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## Cautions when prescribing lithium

I was astonished that Dr. Melvin G. McInnis' article on using lithium to treat bipolar disorder (BD) (CURRENT PSYCHIATRY, June 2014, p. 38-44; [http://bit.ly/1ssZAUr]) did not address all the potential hazards of the medication. He discussed side effects, but only how to manage them so that patients will adhere to treatment.

I have used lithium for patients with BD, and often it is efficacious, although hazardous in overdose. Lithium toxicity can cause cardiac arrhythmias, and must be monitored closely. In addition, the effects of hydration and exercise on the lithium level, especially during summer, often are ignored.

Two of my patients, an adolescent and an adult, were well-maintained

on lithium, adhered to treatment, and had no concurrent medical problems, but developed significant toxicity for no reason that I could determine. The adult had a lithium level of 2.0 mEq/L in the emergency room; the adolescent had a lithium level of 1.8 mEq/L. Levels this high are considered potentially lethal, and because it happened without warning and without a cause that I could determine, I consider lithium to be one of the riskier mood stabilizers. I still prescribe it, but with great caution.

Dr. McInnis also did not mention the possibility of lithium-induced diabetes insipidus, a condition in which the kidneys are no longer able to concentrate urine and that is marked by excessive urination, concomitant water intake, and low urine specific gravity. It is uncommon, but I have seen it 3 times in 30 years, in a practice that specializes in psychotherapy and does not see a high percentage of patients with BD. I consider it a condition that must be kept in mind as we follow our patients in long-term treatment.

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### Dr. McInnis responds

Dr. Davis raises the issue of lithium toxicity and provides examples of 2 patients who developed levels of 2.0 mEq/L and 1.8 mEq/L. These levels clearly are well beyond the toxicity threshold of 1.3 mEq/L, and the patients wisely sought urgent care. These scenarios exemplify the need for regular monitoring of the lithium level—in particular, when there is any change in physical or mental health status. Development of significant toxicity generally has some lead-time with emerging short-term side effects (outlined in **Table 2** of my article), which underscores the importance of discussing

the nature of emerging side effects with your patient.

Dr. Davis is correct in noting that the practitioner must be aware of long-term side effects of lithium. I find it helpful to discuss these effects with the patient in the context of short-term (days or weeks), intermediate (weeks or months), and long-term (months or years) time frames (**Table 2**). Diabetes insipidus is listed as an intermediate side effect.

I am grateful to Dr. Davis for raising the issue of hydration and summer heat, a concern among parents and coaches when student athletes practice strenuously for extended hours.<sup>1</sup> Miller et al<sup>2</sup> found that the concentration of lithium was between 1.2- and 4.6-fold in forearm sweat compared with serum levels, with the implication that heat-induced sweating may lower lithium levels. Jefferson et al<sup>3</sup> studied 4 athletes after a 20-km race and found that all had become dehydrated but had a decrease in the serum lithium level. This is contrary to the widely held belief that excessive sweating predisposes to lithium toxicity.

BD is among the more lethal psychiatric disorders, and lithium is among the few medications shown to mitigate suicidal behavior.<sup>4</sup> As with any medication, lithium is not without risk, and there is a clear need for informed medical management. Any notable change in health status or physical activity in a patient taking lithium is worthy of review, with recommendations based on knowledge of the patient and medical science.

### References

1. Reardon CL, Factor RM. Sport psychiatry: a systematic review of diagnosis and medical treatment of mental illness in athletes. *Sports Med.* 2010;40:961-980.
2. Miller EB, Pain RW, Skripal PJ. Sweat lithium in manic-depression. *Br J Psychiatry.* 1978;133:477-478.
3. Jefferson JW, Greist JH, Clagnaz PJ, et al. Effect of strenuous exercise on serum lithium level in man. *Am J Psychiatry.* 1982;139(12):1593-1595.
4. Goodwin FK, Fireman B, Simon GE, et al. Suicide risk in bipolar disorder during treatment with lithium and divalproex. *JAMA.* 2003;290(11):1467-1473.

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## Monitoring calcium with lithium treatment

I appreciate Dr. McInnis's article and his recommendation to monitor the comprehensive metabolic profile, including the calcium level, before and during lithium treatment. There is an association among lithium treatment, hypercalcemia, and hyperparathyroidism.<sup>1,2</sup> This can occur by lithium reducing parathyroid hormone suppression or stimulating parathyroid glands.<sup>3</sup>

Surprisingly, many guidelines do not include a recommendation to monitor the calcium level; however, the International Society for Bipolar Disorders and other experts do recommend obtaining a calcium level before initiating lithium therapy and at least annually thereafter.<sup>1,4</sup> If hypercalcemia is present, assessing lithium and the parathyroid hormone level is recommended.<sup>3</sup>

Clinicians can continue lithium and monitor calcium if treatment is

beneficial, hypercalcemia is mild, and the patient is asymptomatic.<sup>2</sup> For a symptomatic patient or one who has significant hypercalcemia, clinicians should consider discontinuing lithium and monitoring for a normalizing calcium level.<sup>2</sup> For patients with significant hypercalcemia who need lithium therapy, consultation with an endocrinologist is advised.<sup>3</sup>

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### References

1. McKnight RF, Adida M, Budge K, et al. Lithium toxicity profile: a systematic review and meta-analysis. *Lancet*. 2012;379(9817):721-728.
2. Lehmann SW, Lee J. Lithium-associated hypercalcemia and hyperparathyroidism in the elderly: what do we know? *J Affect Disord*. 2013;146(2):151-157.
3. Broome JT, Solorzano CC. Lithium use and primary hyperparathyroidism. *Endocr Pract*. 2011;17(suppl 1):31-35.
4. Ng F, Mammen OK, Wilting I, et al. The International Society for Bipolar Disorders (ISBD) consensus guidelines for the safety monitoring of bipolar disorder treatments. *Bipolar Disord*. 2009;11(6):559-595.

### Dr. McInnis responds

Generally, calcium is included in the comprehensive biochemistry panel (Table 1). Typically, magnesium or phosphorus is overlooked, and therefore was specifically included in the table of recommendations. There is a complex relationship between lithium and calcium; Dr. Scarff's points highlight this. It is noteworthy that lithium normalizes the calcium amplitude during action potentials in neurons derived from induced pluripotent stem cells from persons with BD<sup>1</sup>; this suggests that there might be a direct mode of action in BD involving lithium and calcium. This finding further emphasizes the importance of monitoring calcium, and the wise clinician will verify that it is included in the comprehensive biochemistry panel.

### Reference

1. Chen HM, DeLong CJ, Bame M, et al. Transcripts involved in calcium signaling and telencephalic neuronal fate are altered in induced pluripotent stem cells from bipolar disorder patients. *Transl Psychiatry*. 2014;4:e375. doi:10.1038/tp.2014.12.

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