

Johan Schioldann: History of the Introduction of Lithium into
Medicine and Psychiatry
Birth of modern psychopharmacology 1949

Part II
Renaissance of lithium therapy. Birth of modern psychopharmacology 1949

Chapter 23. The lithium toxicity scare

The issue of lithium's potential fatal toxicity surfaced again in 1949 in the USA, where the year before lithium substitute salts—Westsal, Foodsal, Salti-salt and Milosal—had been introduced into the treatment of hypertension.¹⁰¹⁰ In February 1949 several newspapers and radio announcements were made as to the likely toxic effects of these remedies.¹⁰¹¹

The American Medical Association as well as the U.S. Food and Drug Administration (FDA) took prompt action. On 26 February 1949 warnings were issued in the *Journal of the American Medical Association (JAMA)*¹⁰¹² with respect to the use of 'preparations that have been sold as salt substitutes', and an 'intensive program' was instituted to recall all lithium-containing salt substitutes from the market.

Two weeks later, Corcoran, Taylor and Page,¹⁰¹³ also in *JAMA*, provided a description of the syndrome: lithium poisoning from the use of salt substitutes. Seven cases had been observed. In two patients the intoxication seemed to have been 'a contributory cause of death' (due to 'Westsal'). The authors commented on the syndrome, based on Cleaveland's experiment with lithium.

In the same issue of the journal, Hanlon and his associates,¹⁰¹⁴ other than reporting another death from lithium intoxication, provided a survey of literature, including Good's 1903 paper.¹⁰¹⁵

¹⁰¹⁰ cf. Johnson, 1984, op. cit., pp.46–57 ('The toxicity panic').

¹⁰¹¹ Anon.: 'Case of the substitute salt'. *Time* 28 February, 1949, p.27, quoted in full in Johnson, op. cit., 1984, p.48.

¹⁰¹² 'Current comment: Salt substitutes—a warning'. *JAMA* 1949;139(Feb. 26):588.

¹⁰¹³ Corcoran AC, Taylor RD, Page IH.: 'Lithium poisoning from the use of salt substitutes'. *JAMA* 1949;139 (March 12):685–688.

¹⁰¹⁴ Hanlon LW, Romaine M, Gilroy FJ, Deitrick JE.: 'Lithium chloride as a substitute for sodium chloride in the diet. Observations on its toxicity'. *JAMA* 1949;139:688–692.

¹⁰¹⁵ Good CA.: 'An experimental study of lithium'. *Am. J. Ment. Sci.* 1903;125:273–284. cf. Kolipinski L.: 'Notes on some toxic effects from the use of citrate of lithium tablets'. *Maryland Med. J.* 1898–1899;40:4.

Additional cautionary papers were provided by Stein¹⁰¹⁶ and Waldron.¹⁰¹⁷

The FDA immediately issued a ban on the use of lithium. It remained in place until 1970; no formal bans were issued in other countries.¹⁰¹⁸

Had Cade not already been aware of these reports, he would have read about them in the *Medical Journal of Australia*, which on 30 July 1949 published the cautionary article *Salt Substitutes and Lithium Poisoning*;¹⁰¹⁹ this came out four to five weeks before the publication of his own paper. Other than drawing attention to the American reports, this paper also made reference to Cleaveland's paper. It can be speculated, therefore, whether the meeting called at Royal Park Hospital, Melbourne, in 1949—Aschburner's communication to Johnson—where Cade discussed his forthcoming paper, also dealt with this lithium alert. However, Cade did not refer to this topic until years later, for instance in 1970, when he recounted that 'in March 1949 lithium was effectively excommunicated as a therapeutic substance, at least in the United States'.¹⁰²⁰

Leusen I, Demeester G.: 'Au sujet de la toxicité du chlorure de lithium'. *Acta Med. Scand.* 1950;138:232–236.

¹⁰¹⁶ Stern RL.: 'Severe lithium chloride poisoning with complete recovery. Report of a case'. *JAMA* 1949;139: 710–711.

¹⁰¹⁷ Waldron AM.: 'Lithium intoxication'. *JAMA* 1949;139(2):733 (cf. Waldron: *Univ. Hosp. Bull., Ann Arbor*, 1949;15(Feb.):9–10 (2 patients)). Peters HA.: 'Lithium intoxication producing chorea athetosis with recovery'. *Wisconsin Med. J.* 1949;48:1075–1076.

¹⁰¹⁸ Amdisen A.: 'Lithium as a pharmacological agent. Historical aspects. Topical aspects in monitoring of psychiatric lithium therapy'. Aarhus, 1985. Amdisen A.: 'The first lithium era', in Johnson FN. (ed.): 'Depression & mania'. *Modern lithium therapy*. Oxford: IRL Press, 1987. pp.24–28.

¹⁰¹⁹ Anon.: 'Salt substitutes and lithium poisoning'. *Med. J. Aust.* 1949;2:175.

¹⁰²⁰ Cade JF.: 'The story of lithium', in Ayd FJ, Blackwell B. (eds.): 'Discoveries in biological psychiatry'. Philadelphia: Lippincott, 1970. pp.218–229.