American Association of Avian Pathologists Biographies of Professionals in Poultry Health

Richard Lawrence Witter 1936 -

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A journey with chickens and tumors

Introduction. This personal reflection focuses on the professional career of Richard Lawrence Witter, veterinarian and scientist. Known as Dick to friends and colleagues, he contributed to research on Marek's disease (MD) and other oncogenic viruses of chickens during a long career at the USDA-ARS Avian Disease and Oncology Laboratory (ADOL) in East Lansing, MI, which was formerly the Regional Poultry Research Laboratory (RPRL). Trained in virology, pathology and epizootiology, he specialized in vaccine development and characterization of MD viruses and the lesions they induced. He was director and research leader of ADOL for 23 years. He was active in the American Association of Avian Pathologists, serving as president and in numerous committee roles. He was involved in international research in the Middle East and the Former Soviet Union. His research, which contributed to most of the current vaccines used for MD control, has been recognized by numerous awards and honors. He was elected to the National Academy of Sciences in 1998. He retired from ADOL in 2002 but continues at this writing to be active in science and veterinary medicine. An addendum covering his retirement years has recently been appended.

Preparing for a career (and life). As the only child of my parents, John Franklin Witter and Verna Harriet Church, I found my way into the world on September 10, 1936 in

Bangor, ME – just a few miles south of Orono which was home for the first 18 years of my life. After initially receiving a B.S. at the University of Maryland, my father earned his D.V.M. at Michigan State College. He spent his entire professional career at the University of Maine and for many years was the Head of the Department of Animal Pathology. My mother earned her B.S. and M.S. at Michigan State, majoring in mathematics, and was the consummate treasurer and record keeper for local organizations. The Orono years provided rich childhood friendships, a chance at sports, piano lesions, and a beginning appreciation for the great outdoors. However, it was my interest in science and academics, coupled with an admiration for my father and his profession, which launched me towards veterinary school. I recall a high school science fair project that demonstrated the osteology of the chicken – accomplished after much boiling of an intact chicken carcass, defleshing and rearticulating. My guide was a book on the subject by Frank Wilbut Chamberlain. My father frequently extolled the virtues of food animal medicine and, especially, poultry, which were becoming a significant part of the agricultural industries in the State of Maine. He also felt it would be desirable for me to do my pre-veterinary work at Michigan State, rather than at the University of Maine, in order to improve my chances of acceptance.

I enrolled at Michigan State College in 1954 (it would change its name to University that same year) in a pre-veterinary undergraduate program. I was accepted into Veterinary School in 1956 and graduated with a B.S. in 1958 and a DVM in 1960 with high honors. I worked hard and was probably considered a good student. I was the only person in my class to receive an "A" in pathogenic bacteriology from the feared professor, John (Black John) Newman. Black John also taught virology, but this consisted of about 5 lectures sandwiched into a composite course on Mycology, Virology and Immunology.

Another of my teachers was Dr. Charles Hall, who taught Poultry Pathology 415 in the Spring of 1959. My notes indicate that Charlie spent 1½ lectures on the avian leukosis complex, which he considered then to be "the most important disease of chickens." However, I did not take much note of this condition at the time. Charlie's class was very well received and he was voted "best teacher" by my classmates – not a small accolade from a group of future dog and cat practitioners. Charlie left shortly for Texas A&M where he became an important person in avian medicine and, particularly, in the American Association of Avian Pathologists (AAAP).

Charlie Cunningham was my faculty advisor during my veterinary training, but he did not teach any of my courses and his stature as a researcher on infectious bronchitis and organized poultry medicine did not become known to me until I returned to East Lansing several years later. Cunningham knew my father and ultimately became a good friend and colleague. I also met Dr. Henrik Stafseth, emeritus professor of microbiology, who had published early research on bacterial diseases of chickens and who, fortuitously for me, had introduced my parents to each other back in 1930 when both were students at Michigan State.

During veterinary school, I took a part-time job in the anatomy department, preparing histological sections. Dr. Lois Calhoun, the department chair, encouraged me to dual

enroll in a graduate program. I actually started this, working on the histology of the trachea in domestic animals, but ultimately lost interest. There was not enough action for me. However, this experience resulted in my first scientific publication on the "histology of the carotid body in six species."

It is worthy of note that during my 6 years as a student at Michigan State, I do not recall any mention of a USDA laboratory located on Mt. Hope Road that did research on avian tumors.

An ancillary accomplishment while at Michigan State was the chance meeting with a beautiful and talented coed, Joan Elizabeth Denny, as arranged by Otis Patrick, a fellow veterinary student. Joan and I kept pretty close company during my last 1½ years in vet school and there seemed to be promise for a lasting relationship.

Following graduation from veterinary school in June 1960, I joined the American Veterinary Medical Association (AVMA), passed State Board Examinations in Maine and Michigan, and applied to continue my selective service deferment since veterinarians were still being drafted during this period. Actually, the draft was a concern for the next 10 years (the Vietnam war years) for me and many others.

Training in poultry health research. Somehow, I never seriously considered a career in veterinary practice, leaning toward more academic applications of my newly acquired knowledge. I worked two summers in my father's laboratory at the University of Maine, even co-authoring a paper with Harold Chute on coccidiosis. Probably with my father's advice, letters of inquiry for graduate programs were sent to a number of candidate universities, including Ben Pomeroy at University of Minnesota, Albert Kleckner of Georgia, Joseph Alberts at the University of Illinois and P.P. Levine at Cornell University. Actually, my initial letter to Cornell was addressed to Dr. Peter Olafson, head of the pathology department, who, fortuitously, forwarded it to Levine. An instant and positive response from Dr. Levine in October 1959 convinced me that Cornell was to be my new home although, in my methodical way, I checked out all the options and did not accept until February 1960. I had no idea just how important this decision would prove to be.

I used the short summer interval before starting graduate school to work in clinical poultry diagnostics with Dr. Jerry Rountree at Samuel Lipman Sons in Augusta, Maine. Lipman was a major broiler integrator and Jerry was the chief health officer, dealing with disease diagnosis and prevention in market broilers. This experience, and Jerry's guidance, helped me establish a sincere appreciation for the practical application of science in poultry health, an attitude that paid many dividends to my career over the years. Jerry was also an innovator and free thinker, looking for ways to utilize knowledge from many sources for the benefit of poultry health. Jerry had trained with my father and Harold Chute at the University of Maine, so was an old family friend.

I enrolled at Cornell in September 1960 on a Master's degree program with Drs. P. Philip Levine and Julius Fabricant. Actually, I was employed as a graduate assistant at an

annual salary of approximately \$4400 (big money for me). Dr. Levine was the chair of my committee but he left the management of my research program largely to Julius. With no preconceived ideas on the area of research I should choose, I recalled that during vet school my training in bacteriology was far stronger than in virology, which seemed to be a new field of emerging importance but was largely unknown to me. Thus, in order to round out my education, I expressed a desire to work with viruses for my Masters research. Fortunately, Julius agreed. This was indeed a pivotal decision for me.

At the suggestion of Julius, I worked on application of agar gel precipitin tests for the diagnosis of infectious bronchitis and Newcastle disease, using a relatively new technique that was being pioneered for poultry disease diagnosis by a German veterinarian, Helmut Woernle. Woernle's papers were published in German and I recall many evenings, armed with a dictionary, trying to decipher the meaning of his work. Julius supervised the completion of the M.S. thesis as Dr. Levine was in Israel on sabbatical leave. I was so inexperienced in authorship that I submitted the paper to Avian Diseases with me as the sole author – and neither Fabricant nor Levine ever said anything. The oversight only occurred to me much later.

As I was launching my career in virology, Joan took a teaching job in Cortland, NY, only 20 convenient miles away. We were married on June 30, 1962, about the same time that I completed requirements for the M.S. degree.

My first formal scientific presentation (on my bronchitis research) was at the Northeastern Conference on Avian Diseases (NECAD), held in Guelph, Ontario in June 1962. I believe Roy Luginbuhl asked the first question – and I somehow survived.

This was also about the time that Bruce Calnek, a former graduate student of Dr. Levine's, returned to Cornell after several years on the faculty at the University of Massachusetts. Bruce was in need of a new project, having just elucidated most of the complexities of avian encephalomyelitis. Bruce became intrigued with tumor viruses and ultimately, Levine concurred. In April 1962, Bruce attended a workshop on avian leukosis held at the RPRL, in East Lansing, Michigan. This was in many respects a landmark moment in the evolution of tumor virus research in chickens. The issue of one type of leukosis or two was becoming more intense. Controversy had been brewing for the last decade with Ben Burmester at the East Lansing laboratory working on leukosis, which was transmitted by a virus following a long latent period. However, leukosis of a different type was being seen in genetic research programs at Cornell, directed by Fred Hutt and Randy Cole, and also in the poultry industry where increased mortality and condemnations of broilers at processing for tumors was on the rise. There was also the issue of viral assay. The bioassay for leukosis virus, developed by Burmester required 9 months and lots of chickens. Pioneering work by Harry Rubin of Berkley (1960 and 1961) had created a new test, conducted in tissue culture, which would detect the avian leukosis virus in less than 3 weeks. This resistance-inducing-factor (RIF) test was a true breakthrough that would surely speed progress in this emerging area. Although Rubin apparently did not attend this workshop, the RIF test methodology and its application was presented by Walt Hughes and several of the East Lansing workers. Bruce returned from the workshop full of excitement, found me still working at the lab late in the evening (probably April 26, 1962), and proceeded to discuss with me the possibility of pursuing this area for my Ph.D. research. I knew little about chicken tumors, but it sounded OK to me. A committee was soon formed with Dr. Levine as chair and Bruce as my research (or thesis) advisor. Another defining moment in my career had occurred.

