

This Week's Citation Classic

Baastrup P C & Schou M. Lithium as a prophylactic agent: its effect against recurrent depressions and manic-depressive psychosis. *Arch. Gen. Psychiat.* **16:162-72**, 1967. [Psychiat. Hosp., Glostrup; Psychopharmacol. Res. Unit, Inst. Psychiat., Risskov; and Aarhus Univ. Sch. Med., Denmark]

Over a period of six and a half years 88 patients with frequent recurrences of mania or depression were observed before and during continuous lithium administration. Lithium treatment led to a marked fall of episode frequency and time ill. On discontinuation of lithium, episodes reappeared. [The **Science Citation Index® (SCI®)** and the **Social Sciences Citation Index® (SSCI™)** indicate that this paper has been cited over 355 times since 1967.]

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"Our study originated in two clinical observations: the first, made by Cade¹ and confirmed in a systematic trial by Schou and associates,² that lithium exerts strong antimanic action; the second, made independently by Hartigan³ and by Baastrup,⁴ that continuous lithium administration may lower the frequency of not only manic but also depressive relapses.

"Collaboration took place across the country. Baastrup, in Glostrup, collected, treated, and observed the patients; Schou, in Risskov, attended to the systematic analysis of the data and to their presentation. The collaboration also involved interaction of different temperaments. Stubbornness crossed swords with impatience, and only friendship and a common goal kept the project going. Our strongest incentive to continue what at times seemed overwhelmingly difficult was that both of us had seen individual patients

whose existence before lithium had been cruelly invalidated by frequent and severe relapses and who during lithium treatment returned miraculously to a normal life with reestablishment of family and working relations. It seemed most unlikely that such dramatic and long-lasting changes could have been spontaneous or accidental, but evidence must clearly be obtained from large numbers of patients treated and observed over long periods of time.

"The outcome of the trial was puzzling. Although of obvious therapeutic value in mania, lithium had not given promise of exerting antidepressive action. Nevertheless, continuous lithium administration significantly attenuated or prevented depressive as well as manic relapses, and a prophylactic action could be seen in unipolar patients, those with depressions only, as well as in bipolar cases. Such a double action, an effect on both clinical manifestations of manic-depressive illness, was, although well established for electric convulsive treatment, not shared by any other antimanic or antidepressive drug treatment, and there were those who found difficulty in accepting the data and the conclusions. A debate on methodological and ethical issues was followed by further trials, carried out by ourselves and by others, in which lithium was compared double-blind with placebo. These studies confirmed the conclusions of the original paper.

"This was the first study demonstrating clear-cut prophylactic drug action against relapses of one of the major psychoses, and it emphasized the importance of longitudinal intervention in diseases with a recurrent course. Continuing interest in our article presumably reflects continuing interest in lithium, which remains without any valid alternative. Maintenance treatment with antidepressant drugs may be of some prophylactic value in unipolar patients; in bipolar patients lithium is without peer."

1. **Cade J F J.** Lithium salts in the treatment of psychotic excitement. *Med. J. Australia* **36:349-52**, 1949.
2. **Schou M, Juel-Nielsen N, Strömngren E & Voldby H.** The treatment of manic psychoses by the administration of lithium salts. *J. Neurol. Neurosurg. Psychiat.* **17:250-60**, 1954.
3. **Hartigan G P.** The use of lithium salts in affective disorders. *Brit. J. Psychiat.* **109:810-14**, 1963.
4. **Baastrup P C.** The use of lithium in manic-depressive psychosis. *Compr. Psychiat.* **5:398-408**, 1964.