

## IN MEMORIAM

# Richard Jed Wyatt, 1939–2002

The ACNP lost one of its favorite sons June 7, 2002. Richard Jed Wyatt succumbed to lung cancer after an heroic three-year fight, which at times seemed as if it might turn miraculously in his favor. It was Richard's third struggle with cancer. He beat the odds the first time when he recovered from stage IV Hodgkin's Disease in his 30s, and he did it again at age 60 in a battle with Burkitt's Lymphoma. In many ways, Richard's scientific career also was characterized by triumphs and achievements that challenged the odds.

Richard Wyatt was one of the preeminent figures of his generation of biological psychiatrists. A clinician, neuroscientist, educator, and mentor to a generation of current leaders in schizophrenia research, Richard spent his career at the intramural research program of the NIMH. He came to NIMH in 1967 after finishing a pediatric internship at Case Western Reserve and two years of psychiatry residency at the Massachusetts Mental Health Center. At that time a military draft was in effect, but a highly select group of doctors were able to fulfill their obligation in the Public Health Service at NIMH. It was the beginning of the golden era of clinical psychopharmacology and neurochemistry research in the intramural research program. His first assignment was to run a clinical research ward with another clinical associate, David Kupfer, under the direction of a clinical associate one year their senior, Herbert Meltzer. Richard's early work focused on sleep, and soon after starting his duties he published a paper about sleep in schizophrenia, which noted that schizophrenics failed to show REM rebound after sleep deprivation. More sleep studies followed, which initiated a long-standing collaboration and friendship with Chris Gillin. His interest in the neuropharmacology of sleep led to the first report that antidepressants (in this case, MAOIs) suppressed REM sleep and could treat narcolepsy. In his second year, Richard worked in the laboratory of Julie Axelrod, which was a privilege coveted by many at NIH, but available to only a few. Richard learned the principles of enzyme assays and with Dennis Murphy, developed a platelet assay for monoamine oxidase. This assay became a cen-



terpiece of Richard's early scientific career and led to one of the first replicated biologic correlates of schizophrenia. The finding of low platelet MAO activity in patients with schizophrenia was seen at the time as a turning point in schizophrenia research and produced highly cited papers in *Nature* and *Science*.

After two years on the main NIH campus, Richard decided to take a road less traveled and accept a position at the St. Elizabeth's Hospital facility in Southeast Washington in the Laboratory of Clinical Psychopharmacology. This took Richard out of the mainstream of NIH life and was seen by his peers as a risky career move. Richard, however, recognized a unique opportunity to work in a rich clinical environment that also was

home to Floyd Bloom, Erminio Costa, Gian Salmoiraghi, and Norton Neff. He once enthusiastically reminisced that the William A. White building at that time was a neuroscience paradise on the grounds of an insane asylum surrounded by a slum. Richard became an NIH lab chief at the age of 33. By 37, he was director of the St. Elizabeth's division of the NIMH Intramural Research Program.

The St. Elizabeth's establishment that Richard created became a preeminent training program for clinicians and basic researchers interested in schizophrenia. Among the schizophrenia investigators whose research careers began there are: Henry Nasrallah, Steven Potkin, Joel Kleinman, Bill Freed, Daniel Luchins, Dilip Jeste, Lynn DeLisi, Craig Karson, Karen Berman, Darrel Kirch, David Shore, John Morihisa, Richard Shelton, Jean-Lud Cadet, William Lawson, Jack Grebb, Michael Egan, and myself. Janice Stevens and Fuller Torrey were frequent contributors to the Wyatt research community for over two decades. Part of Richard's unique vision was to have basic and clinical investigators interacting *de rigueur* in literally the same room, attending clinical rounds together, discussing patients, research protocols, and research findings. Basic scientists were not left isolated at the bench and clinicians were expected to develop bench projects. The clinical research wards were on one side of the building and basic labs studying neuropharmacology in rodents and primates were 50 feet away on the other side. As a mentor, Richard encouraged creativity; he believed in learning by doing. He pushed for new ideas, challenged old ones, and gave his associates the opportunities to pursue their own curiosities. His door was rarely closed, and he always had time to listen and to give advice. The *esprit de corps* and camaraderie in the Adult Psychiatry Branch under Richard Wyatt were widely acknowledged and envied at the NIH.

