

Obituary

In Memoriam

Patricia Ann Webb (1925–2005)

Patricia Ann Webb, M.D., a unique figure in the field of medical virology, died on January 24th 2005 at the age of 79 years. For many years, she served as a distinguished career officer in the US Public Health Service (USPHS). She made important contributions to our knowledge of arboviruses and viral hemorrhagic fevers, serving the USPHS in multiple challenging overseas assignments in the tropics. Patricia Webb will be remembered as an inquisitive, tough and exacting scientist-physician by the many young virologists she inspired to fulfill careers exploring emerging viral diseases.



Pat was born in Cambridge, England on April 5, 1925. Her father, Robert A. Webb, M.D. was an American-born and educated (Johns Hopkins) pathologist who became a renowned Professor of Pathology at the University of Oxford, interested in the pathogenic role of bacteria, such as *Listeria*; he was a close associate of Howard Florey. Patricia, her sister and brother were dispatched to the United States during the Blitz (1940). In 1945, Patricia graduated when only 20 years old from Agnes Scott College in Decatur, Georgia, and went on to medical school at Tulane University, graduating in 1950. After a rotating internship at St. Joseph's Mercy Hospital, Pontiac Michigan, she completed residency training in pediatrics (1951–53) at Kern General Hospital, Bakersfield, California. In the summer of 1952, Pat was deeply influenced by the occurrence of one of the largest epidemics of arboviral encephalitis in the history of the United States. Hundreds of children were hospitalized with western equine encephalomyelitis (WEE), the highest attack rate being in infants <1 year of age. One of Pat's first publications described the clinical features of these pediatric WEE cases. This was her initial foray into the field of arbovirology in an ecological setting that would be the focus of attention of arbovirus research for decades to come.

Pat's subsequent career was spent in a variety of research positions in US Government laboratories studying viral infections. Between 1955 and 1961, she served at the US Army Medical Research Unit in Kuala Lumpur, where she worked with the famous entomologist Col. Robert Traub and her first husband, the well-known rickettsiologist, Bennett Elisberg. Pat became interested in the role of viruses in fevers of unknown origin and respiratory tract infections in a laboratory that was at the forefront of studies on tropical disease ecology. Also engaged in the stimulating research environment in Kuala Lumpur at the time were the late Robert E. Shope and C. E. Gordon Smith, both of whom would become legendary figures in arbovirus research and tropical medicine. In 1957 Pat, Ben Elisberg and their colleagues made

what probably was one of the first isolations of the H2N2 Asian influenza A pandemic strain, but their deliberate attempts to establish the isolate and prepare a lyophilized sample that could be sent for international characterization were overshadowed by a creative Singapore virologist who dispatched the virus to England in inoculated eggs kept viable under a brood hen.

In 1961, Pat began a long and distinguished career in the USPHS, assigned initially to the Laboratory of Infectious Diseases, National Institutes of Health (NIH). Working with Robert Chanock and Karl Johnson, she explored the role of rhinoviruses in human respiratory diseases.

In 1962–63 Pat and Karl Johnson (who became Patricia's second husband) began a remarkable series of endeavors in tropical virology at the NIH's Middle America Research Unit (MARU) in Panama. This era of virological exploration began with an outbreak of viral hemorrhagic fever in the remote Beni Department of northeastern Bolivia. Field and laboratory studies of the causative agent of Bolivian hemorrhagic fever, Machupo virus, expanded into a broadly based program aimed at elucidating the natural history, experimental biology, and virion characterization of rodent-borne viruses in the neotropics.

Young scientists assigned to MARU and strongly influenced by Pat and Karl included some of today's leaders in the field of hemorrhagic fevers and encephalitis: C.J. Peters, T. Walton, R. Tesh, and G. Eddy. Pat and Karl also engaged collaborators among the leading virologists of the day – G.H. Bergold, J. Casals, W. Rowe, W. Rawls, C. Mims, E. Traub, and F.A. Murphy. During this period, Machupo virus was shown to be morphologically and antigenically related to lymphocytic choriomeningitis virus, an observation that led to the creation of a new family of viruses (the *Arenaviridae*). This finding significantly expanded current scientific thinking about zoonotic viruses. Pat went on to discover and describe a number of other new neotropical arenaviruses. She was particularly interested in the role of rodent hosts in perpetuating arenavirus infections. Wild rodents were brought to the laboratory for detailed studies on pathogenesis (a particularly unusual, risky, and difficult endeavor). The mechanisms underlying chronic infection and excretion of virus, the role of host genetics in controlling infection, and the adverse effects of infection on the host mediated by immune responses and damage to reproductive organs were subjected to intensive scrutiny.

