

Impact of VA Research on Health Care for All Contributions Over Nine Decades and Counting

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In 2015, the Veterans Administration (VA) celebrated 90 years of VA research. As Associate Chief of Staff for Research at the Birmingham VA Medical Center, I pondered how to celebrate this momentous occasion for the yearly VA Research Week. My first questions were how has a structured VA Research Program been in existence for 90 years and how did it all start in 1925, 20 years before the National Institutes of Health? My thoughts since then have become especially poignant in view of the recent turmoil within the VA system that has led to questions about its position in the Healthcare System. I respond to this invitation not as the section would imply in its title: Viewpoints, but more so to share the 90-year journey of the VA in melding its tripartite mission of patient care, education, and research.

Before World War I, hospitals were considered charitable institutions for the impoverished, and the sick and injured were cared for in their homes. Passage of the Langley Bill in 1921 marked the transition from a Soldier's home with compensation/pension for injury to a true medical center orientation. The Veterans Bureau took over all Public Health Service Hospitals, and by 1925, the Veterans Bureau oversaw 50 VA hospitals and 30 000 hospitalized veterans. In 1924, a 22-member council on Medical and Hospital Affairs comprised leaders in academic, public, and private medicine endorsed a system of diagnostic hospital beds. They also initiated the US Veterans' Bureau Medical Bulletin, and the establishment of a research program with emphasis on research related to veterans' medical conditions.

The VA *Medical Bulletin* (Figure A) underscored the Medical Council's idea of a hospital-based research program seeking methods to cure disease by systematic bedside observation with an emphasis on outcomes. Before World War II, there was not a strong affiliation with medical schools; nevertheless, VA physicians were required to publish in the *Medical Bulletin*. Under the leadership of Pathologist Dr Philip B. Matz, the *Medical Bulletin* flourished with numerous publications of epidemiological and methodological articles on tuberculosis, syphilis, malaria, long-term health effects of

chemical warfare, and hospitalization and mortality among veterans with mental illness. This work culminated in seminal publications in the *New England Journal of Medicine* reporting the incidence of cardiovascular disease in veterans² and a 1938 *Journal of the American Medical Association* publication reporting a 50% incidence of neuropsychiatric disorders in veterans.³

The 1930s marked the funding of VA Research Laboratories. In 1933, the Tumor Research Laboratory at the Hines Chicago, IL, VA Medical Center (VAMC) became the first research laboratory to receive funds from VA Central Office. Dr Robert Schrek, a leader in the field of radiosensitivity, identified the first connection between sun exposure and skin cancer.⁴ The Neuropsychiatric Research Unit at Northport, NY, VAMC, under the direction of Dr Edward Lazell, pursued intriguing studies connecting immunologic and allergic abnormalities to epilepsy and schizophrenia. The systematic observations of the Cardiovascular Research Unit at Washington, DC, VAMC Unit produced a notable *New England Journal of Medicine* publication that reported the incidence of cardiovascular disease in 19870 World War II veterans under the age of 40 years with a link to hypertension,⁵ a novel connection at a time when treatment of hypertension was a raging controversy.

The exuberance of the individual research efforts waned at the end of 1930s with many of the doctors entering World War II, leaving a huge void to accommodate the many returning veterans. Recognizing a need for reorganization, President Truman appointed General Omar Bradley as Chief Administrator of Veterans Affairs in 1945. His leadership along with Dr Paul Magnuson, a highly respected academic surgeon, possessed the political clout to pass Public Law 293 giving birth to the VA Department of Medicine and Surgery. As chronicled in Magnuson's autobiography, *Ring the Night Bell*,⁶ this bypassed the long delays in the Civil Service to directly hire physicians to VA hospitals and provided the legal basis for affiliations between VA and US medical schools. From 1946 to 1952 each VA hospital had a Research and Education Committee with Service Chiefs and 2 Dean's Committee representatives. Within 6 months, VA full-time physician staff increased from 600 to 4000, and by early 1947, VAMCs—that had no resident physicians in training before 1946—now had some 1000 residents. Today ≈75% of US physicians have received some of their training in the VA hospital system with salary support from the VA.

