Recognizing a Lifetime of Radiopharmaceutical Development

"As de Hevesy was the father of the tracer principle, it is fitting that Bill Eckelman be this year's awardee [of the Georg Charles de Hevesy Nuclear Medicine Pioneer Award] as he has spent his career developing tracers for various applications," said Michael J. Welch, PhD, in his presentation of the award at the SNM Annual Meeting held in June in San Antonio, TX. Early in his career, William C. Eckelman, PhD, worked at Brookhaven National Lab in Upton, NY, where he helped develop a ^{99m}Tc kit for labeling red blood cells and the instant DTPA kit during the early 1970s. "This began the trend in instant technetium kits," said Welch.

As a professor of radiology at George Washington University during the late 1970s, Eckelman worked on receptor ligands for SPECT and used the tracer 3-quinuclidinyl 4-iodobenzilate (IQNB) to obtain the first successful neuroreceptor image in humans. During this time, he published a paper describing the use of cyclic DTPA in hydride to label fatty acids. "This had great application in the labeling of antibodies, proteins and peptides over the years," said Welch.

Eckelman became the associate director and later vice president of The Squibb Institute for Medical Research in 1985 and helped bring the ^{82}Sr/^{82}Rb generator to clinical application enabling ^{82}Sr to become the first PET drug approved for experimental use. He also helped develop a technetium heart agent as well as a gadolinium-labeled MRI agent. In 1991, Eckelman moved to the National Institutes of Health where he now serves as chief of the PET department. There, the PET group is developing ^{18}F- and ^{11}C-labeled receptor ligands and is also working on new techniques for labeling proteins.

Eckelman is currently the editor-in-chief of the journal *Nuclear Medicine and Biology*. He previously received the Paul C. Aebersold Award of the SNM and the Corporate Achievement Award of the ACNP. He earned a PhD in hot atom chemistry at the Washington University in St. Louis.

Upon accepting his award at the SNM Annual Meeting, Eckelman modestly responded by saying: "Developing new radiopharmaceuticals has always been a very satisfying endeavor, but far from a one-man job. I'm very happy to acknowledge the 260 or so colloborators who have really made the development of these radiopharmaceuticals possible. Thank you very much."

A True "Scientist's Scientist" Wins Aebersold Award

Colleagues hail Joanna S. Fowler, PhD, as "truly a scientist's scientist." This year's winner of the 1997 Paul C. Aebersold Award is "extremely hard working, extremely productive, extremely innovative," said Alfred P. Wolf, PhD, in presenting the award to Fowler at the SNM Annual Meeting. During her 26 years at Brookhaven National Laboratory, Fowler has established herself as one of the leading chemists in radiopharmaceutical chemistry and its application to research in the neurosciences using PET. Among her many accomplishments, she played a major role in the development of FDG.

Fowler is perhaps most well known for her dopamine research. She developed a method for measuring enzyme concentrations in the brain quantitatively with the suicide enzyme inhibitor, ^{11}C-L-deprenyl. In addition, she developed the use of the deuterium isotope effect, which decreases the reaction rate of a ligand; some ligands have reaction rates that overlap with the blood flow rate making it difficult to get an accurate modeling of a particular compound. This technique led to a modeling of the enzyme monoamine acid oxidase B (MAO B), which plays a key role in Parkinson's disease. Following this research, Fowler conducted an "almost serendipitous" study of dopamine in the brain of humans during normal aging, said Wolf. Fowler saw that some normal volunteers had extremely low MAO levels, similar to people taking MAO inhibitor drugs. She later found that these individuals happened to be smokers. She then verified that smokers' brains had reduced levels of both

(Top) From left to right: Michael J. Welsh, PhD, presented William C. Eckelman, PhD, the Georg de Hevesy Award at the SNM's Annual Meeting this past June along with outgoing SNM president Michael D. Devous, PhD.

(Bottom) Joanna S. Fowler, PhD, (left) was the 1997 Paul C. Aebersold Award recipient. The award was presented by Alfred P. Wolf, PhD (right).

SNM Annual Award Winners

1997 SNM Presidential Distinguished Service Awards:

Henry M. Chilton, PharmD
B. Leonard Holman, MD
William J. MacInytre, PhD
Kenneth A. McKusick, MD
James A. Ponto, MS, rPh
Mark H. Rotman, PharmD
Mark Tulchinsky, MD

1997 SNM Distinguished Educator Award:

Warren H. Moore, MD

MAO A and MAO B. MAO inhibition by smoke may account for the fact that smokers have a reduced risk of Parkinson's disease. The research could also partly explain why people who suffer from depression are more likely to smoke.