Work on Machupo and other arenaviruses was undertaken in the 1960s using primitive but effective means of laboratory biocontainment. However, field work in the affected area of Bolivia was treacherous, and several MARU investigators, including Karl developed Machupo disease. Pat also developed and survived a severe infection with Machupo virus, probably acquired from Karl. In 1969, Karl and Pat jointly were awarded the prestigious Gorgas Medal for their contributions to medical virology in Latin America. The Gorgas Medal citation reads: "By their worthy contributions to the knowledge of viral diseases of tropical America, Drs. Johnson and Webb have demonstrated outstanding ability in the field of preventive medicine. Their research efforts were instrumental in controlling the 1963 outbreak of Bolivian hemorrhagic fever . . . Their dedicated service is evidence of a deep concern for the improved health of the peoples of Latin America." Their contributions to science were also elaborated in the popular press.

When MARU was closed in 1975, Pat and Karl moved to the Centers for Disease Control (CDC) in Atlanta. This move ushered in a new era of research on hemorrhagic fevers, particularly Lassa fever in West Africa and Ebola virus in Zaire. Pat was the operational force in the Special Pathogens laboratory in Atlanta, supporting field research and epidemiological activities in Africa. The scene surrounding the initial isolation and identification of Ebola virus was described in Richard Preston's book, *The Hot Zone*. Samples from a dying nun with hemorrhagic fever in Yambuku, Zaire arrived at CDC in October 1976. Pat opened the box to find that "the tubes had cracked and broken during shipment . . . the package was

sticky with blood". With minimum regard for her personal safety, Pat collected barely enough residual material to initiate virus isolation attempts in Vero cells. Within a few days she noted cytopathic effects, and provided Fred Murphy with material for electron micrographic examination. The image shocked them all - a filovirus similar to Marburg. However, Pat showed by immunofluorescence that it was an antigenically distinct new agent.

Sierra Leone was the epicenter of Lassa virus activity in West Africa, and CDC established a field station at Kenema in the East of the country to study the epidemiology, diagnosis, transmission and clinical features of the disease. In 1978, Pat succeeded Joe McCormick as director of the Kenema field station. As in Panama and Atlanta, Pat's organizational skills and meticulous approach in the laboratory were critical to success, and she especially enjoyed the application of laboratory methods to field work. With McCormick and Karl Johnson, she carried out clinical studies under extremely difficult circumstances, demonstrating the effectiveness of an antiviral drug (ribavirin) in the treatment of severe Lassa virus infection.

Pat spent the last years of her career (1981–1988) at CDC's Division of Vector-Borne Viral Diseases in Fort Collins CO, where she worked closely with the division director, Tom Monath, on arbovirus problems. In 1982, Colorado was struck by a major epizootic of vesicular stomatitis virus (VSV) disease, affecting horses, cattle, pigs and a few humans. The Colorado epizootic led to a series of important papers by Pat and colleagues showing that VSV transmission between domesticated animals occurred principally by the agency of mechanical vectors such as stable flies.

About this time, and not long after the unfolding of the HIV epidemic in the US, some members of the scientific community suggested that HIV transmission between humans could also be effected by blood-feeding insects. Pat took charge of an investigation in which mosquitoes and bedbugs were inoculated with or orally fed HIV. She showed experimentally that the risk of biological and mechanical transmission by insects was vanishingly small. The work was particularly dangerous due to the use of fine needles for inoculating insects.

In 1988 Pat retired to England and Scotland, living a quiet life with her beloved Labrador retrievers. She retained a keen interest in science and had a huge appetite for books. When Pat's health began to fail, she moved back to the US to be closer to her two sons.

Whether the challenge was hemorrhagic fevers or AIDS, Pat approached her work with enthusiasm, imagination, and precision. She was quick to laugh, particularly at herself. She brooked no fools, had an acerbic wit, and her work was characterized by consummate organization and careful documentation. She also cared deeply for people, and took particular interest in those who were less fortunate than her. She had a love and compassion for both animals and people, and after retirement worked tirelessly for conservation groups and Amnesty International.

All of us who knew her and worked with her consider ourselves fortunate to have had Pat as a colleague and as a friend. She left an indelible impression on all who knew her.

Dr. Webb is survived by her sister, Jill Chance, two sons, Peter and Michael, and two grandchildren Colin and Aaron.

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