The early collaboration between the armed services and medical schools was already in place as explained by Dr Michael DeBakey: "In WWII we had various Army General Hospital Units sponsored by medical schools. My own had the Tulane unit." Tinsley Harrison in his remembrances as Chair of Medicine at the University of Alabama: "There can

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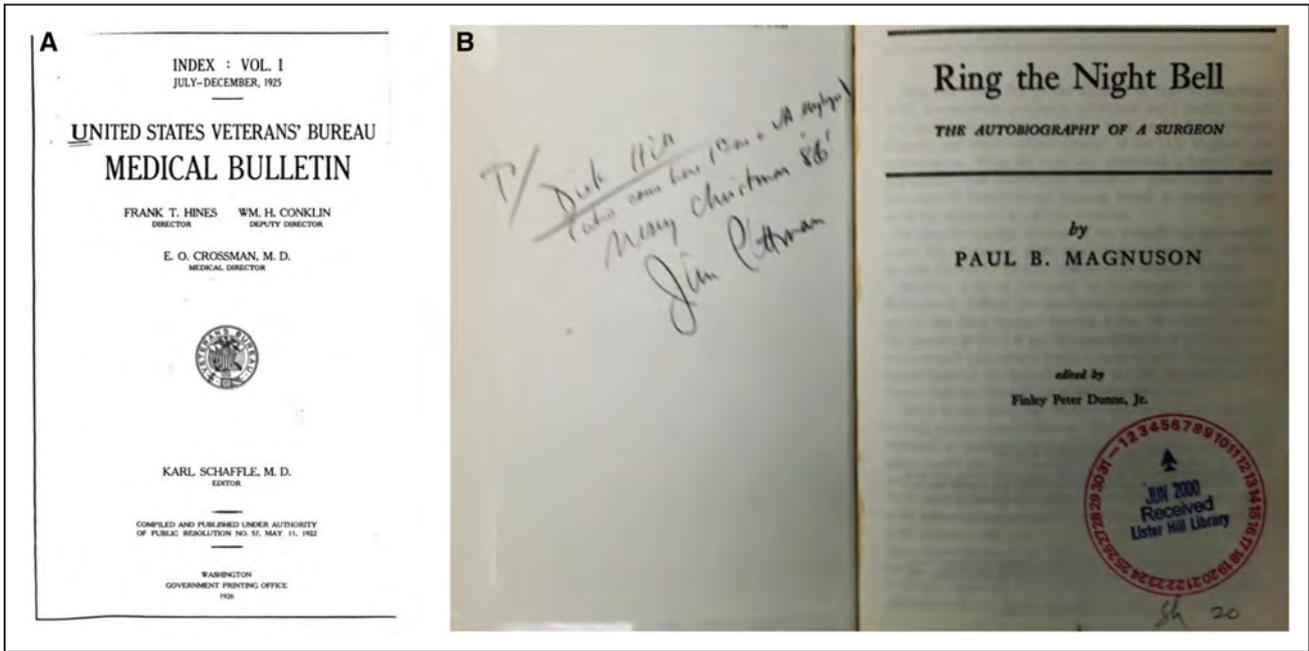


Figure. VA Historical Landmarks. A, Cover of the first edition of the United States Veterans' Bureau Medical Bulletin. **B**, Inscription by University of Alabama at Birmingham (UAB) Dean of the Medical School Dr James Pittman to Dr Richardson Hill President of UAB in a 1986 Christmas gift of the Magnuson's *Ring the Night Bell* reminding Dr Hill that he first came to UAB as a VA employee.

be little doubt that without the University Medical Center affiliation, care in the Birmingham VA Hospital would have been low. But it is equally true that without BVAMC affiliation, Alabama Medical School would have remained second class.⁷ Two of his initial hires at the Birmingham VA Medical Center, Dr James Pittman and Dr Samuel Richardson Hill, became Dean of the University of Alabama at Birmingham School of Medicine and President of the University, respectively (Figure B).

During these early years between 1946 and 1960, dedicated VA staff physicians led clinical studies addressing veterans' health issues that also impacted the general population. Veterans with tuberculosis increased from 4000 to 160 000 from 1940 to 1950. In 1946, the VA Armed Forces Streptomycin Trial led by John Barnwell, MD, included a thorough serial evaluation of all patients and a decision to not include untreated controls for ethical reasons.⁸ This period of growth saw the birth of Nuclear Medicine through the VA Atomic Medicine Program with an emphasis on radioisotope research. By 1946, there were 6 VA radioisotope laboratories, and by 1960, 60 such VA laboratories were in existence. This initiative led to the pioneering work of Rosalyn Yalow, PhD, and Samuel Berson, MD, in the development of radioimmunoassays for many hormones and hepatitis B. For this work, Dr Yalow received the Lasker Award and Nobel Prize for Physiology and Medicine in 1977. In 1955, Dr Rex Huff of the Seattle, WA, VA was the cofounder of the Society of Nuclear Medicine. Many physicians in the early VA radioisotope program were among the pioneers in nuclear medicine.