My PhD project was to define the role of maternal antibodies on the epizootiology of avian leukosis virus infection. I remember use of the terminology "parental antibody" because somehow it was not yet clear to Dr. Levine whether such antibodies were derived from the sire or dam. Tissue culture technology was just emerging for chicken cells when I started my training in Bruce's lab in July 1962. Our first cultures were in 60mm glass dishes contained in a candle jar (one lit a candle and then closed the lid so the candle would increase the CO2 level before it extinguished) placed in a bacteriological incubator. Just the process of obtaining quality monolayer cultures that would support virus growth, including foci induced by Rous sarcoma virus, was a major achievement. These were cutting edge techniques at the time. Part of the project entailed inoculating chickens with avian leukosis virus (which was termed resistance-inducingfactor or RIF virus in my thesis) to create antibody-positive breeders. Virus-free chicks from these breeders were maintained as controls in a pen-type isolation unit. In one study, the uninoculated control chicks developed tumors and nerve lesions at about 15 weeks but remained free of RIF virus or antibody. Of course, this was MD, although we called it "non-RIF lymphomatosis," which resulted from accidental exposure. This accident helped establish separate etiologies for MD and avian leukosis, which was an important unresolved issue at the time and was arguably more important that the principal objective of the work. I recall a job interview seminar given in East Lansing where Ben Burmester seemed interested only in this accidental infection story. This was the first of several unplanned events that produced research opportunities of unusual value in my career

Jobs were plentiful in the mid 60's. I interviewed with Bill Patterson at the Southeast Poultry Research Laboratory in Athens, GA, with Bill Pounden at Wooster, OH, and with Ben Burmester at the RPRL in East Lansing, MI. My knowledge of an opening in East Lansing came from Bruce following his chance conversation with Burmester at a meeting. I wrote to Burmester in December 1963, carefully explaining that I would be available only if a Cornell grant application to NIH was not approved (it was not). Several offers were tendered but the East Lansing job was especially attractive as it would keep me in the field of avian tumors and appeared to offer the best research environment. In retrospect, this was exactly the right choice. I started the East Lansing job on September 8, 1964 at an annual salary of \$10,400 (grade GS-12). My choice may, indirectly, have had an impact on the careers of Charlie Beard and Mo Saif, who were hired and developed stellar careers at Athens and Wooster, respectively, in this same time frame. In the same way, the decision by Torgny Fredrickson to resign his position at East Lansing in 1963 paved the way for the position that was offered to me.

Getting started in East Lansing. Ben Burmester, in 1964, had just become director of the RPRL and was probably at the height of his distinguished career. He was famous for

elucidating the viral etiology of lymphoid leukosis and was a close colleague of others involved in the first wave of viral cancer biology including Ludwig Gross, Joe Beard, Carl Olsen, Frank Rauscher, Werner Schäfer and others. Ben proved to be a role model and mentor for me, which only many years later was fully appreciated and acknowledged. However, I recall holding Ben in high regard from the very first, and I consulted with him often on questions of experimental design in the early years. Since Ben wanted me to work on "acute leukosis", the new form of lymphoid tumors in chickens that were causing increasing losses in both broilers and layers, I prepared a phase of work designated as RPRL project 10, phase 17. At this moment, I was the one person of the 8-9 person staff who was working on this type of leukosis. That would change dramatically over the next several years, but it gave me some breathing space to start my career. We started in October 1964 with some frozen tumor, held in chunks at -70 C., that was labeled strain JM. Chickens had been inoculated with JM tumor at Marty Sevoian's lab at the University of Massachusetts in June, 1962 and carried back to RPRL by my predecessor, Torg Fredrickson. The tumor was then passed in chickens two additional times and frozen. I ground up this material and inoculated newly hatched line 7 chickens which were housed in rooms of a wooden barracks building, formerly used as post-war student housing at Michigan State. Amazingly, considering with hindsight that inocula stored under these conditions should have little or no MD infectivity, the chickens developed clinical signs of leukosis at about 3 weeks of age, along with enlarged peripheral nerves and tumors. My career in MD was launched.

I was given in 1965 a courtesy appointment in the Veterinary Pathology Department at Michigan State University, then chaired by Cleon Morrill, a former classmate and close friend of my father. This appointment and my relationship with Michigan State has continued to the present, being supported in recent years by Willie Reed. The strong connection with Michigan State University over the years has been important to me and also to ADOL.

I did not have to wait long for my research program to gain public attention. In the winter of 1965, the wooden barracks building housing several of my first chicken experiments burned to the ground, probably because of a malfunction of the old oil heaters, and I was suddenly in the local newspapers.

The Technical Workshop Conference on Diseases of the Avian Leukosis Complex, jointly sponsored by ADOL and the University of Georgia, was held in Athens, GA October 13-15, 1965. This was my first opportunity to rub shoulders with the then great figures in the field. Besides Marty Sevoian, who I had met while a student at Cornell, the 41 participants included Peter Biggs, Jim Payne, Bob Huebner, Max Cooper, Peter Vogt and many others. This was probably the point at which laboratories in the United States began using the new nomenclature, "Marek's disease," which had been adopted by the World Veterinary Poultry Association in 1961 but had been largely ignored in the US. The industry was also very interested as the disease was gaining momentum. Nobody understood its etiology and methods for control were nonexistent – but many speakers referred to MD strains as a "virus," even though there was no proof of this. Incidentally,

Jim Payne was at the RPRL on a sabbatical leave in 1965 working with Lyman Crittenden on avian leukosis genetics during which time we became lifelong friends.

An early project, initiated by Burmester with some input from me, was to install isolators at the RPRL, as containment housing appeared to be the key to MD transmission work by both Sevoian and Biggs. I visited the National Animal Disease Center at Ames, IA in October 1964 to inspect plexiglass isolators in use there. Burmester and I ultimately designed a modified Horsfall-Bauer isolator which was fabricated from stainless steel. We bought and installed 62 isolators in 1965 and another 120 in 1966. These isolators proved invaluable to our MD research and are still functioning well at this writing more than 40 years later.

The other key ingredient in successful transmission of MD virus was a source of susceptible chickens. The RPRL line 7 chicken, developed by geneticist Nelson Waters and subsequently maintained by Lyman Crittenden, proved to be highly susceptible to MD (similar to the Cornell S Line). In later years, we utilized an F_1 cross (15x7) which Crittenden found to be nearly as susceptible and much more vigorous.

The availability of a large number of isolators and internally produced susceptible chickens were critical for the work that lay ahead, and probably provided RPRL (and me) an advantage over many other laboratories.

The HVT Story. This section provides historical information on the role I and other ADOL scientists played in the isolation of MD virus, the subsequent isolation of turkey herpesvirus, and the development of the first United States vaccine for MD. This series of events was of huge importance to science and agriculture, and was also pivotal for me, personally. As this was perhaps the signature contribution of my career, a detailed chronology follows.

My earliest efforts on MD research at the RPRL were directed to isolating an etiological agent, using chicken cell cultures. Although it is possible that some virus may have been present in inoculated bone marrow cell cultures in my studies, it was the use of duck embryo fibroblasts (DEF), fortuitously introduced to our lab by Bart Rispens who was doing a sabbatical with Graham Purchase on avian leukosis virus, which proved to be the appropriate system. John Solomon, who was working under my supervision at the time, was a specialist in tissue culture and was already growing DEF in his lab. He, like many other workers, was inoculating all types of available cultured cells with MD tumor material. John probably first observed cytopathic effects in DEF following inoculation with blood from MD affected chickens, in January of 1967. Chickens were quickly inoculated with these cultures and began to die on day 22. I remember well the moment when I visited the isolator and was amazed to see every inoculated chicken with advanced clinical MD – a dramatic sight with obvious significance. These exciting data were presented during the RPRL quarterly reports (an internal review) in March, 1967, and launched a flurry of activity. Keyvan Nazerian employed electron microscopy to determine that these cultures contained a herpesvirus. The ADOL group, led by Nazerian, reported our results at the AAAP Leukosis Workshop on the morning of July 8th in the Hotel Adolphus in Dallas, TX as part of the 1967 AVMA meeting. At the same workshop, Peter Biggs also reported evidence from his group at the Houghton Poultry Research Station (Houghton) in England that MD was caused by a herpesvirus, information that we first learned during a visit by Biggs to RPRL just prior to the Dallas meeting. This was indeed a spectacular moment when, for the first time, the etiology of the disease was revealed, first to the 19 workshop participants and subsequently to the world. The scientific community, the poultry industry and the news media took appropriate note of this event.

The relationship between RPRL and Houghton was both competitive and friendly. Biggs had visited with Burmester at RPRL in the early 1960s, as Biggs was preparing to launch his own career in avian tumor viruses. They established a strong friendship which later extended to other scientists in both labs. More than 40 years later, I still consider Biggs and Payne to be among my closest friends and colleagues. However, the two labs worked on the same subjects and competition was inevitable. In July 1967, the Biggs group had more data to support the herpesvirus etiology of MD than RPRL and managed to publish first – although we both had reached the same conclusion. It seemed to me, looking back, that Houghton was frequently a step ahead although the RPRL had its own moments. The accomplishments of this period were probably sufficient to satisfy egos on both sides of the ocean.

