

Perspective

June 25, 2015

**Risk and Relevance to Lithium Usage**  
**Unpublished Letter to the Editor of JAMA**

**By**

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As an octogenarian psychiatrist, previous author and occasional reader of JAMA, I enjoyed with irony two articles juxtaposed in the 2015 March 24/31 issue. In the Clinical Review and Education Section, Mark Olsen reviews work by Hampton *et al* on “*Psychiatric Medication Adverse Events in Emergency room Visits ADE ED.*” Among these are an estimated 16.4 per 10,000 outpatient visits (0.16%) due to lithium toxicity. Of these “roughly one half” (53.6%) resulted in hospitalization, 0.08% of the total. This finding elicits the following comment from Olsen, “The high frequency and clinical severity of adverse events associated with lithium should be considered amid calls to expand lithium treatment in bipolar disorders.”

In “JAMA Revisited” (p.1273), we find a reprinting of “*Why Physicians Err in Diagnosis*” (March 27. 1915), that identifies social and clinical errors, the former of which include what, at the time, were considered “functional” psychiatric disorders, some that were probably treated with lithium, a panacea at that time.

Today we recognize that lithium is the only naturally occurring, highly specific, remedy for a particular genetically based psychiatric condition, bipolar disorder, and that it is uniquely safe when adequately monitored by regular plasma levels. This is due to classical, but often overlooked work, by Trautner *et al*, (1955), which enabled Cade to rescind the ban he had placed on its use. (See Blackwell, B and others in “*The Lithium Controversy: A Historical Biopsy*”) INHN.Org in “*Controversies*, June 19, 2014 and subsequent postings).

It is a disservice to science, medicine and psychiatry to suggest that sloppy diagnosis or prescribing of a highly specific and effective remedy like lithium for a disabling disorder should become an excuse for limiting its appropriate use.

**References:**

1. Mark Olsen. Surveillance of Adverse Psychiatric Medication Events. *JAMA*, 2015, 313(12):1273
2. Lee, M, Hampton *et al* Emergency Department Visits by Adults for Psychiatric Medication Adverse Events. *JAMA Psychiatry*, 2014, 71(9): 1006-1014.
3. *JAMA Revisited: Why Physicians Err in Diagnosis: 1915:64(13):1076*, *JAMA*, 2015, 313(12).
4. Trautner, EM, Morris, R, Noack, CH & Gershon, S. The Excretion and Retention of Ingested Lithium and its Effect on the Ionic Balance in Man. *Med. J. Aust.*, 1955, 2: 280-291.
5. Blackwell, B in *The Lithium Controversy: A Historical Autopsy*. INHN.Org in “*Controversies*” June 19, 2014.

**Word Count:** 386

The above ‘Letter to the Editor’ of JAMA was duly submitted, meeting demands for fewer than 400 words and 5 references, an arduous process that severely taxed my geriatric computer skills. Several weeks later, I received a formal “Decision Letter” stating, “Considering the opinion of our editorial staff we determined your letter did not receive a high enough priority rating for publication ... we are only able to publish a small fraction of the letters submitted ... which means that published letters must have an extremely high rating.”

I was invited to “contact the author of the article although we cannot guarantee a response.”

This roused my professional ire. A scribe of authors (is this the correct collective noun?) delivered their verdict without seeking input from the reviewer or the original authors for comment on the validity of the concerns expressed.

The article on which the reviewer commented is an example of a massive data set that yielded statistically significant results of dubious clinical significance. The reviewer failed to address how to improve prescribing habits but focused instead on alleged ‘over-prescribing’ without any evidence or mention of how lithium treatment was managed, who the prescribers were (discipline and training) or any details of the patients’ diagnosis, natural history or treatment responses.

A scribe of editors judged the reviewers conclusions and the author’s study design did not merit seeking the opinion of either concerning issues raised by my letter. I could contact them myself

but not expect an answer. This approach raises serious scientific and ethical concerns about editorial disinterest in the quality of what JAMA chooses to publish and how circling the editorial wagons stifles dissent.

The problem identified by this mega data is not new. It was reported 18 years ago by leading European psychopharmacologists (Kores & Lader, 1997), who studied 50 cases of severe lithium toxicity due usually to poor management.

My letter might have suggested a better, more practical solution to this problem compatible with the study design. Every patient admitted with side effects severe enough to warrant admission would be given, at the time of discharge, a brief (one page) outline of ideal management principles and advised to share it with their prescribing physician at a first outpatient visit. This might improve the physician-patient alliance, hopefully viewed by the doctor as prophylaxis for reduced risk of future malpractice litigation.

Of course such a suggestion might have increased the scribes 'priority rating' although adding a sixth reference could have resulted in even more peremptory unthinking rejection.

#### **Additional Reference**

Kores B. Lader MH. Irreversible Lithium Toxicity: An Overview. *Clinical Neuropharmacology* 1997; 20, 283-299.

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