

In Memoriam

William R. Markesbery, M.D.: A Legacy of Excellence in Alzheimer's Disease Research and a Life Well-Lived

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INTRODUCTION

The Alzheimer's disease (AD) research, pathological, and clinical communities suffered a great loss with the untimely death of William R. Markesbery, M.D. on January 30, 2010, from complications of mycobacterium avium-complex.

Dr. Markesbery was a giant in the field of AD research. Consider: (a) Thinking broadly and before the concept of biomarkers for AD was in vogue, in 1980 Markesbery published one of, if not, the first non-central nervous system (CNS) papers on AD [1], followed by another one later in the 1980s [2]. (b) In 1981, Markesbery and colleagues published the first of several important studies that disproved the then prevailing hypothesis of AD pathogenesis, i.e., that accumulation of aluminum was an underlying cause of AD [3–5]. (c) In 1991, along with Earl Stadtman and other collaborators, Markesbery published among the first studies suggesting that oxidative stress was involved in the brain in AD [6]. This paper was followed by a series of papers by Markesbery and collaborators demonstrating elevated lipid peroxidation in the CNS in AD, as indexed by levels of the non-protein bound lipid per-

oxidation products, 4-hydroxy-2-nonenal (HNE), and iso- and neuroprostanes [7–9]. Collaborating with our group in a 1995 paper, Markesbery was instrumental in showing that protein oxidation occurred in AD brain areas rich in amyloid- β ($A\beta$) but not in $A\beta$ -poor cerebellum [10]. Markesbery's seminal review article on the oxidative stress hypothesis of AD [11] remains one of the most cited papers in the AD research field.

Bill Markesbery also provided the first neuropathological description of mild cognitive impairment, arguably the earliest detectable clinical phase of AD [12].

To support his over 400 refereed scientific publications, Bill was continuously funded by the National Institutes of Health (NIH) for his entire academic career. In fact, the University of Kentucky recently reported that Bill Markesbery had more NIH grants in his career than any other UK faculty member.

This prolific research record in AD research is one reason Bill was recently named the 23rd most cited and influential AD researcher in the world [13] and received the 2009 National Alzheimer's Association Zavan Khachaturian Award for Outstanding Achievements in Advancing Alzheimer's Science.

In 1979, Bill Markesbery's vision and entrepreneurial skills led to the establishment of the Sanders-Brown Center of Aging at the University of Kentucky. This center was awarded one of the original 10 Alzheimer's Disease Research (now Clinical) Centers in the United States with Bill as the PI, and the ADC status remains today more than 20 years later. The Sanders-Brown

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Center on Aging, through Bill Markesbery's leadership, has recruited outstanding faculty and faculty associates, who have helped build its enormous international reputation for research in aging and AD.

Bill Markesbery also served the larger AD research communities as well by acting as Chair of the Advisory Council for the National Institute on Aging at NIH and as Chair of the Scientific Advisory Committee of the National Alzheimer's Association.

Dr. Markesbery's research focused almost, but not entirely, on AD. In 1974, he was the first to describe a rare form of tardive distal muscular dystrophy, now known as Finnish-Markesbery disease [14].

In addition to being a superb researcher, Bill Markesbery was also an outstanding clinician. In 1995, he was named one of the 50 most positive doctors in America [15], an achievement consistent with his manner of treating patients and their families with compassion, respect, and dignity. These were values he learned being raised in Florence, Kentucky, and he embodied fully the moniker, Kentucky Southern Gentleman. Everyone who knew Bill was struck by his mannerisms of humility, patience, and grace, in spite of his international reputation as a distinguished AD researcher.

Bill Markesbery graduated from the University of Kentucky in 1960 in Business Administration/Economics, and as an undergraduate, he was a walk-on basketball player for legendary UK coach Adolph Rupp. However, his real sports passion was baseball, and after college he was drafted by the Cincinnati Reds to be a pitcher in their farm system. Fortunately for AD science, he injured his shoulder and realized that his professional career was over. After serving a stint in the US Army, he entered the first class of the then new Albert B. Chandler School of Medicine at the University of Kentucky. He took his residency at Columbia University College of Physicians and Surgeons under the aegis of Dr. Houston Merritt, followed by appointment in Neurology at the University of Rochester. In 1972, he joined the faculty of the Departments of Neurology and Pathology at the University of Kentucky and quickly rose to Full Professor. His great success at UK led to his being named the Commonwealth Chair of Aging.

Bill Markesbery and I were close personal friends for 35 years. In addition to publishing nearly 50 papers together over this time period, we had numerous long chats to discuss science, our families, national trends in politics, and, of course, UK sports. From these discussions I know that as much as he enjoyed using his intellectual skills and drive to provide hope and inspi-

ration to AD patients and their families, the real focal points of his life were his wife of 51 years, Barbara, and his children, Susanne, Allison, and Kendall, along with his grandchildren.

To say the least, Bill Markesbery, researcher, clinician, mentor, family man, and dear friend, will be greatly missed. The day when scientists and physicians will be able to fully understand and treat AD has been made closer because of the prolific legacy of Bill Markesbery.

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