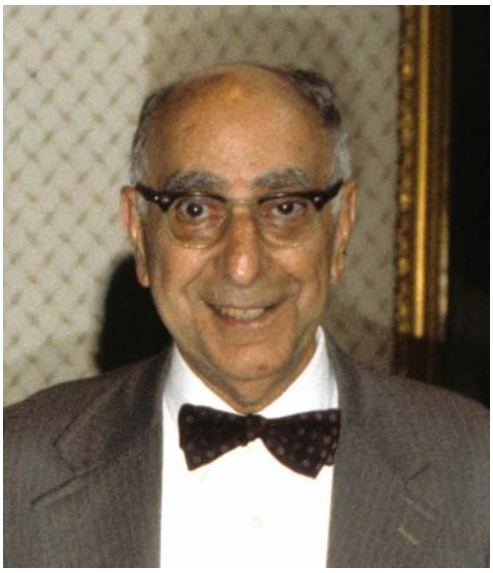
American Association of Avian Pathologists
Biographies of Professionals in Poultry Health



Martin Sevoian

1919- 2005

Prepared by: Bruce W. Calnek
Date: 2007
Revised:

xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

The Life of Martin Sevoian

Dr. Martin Sevoian was world famous for his pioneering work on experimental transmission of Marek's disease (MD) and for his continuing studies on that and other diseases caused by avian tumor viruses. Marty, as he was known to all, was born in Methuen, Massachusetts in 1919. At the age of 12, he took on a large amount of responsibility for his family following his father's death. He worked on the farm and then in factories. During World War II he enlisted in the U.S. Air Force where he became a lieutenant who flew patrols on the eastern coast of the United States and served as a flight instructor. Marty was proud of his Armenian heritage, and in the course of his many travels to scientific meetings, he once had the pleasure of making a side trip to Armenia where he was greeted with open arms.

After his discharge from the Air Force, he entered the University of Massachusetts (UMass) at Amherst, receiving his B.S degree in 1949. This was followed by four years at the University of Pennsylvania in Philadelphia culminating in a degree in veterinary medicine (V.M.D.) in 1953. A year later, at Cornell University in Ithaca, N.Y., he was awarded an M.S. degree. His master's degree program, examining the pathology of infectious bronchitis in the reproductive tract of hens, was under the tutelage of Dr. P. P. Levine. Marty treasured Dr. Levine's guidance and friendship throughout his life, and the author of this biography can attest to the fondness and respect for Marty that was expressed by Dr. Levine. Following the completion of his M.S. program, he accepted the position of Assistant Professor of Pathology at Cornell. Although he stayed at Cornell for only a year, it was there that he met and married Lucile Hieser. They had

been happily married for 51 years at the time of his death. Together, they raised two children, Janna and James.

In 1955, Marty returned to UMass as Professor of Veterinary Science where he served as a veterinary pathologist/virologist for the remainder of his career. Other members of the faculty that were housed in Paige Laboratory at the time of his appointment included Henry Van Roekel, Kenneth Bullis, Roland Winterfield and Glenn Snoeyenbos. Carl Olson and Stephen Hitchner had also been at UMass but they had left by the time Marty arrived. His responsibilities centered mainly on research on the pathogenesis and pathology of chronic viral and bacterial infectious diseases. For most of his career these were directed to diseases of poultry, but in later years he also studied the role of macrophages and other immune mechanisms in cattle and horses.

The author of this biography was first introduced to Marty when he came to Cornell in 1954 (I was a 4th year student in the Veterinary College and worked as a student-technician in the avian medicine group at the time). In 1957, he was instrumental in getting the administration at UMass to take a chance on a young 25-year-old "kid" from Cornell and give him his first real job. He then served as a mentor and helped nurture me with both encouragement and direct help with my research. We co-authored several papers and had innumerable discussions about his and my projects. Also, it was during my 4-year tenure at UMass that he began what was to be his defining work on the transmission of Marek's disease.

The first of his many publications appeared in *Avian Diseases* in 1957. One was a condensation of his MS thesis dealing with the effects of infectious bronchitis on reproductive tract pathology, egg production and egg quality; the other was as a coauthor with his colleague, Roland Winterfield, in a study of avian infectious hepatitis. He subsequently published over 80 papers in various scientific journals, and there were numerous abstracts of his work to be found in the proceedings of various meetings over the years.

His interest in pathology, and his responsibility for the histopathology that was done in conjunction with the poultry diagnostic laboratory in the Department of Veterinary Science at UMass, was reflected in a 1960 publication of a method for rapid diagnosis of avian pox and infectious laryngotracheitis. He also participated in studies by Roland Winterfield and Glenn Snoeyenbos dealing with infectious hepatitis in chickens and turkeys, respectively, and he co-authored papers on avian encephalomyelitis with Bruce Calnek that led to the development of an oral vaccine for the disease. However, without question, he is best known for his work on neoplastic diseases of chickens, most notably Marek's disease and reticuloendotheliosis.

