Celebrating 70 Years of the First Publication on Antipsychotic Treatment in North America by Heinz E. Lehmann and Gorman E. Hanrahan: Would Their Methodology Still Be Conceivable?

Pablo E. P. Dutra, MD,[1] *Richard Balon, MD,*[2] *and Antonio E. Nardi, MD, PhD*[1]

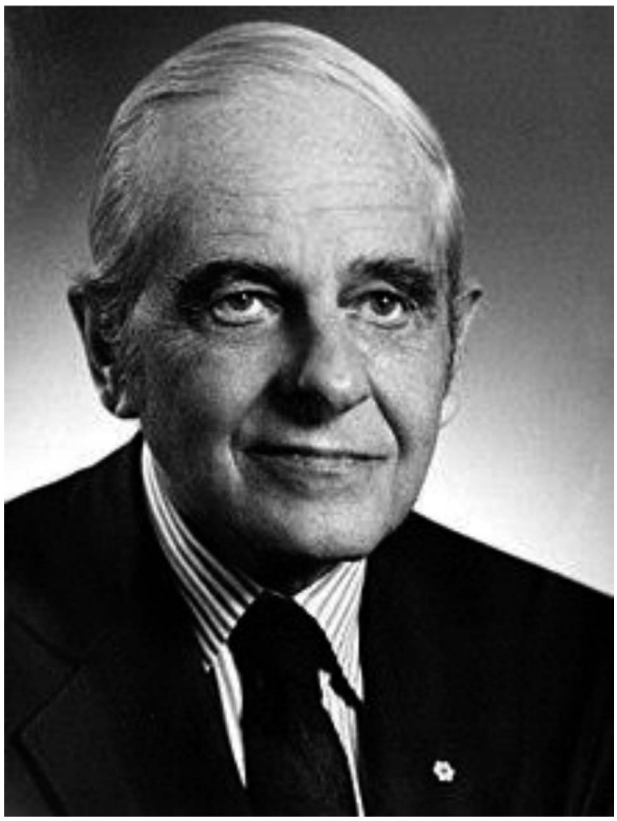
Heinz Edgar Lehmann, a pioneer of psychopharmacology, was born in Berlin, Germany on July 17, 1911, graduated from the University of Berlin in 1935, emigrated to Canada in 1937, fleeing from Nazi Germany, and took a post at the Verdun Protestant Hospital (Montreal's Douglas Hospital) as a junior psychiatrist.[1] In 1944, he published among other interesting papers, an article on the use of massive doses of nicotinic acid in the treatment of posttraumatic confusional state.[2] In 1947, he was appointed Clinical Director of the Verdun Protestant Hospital where he remained affiliated for 60 years.[1] In 1948, he became a naturalized Canadian citizen and he was hired as an assistant professor at McGill, later attaining the rank for full professor. In 1949, he developed a hypnotic with a short half-life made of scopolamine, apomorphine, phenobarbital, hexobarbital, and nicotinic acid.[1,2] From 1970 to 1974, he was Chair of the Department of Psychiatry at McGill University, and he published more than 300 articles, mostly on psychopharmacology.[3,4] In the spring of 1953, Lehmann was seeking a new treatment for his more severely disturbed patients, when a Rhône-Poulenc representative gave him a copy of Delay and Deniker's article about a new compound for treatment of psychosis[5] not specifically schizophrenia, encouraging him and Gorman Hanrahan, to use this compound later called chlorpromazine on a series of psychotic patients. Lehmann read the first article of Delay and Deniker about Chlorpromazine at home in his bathtub[4] and found his curiosity arrested and with Gorman E. Hanrahan conducted their first trial with this new drug.[6]

In February 1954, Heinz Lehmann published the first clinical article on the use of chlorpromazine[6] in Canada. Chlorpromazine was the first synthetic drug used to control states of mania and psychomotor excitement, marking the birth of modern psychopharmacology, and Lehmann gave a full clinical description of what we now call its antipsychotic effects. This groundbreaking clinical observation was responsible for turning chlorpromazine into the first neuroleptic medication in history, hailed as the first "antipsychotic" medication.[1,3] Chlorpromazine reduces the intensity of psychotic symptoms, reducing schizophrenia positive symptoms, such as delusion and hallucinations. It gained attention worldwide because of its safety, becoming a more humane treatment option, which permanently reshaped the landscape of psychiatry for both psychotic patients and psychiatrists.[1,3] After the arrival of chlorpromazine, which affects among others the dopamine 2 receptor, many institutionalized patients could finally leave psychiatric hospitals and return to their families, communities, and continue treatment as an outpatient. This discovery was a revolution in the treatment of psychotic disorders that has spawned at least 2 subsequent generations of antipsychotic medications and contributed to the emptying of huge chronic psychiatric hospitals and contributed to the growth of community mental health treatment of serious psychiatric disorders.

