

This Week's Citation Classic

Schou M. Lithium in psychiatric therapy and prophylaxis.
J. Psychiat. Res. 6: 67-95, 1968.
[Aarhus University Psychiatric Institute, Risskov, Denmark]

The paper reviews the evidence for a therapeutic effect of lithium in mania and a prophylactic effect against manic and depressive recurrences of manic-depressive disease. It further discusses lithium effects on the normal mind, the pharmacokinetics of lithium, side effects, poisoning, preparations, dosage, treatment control, and mode of action. [The Science Citation Index® (SCI®) and the Social Sciences Citation Index™ (SSCI™) indicate that this paper has been cited over 260 times since 1969.]

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"It is not clear why this particular review has reached the rank of 'Citation Classics.' I hope that quality played a role, but it has probably also been of significance that the paper appeared when it did.

"Although introduced into psychiatry in 1949 lithium had during the following eighteen years gained only limited acceptance as a psychotropic drug. It was recognized as having good therapeutic effect in mania, but its rather narrow therapeutic range and the slow onset of action made it a weak competitor of the less specific but more quickly acting neuroleptics. In 1967, however, a new and unexpected effect of lithium was discovered.¹ When the drug was given on a long-term basis, it could to a large extent attenuate or prevent recurrences of mania or depression or both. This was seen in unipolar as well as in bipolar patients.

"It was on this basis that the editor of *journal*

of *Psychiatric Research*, Dr. Seymour Kety, suggested that I review the lithium literature. A review from 1957 had dealt mainly with the biology and pharmacology of lithium.² In this new one, the emphasis was on use in psychiatry as well as on the relevant pharmacokinetics and toxicology. The review aimed at speaking the language of both psychiatrists and pharmacologists. For those about to start clinical or experimental work on this new/old drug, the review may have been a source of information and references.

"Controversy attracts attention, and it so happened that one of the main points of the review, the prophylactic action of lithium in manic-depressive disorder, became the object of heated scientific debate during the following years. Superficially the debate dealt with the methodology of prophylactic trials. Fundamentally, opinions differed about the nature and the course of recurrent manic-depressive disorder as understood by a group of British psychiatrists and a group of Danish psychiatrists. The discussion continued for some years until further studies, some of them double-blind, confirmed the conclusions drawn from the original trial.

"Lithium prophylaxis has served to focus attention on the longitudinal aspects of manic-depressive disorder and on the need for prophylactic or maintenance treatment. This important development started at about 1968, and the consequent colossal upswing of interest in the biology and clinical uses of lithium is reflected in the number of papers published before and after that time. During the five years preceding 1968 the number totalled 500; during the five years following 1968 it was 1,700. I would like to think that my review to some extent contributed to this development.

"Recent publications bring the topic of the 1968 paper up to date."^{3,4}

1. **Baastrop P C & Schou M.** Lithium as prophylactic agent. Its effect against recurrent depressions and manic depressive psychosis. *Arch. Gen. Psychiat.* 16:162-72, 1967.
2. **Schou M.** Biology and pharmacology of the lithium ion. *Pharmacol. Rev.* 9: 17-58, 1957.
3. **Jefferson J W & Greist J H.** *Primer of lithium therapy.* Baltimore, MD: Williams & Wilkins. 1977. 211 p.
4. *Lithium in medical practice.* (Johnson F N & Johnson S, eds.) Lancaster: MTP Press, 1978. 459. p.