Other Nobel Laureates include Andrew Schally, PhD, Director of Laboratory for Hypothalamus Research at the New Orleans, LA, VA for research on peptide hormone production in brain and Ferid Murad, MD, PhD, at the Palo Alto,

CA, VA for discoveries relating to nitric oxide cyclic GMP. By 1958, VA research publications in the *New England Journal of Medicine*, *Journal of the American Medical Association*, and *Annals of Internal Medicine* slightly exceeded the National Institutes of Health with an equal number in *Journal of Clinical Investigation*. This publishing activity reflected 128 VA research programs and 28 ongoing Cooperative Studies Program trials. The vibrant VA clinical research programs were evident by 4 Lasker Awardees:

- 2012: Thomas Starzl, MD, for pioneering techniques used in liver transplantation at the Denver VAMC.
- 1975: Dr William Oldendorf for pioneering concept of computerized tomography at the West Los Angeles VAMC.
- 1974: Dr Ludwig Gross for discovering leukemia- and cancer-causing viruses at the Bronx VAMC
- 1971: Edward Freis, MD, for developing drug therapy for moderate hypertension at the Washington VAMC
- 1963: Dr Michael E. DeBakey for originating new techniques in cardiovascular surgery.

When asked how the Hypertension Trial happened, Dr Freis responded: "We were all VA physicians... We all contributed our time and didn't take any money at all." Another example of the of the VA clinician scientist esprit de corps was Oscar Aurbach, MD, at the East Orange, NJ VAMC where he demonstrated the relationship between smoking and lung cancer in human pathology specimens and in his smoking dogs.⁹ Dr Aurbach was a key participant in the first Surgeon General's Report on Smoking and Health in 1964. Drs William Chardack and Andrew Gage at VA Hospital in Buffalo, NY, and Wilson Greatbatch were responsible for the first successful design of totally implantable pacemaker. In 1956, Dr Leonard Skeggs of the Cleveland VAMC defined the amino acid sequence of angiotensin II.

Examples of recent notable milestones include development of the nicotine patch by Murray Jarvick, Chief of Psychopharmacology at the West Los Angeles VAMC, and the 2005 Shingles Prevention Study in the *New England Journal of Medicine*.¹⁰ Teams of VA investigators led by Dr Jay Cohn conducted the first trials of afterload reduction in patients with heart failure, and Drs Bill Boden and Robert O'Rourke led the COURAGE Trial demonstrating the equivalence of maximal medical therapy and percutaneous intervention in patients with chronic stable angina.¹¹

A formal Health Services Research and Development effort was started in 1958. In 1995, the National Surgical Quality Improvement Program was implemented and was instrumental in identifying ways to improve surgical care, in addition to the Quality Enhancement Research Initiative to translate research results into clinical practice for conditions prevalent among veterans. Most recently, taking advantage of the national VA paperless medical record system, the VA Genomic Medicine Program announced a groundbreaking genetics study—the Million Veteran Program—to study the effects genes have on health, with some 1 million veterans expected to take part for the next 5 to 7 years. In 2009, the VA launched one of the largest studies to date on the genetics of schizophrenia and bipolar disorder to involve 38 000 veterans at >20 VA sites. These initiatives follow discoveries of a gene associated with a major risk for schizophrenia, the gene that causes Werner syndrome, a disease marked by premature aging, and a gene that causes a rare form of dementia providing a potential target for treatment of Alzheimer disease.

In 2013, the VA funded new types of centers of excellence: Collaborative Research to Enhance Transformation and Excellence and Centers of Innovation—promise to speed translation of research results into clinical practice in VA. During the previous 10 years, the VA Office of Research and Development in collaboration with Department of Defense and National Institutes of Health has made important advances in recognition, diagnosis, and management strategies for combat traumatic brain injuries and post-traumatic stress disorder.¹² And recently published in *The Lancet*, a research study from the Cleveland VAMC and Case Western Reserve University published the intracortical brain–computer interface allowing a patient with severe and chronic paralysis to use their own brain activity to move their own arm and hand to perform functional movements.¹³

Unfortunately, because of word limitations, I must come to the end of this snapshot of the past, present, and future of VA Research. For a more detailed account, I recommend the *History of VA Research* thoughtfully written by VA physician scientist Margaurite Hays, MD,¹ and the VA Research and Development website <https://www.research.va.gov/about/>

crado.cfm. Having so much to draw from, it is my hope that this review elicits letters to the Journal sharing personal stories, additional facts and viewpoints, and other seminal studies that embellish VA research in its mission to enhance patient-centered care for everyone.

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