JM virus

The research that literally "made" his reputation was his pioneering work in the field of avian tumor viruses. He had spoken to Dr. P. P. Levine about his desire to work on "leukosis" and was advised (in a friendly way) to avoid the subject because it was an "old man's disease." By that, Dr. Levine meant that it could be a futile effort that would be best suited to persons who were approaching the end of their career when they had already established their credentials and it would not matter if they did not make much progress. Luckily for the field of avian medicine, Marty did not heed this advice. He wisely sought the help of Dr. Randall Cole at Cornell University. Randy, along with Frederick Hutt, in the Department of Poultry Science, had been

studying the genetic basis for resistance to “avian leukosis” for some time and had developed strains of chickens remarkably and consistently susceptible or resistant to the form of the disease now known as Marek’s disease. Marty received periodic but regular shipments of day-old, genetically susceptible S-strain chicks from Randy and he inoculated these with tumor or blood cells from MD-affected birds. He soon had a succession of passages of an “agent” that faithfully reproduced the disease in a matter of a few weeks. The strain chosen for continuous passage and further study was named “JM.” Prodding by his colleagues failed to uncover the significance of the term JM until many years later when he finally related that the initials were derived from the given names of a stillborn son, James Martin. Although Drs. Peter Biggs and Jim Payne almost simultaneously carried out similar transmission studies at the Houghton Poultry Research Laboratory in England, their work and Dr. Sevoian’s work were done totally independently and without knowledge of each other’s studies.

The JM strain of MD virus (MDV) soon became a virus of choice for research by many others throughout the United States and elsewhere, particularly in 1970s, and it remains useful for comparative studies to this day.

Terminology

Martin was not swept up in the mainstream. This was apparent early in his career with neoplastic diseases of chickens. Avian disease specialists in the United States had classified tumors according to pathologic descriptions. Several types of leukotic and related tumors were lumped together as members of the “avian leukosis complex.” The situation was clarified when European workers recognized an etiologic difference between two leukotic diseases which they proposed to call lymphoid leukosis and Marek’s disease, the latter name selected to recognize Josef Marek’s description of a polyneuritis (later found to be associated with leukotic neoplasms)in the early 1900s. Workers in the United States largely accepted this differentiating terminology. Marty was an exception. He came up with a counter proposal in which all leukotic tumors would be separated into categories using a universal, open-ended classification based on cellular origin and etiology. Under his system, lymphoid tumors would be identified as Type I (caused by avian leukosis virus), Type II (“JM-type”, *i.e.*, later known to be caused by a herpesvirus), and Type III (caused by reticuloendotheliosis virus). Other types could be added as needed. Although many people agreed that this could be a workable system of terminology, the use of the European terms had become so commonplace that there was little or no enthusiasm for changing. Marty became the sole proponent of the alternative system and for several years, he refused to refer to JM or other viruses as Marek’s disease virus, preferring to call them Type II leukosis viruses. Ultimately, he capitulated.

JMV development

Rapid passage of the JM strain in S-strain chicks resulted in the development of a subline called JMV which was described as a “virulent” form of JM virus because it caused the death of inoculated chicks with massive tumors within a very few days. It was considered by Dr. Sevoian to be a more virulent subline of the JM virus. He mistakenly reported that it was lethal even in a cell-free form; it was later proven by others to be a cell transplant. JMV was the subject of a large number of studies by Marty and several of his associates and graduate students in the 1970s and 1980s. They reported the development of a continuous cell line from JMV, serum-neutralizing antibody responses following inoculation of JMV into chickens, and attenuation of

JMV by yolk-sac passage in chicken embryos. “Attenuated” JMV was claimed to be nonpathogenic for chicks and capable of immunizing against challenge with virulent MDV. The attenuated JMV was the subject of a patent, and it was touted as an alternative to the commonly used turkey herpesvirus (HVT) vaccine in use throughout the world. However, it did not receive much attention and was never a factor in the protection of commercial poultry against MD. None-the-less, this transplantable cell line was found by some manufacturers to be helpful as a challenge to determine the efficacy of commercial lots of HVT vaccine and it most certainly served a useful purpose in a variety of studies on Marek’s disease in many laboratories.

T-virus studies

In 1964 and 1965, Martin and colleagues published papers dealing with a virus which they called T virus. This agent was obtained from Marvin Twiehaus who had isolated it from a turkey in 1958 and passaged it over 300 times in chicks or turkey poults. There was confusion over whether Sevoian called it T virus because he obtained it from Twiehaus or because it came from a turkey; the point was later settled by Twiehaus as being the latter. It was subsequently renamed reticuloendotheliosis virus (REV), strain T. The work that Marty did was to provide a description of the pathogenicity and pathologic responses following inoculation of chicks of different genetic strains. He and colleagues showed that the virus could be grown in chicken embryos and tissue cultures, and they demonstrated age resistance, humoral antibody responses and contact transmission of the virus. Much later, in 1979, he helped in the development of an REV-transformed lymphoblastoid cell line.

