

Thomas A. Ban: Neuropsychopharmacology in Historical Perspective

Collated 29

**Profiles of clinicians and researchers who were instrumental for the birth
and/or contributed to the development of neuropsychopharmacology**

Nathan S. Kline, Roland Kuhn, Heinz E. Lehmann, Laszlo Meduna and

Dionisio Nieto Gomez

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Nathan S. Klein by Barry Blackwell

Nathan Kline was born in 1916 and died tragically at the age of 66 in 1983 following open heart surgery. A graduate of Swarthmore College and New York University College of Medicine, Kline was a practicing psychiatrist. He was one of the very first pioneers to use and study drugs for the treatment of mental illness, beginning in 1952, when at the age of 36 he started a research unit at Rockland State Hospital York in New York, named the Nathan Kline Research Institute after his death.



He was a founding member of the American College of Neuropsychopharmacology (1961) and its sixth President (1967). Kline was the only two-time recipient of the Albert Lasker Clinical Medical Research Award: in 1957 for work on Rauwolfia Serpentina in the early treatment of neuropsychiatric disorders and in 1964 for introducing the first MAO inhibitor (iproniazid) as an “energizer” in the treatment of mood disorders. Within a decade, Rockland Research Institute had established a worldwide reputation and a staff of more than 300, attracting students and colleagues from around the world, who Kline insisted live in close proximity to their patients.

He was also a major proponent of lithium in bipolar disorder and also recognized its potential usefulness in alcoholism. In 1968 he installed one of the early computers at Rockland State to facilitate research. The early treatment successes helped initiate the process of de-institutionalization, leading to the closure of asylums nationwide. Kline did much to publicize and de-stigmatize mental illness with more than 500 publications directed to both the medical profession and general public. His book, *From Sad to Glad*, became a best seller. Kline was founder and Director of The International Committee Against Mental Illness, consulted with the World Health Organization and devoted much time and effort to promoting treatment of mental illness in developing countries.

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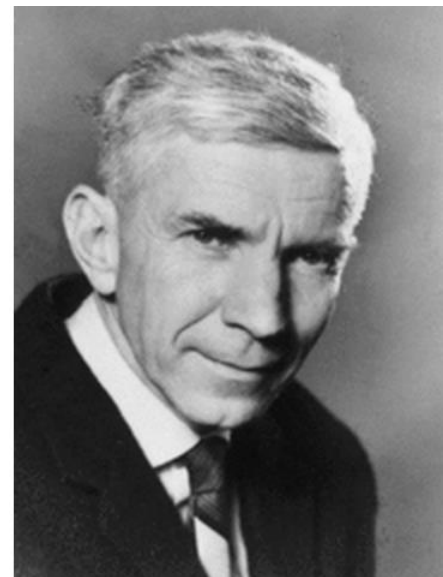
Kline NS. Clinical experience with iproniazid (Marsilid). J Clin Exp Pathol 1958; 19(suppl.1):72-8.

June 13, 2013

Roland Kuhn by Thomas A. Ban

Roland Kuhn was born in Biel, Switzerland, in 1912. He was trained in psychiatry at the University of Bern and in 1939 was appointed senior physician at the Cantonal mental hospital in Münsterlingen.

Kuhn became involved in the clinical testing of new drugs for Geigy, one of the major drug companies in the mid-1950s. He suggested the testing of one of the antihistamines, G22,355, a tricyclic dibenzazepine, because it showed the closest structural resemblance to chlorpromazine, a substance that was widely used in the treatment of schizophrenia. Contrary to his expectations, G22,355 had no therapeutic effect in schizophrenia. Instead, he observed that it was effective in some depressed patients, and especially in those with endogenous depression in whom vital disturbance was in the foreground. Kuhn published his observations with G22,355 in 40 depressed patients in the August 31, 1957, issue of the Swiss Medical Journal, and the substance was released in the same year for clinical use in Switzerland for the treatment of depression with the generic name of imipramine and the brand name of Tofranil. There was a strong opposition by mainstream psychiatry against pharmacological treatment of depression, but Kuhn prevailed and the introduction of imipramine was instrumental in encouraging the development of other drugs for the treatment of depression. Kuhn died in 2005.



