A Profile of Dr. Leonard Berg

This profile of Dr. Berg, written by Linda Sage, appeared in the Washington University Record newspaper in September 1995. It is reprinted here in its original form. Certain references are now inaccurate.

In 1972, when neurologist Leonard Berg, M.D., was a successful private practitioner, he wanted to improve the diagnosis of dementia. So he asked his department head, William Landau, M.D., if he could start a faculty discussion group. Landau was glad to oblige and offered to supply lunch. We'll bring brown bags, Berg insisted.

Berg, professor of neurology and director of the Alzheimer's Disease Research Center, is now the recipient of $19.4 million in federal grants for dementia research. "This tremendous operation is the result of his initiative to establish a long-term scientific effort," said Landau, professor of neurology. "He began with the modest lunch-time meetings and now is one of the father figures in the field."

Berg chairs the medical and scientific advisory board of the national Alzheimer's Association and sits on the parent board. When the group organized a congressional hearing in 1992, he spoke about the burden of the disease and hopes for a treatment in the not-too-distant future. Several C-SPAN viewers called the association the next day, impressed that this erudite man, with his broad grasp of scientific issues, also was the type of person they would want for a family physician.

"He comes across as very knowledgeable but very caring," said Creighton Phelps, Ph.D., director of the Alzheimer's Disease Research Centers Program at the National Institute on Aging (NIA). "To be a scientific leader as well as a compassionate doctor makes him a unique person."

Berg's connection with Washington University began in 1943, after he graduated from Soldan High School at age 15. He enrolled in an accelerated pre-med program in psychology and chemistry, and worked his way through school by playing dance music on his clarinet and saxophone. In 1945, when tuition was $500 per year and dementia was considered a normal part of aging, he entered the School of Medicine. He decided to become a neurologist during a freshman neuroanatomy class taught by neurologist James L. O'Leary, M.D., Ph.D.

After internships and residencies at Barnes Hospital, the Neurological Institute in New York and the National Institutes of Health in Bethesda, Md., Berg returned to St. Louis in 1955. He turned down a full-time faculty position, preferring to teach part time. "I was concerned that I wouldn't be successful in research," he recalled. Instead, he went into practice with Irwin Levy, M.D., then professor of clinical neurology.

That partnership survived until Levy's death 24 years later, eventually moving to Barnes Hospital West Pavilion. During this time, Berg encountered older patients with a dementing condition caused by hydrocephalus--excess fluid in the brain's cavities. "The burning question was how to distinguish patients who would benefit from surgery to drain the fluid from those with cerebral atrophy, which also enlarges the cavities," Berg explained.

Alzheimer's disease now is known to be the leading cause of cerebral atrophy--shrinkage of the brain. First identified in 1906 by the presence in the brain of tangled neurons and plaques of a protein called amyloid, it was thought to be a rare condition. But Berg was noting these features in autopsy specimens from some of his demented patients. So were pathologists elsewhere as more people lived into their 80s and 90s. "So a few people started sounding the trumpets and suggesting that Alzheimer's was a big problem," Berg recalled.
Alzheimer's disease now afflicts 4 million Americans. The fourth leading cause of death among adults, it costs the United States $100 billion per year. But the federal government spends only $300 million per year on Alzheimer's research. "This is not nearly enough because the number of cases could triple in the next 50 years," Berg said. "This will lead to financial disaster for our country, unless we find some way to prevent the disease or delay its onset or progression."

The brown-bag group and literature surveys for a book chapter prompted Berg to apply for federal research funds in the mid-1970s. After his first two applications were rejected, he read an article in the Washington University magazine about the research of Jack Botwinick, Ph.D., now professor emeritus of psychology, and Martha Storandt, Ph.D., professor of psychology, on the Hilltop Campus. Drawing upon their expertise in the psychology of aging, Berg submitted a proposal to the National Institute of Mental Health (NIMH).

After the collaborators showed they could distinguish healthy subjects from persons with mild dementia, NIMH awarded a four-year grant in 1979 to compare the two groups over time. This grant evolved into three five-year program project awards from the National Institute on Aging. For the past 16 years, Berg and his colleagues have followed the yearly progress of healthy and demented participants through clinical, psychometric, radiologic and electrophysiologic studies. To date, 1,200 subjects have participated in the study.