The next year (1968) my research schedule was filled with efforts to confirm that this herpesvirus was indeed the cause of MD, using circumstantial proofs. This was some of my best work, but it pales in history because it simply confirmed what had already been suggested to be true, and was similar to parallel studies by Biggs. However, there were prominent persons, including Robert Huebner at the National Cancer Institute, who felt strongly that all cancer was related to retroviral oncogenes, and these objections had to be overcome.

By the fall of 1968, I began to utilize the newly available techniques of virus isolation and antibody detection to study the epizootiology of MD virus (RPRL project 46). I started a major project on broiler flock infection with MD virus, using samples sent from Georgia by Jim Moulthrop. However, it also occurred to me that a study of turkey flocks might be fruitful, especially since turkeys had sporadically developed lymphoid tumors that might be MD. RPRL had a relationship with Dr. Joe Ostendorf, a veterinary practitioner in Milford, IN who sent us 10 live turkeys from a 23 week old flock on the Ernie Schrock farm located in New Paris, IN. Some lymphoid tumors had been noted in this flock. The turkeys arrived at RPRL on September 24, 1968 and blood and kidney tissues were collected. We immediately inoculated chicken kidney and duck embryo fibroblast cultures and a few days later my technician, Harvey Burgoyne, asked me to examine one of the cultures because he had observed something strange. In fact, cellular inocula from 8 of 10 turkeys had induced cytopathic effects in either DEF or chick kidney cultures. The cytopathic effects (plaques) were much larger than and easily distinguished from those of MD virus, although certain similarities were apparent. This time, when we inoculated infected cultures into chickens or turkeys, nothing happened. However, the serum from inoculated chickens reacted with MD viral antigens by

immunofluorescence and other tests, indicating that this virus shared an antigenic relationship to MD. We named our original strain "FC126" because at the time there was a single book to record field case accessions for the entire lab, initiated by Frank Siccardi. This accession was recorded as field case 126 in this book. I subsequently started my own series of accession numbers, many of which became names for future virus isolates, but FC126 stuck. At the American Cyanamid 10th Poultry Pathologists Conference held at the Nassau Inn in Princeton, NJ in November, 1968, I met Dave Anderson, then working at the University of Wisconsin. While standing in line for lunch, I learned for the first time of his findings, obtained with the help of Hitoshi Kawamura, of a herpesvirus isolated from cell cultures prepared from kidneys from adult turkeys. I also shared my findings, which at this moment were only a couple of months old. Dave generously sent me his isolate (WTHV-1) which proved to be similar to ours. This was a time when it was easy to share data and materials prior to publication.

The Wisconsin group published on HVT first (in 1969) but failed to recognize the antigenic association of this virus with MD virus. Our study, published in 1970, revealed this antigenic relationship which, of course, was the key to its ultimate use as a vaccine. We saw immediately what needed to be done and had the resources to accomplish it. In contrast, shortly after their report Kawamura returned to Japan and Anderson left Wisconsin for Georgia. Thus, circumstances favored East Lansing and illustrate how fragile is the process of discovery.

While all this was going on, Tony Churchill and others at Houghton had published on a successful vaccine for MD, prepared by classical attenuation of the virulent HPRS-16 strain. At our lab, Bill Okazaki immediately started to attenuate some of the RPRL strains of MD virus and test them as vaccines with help from Graham Purchase. It seemed natural to me at the time to offer our FC126 isolate to Okazaki for testing as a vaccine in his established system. He did, and the rest is history. Peter Biggs asked me once why I gave up FC126 for someone else to develop as a vaccine. In retrospect, however, I gained much from my role in the development of the FC126 vaccine, even though my name did not appear on the seminal paper.

In 1969, I was scheduled to attend and present papers at two summer meetings, NECAD and the American Veterinary Medical Association (AVMA) meetings which included the program of the American Association of Avian Pathologists. To AVMA, I submitted my work on epidemiology of MD virus in broiler flocks, thinking this would be my most important work. The lesser paper, on turkey herpesvirus, was submitted to the 41st NECAD meeting in Orono, ME. However, history will record my presentation on June 23, 1969 in Orono as one that attracted the most attention – it effectively, although unintentionally, announced the development of a MD vaccine. No protection data were presented but following the presentation a question from the audience asked whether this virus induced protection and my answer, that preliminary results were "very promising," was sufficient to let the cat out of the bag. Results of protection tests with FC126 would be presented by Okazaki and Purchase later, and showed dramatic benefit, both in laboratory and field trials. Another landmark achievement in the history of MD was in hand. Application of this vaccine to industry is best marked from the issuance of the first

federal licenses for production on March 1, 1971, although some state licenses for HVT were issued earlier and some poultry operations without HVT vaccine utilized whole blood from commercial turkeys (but this is another story).

Nomenclature was an issue. We initially referred to turkey herpesvirus by the obvious acronym, THV. Immediately following my presentation at Orono, Bruce Calnek stood up and reminded me that THV had been preempted by Glenn Snoeyenbos for turkey hepatitis virus. This prompted our group at RPRL to reevaluate, and create at my suggestion the unwieldy designation, *herpesvirus of turkeys* (HVT), which became the official designation in my 1970 paper. This nomenclature has stuck well, but I regret caving in on this issue and continue to occasionally refer to the virus as turkey herpesvirus (HVT). Turkey hepatitis virus, now known as turkey viral hepatitis (TVH) virus, has remained obscure.

The technology was the subject of one of the early patents undertaken by USDA and when USDA declined to pursue foreign rights, these were returned to the inventors (Okazaki, Purchase, Burmester and me). Patents were new in agricultural science and the possibility that government scientists could benefit financially from their work was novel and, in some cases, distasteful to other colleagues. The USDA provided royalty-free licenses to several US companies. Merck Inc., under the guidance of Maurice Hilleman, licensed the foreign rights. This might have made us all wealthy except for two circumstances. First, my initial paper on the turkey herpesvirus contained one famous sentence in the discussion (pg. 537, paragraph 2) citing unpublished RPRL data on the ability of HVT to protect against MD, and my paper was published a few days outside the 12 month grace period before the patent was filed, effectively invalidating it. Second, Merck was a neophyte in the poultry vaccine business and could not compete against existing poultry vaccine companies in either the domestic or foreign markets and soon abandoned this business, thus royalties were minimal. Obviously, we inventors were also neophytes. In later years policies were changed so that domestic patent rights would have generated royalties with a share going to inventors. The failure to capitalize financially was never an issue to me. Our group looked askance at Tony Churchill, a researcher who started his own MD vaccine company about this time and became wealthy. I received a life-long benefit through the enhancement of my reputation which was something money could not buy. This was plenty good enough for me. My colleagues (Burmester, Purchase and Okazaki) probably received less benefit because each of them soon left the field of MD research for various reasons.

The development of the HVT vaccine and its commercial use was widely recognized. Maurice Hilleman, an outstanding vaccinologist at the Merck Institute for Therapeutic Research said that this was "the most outstanding achievement in the virus cancer field in the last decade or two." Reed Rumsey, of DeKalb AgResearch Inc. said "we have seen a near miracle occur in the control of a disease that just 2 years ago was the scourge of our industry." The percent of commercial broilers condemned for leukosis dropped by 90% within 3 years after introduction of the vaccine. Layer livability surged and resulted in a glut of eggs. This was indeed a happy time, but was not to last long.

Reflections on the bigger MD story. The work at ADOL on the etiology of and a vaccine for MD, was only one part of the story. The evolution of knowledge on MD culminating with the licensing of a vaccine in the United States, mainly from 1961 to 1971, has been documented in many places and was the subject of a special historical program held as part of the 5th International Symposium on Marek's Disease in 1996. This period was so big and so important that it will surely be viewed differently by the persons involved. The following are a few of my personal recollections.

Interest in MD was driven by a major increase in broiler condemnations, much easier to measure after the advent of federal inspection data in 1961, and layer mortality. Even in the early 1960s, the economic impact was of great concern, and this only became worse with each passing year. MD was clearly the most important poultry disease by a wide margin. The origin of the problem in Delmarva and subsequent spread to the southern broiler states was duly noted, but nobody really understood what was going on. Other countries were also involved, but this attracted less attention.

Then, as now, the broiler and layer industries had a number of prominent spokespersons in the health area who were looking for ways to control MD losses. At ADOL, frequent visits by Walter Staples (Cobb), Carl Weston (Hubbard), Egon Vielitz (Lohmann) and others provided a glimpse into the real world. The questions were always the same, "what have you learned lately?" and "what can we do to reduce our losses?" There were few answers but our industry contacts were a critical source of field data and experimental materials.