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June 13, 2013

Heinz E. Lehmann by Antonio E. Nardi

Heinz Lehmann was born in Berlin, Germany, in 1911 and received his MD from the University of Berlin in 1935. In 1937 he immigrated to Canada and in the same year he took a post at the Verdun Protestant (later Douglas) Hospital, a psychiatric inpatient facility in the suburbs of Montreal, with which he remained affiliated for 60 years. In 1948 he was appointed lecturer in the Department of Psychiatry, McGill University, in Montreal and became actively involved in teaching. He rose on the academic ladder to full professor and served as the Chairman of the Department from 1970 to 1974 (Shorter 2011).

Lehmann became involved in psychiatric research with drugs in the early 1940s. In his first project, the findings of which were published only in 1979, he studied the differential effect of pentobarbital on yawning in psychiatric patients (Lehmann 1979, 1993). Subsequently, in 1944, he published a report on the therapeutic effect of massive doses of nicotinic acid on post-traumatic confusional state (Lehmann 1944) and in the late 1940s developed a short-lived hypnotic containing nicotinic acid, a barbiturate, scopolamine and apomorphine (Lehmann 1949).

In 1954 Lehmann was propelled into dominance by being the first in North America to publish his findings on the effect of chlorpromazine in psychomotor excitement and manic states (Lehmann and Hanrahan 1954). The impact of his paper was so profound that in 1957 he was presented with the prestigious Lasker Award (Ban 2011). Lehmann was also the first in North America, in 1958, to report on the effects of imipramine in the treatment of depression (Lehmann, Cahn and DeVerteuil 1958) and among the first in the same year to report on findings in a clinical trial with iproniazid in depressed and apathetic patients (DeVerteuil and Lehmann 1958). During

the 1960s he was also involved in developing one of the first rating scales for the assessment of changes in the treatment of depression (Lehmann, Cahn and DeVerteuil 1958) and methods for the evaluation of psychoactive drug effects that were based on psychological performance tests (Lehmann and Knight 1961). As the Principal Investigator of a grant from the US Public Health Service to support the operation of an Early Clinical Drug Evaluation Unit of the network organized by the Psychopharmacology Service Center of the United States, Lehmann was also involved during the 1960s and 1970s in the clinical evaluation of numerous new psychotropic drugs in development (Lehmann and Ban 1963).

In recognition of his contributions, in 1976 he became an Officer of the Order of Canada; and in 1998 he was recipient of the Pioneers in Psychopharmacology Award of the *Collegium Internationale Neuro-Psychopharmacologicum*. There are also several awards honoring his name: The Heinz Lehmann Award of the Canadian College of Neuropsychopharmacology, the Heinz Lehmann Award of Excellence of the Quebec Psychiatric Association and the Heinz Lehmann Research Award, established by the New York State Office of Mental Health, where he served in the last decade of his life as Deputy Commissioner in the Research Division.

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April 17, 2014

Laszlo J. Meduna by Antonio E. Nardi

Lászlo Meduna was born on March 27, 1896, in Budapest and received his MD in 1921 from the Medical Faculty of Pázmány Péter University. Subsequently, in 1922 he joined Károly Schaffer, a psychiatrist and neurohistologist, in his Interacademic Institute for Brain Research in Budapest. After Schaffer's appointment, in 1927, as professor (chair) of the Department of Psychiatry at the University, he became a member of his faculty (Shorter and Healy 2007).