**Setting international standards**

This Healthy Aging and Senile Dementia program project has set international standards for evaluating patients with Alzheimer's disease. "Diagnosis is what I associate with Dr. Berg and his colleagues," said the NIA's Phelps. "They have developed a dementia rating scale that allows one to find patients at a very early stage and then track them to see how the disease develops."

This diagnostic expertise permits patients to plan for care while they are still able. "And being able to identify patients at a very early stage will be extremely useful when there is some treatment that will stall the progress of the disease," Phelps explained.

The Washington University team was the first to validate its criteria through autopsy studies. Ninety-five percent of the patients they have diagnosed as having Alzheimer's disease are found to have plaques in the brain when they die. The criteria are accurate even for patients in the initial stages of the disease.

The Healthy Aging and Senile Dementia project also has shown that the disease prevents the brain from ignoring irrelevant information as a person tries to learn new tasks. And one component studied the effects of the disease on patients' families. Researchers also have discovered that neurofibrillary tangles accumulate in certain regions of the healthy brain and therefore do not necessarily indicate Alzheimer's disease. Plaques, on the other hand, appear to be a hallmark because "control" subjects with plaques and without head injuries always turn out to have had some indications of impairment.

**Grant creates center**

In October 1985, about 18 months after the program project grant was awarded, Berg received one of the NIA's Alzheimer's Disease Research Center grants. This award recently was renewed for the third five-year period. Early studies focused on the part of the brain that uses acetylcholine as a chemical messenger. Another project identified subtle changes in visual perception among Alzheimer's patients. Then attention shifted to brain cell damage by the chemical messenger glutamate and the programmed cell death that can destroy neurons. Both of these topics now are major foci of research at the School of Medicine and are pertinent to many other neurologic disorders.

The center grant has supported many pilot projects that have led to independent funding. These include studies of the interrelationship between Parkinson's and Alzheimer's diseases, the effect of blood sugar and insulin levels on brain function, the ability of Alzheimer's patients to drive, and the molecular genetics of Alzheimer's disease.
"Recent advances here and elsewhere have been spectacular in terms of understanding the causes of Alzheimer's disease," Berg said. "So it is important to support research that will follow up on these leads. Because Alzheimer's affects mainly the elderly, finding ways to delay the onset of the disease by just five or 10 years would halve the number of affected people," he explained.

Shortly after the first grant was awarded, Berg realized that families in the research study needed a support group, so he helped establish a St. Louis chapter of the association. Various members of his team still are involved, and Berg is a frequent speaker on the Alzheimer's Association's behalf. "He is very willing, kind and insightful," said Executive Director Kathleen O'Brien. "He can see how laboratory research, clinical research and ways to help families all fit into the big picture."

In 1986, Berg was elected to the national Alzheimer's Association's medical and scientific advisory board, which he now chairs. The board assigns about $6 million in research funds each year. He joined the association's parent board in 1989, is on its ethics advisory panel and often acts as a spokesman. "Leonard has been instrumental in linking our medical, scientific and caregiving programs," said Edward Truschke, president and chief executive officer of the Alzheimer's Association. "He is particularly adroit in driving a consensus by hearing all sides of a story and tying everything together in cogent ways that make people feel good about the solution."

Berg's 65-hour workweek has shrunk since he suffered a heart attack in 1993. For several months after his bypass surgery, his office received thousands of phone calls and letters from around the world. "It seemed like everyone on earth knew of his illness and was concerned," said Kathy Mann Koepke, Ph.D., research assistant professor of neurology and executive director of the Alzheimer's Disease Research Center. "Many had only heard him speak but were very moved by his knowledge and compassion." After Mann Koepke had surgery the following year, Berg did her weekly grocery shopping.

In 1997, Berg will pass the directorship of the ADRC to Eugene M. Johnson Jr., Ph.D., Norman J. Stupp Professor of Neurology, and John C. Morris, M.D., associate professor of neurology. But he intends to remain active in public service and advocacy. He also will spend time with family members. (Berg is the father of John A. Berg, associate vice chancellor for finance.)

His top priority for the next five years is to persuade more School of Medicine colleagues to study Alzheimer's disease --though 16 departments and divisions already are collaborating. "It is such an intriguing scientific problem because it has complex causes and mechanisms," Berg said. "The challenge is to understand how multiple genetic, environmental and aging factors interact to bring about the disease and all of its human and social consequences."