Money for research started to flow. By the mid 1960s, ADOL was dispensing money on contract to a number of laboratories including Massachusetts (Marty Sevoian), Georgia (Sam Schmittle and Caswell Eidson), Arkansas (Joe Beasley), Cornell (Randy Cole), California (Ray Bankowski), Connecticut (Roy Luginbuhl) and Washington State (Sam Kenzy). In addition, money from the National Institutes of Health was available due to the interest in virus-induced cancer in animals. Thus, many new laboratories were entering the MD research community, each trying to contribute in their own way. This was a healthy situation but at the time it seemed chaotic and competitive. Everybody seemed to recognize that the stakes were large. A backdrop to this scenario was the emphasis placed by the National Cancer Institute (NCI) on cancer virology, prompted by a prevailing but misguided view that animal virus systems would be good models for human cancer. Funds for the contracts above were derived from the NCI Special Virus Cancer Program. NCI continued to fund MD research for many years.

The poultry industry was desperate and not inclined to wait for the ivory tower folks to develop answers. Many strategies were attempted, with generally poor success. The "new house syndrome" reflected the propensity of chickens in a new house to develop severe MD and caused some to seed houses with old litter. Once HVT was isolated, producers would inoculate chicks with turkey blood in hopes of providing protection. In 1970, an AAAP resolution to urge the quick licensing of MD vaccines was motivated in part by a desire to curb the use of turkey blood and other empirical techniques.

The major successes of the period need little attention here; each was confirmed quickly and proved to be building blocks for advancement of knowledge. However, a number of reports created temporary excitement but proved to be blind alleys when they could not be confirmed by other laboratories. Examples would include: (1) darkling beetles are an important method of transmission, (2) MD is egg transmitted, (3) JMV is a cell-free virus of high virulence, (4) MD virus can be grown in mammalian cells, (5) retroviruses are required for induction of MD, and (6) MD is a public health hazard. As one who was directly involved in refuting several of the above, I can attest to the effort required and the strain this sometime caused on personal relationships. However, at the end of the day, the scientific method worked.

The administrative years. As a staff member, there were various administrative roles to be played out. In the early 1970s, I helped reorganize the laboratory breeding flock testing program with Howard Stone. I also was instrumental in starting a weekly lunchtime research group discussion so that senior staff could share results with all on a timely basis. This type of weekly research discussion has been maintained at ADOL, with some modifications, to the present day.

In December, 1974, Ben Burmester abruptly announced his retirement, to be effective in a month. I was asked to step in as the acting director in January 1975 pending a national search. The search commenced, with colleagues Lyman Crittenden, Graham Purchase and Padman Sarma in the running. I submitted my own application in May 1975, brazenly specifying that "my acceptance of the position of Director would be contingent on the successful negotiation of ways to limit the non-research administrative duties." I was in Tübingen, Germany in July 1975 when the United States Consulate called with the news that I had been selected. Another chapter begins for me, at age 38.

The challenges of administration were considerable, especially for one who had minimal prior experience. There were budgets, personnel and physical plant problems. My request for ways to limit non-research duties (above) had fallen on deaf ears. There was the need to provide direction for the lab research program. It was also essential for me to maintain my personal research, as my evaluations were still based mostly on research productivity. All of a sudden I even had a secretary, and supervised a farm manager, maintenance manager, and administrative officer. Dora Post (Westbrook) was my secretary for many of these administrative years.

In my 23 years as director and research leader, I hired many new staff including principal scientists Aly Fadly, Larry Bacon, Bob Silva, Hans Cheng and Henry Hunt. We focused mainly on MD and avian retroviruses, but there were several new initiatives. In the 1970s, I started a new program on infectious bursal disease and hemorrhagic enteritis of turkeys, in order to achieve more diversity. I launched a viral vector program in the 1980s, which ultimately focused on fowlpox vectors. I supported a change in our traditional genetics program to embrace the new field of genomics, mostly at the urging of Lyman Crittenden. I attempted to launch an effort in transgenic chickens, sending Larry Bacon to the University of Guelph for a year to work with Rob Etches, but this ultimately floundered and was abandoned. When myeloid tumors in broiler breeders

became an industry problem in the 1990s, I instituted a crash program on the causative virus, avian leukosis virus subgroup J (ALV-J). This was a successful venture and assisted the industry in dealing with a significant economic problem.

The ADOL celebrated its 50th anniversary on the 16th of June, 1989. Peter Biggs (from Houghton), Dean Plowman (administrator of ARS) and many other dignitaries attended and presented accolades to the laboratory for its many contributions. As one would expect, I was very much involved with this activity, and many of our staff played significant roles.

The ADOL hosted the 5th International Symposium on Marek's disease which was held in East Lansing in September, 1996. I co-chaired with Lee Velicer this 4 year effort which featured a historical theme (Legacy of the 1960's) that celebrated the anniversary of the many major findings on MD during the subject decade. Carol Cardona worked closely with me on the historical part which featured a workshop with many of the original scientific contributors. A video was produced of this workshop and with interviews with several of the principals. This video is sold by AAAP and is deposited in its historical archives. Coincidentally, the symposium banquet was held on my 60th birthday, which was well celebrated by those present.

In my role as laboratory director, I tried hard to improve the research environment at ADOL. Following a strategic planning conference in 1988, I created an industry liaison group which met several times in the 1990s to advise us on programs and other issues. Effective May 17, 1991 we changed the name of the laboratory from RPRL to ADOL to improve our image with our public. When outside consultants were brought in to discuss communication issues and improve the workplace environment, I realized the extent to which the leader of a group is responsible for its culture. I was perceived for a time as having some talent as an administrator, and was even invited to give lectures to outside laboratories on my various leadership initiatives. Starting in about 1988, a need for improved physical facilities was identified and enough support from ARS was obtained to initiate planning, a process that went on for years and consumed untold hours of staff effort. Perhaps my greatest career disappointment was the ultimate failure to receive construction funds that would have provided ADOL with a world class physical plant. On the other hand, occasionally adversity could be turned into a success. When called to task for violation of a wetland ordinance on our 50 acre property, we shifted course, established a 4 acre wetland improvement area and were the recipient of a USDA award in 1988 for the effort.

During my watch, others at ADOL made many significant contributions of which I was most proud. Improved diagnostic tests for avian leukosis virus by Lloyd Spencer (visiting scientist), development of in ovo vaccine technology for MD by Jagdev Sharma, monoclonal antibodies against MD virus by Lucy Lee, the first transgenic chickens by Lyman Crittenden and Don Salter, a credible vaccine for hemorrhagic enteritis virus of turkeys by Keyvan Nazerian, new diagnostics for avian leukosis virus subgroup J by Aly Fadly, elucidation of lymphoid leukosis enhancement by serotype 2 MD virus by Larry Bacon, the genome sequence of MD virus by Lucy Lee, and a genomics program led by

Hans Cheng that has identified many markers and led ultimately to the sequencing of the chicken genome are just a few of the many highlights that occurred in my era. Truly, ADOL appeared to me to be special. The scientists there established a tradition of excellence by blending high science with practical application. Productivity per square inch of laboratory bench space was undoubtedly at the top of the list. Times are harder now, but I am grateful for the chance to experience some wonderful years at ADOL in the company of highly skilled colleagues.

Research – **my first love.** My personal research focused on MD, with occasional digressions with REV and ALV. Most of the work was accomplished solo, with the help of one or more technicians, although I collaborated often with other senior investigators. The decision in 1980 to select Barbara Riegle for the open position as my principal technician was a key to my productivity in subsequent years. She managed my personal research with a minimum of supervision until my retirement during a period when my life was filled with heavy administrative responsibilities. Every once in a while there would be a contribution of significance, or at least of personal satisfaction.

As my career progressed, there seemed to be a paradigm shift from individual studies to what might be termed "great projects." It was easy for me to maintain several long term projects at the same time, some of which might continue for 20 years or more. I will relate just a few examples, small and large, by way of illustration.

- MATSA just before becoming director, I was involved with Ann Stephens with research, stimulated by a publication from Patrick Powell at Houghton, on tumor antigens in MD. Ann and I crashed hard for several months using the JMV tumor transplant model and produced a paper that established the nomenclature and some properties of the antigen, but did not define it (MATSA = Marek's associated tumor specific antigen). This antigen spawned follow up work by numerous workers, but ultimately was determined to be a host antigen and interest decreased.
- <u>Bivalent vaccine and synergism</u> I reentered the MD vaccine business in the late 1970s with HVT and two new strains, my attenuated serotype 1 virus (Md11/75C) and the SB-1 strain from the Cornell group. None of these strains offered good protection alone against challenge with hot field strains, but I followed a casual suggestion by Abdu El Mubarak, a visitor from Sudan, that the several vaccines should be tried together as a polyvalent cocktail. This approach gave a dramatic improvement on the first try and was included in a paper I submitted in April 1981 (published in 1982). USDA-ARS published a news release in August 1981 which was picked up by several trade publications. I published more details of synergism between HVT and SB-1 in 1983 and 1984, and continued to work on synergism for the next 10 years. Even though Schat included data that bivalent vaccines improved protection in line P (but not PDRC or line N) chickens in his 1982 paper on characterization of the RB1B strain, I knew nothing of this when my research on synergism was initiated. Because of my several publications on bivalent vaccines and protective synergism, I feel like something of a father to

this technology, although much of the credit went to Cornell because of the widespread use of the SB-1 strain. Without synergism, however, it seems unlikely that SB-1 or any other serotype 2 vaccine strain would have been successful.

