

## Lithium – Back to the elements

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A patient recently asked me, “Why are you starting me on lithium? Isn’t that what’s in batteries? If I’m supposed to be getting my mood stabilized, isn’t this going to make me like the Energizer® Bunny...?” I really couldn’t blame him for asking such questions. Why are we using battery contents to flatten out mood episodes? Why is a deadly former salt-substitute now doled out in prescription bottles? With its many and varied uses medicinally and non-medicinally as well as the urban legends surrounding lithium and its side effects, it’s no wonder there is a bit of mystery and maybe even mistrust surrounding lithium on the part of patients and providers alike.

Lithium, the third element in the periodic table, was found, quite by accident in 1817 by a Swedish Scientist named Arfwedson. He detected the presence of lithium in a metal ore and gave it its name, which is from the Greek word for “stone.”<sup>1</sup> Lithium was not isolated to its pure elemental form until 1821. In the ensuing years lithium was first little more than a laboratory curiosity, but was later put to use as a compact, light-weight source of hydrogen for emergency signaling balloons, and was used during World War II in the development of lubricating greases and heat-resistant ceramics. When a tablet form of lithium was used as a salt substitute in low-sodium diets in 1949-50, there were many reports of severe lithium side effects, and some deaths.<sup>2</sup> Lithium was in high demand during the Cold War era with the production of nuclear fusion weapons. Both lithium-6 and lithium-7 produce tritium when irradiated by neutrons, and are thus useful for the production of tritium, which is used as a component in the triggering mechanism of thermonuclear weapons.<sup>3</sup> Today, just 2% of lithium use in the United States is for pharmaceutical purposes, with the remaining 98% put to use in ceramics, batteries, lubricating greases, continuous casting, air treatment and other varied purposes.<sup>4</sup>

The first recorded use of lithium for the treatment of mania took place in 1871. This was based in part on the theory that “urate imbalances” were responsible for disease. Around this time, it was discovered that a solution of lithium carbonate could dissolve stones made of urate. Use of lithium carbonate (the current pill form of

lithium) to prevent depression came in 1886.<sup>2</sup> In 1948, Australian psychiatrist, John Cade used lithium to treat patients with mania after noting that pigs injected with lithium urate became placid and somewhat tranquilized. Use of lithium for the treatment of bipolar disorder did not catch on quickly though, as lithium therapy was hotly debated and was not approved for use in the treatment of mania in the United States until 1970.<sup>5</sup> Following this, lithium therapy expanded and was utilized widely for the treatment of bipolar mania and depression and in other psychological disorders as well. However, owing to its adverse effects with chronic therapy, sometimes inconsistent efficacy, and possibly also because of the continued lack of full explanation regarding its mechanism of action, the idea of medication therapy using lithium has become somewhat tarnished of late. Further, the fact that lithium is no longer a particularly profitable or highly marketed treatment, coupled with the introduction of dozens of potential therapeutic alternatives for bipolar disorder treatment have further reduced lithium’s prominence in the world of psychopharmacology. Somewhat ironically, this soft, silvery-white metal exhibits a metallic luster when cut open, but contact with moist air corrodes the surface quickly to a dull silvery gray, then black tarnish. Throughout its history, the employment of lithium for the treatment of mental illness has followed a similar storyline, shining initially, then becoming clouded and somewhat obscure.

In this issue of the MHC, we intended to polish lithium off a bit to remind us of its usefulness and provide some tips for maintaining its luster. Goucher and DeJongh review the literature to comment and update us on lithium’s use in bipolar disorder and major depressive disorder, respectively. Additional commentary will refresh your memory regarding lithium’s complex pharmacokinetics, its unique niche when used in combination with clozapine, and its surprising relative safety when used in pregnancy.

### REFERENCES

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