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Obituary

Roland Kuhn (1912–2005)

DAVID HEALY*

Roland Kuhn was born at Bienne, a small town near Berne, on 4 March 1912. He studied medicine at Berne and Paris. He originally wanted to do surgery but was frustrated by the retirement of the surgeon with whom he planned to train, and as a temporary measure he went into psychiatry. The leading figure in Berne psychiatry at the time was Jacob Klaesi, who had introduced prolonged sleep treatment. The buzz surrounding sleep and malaria therapies, and later the presence locally of Ludwig Binswanger the developer of existential psychiatry, captured Kuhn's interest. Binswanger's influence played a part in Kuhn taking up a post in the psychiatric hospital in Münsterlingen. At the time the hospital had up to 700 patients and a growing outpatient service. Still not committed to psychiatry, he was trapped in his new career by World War II (Kuhn, 1998).

After the war, the Basle-based Geigy pharmaceuticals, now part of Novartis, recruited him to test out new drugs, especially new antihistamines, which in 1950 were a key growth area in clinical medicine. The Geigy antihistamine series was derived from an iminodibenzyl dye, summer blue. The first compound given to Kuhn, G22150, seemed ineffective clinically. When the effects of another antihistamine, Rhone-Poulenc's chlorpromazine, became apparent in 1953, Otto Kym and Paul Schmidlin from Geigy persuaded Kuhn to try G22150 again but on second exposure there still seemed little effect – in schizophrenia. Geigy then sent Kuhn G22355, the iminodibenzyl derivative closest in structure to chlorpromazine. This turned out to be imipramine, the first tricyclic antidepressant. There is an

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unresolved dispute between Kuhn and Robert Domenjoz of Geigy as to whose idea it was to try this compound. Imipramine was first given to a group of patients with schizophrenia with adverse results. However, Schmidlin and Kym from Geigy appear to have persuaded Kuhn to try it again in depressed patients. This he did, and the response was dramatic. So dramatic that again there is some dispute as to who noticed the benefits first, nursing and company staff or Kuhn.

What is undisputed is that Kuhn was the first to present a paper on the new drug and the first to have an article published on it, and that he then mapped out its profile, both as regards which patients were likely to respond and what the side effects of the drug were, in a manner that has stood the test of time (Kuhn, 1958). In addition he and his wife Verbena were among the first to report on the treatment of childhood depression with psychotropic drugs. But he was not a particularly effective advocate for the drug, which languished for several years within Geigy before being marketed, and nor was he someone to persuade (or mislead) the wider world into thinking that depression was an important public health problem. These factors may have played a part in his failure to secure a Nobel Prize or other recognition, a fact that deeply upset him.

There were several factors operating against any celebration of Kuhn's role in psychiatry. First, he was older than most of the key group that became influential in psychopharmacology. Second, he was not a clubbable man. Third, he worked outside the main academic centres – '*un petit psychiatre de campagne*' as Jean Thuillier called him. Fourth, a series of bitter priority disputes over chlorpromazine meant that no one got a Nobel Prize for this breakthrough, and against this background it was all but impossible to award honours for the discovery of the less important antidepressants. Fifth, he framed his insights in the language of classic German psychopathology, a language for which the atheoretic world of the new biological psychiatry spawned by imipramine and chlorpromazine had little time. Sixth, he rather magnificently rejected the language of statistics towards which the new world was moving. He put greater store in the close observations of individual cases than in the aggregated data of cohort studies.

This lack of recognition may have distorted the historical record, in that it almost certainly made it difficult for Kuhn to give an expansive account of what happened and to some extent forced him to emphasize his own contribution at the expense of the contributions of others. He would probably be quite unhappy to hear that I was asked to write his obituary because my efforts in the late 1990s to find out more of what had happened, and to get competing accounts onto the record, led him close to threatening a legal action. His anger at what he saw as efforts to downplay his role, however, in the hands of Tom Ban and Ned Shorter was finessed into a series of contributions on the discovery of imipramine that helped push the story forward (Healy, Kuhn, Simon, Broadhurst, *et al.*, 2002).

But aside from imipramine, Kuhn was involved in other discoveries, and this involvement makes it clear that his role as a pioneer was not simply an accident. He was the key clinician in the development of maprotiline, which at one point in the 1970s was the best-selling antidepressant in Europe. This was a minor but not unimportant drug, whose significance has been written out of psychopharmacology's script by the later development of the SSRIs. He was also a champion for levoprotiline, a derivative of maprotiline. This drug, which had no effects on either catecholamine or serotonergic systems, was not developed further by Ciba-Geigy, despite positive reports by Kuhn. It may well have interesting psychotropic properties. In a field that was more genuinely scientific and less commercial, this would have been taken further and we might all be the wiser, and Kuhn's contributions might have been harder to ignore, and might have been more generally celebrated.

A photograph of Roland Kuhn was published quite recently in this journal (Kuhn, 2004). He died at Scherzingen, Switzerland, on 10 October 2005.

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