- REV Sometime about 1968 ADOL received several samples of strain T reticuloendotheliosis virus (REV) and also of chick syncytial virus, which was initially associated with the CAL-1 strain of MD virus. Although Graham Purchase was driving much of the original work, I developed an academic interest in this new type of avian retrovirus. In 1970 I described enlarged nerves in REV-inoculated chickens, a finding of interest to me since enlarged nerves were previously considered pathognomonic for MD. Later, with help from Lyman Crittenden and others, I described induction of both B and T lymphomas in chickens by REV and conducted studies on tolerance and shedding, immunodepression, and field prevalence. All this established me as something of an expert in the pathology and epizootiology of this virus.
- <u>Insertional mutagenesis</u> An accidental contamination by REV of the JM strain of MDV during serial passage in my lab during the 1970s paved the way for Hsing-Jien Kung to describe in 1992 the insertion of retroviral DNA into herpesvirus, which was at that time a unique phenomenon in biology. Hsing-Jien provided the brains, but I provided the materials and later characterized the RM1 strain which consisted of the JM strain of MDV with an REV LTR insert. This natural recombinant virus proved to be a candidate vaccine strain.
- New MD vaccines. In the 1980s and 1990s, I developed and evaluated a series of new candidate vaccine strains, including (but not limited to) 301B/1 and 471B/1 (serotype 2) and R2, R2/23, 648A/80, RM1 and CVI988/BP5 (serotype 1). Although 4 of these strains were patented, only 301B/1 achieved significant commercial use. I also conducted a critical evaluation of the CVI988 strain and my paper at the 1992 International Symposium on MD in Amsterdam on the superior efficacy of this strain helped speed its introduction to the United States. A number of challenge models for vaccine evaluation under laboratory conditions were developed and improved. However, I eventually concluded that large scale challenge under semi-commercial conditions, such as that conducted by Kenton Kreager at Hy-Line International, was superior.
- Evolution of virulence Following a suggestion from Graham Purchase, then a National Program Leader with ARS in Beltsville, I isolated a clutch of MDVs from field flocks in the late 1970s and early 1980s and described the vv pathotype. This initiative was stimulated by observations by Caswell Eidson in Georgia of MD virus strains with increased virulence and reports of field problems from Delmarva and continued off and on for 25 years. The term vv was a take off on the velogenic viscerotropic Newcastle disease virus, and initially designated a "virulent variant" strain. Calnek objected to the word "variant" because it was not an antigenic variant. I revised the manuscript and

ultimately designated the virus as a "very virulent" strain (vvMDV). Later, in the 1990s, I isolated additional viruses and described a further pathotype, designated as vv+. My 1997 paper on the evolution of virulence in MD has been cited more times than most of the others, and my original diagram illustrating this step-wise phenomenon has been reproduced so many times by various speakers that it brings a smile or chuckle when somebody new rolls it out.

My research career had several distinct phases. The initial phase concerned with MD etiology and HVT vaccine was a circumstance of time and place – one simply went with the flow as the goals were obvious. Then came a less inspired period during the 1970s when I tried a number of ideas, some more productive than others. By the end of the 1970s, however, I made two decisions that set the stage for the rest of my career. One was to start isolating MD virus from the field in order to characterize its evolving properties. The other was to get serious about the development of improved vaccines.

At least some of my research attracted attention from peers. I received the P.P. Levine award 5 times for the best paper published in Avian Diseases and once received the Bart Rispens award for the best paper published in Avian Pathology. In addition, my description of HVT, published in the American Journal of Veterinary Research, was recognized by ISI as a citation classic (a high number of citations). I was a junior author on two other best paper award publications in Avian Diseases, authored by Aly Fadly and Larry Bacon, respectively.

I was also recognized within my agency, the ARS, through regular promotions which were always based on research achievement, rather than administrative accomplishment. I entered federal service at grade GS-12 and, after promotions at each of 5 successive evaluations, attained in 1990 grade GS-17 (considered a "supergrade" in federal service).

Equally meaningful were the frequent invitations to present lectures, sometimes in quite exotic places. The keynote talks and a number of other special presentations stand out in my mind. Probably the most notable of these was the Bart Rispens Lecture presented in 2000 to the International Symposium on Marek's Disease, in Montreal. But there were many others.

My relationship with the AAAP. I joined AAAP in 1963, after I had satisfied the then requirement for 3 years of experience in the poultry field. My application, mailed in June, was approved first by Bill Benton, chair of the membership committee. The letter of final approval was posted by Glenn Snoeyenbos on December 18th – along with a bill for a \$5 initiation fee and \$8 dues (which included a subscription to Avian Diseases). This decision was never regretted, as the AAAP has provided important venues for my professional growth. I served and continue to serve in many different capacities.

I became a member of the AAAP leukosis committee and participated in a landmark committee workshop, organized by chairman Bruce Calnek in 1967 at the Dallas meeting, as discussed earlier.

I was chair of the AAAP leukosis committee in 1970 when interest in MD etiology and vaccines reached its peak. In this capacity, I organized a workshop for the 1970 AVMA annual meeting in Las Vegas. There was a question of whether this workshop should be restricted to committee members and special invitees (workers in the MD field) or open to all. I supported a closed meeting but this view was not popular with those not on the invited list. I recall discussing this with Frank Craig, then president of AAAP, who ultimately supported me and earned my lasting respect in the process. The meeting was closed and the report published in Avian Diseases, but the whole situation was controversial. After all, at 34 years of age, I was pretty young to be telling the senior membership of AAAP they could not attend our workshop. It would be done differently now, for sure.

In 1971, I chaired the AAAP leukosis committee again and presided over a major symposium on MD held with the AVMA meetings in Detroit, MI. This was a most successful meeting (open to all), showcasing the considerable progress on MD culminating with commercial vaccine development and essentially announcing that a cure was now in hand. How little did we know about the power of viruses to evolve and evade. Among other things, the symposium proceedings, published by Avian Diseases as a special issue, provided the vehicle for Bart Rispens to publish his work on the CVI988 strain. Bart was invited to give one talk, and ended up sending me two long manuscripts, both in dire need of revision. I personally did extensive work on these manuscripts, which have been highly cited in later years. Indeed, these two papers represented, arguably, Rispens' most important senior authorships on the subject of MD.

I served on the AVMA program committee during 1979-1983, first with Reed Rumsey and later with Bob Eckroade. During this period, Eckroade and I initiated the use of poster presentations at annual AAAP meetings, first displayed at the Washington DC meeting in 1980. Posters have since become a tradition at the annual meeting.

During my year as president (1987-1988) I initiated a new committee devoted to biotechnology, because molecular biology was yet a new science and just beginning to be applied in poultry disease research. Nearly 20 years later, this committee remains active and communicates high tech issues to the AAAP membership.

In 1993, I joined the AAAP History Committee, a committee chaired by my father in the 1970s. As chair, I launched an effort to document biographical information on prominent poultry health specialists. My interest in this work has continued as evidenced by the present document. The history preserved in these biographies represents an important chapter in veterinary science, the value of which can only increase with the years.

At the request of Bob Eckroade, I chaired an ad hoc organizing committee for the World Veterinary Poultry Association (WVPA) congress, held in conjunction with the AVMA/AAAP meetings in Denver, CO in July 2003. This was another 4 year effort and seemed to me to be a success, judging by comments from participants and also by the AVMA. A Saturday night welcome reception, inaugurated at this congress, has now become a tradition at AAAP meetings.

I have supported AAAP educational publications, authoring or co-authoring 71 papers in Avian Diseases (1961-2006), contributing to chapters on Marek's disease (editions 6 through 11) and Reticuloendotheliosis (editions 7 through 12) of Diseases of Poultry, and authoring two comprehensive slide study sets in 2005 (my first publications in electronic format). I served on the editorial board of Avian Diseases 1969-2003 (35 years).

The AAAP recognized my efforts with its Special Service Award in 1998 and Life Membership in 2007 for which I am most grateful. Although I have joined and participated with other professional organizations, the AAAP has provided me a sense of family and unity of purpose that I have not encountered elsewhere. This organization has been instrumental in my professional development and continues to be a focus of my energies in retirement. My election to Life Membership allowed me to join my father as the first father-son life member combination in this organization's history.

On the occasion of the AAAP's 50th anniversary meeting in 2007, I was honored to present the Lasher History Lecture, documenting the first 50 years of the organization, which I dedicated to my friends Charlie Hall and Bob Eckroade. I also contributed to the genesis of a commemorative book, ably edited by John Dunn, to mark this auspicious occasion.

The international dimension. My international experiences commenced in 1971 with a one-year sabbatical with Prof. Werner Schäfer at the Max Planck Institute für Virusförschung in Tübingen, Germany. This was first suggested by Ben Burmester, who was a good friend of Schäfer, a fellow retrovirologist. This experience instilled a life long appreciation for high tech, basic science, European culture and fine wines. Schäfer's technician, Liselotte Pister, was especially helpful, and provided valuable instruction in science and also in German culture and language.

In 1994, I was recruited by Tom Walton along with Mo Saif of Wooster, OH to represent the United States in a USAID-funded program (MERC) with scientists from Egypt, Jordan and Israel, effectively breaking down long time barriers to communication and cooperation. Unfortunately, political realities later asserted themselves and the progress achieved with so much effort appears now to be largely lost. Nonetheless, this was an inspiring experience with the promise of advancing science in countries with limited resources and significant political issues. The opportunity to work closely with Mo on this project for nearly 10 years cemented a valued friendship.

