formalised regulatory mechanisms for reporting this anomaly, it is important that lithium prescribers are aware of the possibility.

## CONCLUSION

When I informally reported this vignette to a number of distinguished Australian, US and UK psychiatrists, all but one excluded lithium toxicity on the basis of the three lithium assay levels of 0.4 mmol/L.

However, one observed that, in medicine, it is better to go by clinical impression rather than put too much faith in 'tests'. So, if it looks like lithium toxicity, seek a repeat test and request a manual – rather than automated – lithium assay. 

1. Parker, G. *Australian and New Zealand Journal of Psychiatry* 2008; 42(7):643-45.