

GUEST EDITORIAL

Julius Axelrod (1912–2004)

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Julius ('Julie') Axelrod passed away in his sleep at his home in Rockville, Maryland, on December 29, 2004 at the age of 92. Pre-deceased by his wife Sally Taub Axelrod, he leaves two sons, Paul Axelrod of Ripon, Wisconsin, Alfred Axelrod of Wausaukee, Wisconsin, and three grand children.

Julie was born on the Lower East Side of Manhattan on May 30, 1912, the son of Polish immigrant parents. His father supported the family as a basket-maker. Julie graduated with a bachelor degree in biology in 1933 from tuition-free City College of New York, which he described as 'proletarian Harvard.' He applied to several medical schools, but was accepted by none. At the time, there was a quota on the admission of Jews to medical schools. Julie noted in an interview 'I wasn't that good a student but if my name were Bigelow I probably would have gotten in.' Work was difficult to find in the Depression. He first worked as a laboratory technician at the Harriman Research Laboratory at the New York University School of Medicine. In 1935, he obtained a position testing vitamin supplements for the New York City, Department of Health's Laboratory of Industrial Hygiene, where he remained until 1946. Julie took night classes at New York University and completed a Master of Science in chemistry in 1941.

In 1946, he joined the laboratory of Bernard Brodie at the Goldwater Memorial Hospital on Welfare Island as a technician and began his research on metabolism of analgesic medications. When Brodie moved his laboratory to the National Heart Institute in 1949, Julie joined him and was appointed a research chemist at the NIH. He continued his work on drug metabolism and began his studies on sympathetic amines. But, Julie came to realize that his research contributions would not be fully recognized unless he had a doctorate. In 1954, he took a leave of absence from NIH and enrolled in the PhD program in the Department of Pharmacology at George Washington University and completed his thesis, 'The Fate of Phenylisopropylamines' under George Mandel in 1955. Seymour Kety then recruited Julie to become the Chief of the Section on Pharmacology in the intramural program of the National Institute of Mental Health, a position that he held until 1984.

In 1957, he commenced his very productive research on the disposition of biogenic amines. He identified and characterized the enzyme catechol-*o*-methyl transferase, as well as several other methyl transferases involved in biogenic amine metabolism. Using the first batch of [14C]norepinephrine, he



Julius Axelrod, Ph.D. (05/30/1912–12/29/2004). Photo credit: National Library of Medicine.

observed that after its intravenous injection into rats the vast majority was rapidly metabolized, as expected, but a very small amount of intact norepinephrine persisted in the tissues. In the typical Axelrodian strategy of pursuing the unexpected, he was able to show that the sequestered norepinephrine had been transported into sympathetic nerve terminals and that tricyclic antidepressant drugs inhibited this transport process. As the monoamine oxidase inhibitors were thought to exert their antidepressant effects by preventing the degradation of biogenic amines, he proposed that the tricyclic antidepressants worked by prolonging the action of norepinephrine at brain synapses by inhibiting its re-uptake.

In 1970, Julie was awarded the Nobel Prize in Medicine or Physiology along with Sir Bernard Katz of the University College London and Ulf von Euler of the Karolinska Institute in Stockholm for 'discoveries concerning the humoral transmitters in the nerve terminals and the mechanism for their storage, release and inactivation.'

While this chronology depicts an extraordinary life from humble beginnings to the dais in Stockholm for the Nobel Prize, it does not do justice to his remarkable personal qualities. Julie was the ultimate mentor. His laboratory was not simply a place where good science was done, but one where the fellows learned how to do good science. Julie's government-issue steel desk was strategically placed in the laboratory, where it was 4 feet from the reagent scale

and 10 feet from the scintillation counter so that every fellow would have to chat with him when either starting or finishing an experiment. He took his annual vacation in July, just as the new fellows were arriving. This unnerving practice forced the new fellows to work with the established fellows so that they became familiar with the ongoing research of the laboratory by the time Julie returned. Then, the new fellow could decide with him on potential projects that fit into the general themes of the laboratory.

Julie made sure his fellows were visible. Every fellow presented a slide talk at the annual American Society for Pharmacology and Experimental Therapeutics meeting, which was the meeting of the year. Julie would turn down seminar invitations and recommend a fellow to speak in his stead. Julie would give fellows journal articles to review. After he felt confident in the quality of these reviews, he would let the fellow sign the review so that soon the journal was soliciting reviews directly from the fellow. Once, I wrote a sarcastic review of what was a weak scientific manuscript. Julie caught me at the reagent scale and said 'Joe, a scientific article is like the person's child. You shouldn't attack it. Be constructive with your criticism.' I learned humility from a Nobel Prize winner.

Julie taught us that the best science is not simply confirming your beliefs but watching out for the anomalous results that may point to novel insights. He encouraged us to be aggressive in our research—'Be the firstest with the mostest.' He bridled a bit at the introduction of statistics into data analysis, commenting 'If you have to do a *t*-test to prove something is different, it probably isn't important.' This skepticism about statistics derived from his

uncanny ability to pose experimental questions with such clarity that the results were unequivocal. For 30 years, he trained a series of fellows, who invariably went on to distinguished careers in science and academe, a testimonial to his skills as a mentor. But there was not an arrogant fiber in him. On the day that he won the Nobel Prize, the Director of NIH asked what he would like. Julie thought for a moment and then replied, 'A parking space would be nice.'

While in his mid 80s, Phil Sharp and Dick Wurtman invited him to MIT to give a seminar. The room was filled with young students and fellows. He apologized that he had no new findings to discuss as he had closed down his laboratory. He then proceeded to review his Nobel Prize research, which was a *tour de force* on the logic of experimental design. The students gave him a standing ovation.

In 1992 and again 2002, a symposium was held in Julie's honor at the NIH to celebrate his 80th and 90th birthdays. He thoroughly enjoyed learning what his mentees were doing scientifically. But he seemed surprised at the affection with which he was held, commenting at the most recent one — 'You really do care about me!' In 'An Unexpected Life in Research,' Julie wrote 'F. Scott Fitzgerald once stated that there are no second acts in American lives. After a mediocre first act, my second act was a smash. So far the third has not been so bad' (1988). All who knew him will profoundly miss his great mind and his generous and graceful spirit.

JT Coyle

Eben S Draper, Professor of Psychiatry and
Neuroscience, Harvard Medical School
E-mail: joseph_coyle@hms.harvard.edu