In 1998, I was asked by Floyd Horn, administrator of ARS, to chair a committee on a new international program designed to provide funds to scientists in the former Soviet Union who were formerly involved in biological weapons research. Under the initial guidance of Arlene Meyers, and subsequent leadership by Melanie Peterson in the ARS Office of International Research Programs, this program has mushroomed to a \$6 million/year operation, and in 2006 involves about 80 projects in Russia, Kazakhstan, Uzbekistan and other countries. I was instrumental in developing the initial concept and

operating procedures, and continue to serve as scientific advisor to this program in retirement.

Throughout my career, collaboration with international scientists has been an important and exciting part of my personal research program. There have been more than 50 trips outside the United States to lecture or collaborate. Germany and Russia have become my adopted countries. There were several BARD grants with Mertyn Malkinson and Irit Davidson in Israel. My involvement on an MD research project in Moscow, first with Leonid Dudnikov and later with Kate Dudnikova, resulted in more than a half dozen trips to this interesting city. Lucy Lee has brought so many scholars and scientists to ADOL from China that I have acquired a considerable knowledge of Asian culture.

I have been a member of the World Veterinary Poultry Association for many years, attending many of the congresses and chairing the 13th Congress held in conjunction with the AAAP meetings in Denver in 2003. In 2007, I was elected by this organization to Life Membership, probably in recognition of my contributions for the Denver meeting. My very first international meeting was the WVPA Congress held in Belgrade, Yugoslavia in 1969.

At ADOL, for more than 40 years, I was part of a scientific staff characterized by significant ethnic and cultural diversity, a most enjoyable and beneficial circumstance. Our many international visitors have added to this diversity. Persons such as Jim Payne, Dan Gaudry, Uli Neumann, Marius Ianconescu, Laurent Cauchy, Mertyn Malkinson, Puyan Chen, Xiufan Liu, Zhizhong Cui, Mona Aly, Isabel Gimeno and Leonid Dudnikov did projects at ADOL and became my long term friends in the process, just to name a few. The list of international colleagues with whom I have fashioned important scientific and personal relationships through meetings and correspondence is extensive and contributed much to my career.

Transition back to the bench. For the 23 years I served as director of ADOL, it never occurred to me that one could actually step down and return to full time research. However, towards the end of 1997, my administrative life became more stressful at several levels. After considerable soul searching, I submitted a formal request to step down. Rick Dunkle, the Area Director in Peoria, IL not only approved my request immediately, but determined that I was to be replaced in 30 days. Folks were obviously anxious to see me go and, in retrospect, it truly was time. It was back to the bench for yet another chapter.

This provided me quality time to focus on several continuing projects. I completed a couple of large studies on ALV-J epidemiology which were among my best work, even though they seemed to have little impact on industry control programs. I completed the last of a 20 year series of studies on various candidate MD vaccine strains. New information was provided but I was disappointed at my failure to improve on existing products. I probably never worked harder or was any happier than in the years between my return to the bench and my retirement. I never thought it would be possible.

The National Academy. A phone call from Harley Moon in April, 1998 changed my life forever. I am not sure if I really understood what the National Academy of Sciences (NAS) was, and suddenly I was informed that I had been elected, joining fewer than 2000 United States scientists representing all scientific disciplines from astrophysics to chemistry to plant biology. I later realized that this was very close to the top recognition in science and was highly coveted. In the ensuing years, I have participated in Academy business and joined a committee that deals with science projects in Russia (much like my involvement with the ARS program). I have helped a number of authors publish in the Proceedings of the National Academy of Sciences. This recognition has become closely linked to my name, opening some new opportunities for service in science. In my view, I am far less qualified than most who have been elected. However, as one of 7 veterinarian members (in 2007), only 4 of whom are involved with agricultural research, I have been presented with a unique opportunity to serve as a spokesperson for veterinarian scientists everywhere. I do not intend to shirk this responsibility. To my knowledge, the only previous worker in poultry diseases to be elected to the NAS was Robert Hanson, who worked on Newcastle disease and was not a veterinarian. Subsequently, I was joined in NAS by the election of Roy Curtiss III, a molecular microbiologist who developed recombinant vaccines for Salmonellae and other pathogens of poultry. Curtiss was not a veterinarian either. All three of us are or were members of AAAP.

Transition to retirement. Retirement on May 31, 2002, was long planned and appropriately timed. ADOL kindly provided me status as a collaborator and an office, which enabled me to complete many continuing projects. The fact that my last chicken experiment was killed a week before my retirement party suggests that there was still work to be done. A subtle point, not originally clear to me, is that retirement from employment does not mean one has to retire from science.

Retirement also provided the chance to wrap-up several of the "great projects" of my career, including some that were not strictly research. With the help of Barbara Riegle, a comprehensive list of virus isolates was assembled (2004) and freezer inventories were adjusted to accommodate long term use by others. The review paper in Avian Pathology on pathotyping (2005) was a chance to lay out my vision in this field. The slide set (#27) on differential diagnosis of tumors (2005) included a comprehensive treatment of diagnostic philosophy and strategy, but may not be widely read because of its electronic format. The opportunity to bring closure to my activities in these and other areas has been a true blessing.

Goals realized. In my view, my career has focused on three goals: (1) advancing knowledge, (2) promoting the institution of science and (3) passing the torch. I feel I have made progress towards each of these goals, but it is for others and history to make the final assessment.

The publications arising from my personal research (>300 at last count) plus those produced by scientists in groups under my direction probably qualify as at least a modest advancement of knowledge based on volume alone. More importantly, some of the work has had an impact and some of the technologies have come into general use. My work

has played some role in each of the 3 vaccine strategies in common use for MD control, HVT vaccine, bivalent vaccine and CVI988 (where I did the studies that confirmed its superior efficacy and paved the way for its use in the United States). The number of HVT vaccine doses administered during the past 35 years probably approaches one trillion and strain FC126 is still used worldwide. The cumulative number of chickens in the United States that have been "saved" (protected) by MD vaccination exceed 2 billion through 2004. More importantly, the incidence and economic impact of MD is lower at this writing than at any time during the past 45 years. I like to think that perhaps I played at least a small role in this development. I have helped synthesize available information in chapters in Diseases of Poultry (and elsewhere) and have created a bank of pathotyped MD viruses which is in use worldwide. My contributions have been noticed by others from time to time. Of the nearly 30 major awards and recognitions I have received, the best paper awards and an honorary degree from the Tierärztliche Hochschule in Hannover, Germany are especially memorable. Michigan State University has also recognized me generously, perhaps a testimony to the close collaboration between ADOL and MSU over the years. I also received awards from USDA-ARS, my employer for 38 years. Recognition by scientific peers has been gratifying, culminating in the NAS membership. Recognition by the poultry and biologics industries, including election to the Poultry Hall of Fame, brought special satisfaction since this indicated that some of my work must have had practical importance. There has been some kind of accolade from virtually all of my professional constituencies (list available in cv).

Promotion of the institutions of science has been a more recent goal, stimulated in part by my acceptance of some sort of elder statesman role in my field. Some of this accrues from longevity, as many of my peers are gone or have become less active. Activities in this sector include those with professional societies, international programs and the National Academy of Sciences. I published one article on the need to train veterinarians in agricultural research and have supported programs to provide veterinary students summer experiences in research. I look forward to additional opportunities to contribute to the scientific community, which provided me a framework for my own research accomplishments in earlier years.

The act of passing the torch was not initially a priority in my career, but upon current reflection, it is probably the most significant of all. Relatively few students worked with me personally. Harvey Burgoyne and Ann Stephens did degrees under my guidance in the 1970s. Puyan Chen, a scholar from China, spent a year with me in the 1980s. Then came the fortuitous appearance of Isabel Gimeno, a talented and enthusiastic veterinarian from Spain who completed her PhD research with me in the 1990s and continued to collaborate with me and others at ADOL as a post doc for several years. We are still collaborating. Some of the student employees in my laboratory, such as Nadine Bowden, went on to careers in science. Subsequently, I have contributed to research conducted by veterinarians Kate Dudnikova (in Russia) and John Dunn (at ADOL). These and other persons who have interacted with me in various ways are perhaps my most important legacy. These efforts have also provided me with great personal satisfaction.

Mentors and role models. The five persons who played exceptional mentoring roles in my life and career, and who also served as role models, are J. Franklin Witter (my father), P.P. Levine, Bruce Calnek, Ben Burmester and Werner Schäfer, each of whom guided my professional development at critical stages. Each of these persons was highly successful in his career and had a strong character that engendered respect. In addition, each had human qualities and treated me kindly. I owe them everything.

A few others should be acknowledged for their help at certain stages. Charlie Hall was my teacher of poultry diseases in veterinary school. Julius Fabricant contributed to my M.S. program. Jerry Rountree provided my first real lesson in clinical poultry medicine. Harold Chute provided me my first summer experience in poultry disease research. Mal Peckham taught me poultry necropsy and diagnosis.

I respected many other colleagues as role models, some of whom became close friends. In this group, Peter Biggs, Jim Payne, Harley Moon, John Gorham, Reed Rumsey, Frank Craig, Mo Saif and Hsing-Jien Kung deserve special mention but there are many others, too numerous to mention here.

My many colleagues at ADOL also contributed in a variety of ways. I considered my relationships with Jagdev Sharma and Larry Bacon to have special value to my research but many others played invaluable roles. One does not succeed in a vacuum.

Secrets of success. This section describes a few of the things that seem to have worked for me.