In another aspect of her work, Fowler successfully labeled cocaine with ^{11}C and was the first to show that the major site of ^{11}C-cocaine binding in humans was to dopamine transporters in the basal ganglia. She was also able to demonstrate that the pharmacokinetic profile of ^{11}C-cocaine paralleled the euphoria profile in cocaine users that was established by other groups.

Fowler earned a PhD at the University of Colorado, Boulder in 1967. She earned a post-doctorate degree at the University of East Anglia in England and was hired by Brookhaven as a chemist in the chemistry department in 1971. She twice received the Jacob Javits Investigator Award in the Neurosciences and is currently serving as a member of the Board of Scientific Counselors for the National Institutes on Drug Abuse and as a member of TRIUMF, Life Sciences Visiting Committee.

Education and Research Foundation Awards

Tetalman Memorial Award

Malik E. Juweid, MD, the 1997 winner of the Tetalman Memorial Award in Nuclear Medicine presented by the Education and Research Foundation, has conducted a significant body of research in the eight years since coming to the United States after receiving his medical training in Germany. As a research fellow at Massachusetts General Hospital, Juweid worked on the use of polyclonal human IgG for inflammation imaging. He was then awarded a Fogarty fellowship from the National Institutes of Health to work on proving the "binding-site barrier" hypothesis, namely, that the penetration of antibodies in tumors may be prevented by the antibodies' success in binding to the first layers of tumor cells. Juweid completed an additional year of clinical training at the University of Pennsylvania and became board certified by the American Board of Nuclear Medicine in September, 1992.

In December, 1993, he joined the Center for Molecular Medicine and Immunology in Newark, NJ as the director of nuclear medicine. He is currently conducting phase-1 trials in radioimmunotherapy of medullary thyroid cancer. He also serves as an adjunct assistant professor of radiology at the University of Pennsylvania and as a reviewer for the FDA orphan drug grants program.

Student Fellowships

Brian Auster — Martin Zalesak

Pilot Research Grants

Francois Bernard, MD — David E. Modrack, PhD

Cassen Fellowship

Kurt R. Zinn, DVM, PhD

Paul Cole Fellowships

Twelve $1000 scholarships are awarded every year to student technologists who have shown a financial need and a strong academic performance. The money goes toward financing their nuclear medicine education. This year's winners are:

- Karen Auger
- Maria Carter
- Hanh Nguyen
- Jennifer Bowers
- Stephanie Krause
- Eleni Kourembanas
- Greg Smith
- Ashley Tilman
- Corey Comeaux
- Bradley Wells
- Gerry Hechanova
- Renee Moyer

Finding a New Way to Target Cancer Cells

Intrigued by the tenaciousness of cancer cells, this year's winner of the Mallinkrodt fellowship would like to beat them at their own game. Vikas Kundra, MD, PhD, a resident/fellow in the department of radiology at Brigham and Women's Hospital in Boston, will investigate using telomerase as a target for imaging cancer cells. Telomerase, a recently discovered ribonucleoprotein enzyme, has been found to be active in more than 80% of cancers tested for its presence including lung, breast, colon and prostate. It is thought to play a role in enabling cancer cells to undergo indefinite divisions and subvert the aging process that occurs in normal cells.

When nonmalignant cells divide, the ends of chromosomes, called telomeres, shorten with each division. Gradual telomere shortening is thought to act like an hourglass in determining the number of times a cell can divide before it dies. Normal tissues of the body (except for germ cells) express zero or low levels of telomerase activity. In contrast, cancer cells have high levels of telomerase activity. It is thought the cells activate telomerase to add DNA to the ends of chromosomes and thus prevent telomere shortening.

In his research proposal, Kundra outlined four specific aims that he would accomplish with the Mallinkrodt grant: First, he will identify an altered form of DNA that serves as a telomerase substrate and is resistant to enzymatic degradation. Next, he will synthesize a stable telomerase substrate that is specifically retained by neoplastic cells. He will then label the stable telomerase substrate with a radionuclide such as ^{111}In, ^{99m}Tc or ^{123}I. Lastly, Kundra will inject the stable, tagged telomerase substrate into mice to see if it localizes human tumor cells that possess telomerase activity. If the project is successful, therapeutic radiopharmaceuticals can be designed to shut off telomerase activity in cancer cells, vastly shortening the cells' lifespans.

Kundra's illustrous career as a researcher is marked with many academic accomplishments. He graduated with honors from Harvard Medical School in Cambridge, MA, in 1995 and was a Fulbright scholar. He previously worked in Dr. Bruce Zetter's laboratory at Harvard on the signal transduction pathways involved in Platelet Derived

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SNM Award Winners

(Continued from page 24N)

Growth Factor receptor-mediated chemotaxis versus cell division, which was the basis for his PhD thesis.