Meduna began research in histopathology in the mid-1920s. While studying microglia cells in the rabbit, he found disease dependent differential changes, i.e., atrophy, in some diseases and swelling in others (Meduna 1927). Extending his research to autopsied material from psychiatric patients, in the early 1930s he noted a marked decrease of microglia cells in the brains of patients with schizophrenia and a marked increase in patients with epilepsy (Fink 1985; Meduna 1932). Considering the findings of Nyirö and Jablonsky (1929) that the incidence of seizures decreased in those epileptics who developed schizophrenia, the observations of Glaus (1931) that

schizophrenic psychopathology was transiently alleviated in schizophrenic patients with epilepsy and the report of Müller (1930) that two patients with schizophrenia “recovered” when they developed epilepsy, Meduna, in 1934, introduced pharmacologically-induced convulsions in the treatment of schizophrenia with camphor first, then with pentylenetetrazol (Meduna 1935, 1937). In the late 1930s Meduna emigrated from Hungary to the United States (Kuncz 1993). He became professor of Neurology at Loyola University and became settled for the rest of his life at the Illinois Psychiatric Institute. In the mid-1940s he coined the term “oneirophrenia” for a small group of “atypical psychoses” conventionally diagnosed as schizophrenia (Meduna and McCulloch 1945, 1946) and in the late 1940s he introduced carbon dioxide therapy, a “pharmacodynamic treatment of psychoneuroses” (Meduna 1947, 1948). In 1950 he published a monograph on both, with the title “Oneirophrenia and Carbon Dioxide Therapy” (Meduna 1950). In 1958 Meduna became founding editor of the journal *International Neuropsychiatry*. Finally, in 1959, Meduna in collaboration with Abood, was one of the first to explore Ditrán (1-ethyl-3 piperidyl cyclopentylphenylglycolate), an anticholinergic substance with atropine-like actions, in the treatment of depression (Meduna and Abood 1959).

Meduna died in Chicago on November 30, 1964, at age 68.

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November 27, 2014

Dionisio Nieto Gómez by Antonio Torres-Ruiz

Dionísio Nieto Gómez was born in Madrid on March 13, 1908. In 1929 he received his MD from the Faculty of Medicine, Complutense University in Madrid. Subsequently, he spent five years, from 1931 to 1935, in Germany studying neuropsychiatry. After returning to Spain, he worked from 1935 to 1937 at the Psychiatric Clinic of the General Hospital of Madrid and in the Cajal Institute.

Nieto left Spain in 1939 after the Civil War and arrived in Mexico via France and Santo Domingo, in April 1940. In Mexico City he worked first at the National Psychiatric Hospital, commonly known as *La Castañeda*, and was instrumental in establishing the foundation of the Laboratory of Medical and Biological Research that was to become UNAM's (*Universidad Nacional Autónoma de México*) Institute of Biomedical Research.

In 1964 Nieto joined the National Institute of Neurology and Neurosurgery in Mexico City and soon after he became head of the Department of Psychiatry and Research of the Institute. In the mid-1950s he was involved in studying copper metabolism in the CNS (Escobar and Nieto 1957) and its effect on mental disorder. He also developed a chemical reaction, the "Nieto Reaction," for the diagnosis of neurocysticercosis in the cerebrospinal fluid (Nieto 1956).

In the late 1950s Nieto's interest turned to psychopharmacology and he was among the firsts to explore the psychopathology induced by *stropharia cubensis*, a potent species of psychedelic mushroom, whose principal active compounds are psilocybin and psilocin (Nieto 1959, 1962). In the 1960s he contributed with his research to the treatment of epilepsy with methaminodiazepoxide (chlordiazepoxide) (Nieto, Escobar, Castro and Roldan 1960) and to the prophylactic treatment of manic-depressive psychosis with lithium carbonate (Nieto 1963, 1969). In the 1970s he studied the effects of Prussian blue, ferric hexanocyanate ferrate, a substance in use at the time in heavy metal poisoning and in 1980 he reported his findings with the substance in schizophrenia and in the treatment of thallium, arsenic, lithium, etc., poisoning (Nieto 1980).

In 1970 Nieto was appointed head of the Mexican National Reference Center of the International Reference Center Network of Psychopharmacology of the World Health Organization. He was instrumental in setting a foundation of psychopharmacological research in Mexico and will be remembered as the beloved teacher of the first generation of psychopharmacologists in this country.

Nieto died on January 2, 1985, in Mexico City.

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April 3, 2014

April 30, 2020