In 1958, Heinz Lehmann, inspired by the astute observation of Roland Kuhn, published his works on the effects of imipramine and iproniazid in depression.[7,8] One of Lehmann's most significant contributions was the development of the first rating scales for the assessment of changes in the treatment of depression, and methods for the evaluation of psychoactive drug effects based on psychological performance tests because of lack of objectivity on clinical evaluation itself. He collaborated on the development of the Hamilton Rating Scale for Depression, published in 1960, and with his work, he helped identify not only the therapeutic effects of medications but their potential risks, through the development of psychological tests aimed to evaluate their emotional and cognitive effects, allowing mental health science to rely

From the [1]Panic and Respiration Laboratory, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil; and [2]Departments of Psychiatry and Behavioral Neurosciences and Anesthesiology, Wayne State University, Detroit, MI.
Received September 14, 2023; accepted after revision October 11, 2023.
Address correspondence to: Antonio E, Nardi, MD, PhD, Panic and Respiration Laboratory, Institute of Psychiatry, Federal University of Rio de Janeiro, Rua Visconde de Pirajá 407/702, Rio de Janeiro, RJ, 22410-003, Brazil (e-mail: antonoenardi@gmail.com).
The authors declare no conflicts of interest.
A podcast discussing this article is available online at the journal website.

ISSN: 0271-0749
DOI: 10.1097/JCP.0000000000001788



HEINZ EDGAR LEHMANN (1911-1999)

on empirical evidence[8,9] raising the bars for upcoming medications and for mental health practitioners to make significant strides in understanding and treating mental health disorders.[10]

As the principal investigator of a grant from the US Public Health Service, Lehmann was also involved during the 1960s and 1970s in the clinical evaluation of numerous new psychotropic drugs in development.[3,9,10] Lehmann simplified complex concepts, developed innovations in psychiatric treatment, started a revolution toward deinstitutionalization and reduction of prejudice against psychiatric patients, produced many important papers, contributed enormously to the development of psychopharmacology, and worked on medical education in Canada and North America. Interestingly, Lehmann, who read Freud's work as a school boy in Berlin, viewed some aspects of psychoanalysis positively, similarly to Roland Kuhn. This holistic patient view may have helped him in his clinical observations and his deeply humanistic care of his patients.[1,3,4]

Heinz Lehmann was a member of the generation of pioneers of psychopharmacology who "did it all," combined astute clinical observations with the use of objective tools, worked on developing new tools and medications, conducted clinical trials, and moved the nascent field of clinical psychopharmacology forward. It is of great interest to catch the attention of young psychiatrists to bring up the example of Professor Heinz Lehmann in the context of some voices in the field who argue that opportunities for empirical clinical investigations have been curtailed and essentially abandoned in current times. Psychiatrists need to identify the most relevant features of what made it possible for him to do what he did and provide an insightful clinical view that returns to the extent possible in supporting analogous efforts with the array of new entities that work on different molecular targets.

REFERENCES

1. Paris J. In memoriam: Heinz Lehmann. McGill Reporter. April 22, 1999. Available at: http://reporter-archive.mcgill.ca/Rep/r3115/memoriam.html. Accessed September 5, 2023.
2. Lehmann H. Post-traumatic confusional state treated with massive doses of nicotinic acid. *Can Med Assoc J.* 1944;51:558–560.
3. Shorter E. Starting Up. In: Ban TA, ed. *An Oral History of Neuropsychopharmacology: The First Fifty Years: Peer Interviews*. Brentwood: American College of Neuropsychopharmacology (ACNP); 2011:XVIII–LXIV.
4. Shorter E. *Historical Dictionary of Psychiatry.* New York: Oxford University Press; 2005:160–161.
5. Delay J, Deniker P. Le traitments de psychoses par une méthode neurolytique dérivée de l'hibernothérapie; le 4560 RP utilisée seul en cure prolongée et continue. *CR Congr Méd Alién Neurol (France) 1952a*. 1952; 50:497–502.
6. Lehmann HE, Hanrahan GE. Chlorpromazine: new inhibiting agent for psychomotor excitement and manic states. *AMA Arch Neurol Psychiatry.* 1954;71:227–237.
7. Lehmann HE, Cahn CH, DeVerteuil RL. The treatment of depressive conditions with imipramine (G 22355). *Can Psychiatr Assoc J.* 1958;3: 155–164.
8. DeVerteuil RL, Lehmann HE. Therapeutic trial of iproniazid (marsilid) in depressed and apathetic patients. *Can Med Assoc J.* 1958;78:131–133.
9. Lehmann HE. A simple psychometric test for the diagnosis of minimal cerebral dysfunction. *JAMA*. 1955;159:1458–1460.
10. Lehmann HE, Knight DA. In: Rothlin E, ed. *Measurement of changes in human behavior under the effects of psychotropic drugs* vol. 2. Proceedings of the 2nd International Meeting of the Collegium Internationale Neuropsychopharmacologicum; 1961:291–303.