

## Obituary

### Joseph J Schildkraut, 1934–2006

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Joseph J Schildkraut, 1996 (Photo by Dan Dehainaut)

Joseph Jacob Schildkraut died in June last year following a year-long struggle with esophageal cancer. With his death, our field lost one of its true giants, a man whose work from the early- to mid-1960s essentially set the stage for psychopharmacological research in affective disorders for the years since.

Joe (everyone called him Joe) was born in Brooklyn, NY, in 1934, but he lived the overwhelming majority of his life from college onward in the Boston area. He attended public schools in Brooklyn, and from there, he went to Harvard College, where he was a chemistry major with an interest in philosophy (and was elected to Phi Beta Kappa in his junior year, graduating Summa Cum Laude, first in his class). His experiences as a student at Harvard Medical School, particularly the clinical rotations he had at the Massachusetts Mental Health Center (MMHC), encouraged him to go into psychiatry with an eye to becoming a psychoanalyst.

Following a medical internship in California, Joe returned to Boston for his residency at MMHC, which at the time was a hotbed of psychoanalytic thinking and training. As he told the story, it was the experience of watching a patient with a severe depression have a dramatic recovery from a course of electroconvulsive therapy (ECT) that initially got him interested in biological psychiatry. During this era, psychopharmacology was in its infancy (certainly at MMHC), and Joe (along with other residents at MMHC) was treating patients with depression utilizing psychoanalytic-oriented

therapy; but one very ill patient was given ECT and had a remarkable response. A few other experiences of patients having astonishing recoveries after being given imipramine or phenelzine (the only antidepressants then available) piqued his interest.

Fortunately for Joe, Milton Greenblatt was setting up a depression research unit at MMHC to study the effects of these new antidepressant medications, and a research laboratory at the Peter Bent Brigham Hospital across the street had developed the capacity to measure the deaminated metabolite of norepinephrine, vanillylmandelic acid (or VMA), in urine. Working with Gerry Klerman, Dick Shader, and George Henninger, he began treating patients with various new experimental agents. Moreover, he assessed VMA in the urine of patients who were given these and other medications. What these original studies demonstrated was that imipramine and phenelzine both cause an increase in VMA (signaling extraneuronal metabolism), which he was able to link to their antidepressant effects. With a few papers related to this research under his belt, he went to National Institute of Mental Health (NIMH) as a Clinical Associate in 1963, and eventually stayed for 4 years, working as a Research Scientist from 1965 to 1967 (with, among others, Seymour Kety, Irv Kopin, Jack Durell, and Saul Schanberg). It was during these years that Joe wrote the landmark paper, entitled 'The Catecholamine Hypothesis of Affective Disorders: A Review of Supporting Evidence', published in the *American Journal of Psychiatry* (AJP) in 1965 (the 4th paper he wrote).

This paper, which, it may be fairly said, launched a revolution in the general understanding of neurotransmitter function and affective disorders and formed the basis for research in the field for at least the following 20 years, is the most frequently cited paper ever published in the AJP. Revised and updated versions of the ideas contained in this paper were also published in *Science* in 1967 (with Seymour Kety as a co-author) and in the *New England Journal of Medicine* (in 1969).

After his time at NIMH, Joe returned to Boston in 1967 and set up the Neuropsychopharmacology Laboratory at MMHC, which remained his base for the rest of his scientific career. At MMHC, working with a group of collaborators, his continued research in animals and patients with depression resulted in the publication of a series of papers entitled 'Toward the Biochemical Classification of Depressive Disorders (I-X)', in which he and his colleagues described data from urinary measures of norepinephrine and its metabolites suggesting that depression was actually a group of disorders, each with a particular 'signature' that could be divined from the study of the noradrenergic components of the urine. Thus, he delineated biochemical subtypes such as 'unipolar endogenous', 'schizophrenia-related', etc that were predictive of the clinical groupings. This work, coming before the advent of modern neuroimaging or genomics, presaged much of the current research within neuropsychopharmacology

regarding the development of biomarkers of subtypes of psychiatric disorders.

Joe was the editor of the *Journal of Psychiatric Research* for over 10 years, and a member of the American College of Neuropsychopharmacology (ACNP) since 1966. He was an ACNP Life Fellow Emeritus at the time of his death. We can picture Joe as a constant presence at ACNP meetings, quietly listening to presentations, prepared to pull us aside to talk about the implications of what he was hearing. At the meetings, he was often quiet, but his mind was constantly at work.

At MMHC, Joe became the senior mentor for a string of young investigators—Danny Weinberger, Carl Salzman, Jon Gudeman, Gerry Cassens, Paul Orsulak, Carl Schwartz, Rick Shelton, and Jon Mooney, with the two authors of this memorial piece also among them. All of us would probably say the same thing about Joe—that he was a masterly mentor, that he was willing to listen, to carefully dissect what we wrote, to argue with us about the rationale for our experiments, and to force us to hone our thinking to be more precise. When he took someone on as a mentee, nothing was more important—not his own work, not his own sleep. The two of us owe our scientific careers, in large measure, to Joe; he taught us how to demand the best of ourselves, largely by giving us the best that he had to offer.

Another aspect of Joe's creative energies had a different bent. He was honored by the *New York Times* on December 31st, 2006, by being listed as one of the people of significance in 'The Lives They Lived' section. This was not for this work on the biochemistry of depression, rather it was for his contributions to the understanding of artistic creativity and mood. In his writings, he focused on Rembrandt, Miro, and Rothko, primarily, but, as with his

research on catecholamines, this was not a superficial avocation. Within the art world, he was seen as a serious and creative scholar, as reflected in the *New York Times* recognition.

Joe leaves Betsy, his wife of 40 years, and two sons, Peter and Michael. Working together with some of Joe's friends and with the faculty at the MMHC (now part of the Beth Israel Deaconess Medical Center Department of Psychiatry in Boston), Joe's family established a fund to perpetuate Joe's name and his interest in promoting research—the Joseph J Schildkraut Prize for Research Excellence. This prize to reward and encourage research of psychiatric residents in the MMHC-sponsored Harvard Longwood Psychiatry Residency will continue to link Joe's name to his key role as a mentor, a fitting way, we believe, to honor him.

A Memorial Service was held at Harvard for Joe 3 months following his death. Following the service in Memorial Church within Harvard Yard, the Harvard College band played a medley of Harvard songs as Joe's family, friends, and colleagues marched through the campus to the Harvard Faculty Club for a celebration in his honor. We learned then about yet one other aspect of Joe—that he followed football games, particularly Harvard games, with great interest. Just one more thing that Joe knew about in great detail.

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