Kundra, however, also has a strong personal interest in cancer research. He was diagnosed with cancer when he was in tenth grade. "As a patient going through surgery, radiation and chemotherapy, I felt that the cure was worse than the disease," he wrote on his application to the residency training program at Brigham and Women's Hospital. "In twelfth grade, I had my last treatment. The experience taught me the extent of life, its shortness, its wonder, its beauty." Kundra has taken those insights to a microcosmic level to explore the beauty and transience in the life of a cell.

Testing a New Tracer for Cardiac PET Studies

William F. Oellerich, MD, PhD, winner of this year's DuPont Pharma/Society of Nuclear Medicine Research Fellowship for Cardiovascular Nuclear Medicine, recognizes the need for a radiopharmaceutical that can reliably quantify glucose metabolism in cardiac studies. He plans to determine if ^{11}C-glucose can achieve more accurate measurements of glucose metabolism in the heart than FDG. It is well recognized that FDG is limited by its nonspecificity relative to the overall glucose utilization, thus there is the need to correct mathematically for the differences in metabolism between FDG and glucose. Recent research at Washington University in St. Louis has shown that ^{11}C-glucose (radiolabeled with ^{11}C specifically at the one-carbon position) can provide accurate measurements of glucose utilization in the brain, which leaves the possibility that it could provide accurate measurements in the heart.

In his project, Oellerich's overall objective is to validate that myocardial glucose utilization can be quantified by PET and ^{11}C-glucose using an appropriate compartmental model of ^{11}C-glucose kinetics. He plans to test the method in canine studies to see if the measurement of myocardial glucose utilization using PET correlates with direct measurements of glucose utilization in blood samples.

Oellerich earned his MD and PhD from the University of Tennessee in Memphis and is currently a postdoctoral research fellow in the cardiovascular division at Washington University. During the course of his PhD training, he published two manuscripts and four abstracts describing the impact of neuropeptide Y on adrenergic transmitter release.

—Deborah Kotz

Past President's Message

(Continued from page 30N)

the initiation of its first programs!

NRC. Stimulated by the National Academy of Sciences Institute of Medicine report, substantial progress toward significant regulatory reform regarding the medical use of byproduct material has been made, largely through the auspices of the SNM/ACNP leadership and our joint Government Relations Committee. The NRC Commissioners, weighing all the comments received regarding the reform of the medical program, have directed the NRC staff to submit a plan for revising 10 CFR Part 35 and associated guidance documents, as well as the Commission's 1979 Medical Policy Statement by June 6, 1997. The program should describe how 10 CFR Part 35 can be restructured into a risk-informed, more performance-based regulation to be implemented by June 30, 1999. In addition, the Commission decided to terminate the "Unauthorized Usage" rule-making, consistent with the comments provided to the Commission from ACNP and SNM.

FDA. I have worked with others on two fronts to improve approval processes. With NEMA, we achieved approval of 511-keV collimators, which had previously been rejected by the devices branch. Also, I met with many FDA leaders, across several centers, in cooperation with CORAR and ICP, to successfully add diagnostics to the recently announced Cancer Fast-Track approval initiative. The SNM also worked with Syncor to file an appeal brief in Syncor's suit against the FDA regarding the authority to regulate PET radiopharmaceuticals. The case awaits oral arguments which are scheduled for September 11, 1997. SNM has also assisted Senator Ted Stevens (R-AK) in drafting language for legislation that would reform the regulation and use of PET under the FDA. Finally, Representatives Richard Burr (R-NC), Gary Condit (D-CA) and Tom Delay (R-TX) have introduced legislation (HR 1060) that would provide important protection for physicians and pharmacists against unwarranted regulation by the FDA. The legislation clarifies that states, and not the FDA, have regulatory authority over pharmacy compounding. The bill also applies to licensed physicians involved in compounding. In addition to compounding provisions, the legislation would also withdraw FDA-proposed regulations of PET drug products. The legislation would make null and void the FDA proposal to expand regulation of PET drugs, and return this issue to the state boards of pharmacy.

Brain Attack. I represented the SNM at a symposium sponsored by NIH/NINDS to launch a national program focused on the treatment of acute stroke (watch for national ads about brain attacks that will parallel the public education programs of the 1960s for heart attacks), subsequent to the approval of rt-PA for such treatment. This has resulted in the design and approval of a clinical trial in cooperation with Genentech to combine SPECT imaging of regional cerebral blood flow with acute stroke treatment by thrombolysis to determine if SPECT can be used to screen patients at risk for hemorrhagic transformation.

Whew, and that's just a sample! I hope you continue to read the journal and visit our home page to get more details on these and the many other SNM activities the come along with your membership. I've had a wonderful year as your president and want to extend my thanks to you for providing me with this opportunity.