LITHIUM: THE MINERAL AS MEDICINE

Lithium is one of the original earth elements.

As far as cosmologists know, there were only three elements present when the universe was first formed some 13.8 billion years ago: hydrogen, helium and lithium. As one of the three original elements, lithium can still be found in plenty throughout our atmosphere. Meteorites, the sun and stars burn brightly with the flame of this highly reactive element. Here on earth, lithium remains a major mineral component of granite rock, and also lingers in significant amounts in sea water, mineral springs and soils. Every organ and tissue in the human body also contains the mineral

lithium.

Lithium was given its official name by a chemist named Johan August Arfvedson in 1817. He found the element when researching petalite - a rich mineral deposit found in soils- on a remote Swedish island. The metal was aptly named lithium, a term derived from the Greek word *lithos* meaning literally "from stone." Subsequent research has given scientists a greater appreciation of this alkali earth metal, which is now known to be relatively common in the Earth's upper crust. As the 27th most abundant element it can be found in rock sediments, salt flats and mineral springs at varying concentrations throughout the globe. The largest deposits of lithium are salars or vast saline basins in the deserts of South America. But the mineral is also highly concentrated in clay beds and hard rock underground mines dotting Australia, China and some parts of North America.

As the lightest of all solid elements, lithium is highly reactive, malleable, and also a good conductor of heat and electricity. These characteristics have contributed to its wide applications in industry today, such as in the development of technologies like batteries and devices for telecommunication, aircraft parts, focal lenses and even the fusion material in power plants. The demand for lithium-ion batteries as a durable power source for camcorders, cameras, cell phones, portable computers and eco-friendly vehicles has caused lithium commodity prices to rise in recent years, creating speculation as to whether sufficient volumes of lithium are even available to sustain global demand. This will become an increasingly important issue for us to consider in research and practice, as over-mining and environmental contamination threaten stores of lithium in certain regions around the globe.

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The healing properties of lithium have been recognized for centuries.

A physician from ancient Ephesus observed its benefits but did not know its name. When asked how to treat people undergoing manic episodes, he responded, "*Utendum quoque naturalibus aquis, ut sunt nitrosae,*" meaning,"Use should be made of natural waters, such as alkaline springs." Lithium, it turned out, was present in abundance in these springs.

Since this observation from ancient times, lithium has undergone a shifting and dramatic history in medicine, sometimes celebrated as a panacea, sometimes reviled as toxic, sometimes totally forgotten before reappearing in scientific experiments in another country in another context. Still, after the intervening centuries and billion dollar pharmaceutical breakthroughs, no drug has superseded lithium for stabilizing mood and preventing suicide in patients with bipolar disorder.

Soranus from Ephesus was followed by centuries of silence on the issue. Almost 2000 years later, the treatment benefits of lithium were publicized by London doctor Alfred Baring Garrod, who used it to treat patients with gout. After discovering uric acid in the blood of his patients with gout, he wrote about pioneering the use of lithium in his 1859 treatise, *The Nature and Treatment of Gout and Rheumatic Gout.* He explained that uric acid deposits in cartilage are dissolved in vitro by carbonate lithium. Between the 1850's and the 1890's, several other physicians experimented with lithium treatment because at the time uric acid was viewed as a critical factor in many diseases.

Both the popular and medical literature of the period contain enthusiastic reports of the benefits of lithia waters. For example, Manadnock Lithia Spring Water was touted as "the most wonderful natural lithia spring water now known in the world. Recommended for gout, dyspepsia, rheumatism, eczema, sugar diabetes, Bright's disease, gall stones; also reduces temperature in all fevers; and all disease of the kidneys, asthma, etc. As a beautifier of the complexion it has no equal" (Strobusch, AD, Jefferson, JW, 73).

Soon after this rave review, public enthusiasm for alkaline springs fizzled. A study by the U.S. Bureau of Chemistry had found that all the lithia waters on the American market contained only infinitesimal traces, or less than one part per million, of lithium, not nearly enough to bring about the cures for which they were advertised. So the lithia springs as a treatment for disease fell out of favor.

