

Thomas A. Ban: Neuropsychopharmacology in Historical Perspective

Collated 32

Thomas A. Ban: Lithium in Psychiatry in Historical Perspective

2. Introduction into treatment in psychiatry

Samuel Gershon: Profiles of John Cade and Edward Trautner

Contents

Samuel Gershon: John Cade and Edward Trautner

John Cade by Samuel Gershon

John Cade was born in 1912 in Murtora, Australia, and received his M.D. in 1933 from the University of Melbourne. He worked as House Officer at St. Vincent's Hospital and trained in psychiatry before joining the Australian Armed Medical Corps where he rose to the rank of major in 1941. After spending two years as prisoner of war, Cade returned home and joined Bundoora Repatriation Hospital in Melbourne.

Influenced by Rolv Gjessing's reports that altered metabolism with the production of mescaline-like substances was possibly responsible for a form of catatonia, and Albert



Hofmann's discovery that lysergic acid diethylamide, an ergot alkaloid, has psychomimetic effect in minute amounts, Cade began his research in the mid-1940s at Bundoora. He assumed that manic-depressive illness is analogous to thyrotoxicosis and myxedema and hypothesized that mania is a state of intoxication by a normal product of the body in excess and melancholia is a state of deficiency of the same substance. To test this hypothesis, he compared the effects of intra-peritoneally injected manic urine with urine from normal subjects in guinea pigs and found the former more toxic in killing the animals than the latter. Cade identified urea as the culprit that killed the animals; but when he administered lithium urate to establish uric acid's toxicity enhancing effect on manic urine, he found that instead of enhancing toxicity, it protected the animals from urea's toxic effects. He attributed the protective effect of the substance to lithium and when trying to determine whether lithium salts alone have any discernable effect, he found that after injecting large doses of aqueous solution into guinea pigs, the animals became lethargic and unresponsive. Since Cade's investigations had commenced in an attempt to demonstrate the presence of a toxic substance excreted in the urine of manic patients, he compared the effect of lithium in 10 manic, 6 schizophrenic and 5 depressed patients, after taking the substance himself for about two-weeks to ascertain its safety, in the dose at which it was used before in gout, epilepsy, etc. He found that lithium was effective in controlling psychotic excitement, especially in manic patients. The publication of his findings, in 1949, in the Medical Journal of Australia, signals the rediscovery of lithium treatment in psychiatry.

Cade recognized that lithium exhibited remarkable specificity for mania, that it was not sedating to patients and that the treatment could be continued with a possible prophylactic benefit. Yet, concerned about its toxicity, after the death of one of his patients included in his first experiment, he virtually stopped using lithium in his hospital and stopped experiments with the substance.

In 1953 Cade was appointed Medical Superintendent of Royal Park Hospital in Melbourne. In the years that followed, he did no further research with lithium but carried out investigations with protective foods in psychiatry and with high doses of thiamin in the prevention and treatment of memory disturbances in alcoholism. About 15 years after the publication of his historical paper on lithium, he reported high magnesium levels in schizophrenia; during the 1960s, he studied the effects of manganese in mongolism.

Cade retired from his position at Royal Park in 1977 and died at age 68 in 1980.

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August 1, 2013

Edward Trautner by Samuel Gershon

Edward Trautner was born in 1886 in Germany and received his medical degree in his native country. He left Germany in the 1930s and after a short stay in Spain and England, he arrived as a refugee to Australia in the 1940s when he was invited by Professor Douglas Wright, head of the joint Department of Physiology and Pharmacology at the University of Melbourne, to join his faculty.

In 1949 John Cade published his report in the *Medical Journal of Australia* on “Lithium salts in maniacal excitement” that led to the re-introduction of lithium therapy in psychiatry. Yet, the clinical use of the new treatment entailed difficulties because of lithium’s toxicity that was to the extent that Cade himself prohibited the use of the substance in his own hospital. Recognizing the importance of rendering lithium feasible for clinical use, Trautner, with his junior associates who included Charles Noack, Douglas Coats and Samuel Gershon, conducted a series of four studies during the 1950s that set the foundation for lithium therapy.

In the first of these reports, published in 1951, it was established that lithium, if administered in a dose in which plasma lithium levels are kept within 0.6 mEq/l to 1.2 mEq/l, is a safe and effective treatment in manic depressive patients. Plasma level determinations in the study were carried out

with the flame photometer, an instrument constructed by Victor Wynn at the University just a year before. The other three reports, one published in 1955, showed increase of lithium retention in mania and of lithium excretion when mania is resolved; another, published in 1956, revealed possible use of lithium in maintaining manic depressive patients in remission; and the third, published in 1957, dealt with the treatment of lithium toxicity. Without Trautner's contributions, implementation of lithium treatment would have been considerably delayed.

Trautner died in Queensland in 1979 at age 93.

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August 1, 2013

May 21, 2020