A life outside of science is critical. My wife and children top the list but hobbies, community service, philanthropy and spiritual pursuits all meld together to create a purpose beyond scientific endeavors. After a stressful day at the office, activities such as playing a Hoagy Carmichael tune on the piano, weeding the vegetables, or waiting with my bow in a treestand for a deer to pass by help me regroup. Our "camp" on a scenic lake in Maine has served as a special family retreat for more than 50 years. The local Kiwanis club and church choir also provide opportunities for service and friendships. Once in a while there is an opportunity for fishing or photography. All this has made me a better scientist and person.

<u>Serendipity</u>. My career benefited from the fortuitous convergence of my entry to the job market with the emergence of a major viral disease which was amenable to study. I was surely at the right place at the right time, through no particular planning on my part. All scientists should be so fortunate. Chance continued to play an important role as my career matured, although one needed to recognize what to do when the opportunity occurred.

<u>The right questions</u>. In research, ideas come easily but not all will be productive paths to follow. In many cases I was able to ask the right questions – where approaches were feasible and the answers could be utilized by others. Often in my career, the right

questions derived from my interactions with colleagues in the poultry industry, or from the ability to see something in a set of research data that was not obvious to others.

<u>The big picture</u>. An ability to see the broad practical applications of the work, even though the work itself was tedious and detail oriented, has been most helpful. The detail is also important, because concepts are exciting but rarely can be implemented without due attention to the fine points. My veterinary training was helpful in this regard, by instilling a vision of animal disease issues on a population basis.

<u>Communication</u>. Research is worthless unless it is communicated. Skills at oral and written communication have helped me make useful contributions out of ordinary findings. For one who was a severe stutterer for many years, oral presentations were a challenge but one that I was able to mostly conquer in the latter part of my career. I finally realized that what you said was more important than how you say it. The advent of computer keyboards allowed me to compensate for increasingly poor and labored hand writing and allowed me to communicate effectively throughout my career.

<u>Human values</u>. Without respect for colleagues, supervisors, and support staff (the people one deals with in science and in life), the cooperation that is so essential for success may be absent. One cannot burn too many bridges without paying a price. Although it is difficult to be friends with everyone, the many sincere friendships in my work are deeply valued and have served me well.

<u>Bias and credibility</u>. The ability to minimize bias in all aspects of the research process and the willingness to acknowledge errors when they occurred were critical to my success. The advent of proprietary technology has made financial incentives a particularly important consideration. It has been easy for me to subordinate personal financial gain to the principles of fair and ethical reporting in science. I have witnessed the damage done when other scientists have not followed these precepts. In science, truth is power, and credibility is everything.

<u>Organization.</u> For me, the idea of keeping careful records and having a good organizational system was second nature. Although the value seems obvious, I believe only a few scientists take this part seriously. I suspect that this characteristic, no doubt inherited from my mother, has helped my research.

<u>Publish</u>. It is self evident that a scientist needs to publish. I took much pride in my publications and invested the effort to make them the very best. I resisted the tendency of my peers to publish only in the highest quality biomedical journals, and instead directed much of my best work to poultry disease journals. I do not think my career suffered as a result of this decision.

Excellence above all. At the end of the day, success rarely comes in the absence of hard work, and lots of it. I have endeavored to achieve excellence in all aspects of research, regardless of time or effort or cost. I rarely took a shortcut, whether it was in a research

design or a manuscript or an oral presentation. I believe that this ethos has paid large dividends to me and my work.

Another thing that has made the conduct of research enjoyable to me (as opposed to successful) was the happy circumstance of having sufficient independence to choose my own projects and follow my instincts. I fail to recall any time during my employment with ADOL that I was told or asked to conduct a particular piece of research by persons higher up in the chain of command. Likewise, I do not recall conducting a piece of research just because someone was offering to fund it. In more modern times, scientists will often be part of large teams, or changing subjects as needed to keep the flow of grant dollars intact. It was easy for me to be content with my work, because I decided what to do, when to do it, and how to do it – for 38 years. Few others in any profession can say the same.

Opportunities missed or denied were also important. I recall applying for an NIH grant at Cornell on experimental pathology, agreeing to be nominated for major AAAP service positions and even applying for a deanship. All these misguided initiatives were unsuccessful, a circumstance which I consider in retrospect to have been extremely fortuitous, since any one would have seriously diverted me from my ultimate path. Learning to say no is critical, but was never easy for me.

The accolades and awards received during my career are appreciated but are almost certainly out of proportion to my talents and accomplishments. To what extent do awards beget awards? There are so many of my colleagues with superior skills who have been less frequently recognized.

Changes I have witnessed. During my career, I have seen many changes in the way science is conducted. The change in attitudes of scientists and the involvement of public opinion on the welfare of experimental animals has been huge. The treatment of scientific findings as intellectual property and the increased confidentiality has transformed the style of communication between scientists. Our lab used to send "preprints" to a long list of collaborators, but no more. Also, a change from teams of a single scientist and a technician who worked alone or collaborated with other scientists in similar situations, to larger teams of students and post docs supervised by a senior scientist who may have lesser need to collaborate with peers has been evident, no doubt fueled by a shift, even in government research, to more soft funding. My PhD thesis and early papers were all hand written, laboriously transcribed by typists, corrected by hand, transcribed again, and ultimately finalized, yielding an original and up to 4 copies on onionskin paper. On one occasion, the typist, realizing the importance of protecting my final typed copy, placed it in the lab refrigerator for safe keeping. Mal Peckham found it the next day, and repeatedly chided me for the "hot stuff" that required refrigeration prior to publication.

I have also seen changes in the way the poultry industry deals with disease problems. Increasingly, the bottom financial line takes precedence over disease control procedures. Broiler companies will not implement the strict biosecurity needed for proper function of

MD vaccines if the cost of such procedures exceeds the short term benefit. One can develop the next great vaccine but it will be used only if the benefits exceed the costs in next week's balance sheet. It is essential that scientists understand this new paradigm, as it will influence the type of research that should be conducted. I do not recall such a short range vision in the early days of my career.

As the adage says, "the only constant, is change itself."

Final reflections. My career encompassed an exciting time in the history of avian medicine. Fate and diligence allowed me to make certain contributions that may have been of value to science and the poultry industry. But in as much as I have given or provided, I have also received. My career has given me much satisfaction for the work accomplished, for the harmony and beauty of the scientific method, and for the many friendships collected along the way. I was able to come to work each day with a sense of excitement and mission – the chance to do something I felt was really *creative* and *important*. Those who follow should be so fortunate.

2017 Addendum – The Blessings of a Long Retirement

My earlier biography (front pages of this document) describes the details of my happy and productive career as a veterinary scientist at the Avian Disease and Oncology Laboratory. It remains accurate, to the best of my recollection.

I am now at the point where my post retirement years have taken on their own identity – a second career, so to speak. Thus, a summary of this phase seems an appropriate addition to my earlier biography.

Some of my colleagues have walked away from science the day they retired, but as you will see, I have not followed that path. In the summer of 2001, 10 months prior to my retirement, I set down a *master plan* containing 17 specific projects I intended to complete. This was equivalent to my professional "bucket list" with most of the items to be finished post retirement. Upon reading this list again after so many years, I was surprised to find that virtually every item from #1 (conventional MDV pathotyping) to #17 (ADOL history) has been completed. Since #16 is "Witter biography," the present document may represent its completion as well. However, it has taken a while. It also has taken a plan.

My professional activities in retirement fall into several discrete chapters.

ADOL activities. I have already mentioned in earlier chapters my efforts to organize my extensive virus collection (for posterity) and make my final contribution to MD vaccine development and MDV pathotyping through appropriate publications. Of course, I had some help. For example, I shared my preliminary studies on double vaccination with Isabel Gimeno who, ultimately, produced a fine paper on this topic that included much of her own work. Indeed, my publication list has grown substantially since 2002.

My interest in differential diagnosis of tumors goes back to the 1990s when we started a project involving several ADOL staff members, but this ultimately floundered. I resurrected this after retirement to produce, with Isabel Gimeno, a slide study set on MD diagnosis. Shortly thereafter and stimulated by a conversation with Gregorio Rosales, I and several co-authors took the teachings of the slide study set and produced a Tumor Diagnosis Manual, which was first published by the AAAP in 2010.

In 2014 I authored a book on the 75 year history of ADOL. Its publication coincided with the 10th International Symposium on Marek's Disease held at East Lansing. Given that ADOL is now scheduled for closure with transfer of its activities to Athens, Georgia, the timing of this book is fitting.

John Dunn, a veterinarian with an M.S. degree, joined ADOL in 2004 as a trainee. He conducted his Ph.D. research under my guidance. After completing his degree in 2009, he was converted to a permanent research position as Veterinary Medical Officer. He has continued work on MD, focusing on diagnostics, vaccines, epidemiology and other topics. In many ways he is my successor at ADOL, doing much the same type of work

that I did. He has also developed an interest in history and has chaired the AAAP History Committee for several years. John and I have maintained a relationship which has kept me close to his research as well as developments at ADOL and the AAAP.

My mentees, Isabel Gimeno and John Dunn, have stayed in the poultry disease field. Both have won awards for their research and the respect of their peers – and continue to make me proud.