Richard presided over a research portfolio that was as varied as it was innovative. His lab tested numerous biochemical theories of schizophrenia, from the dopamine hypothesis, to abnormal methylation of indoleamines, to autoimmunity. He was instrumental in the development of a variety of neurochemical assays and in their applications in basic and clinical studies. Richard probably never gave up the notion that if he just had the right molecule and a good assay, he could get to the core of schizophrenia. His laboratory was responsible for several archival developments in schizophrenia research, including the first systematic brain imaging studies, the first brain tissue archiving for postmortem neurochemical analyses, and the first systematic approach to experimental therapeutics. His contributions were honored with a number of prestigious awards, including the Efron Prize of the ACNP and the Lieber Prize of NARSAD.

Richard's vision, curiosity, and scientific instincts were ideally suited to the IRP environment of the 1970s and

1980s. Investigators had extraordinary opportunities to pursue their scientific interests, make frequent and rapid midcourse corrections, and take almost instant advantage of new technologies and scientific discoveries. It was in the context of this opportunity for scientific adventure that Richard launched a landmark series of studies of brain plasticity, long before it was widely appreciated as important, let alone a hot topic. In collaboration with Bill Freed, Richard carried out a series of pioneering studies of the effects of brain grafting in rodents and primates. His group was the first to demonstrate the viability of fetal substantia nigra grafts and of autologous adrenal medulla grafts to reverse aspects of experimental Parkinsonism.

Richard was willing to take risks and to let projects fail and be wrong, and was not afraid to call it as he saw it. In the last 10 years of his life, he became especially interested in the possibility that untreated psychosis was neurotoxic and could produce irreversible neurodegeneration. He reanalyzed the seminal data of Philip May at Camarillo State Hospital, and believed it showed that delaying treatment led to a poor outcome. Richard became a vocal public advocate for the view that untreated psychosis was neurotoxic, but when he was unable to confirm this hypothesis in a large study of the effects of repeated and prolonged drug-free episodes, he had the courage and objectivity to revise his position and reject what had attracted a considerable following. His last scientific project was an ambitious epidemiological study of first-break psychosis in collaboration with the Department of Defense to characterize premorbid risk and protective factors. He continued to collect and analyze data until the final days of his life.

Richard was also a tireless advocate for raising the public consciousness about mental illness and lobbying for increased research funding. He volunteered generously of his time and energies to help organize NAMI, to serve on the board of NARSAD, to serve as president of the Manic-Depressive Illness Foundation, and to lobby government officials. He was an active participant in the educational and executive functions of the ACNP. In collaboration with his wife, Kay Jamaison, he produced a series of award-winning public television programs about the arts and mental illness. Richard's struggles with cancer were inspirational, especially so in the past three years. He faced disheartening and repeated bad luck with exceptional dignity, optimism, and wisdom. It was impossible to see him during these last three years and not be deeply moved and in awe of his strength and humanity.

In May of 2001, the NIMH IRP held an all-day scientific symposium in honor of Richard Wyatt, focused on areas of neuroscience that had interested him during his career. The participants, including Sol Snyder, Floyd Bloom, Erminio Costa, Pat Goldman-Rakic, Chris Gillin, and Robert Belmaker, made note of Richard's role in shaping the intramural research environment and in changing

the landscape of schizophrenia research. Psychiatric research owes an immeasurable amount to this man.

As involved as Richard was with the world of neuroscience research and with the public policy challenges of mental illness, he was a very private person. He often said that he had difficulty expressing emotion. This is ironic considering how much his scientific offspring felt for him. However, when it came to the four principal people in his life, his wife, Kay, and his three children,

Chris, Justin, and Elizabeth, he had no limitations in expressing his love and appreciation for them, and the degree to which he was grateful for their love and support. We are all grateful and better for having had Richard Wyatt in our lives.

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