Antibody responses to HVT, JM, JMV and the influence of passive antibodies

Immunologic responses and their interactions in Marek’s disease were the subject of a number of publications in the 1970s and 1980s authored by Martin and various graduate students and assistants. These studies added to the wealth of information coming from many laboratories during this period of trying to understand the responses of chickens to infection with MDV as an oncogenic virus and the influence those responses had on the susceptibility and resistance of chickens to MD.

Susceptibility of mammalian cells to MDV and HVT

Another series of publications from Dr. Sevoian’s laboratory dealt with the susceptibility of mammalian cells to HVT and MDV infection. It was claimed that guinea pig and hamster cells were susceptible to infection with both cellular and cell-free preparations of JM and JMV. It now seems probable that the conclusions drawn from these studies were in error. Work in another laboratory done as a follow-up to the published work from UMass showed that in all likelihood, a misinterpretation occurred as a result of cell fusion between the inoculum (JM) cells and the recipient (mammalian) cells. Also, JMV was shown to be free of infectious virus (it was a transplantable cell) so it is improbable that this inoculum caused infection of the mammalian cells.

Miscellaneous

Marty had a special interest in the area of immunology and he studied the role of macrophages and interferon in chickens. In addition to his work on avian diseases, he entered into collaborative research on equine infectious anemia and bovine immunoglobulins with colleagues at Umass toward the end of his research career. An important part of his collaborative work had

to do with the development of bio-degradeable, non toxic, synthetic polymers that could be coupled with various antigens to be used as immunogens, some of which were to be developed using hybridoma techniques.

Recognitions

Martin Sevoian lectured worldwide on his work. He was a member of the AAAP and the American Veterinary Medical Association, and he was a diplomate of the American College of Veterinary Microbiology. In 1985, his first papers on Marek's disease transmission were recalled in a special feature of *Current Contents* entitled "This Week's Citation Classic." Which recognizes highly cited research publications and allows the author to provide some of the interesting background information relating to the work. Also in 1985, he received the Distinguished Service Award from the Massachusetts Poultry Association, a citation from Governor Michael Dukakis praising his 30 years' distinguished service to the state's poultry industry, and also one from the Massachusetts House of Representatives, commending his contributions to research in avian medicine.

The man

Marty was a really nice person who was dedicated to his family, his work, and his church. He was an avid gardener who simply could not wait for the first corn from his garden and would stop at a roadside stand for a few ears even when his own would be ready within a day or two. He produced prodigious quantities of squash, and delivered it to colleagues at Paige Laboratory until his friends would finally lock their cars so that he could no longer pass on more. He was quick to offer help to those who needed it. Marty had a great sense of humor and he often "entertained" those of us at Paige Laboratory with hilarious mimicry.

This biographer would be remiss if he did not note that in spite of the major and ground-breaking contributions of Martin Sevoian's scientific career in the field of avian medicine, there is another side of his story that should be told. In a memorial service after his death, Marty's daughter Janna described him thusly: "…. he was a complex man with his own way of doing things. He was sometimes misunderstood and people did not always agree with him, but he had a great many friends. He was a man of contrasts: to say he was thrifty would be an understatement – but he was also extremely generous. He could be judgmental – but he was also forgiving. He was introverted, keeping his troubles to himself – at the same time, he was friendly and outgoing, and was able to strike up a conversation and talk with anyone he met."

I believe that Janna was right on the mark. The word "stubborn" comes to mind as one that should be added to her list. An example was his strong opinion on nomenclature for avian tumors, as noted above. He may have been right, but it was akin to fighting windmills. Marty's strong will (should I say obstinacy) persisted for many years, but in fairness it must be noted that he finally, albeit reluctantly, accepted the terminology used by everyone else. Sometimes Marty also was slow, or unable, to admit mistakes. As an example, for several years he refused to acknowledge that he was in error regarding a subline of his JM strain of Marek's disease virus, which he called JMV (the V for virulent). He claimed that the *virus* was modified to become rapidly lethal, even as a cell-free extract whereas in reality he had selected for a transplantable tumor line devoid of infectious virus. As his friend, I once tried to point out one possible explanation for his mistaken conclusion regarding the reason for the lethality of JMV (it was

based on an assay method he was using which was nonspecific and could cause misinterpretations); it caused a rift because “I did not trust him.” I am not sure if he ever acknowledged that he had been wrong. This type of defensiveness caused many of his colleagues to question some of his research, or at least be wary of his conclusions. In turn it caused him to isolate himself even more within the scientific community. This was unfortunate. It would be a rare scientist, indeed, who did not make errors in interpretation, and most certainly Martin Sevoian was not the only one who found it difficult to be “wrong” (remember the inability of Frederick Beaudette to admit that Stephen Hitchner’s B-1 strain of Newcastle disease virus was anything other than the infectious bronchitis virus he claimed have sent to Steve). None-the-less, it is important that we remember Martin Sevoian for the ground-breaking work he did, the opening of new research avenues he created, and his life-long dedication to advancing our knowledge in the field of avian medicine. We truly owe him a great deal.

Biography solicited by the Committee on the History of Avian Medicine, American Association of Avian Pathologists.