As lithia springs faded from the news, lithium tablets appeared on the market. For several decades tablets and other products containing lithium were recommended for treating kidney and bladder problems as well as gallstones. The Sears, Roebuck & Company Catalogue of 1908 advertised Schieffelin's Effervescent Lithia Tablets for a variety of uric acid afflictions. By 1907, The *Merck Index* listed 43 different medicinal preparations containing lithium. In 1929, a soft drink inventor named Charles Leiper Grigg even created a new lithiated beverage he called Bib-Label Lithiated Lemon-Lime Soda, now known as "7-Up." The beverage contained lithium citrate until 1950, and was originally known and marketed for its potential to cure hang-overs after a night of drinking alcohol, and to lift mood. In the 1930's, the varied products containing lithium on the market were advertised to control renal calculi and uric acid problems. In 1939, the German pharmaceutical index, *The Red*

List, featured "Lithosanal Bauer," a combination of lithium citrate and other components for the purposes of treating kidney and bladder problems and gallstones.

Meanwhile, toward the end of the 1800's, some American physicians were investigating possible psychiatric benefits of lithium. In 1870, Philadelphia neurologist Silas Weir Mitchell recommended lithium bromide as an anticonvulsant and a hypnotic. William Hammond, professor of diseases of the mind and nervous system at the Bellevue Hospital Medical College in New York, was the first physician to prescribe lithium for mania. He found it more effective than any other treatment he had ever used for calming mood in his patients with manic episodes.

A significant twentieth century revival of lithium as a possible psychiatric remedy began in 1949 in Melbourne, Australia, when John Cade, who knew of Garrod's success in lithium treatment a century before, speculated that a condition involving uric acid might underlie his patients' mania. He began treating patients with lithium citrate and lithium carbonate. Some patients responded strikingly well, even after years of illness and unsuccessful treatment with other preparations. Although it was published in an obscure journal, Cade's article described a well-designed and executed research study and focused on rational presentation of results rather than rhapsodizing about the virtues of a particular treatment. The benefits that lithium conferred to patients with mania were dramatic. Because of his well-structured study and the dramatic results, some historians of medicine consider that John Cade ushered in modern psychopharmacology.

Unfortunately, the timing of Cade's treatment successes was ill-fated. The very same year, 1949, adverse reaction reports surfaced in the media about patients who were taking lithium in a different form for a completely different purpose. As physicians encouraged their patients with heart disease and hypertension to avoid sodium chloride, lithium chloride was marketed as an alternative to sodium chloride in four different preparations: Salti-salt, Milosal, Foodsal, and Westsal. In the late 1940's and early 1950s, physicians around the country released reports of patients who developed lithium poisoning after they had used Westsal. Dr. A.M. Waldron documented that four of his patients who used Westsal developed weakness and blurred vision. The next year, Dr. John H. Talbott collected and released case studies of his patients who suffered lithium poisoning. Excessive intake of lithium coupled with the tendency of the body to retain more lithium when sodium intake was low led to disastrous results. Several deaths were also reported, leading the FDA to ban the use of lithium salt substitutes. "Stop using this dangerous poisoning at once!" exhorted the FDA. Lithium fell out of favor with the medical community.

Despite the lithium chloride debacle, Cade's study prompted a few isolated studies of lithium in

Australia and in France. Cade himself left lithium research behind and began to explore the psychotropic effects of other alkali metals in his lab in Australia.

Yet by the end of the decade a "lithium underground" had formed of American physicians prescribing lithium in the absence of official FDA approval. Finally, the FDA approved lithium in 1970 as a new investigational drug for use in treatment of acute mania. By this time many other countries had already approved lithium, including France, the United Kingdom, Germany, and Italy. In 1974, lithium was approved to prevent recurrent mania.

What will be the next chapter in the dramatic and shifting history of lithium? It seems paradoxical that this simple substance, the third element in the Periodic Table, still achieves better treatment results in bipolar patients than the new and expensive products of pharmaceutical research and development. If lithium as treatment once again fades from view, the loss will not be to the pharmaceutical companies which, after all, have nothing to gain from the success of a low-cost treatment. Those who will lose are the patients whose uncomfortable highs and lows and suicidal impulses could be better kept in check by psychiatry's best and oldest drug.

Image Credit: Illustration of the Londonderry Lithia bottling plant from Hurd Town & City Atlas of New Hampshire, 1892