

GENERAL PSYCHIATRY*Key Words: antidepressants, history of pharmacopsychiatry, Roland Kuhn*

Roland Kuhn—100th Birthday of an Innovator of Clinical Psychopharmacology

By Holger Steinberg, Hubertus Himmerich

ABSTRACT ~ *On the occasion of his 100th birthday this letter is to pay tribute to Swiss psychiatrist and psychopharmacologist Roland Kuhn (1912–2005), who established the antidepressant effects of imipramine starting in 1956. Since until now only monoaminergic-based antidepressants such as this substance found their way into psychopharmacological therapy, one can say that Kuhn established the lead antidepressant substance and has hence fundamentally changed clinical psychiatry and care for the mentally ill. Psychopharmacology Bulletin. 2012;45(1):48–50.*

Roland Kuhn (Figure 1) was born in Biel (Switzerland) on 4 March 1912, studied medicine at Bern and Paris. After his MD degree in 1937 he worked for two years at Bern University with Jakob Klaesi, before starting at the 700-bed Münsterlingen psychiatric hospital, which he headed from 1970 to 1980. In 1957 Kuhn habilitated at Zurich University and started to teach there as honorary professor in 1966. After 1980 he retired into a private practice in Scherzingen. He wrote some 200 papers and book chapters, but only a few monographs. (list of publications: see¹). From the mid-1950s, after dealing with the Rorschach (inkblot) test and philosophical *Daseinsanalysis*, he did clinical psychopharmacological research, which earned him worldwide recognition due to the discovery of the first antidepressant imipramine. Kuhn died on October 10, 2005, aged 94, in Scherzingen.

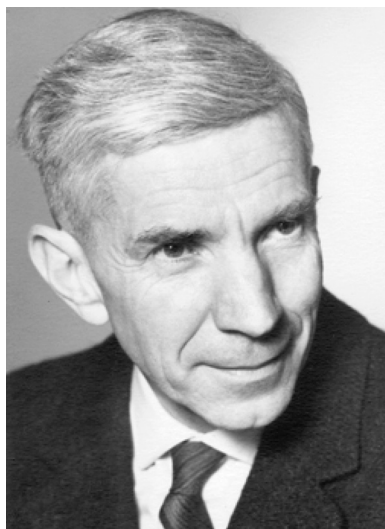
Kuhn came to psychopharmacological research, when the Münsterlingen institution got involved in clinical trials investigating the antihistaminic chlorpromazine for which Pierre Deniker and Jean Delay had found sedative and antipsychotic effects. When the hospital no longer received chlorpromazine for

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FIGURE 1

THE SWISS PSYCHIATRIST AND PSYCHOPHARMACOLOGIST ROLAND KUHN ABOUT 1957 (PERMISSION BY COURTESY OF DR. VERENA KUHN-GEBHART, SCHERZINGEN/SWITZERLAND)



testing, Kuhn approached Geigy for clinical trials with other antihistaminic drugs to replace the ostentatiously expensive chlorpromazine.² Other reports award the initiative to Geigy employees Robert Domenjoz, Paul E. Schmidlin and Otto Kym.^{3,4} Whatever the truth, from the beginning in 1956, Kuhn trialed imipramine, differing from chlorpromazine in just one side chain. For the first time, in 1957 he published his clinical observations of an antidepressant effect of imipramine in a group of 40 patients.⁵ Only one year later, the results of a repeat study on more than 500 psychiatric patients of various diagnostic categories treated with this new antidepressant were published in the *American Journal of Psychiatry*.⁶ Therein Kuhn found antidepressant effects mainly in major depression, but also in depressive syndromes in the framework of other psychiatric conditions such as schizophrenia, organic psychiatric disorders or anxiety disorders—and thus found the first antidepressant drug.⁶ This is the more remarkable since until the mid-1950s opium treatment was the standard, yet extremely lengthy and in many cases ineffective therapy, which had a high addictive potential. For major depressions insulin or cardiazol shock as well as electro-convulsive therapies had been in use since the 1930s and much under discussion for their serious side effects.

Kuhn admitted freely that he could not yet explain how imipramine works. The fact that tricyclic antidepressants were monoamine reuptake

inhibitors led to the monoamine or catecholamine deficiency hypothesis of affective disorders.⁷ Up to the present day, however, the core mechanism of action of antidepressants is still unknown. Hypotheses exist ranging from the normalization of the hypothalamo-pituitary-adrenal axis,⁸ changes in the brain structure by neurogenesis and gliogenesis,⁹ and changes regarding cytokines and immune cells¹⁰ to changes in neurotrophic factors, glutamate receptors, hypothalamic feeding peptides, nuclear hormone receptors, and epigenetic mechanisms,¹¹ to mention just a few of them.

Since until now only monoaminergic-based antidepressants such as imipramine found their way into psychopharmacological therapy,¹¹ it is justified to pay tribute to Roland Kuhn as the father of the first antidepressant imipramine, which became the lead substance for a long row of successors and generics that have fundamentally changed clinical psychiatry and care for the mentally ill.¹² ❀

CONFLICTS OF INTEREST

Dr. Hubertus Himmerich received speaker honoraria from AstraZeneca, Servier, Bristol-Myers Squibb and Lilly. Dr. Holger Steinberg has no potential conflict of interest.

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