Beginning in the fall of 2002 I was appointed as a collaborator at ADOL, a title that paid no money but gave me access to the building and a small office, which I maintained until about 2012. I found that my home office was ultimately a much better place to work anyway. My collaborator status was terminated in 2014.

Russia. With the demise of the Soviet Union in 1991, science had fallen on hard times and many scientists working in institutes with expertise in biological warfare were at risk of leaving for more lucrative jobs in rogue countries. Money was available from the US Department of State to sponsor collaborative research to sustain and retain key scientists in certain countries of the Former Soviet Union (FSU).

The ARS-FSU Scientific Cooperation Program was established by the Office of International Research Programs (OIRP) of the Agricultural Research Service (ARS) to address this new opportunity.

I was appointed in 1998 by Floyd Horn, ARS Administrator, to chair the original ARS committee. In this role, I personally provided much of the input to the operational guidelines of the new program which provided research grants to FSU scientists. The mission was (1) to advance agricultural science in FSU countries, (2) to enhance ARS research programs, (3) to improve the economy of FSU countries and (4) to reduce the threat of biological weapon development and usage in the world.

After my retirement, I was appointed as Scientific Advisor to this program (2002-2008) This gave me a say in which projects to fund and the chance to visit several ongoing and potential program sites in Russia and Kazakhstan. The program was run by the ARS Office of International Research Programs (OIRP). My chief ARS-OIRP contacts, Arlyne Meyers and, later, Melanie Peterson, were both a joy to work with. This program, which ultimately involved about 50 projects, was considered one of the most successful of the US efforts to support FSU scientists.

In the course of this, I became a co-principal investigator on a project in Russia dealing with MD in chickens. Initially, my collaborator was Leonid Dudnikov of NARVAC, a veterinary vaccine company located in Moscow. The project funding started in 2002. Leonid left the project after the first year and was replaced by his former wife, Kate Dudnikova. Kate and I worked together until about 2009 and published two good papers. Project funds supported my travel to Russia and to a number of other professional meetings during this period.

Meanwhile, my membership in NAS provided me the chance to participate on a series of four National Research Council (NRC) committees related to biological research in the FSU. First was a committee to review FSU research projects for US Government funding (1999-2006). Next was a committee on Future Contributions of Biosciences to Public Health, Agriculture, Basic Research, Counterterrorism and Nonproliferation Activities in Russia (2003-2006). Then followed a committee on Prevention of Biological Weapons in States Beyond the Former Soviet Union (2008-2009). The last was a committee on US-Russia Bioengagement, (2010-13). Each of these committees was coordinated by Glenn Schweitzer, an NRC staff person with special expertise in the FSU countries. This was a special experience. My role was to represent agriculture in the midst of a group of high-powered basic scientists and, believe it or not, I think I held my own.

In summary, I traveled to Russia 10 times from 1998-2011. I became close friends with the scientists working on my project, and generally acquainted with many of the key persons and institutes working on animal diseases in Russia. Also, I hosted many Russian visitors, a few of which spent time at ADOL learning techniques. The confluence of the ARS and NAS programs provided a special opportunity which was a jewel in my retirement years, and left my cellar with enough vodka for several lifetimes.

The National Academy. I mentioned in the previous section that my election to NAS was a life changing event. It is true. I have tried hard to contribute to the best of my abilities even though surrounded by eminent scholars. In addition to the NRC committees (see above), I have functioned as the secretary of Section 61, taking minutes at the annual meeting. I also was for many years the Section 61 Liaison to the NRC, recommending persons for service on committees or as project reviewers. I have attended every annual meeting since my election and have given priority to opportunities for service as they would arise. Indeed, Michigan State University has "adopted" me and provided some funds for my NAS travel. NAS membership has proved to be not only an honor but also a responsibility, which I continue to take seriously.

As I write this, I have just joined a NAS committee to review nominations for the NAS Prize in Agriculture, a \$100,000 award for a midcareer scientist which should attract the very best of candidates.

The AAAP. The AAAP has always been important and this has continued in my retirement years. I attended annual meetings every year through 2010 and sporadically thereafter. My membership on the Tumor Virus Committee has continued through this writing, although my role is largely ceremonial. In contrast, my role on the History of Avian Medicine Committee has continued at a high level. Let me mention a few of my projects and efforts on this committee.

Biographies – having launched the AAAP Biography project in 1996, I have done what I could to recruit or prepare biographies. Of the 43 biographies completed to date, I have been the lead person (author) on 12, and have helped on some others. On the biographies for Hiram Lasher, Harold Chute and Lucy Lee, I was able to work directly with the subject person. On the biographies for Graham Purchase, Ben Burmester and my father,

I used other sources. Although Egon Vielitz wrote his own biography, I helped get it into proper English and format. Each has been a labor of love - a gift to the memory of the person as well as for posterity.

Archives – The AAAP Archives was founded in 1991 and now comprises 29 linear feet of assorted materials. But few AAAP members have utilized its contents. I have maintained a keen interest and have used some materials for talks and posters. Art Bickford and I spent several days reviewing the archives in 2008. I have been personally responsible for many of the deposits of materials to the archives, including a large deposit scheduled for 2017. Although much work remains to be done, I feel I have helped make this resource more accessible and complete.

Meeting Organization – My role as chair of the joint meeting of the AAAP and WVPA in Denver, 2003 has already been described. Along with my role as chair (1996) of the 5th International Symposium on Marek's disease in East Lansing, these stand in my view as singular achievements. However, I also served on the organizing committee for the 2007 50th anniversary meeting of the AAAP in Washington DC. In addition to giving the Lasher-Eckroade lecture, I was involved with the concept of a commemorative book for the occasion and gave John Dunn strong encouragement to lead this project to completion. I have attended many meetings but these 3 stand out, and not just because I was involved.

50 year history – A highlight of my career was the chance to deliver the Lasher-Eckroade Lecture in 2007 on the 50 year history of AAAP. Not long afterwards, I was inspired to put this material in writing. I found, of course, that new material needed to be added and the preparation of a manuscript became a significant new project, one that caused me to visit the archives for more material (see above). The finished manuscript was posted on the AAAP website in 2012. However, it is planned that a print version of this paper will be included in the book being prepared for the 60th anniversary celebration. Although previous histories exist, I felt that my piece provided a deeper and more personal view of our great organization.

60 year history – This project started with a request from the Board of Directors to Patty Dunn, the chair of the history committee, to prepare a celebratory video (about 15 minutes) covering several aspects of the early history of AAAP. The video was to be shown (presented) at the 2017 annual meeting in Indianapolis. I agreed to chair a subcommittee with Bruce Calnek and Art Bickford to accomplish this. This was unlike any prior project; it occupied most of my free time for about 5 months. With contributions from several others and professional technical help I was able to deliver the requested product. The video was shown at the Indianapolis meeting and I gather it was a success.

I also helped John Dunn prepare a 10 year history to be included in a celebratory book, which will be produced by John. The book is formatted as a companion volume to the earlier 50 year history book. It includes my 50 year history, which has been available on the AAAP website, but is now in print.

All this, but especially the video, has involved a great deal of nit-picking detail work that, somehow, is still possible for me at age 80 and is even fun. I should be thankful.

Honors and Recognitions. My list has continued to grow in retirement, much to my surprise. I was especially pleased to receive honorary doctorates from two different universities – the School of Veterinary Medicine in Hannover, Germany and the University of Guelph, in Canada. In addition, I was included in the inaugural class inducted into the Hall of Honour of the World Veterinary Poultry Association (2013) and also in the inaugural class inducted into the Hall of Honor of the AAAP (2016). I continue to be humbled by the accolades I have received over the years.

A complete list is included in my CV (also deposited in the archives).

Leisure time pursuits. In reading the above, one may deduce that I have spent my retirement totally involved with professional activities. I assure you this is not the case.

I have always had multiple avocations and interests but retirement has provided more time for their nuture. Joan and I share interests in family, travel and gardening. I have devoted more time to photography, bow hunting, fishing, church choir and piano. Joan and I helped launch a nonprofit organization to conduct and manage a local chamber music series. I was even president for 4 of its first 5 years. This was also a labor of love that is renewed every time we attend a concert. I continue my long time membership in a local Kiwanis club, serving our community and the world. Too many things to do, not enough time.

Looking Back. My retirement life, now at 15 years and counting, has been a distinct chapter that surely deserves mention in my professional history. I had hoped for a continued involvement in research and science, and this was realized. Instead of the abrupt transition experienced by so many at retirement, I had the privilege of a gradually tapering professional life – just about perfect.

In retrospect, one's research accomplishments have a surprisingly short life but one's influence on people can pay dividends forever. Although many of my personal goals have now been accomplished, I also realize that the list of important things to do will never be empty. And may it always be so.

My father wrote (1976) that "history is a compass bearing that gives a sense of direction for a continuing journey over winding roads. A look at the past is not a backward turn; it can lay the foundation of future progress." This biography is now history.

Addendum

Selected aspects of the career of Dick Witter are also documented in several talks, including the Bart Rispens Lecture (2000), a talk at Elanco, Indianapolis, IN (2001) and a talk at the Tierarztliche Hochschule, Hannover, Germany (2003). These talks along with a cv and list of publications will be deposited in the AAAP Archives.

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

Additional biographical materials may be available from the AAAP Historical Archives located at Iowa State University. Contact information is as follows:

Special Collections Dept. & University Archives 403 Parks Library Iowa State University Ames, IA 50011-2140