Randall Knight Cole

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The Life of Randy Cole – consummate geneticist

Randy Cole was born 21 September 1912 in Putnam, CT. His parents were Alden Brigham Cole and Sarah Elizabeth Medbury.

My interest in chickens goes back to my grandparents, who were farmers in northeastern Connecticut, where both families had small flocks of chickens. Just before I became five years old I spent some time with my paternal grandparents, while my younger brother was joining the family. I helped grandma (Nana) feed her chickens, and collect the eggs that grandpa sold. I still remember going into the chicken house one late - summer day and moving all the few eggs to one nest, which upset grandma! I liked one hen that had a damaged leg but could lay. When my family became re-organized grandma sent us some eggs by mail quite frequently and often marked one for me as coming from that interesting hen. In 1923 a new home in Massachusetts (W. Medway) included a small house that could be used for chickens. Very soon, I was provided with some chickens that a friend of my father had to discard. They were English Pit Games!

Joining the local 4 - H Club, that was limited to those having chickens, soon led to information about chickens and eggs, how to judge chickens, prepare them for shows,

etc. Within a year I obtained a job at the only local poultry farm (Harold Rotzel's) where I spent most of my time after school, on weekends and holidays, as well as ‘vacations' from school, doing chores that included feeding, collecting eggs and preparing them for market, brooding chicks and caring for them on the open range until maturity. This included living in a tent at night on the range with my dog during the summer months so as to keep the foxes away. Most of the growing birds (White Leghorns) roosted in a tree at night. Birds affected with range paralysis could not do so and thus were the primary game of the foxes. Other health problems existed, such as laryngotracheitis. A severe outbreak was diagnosed after affected birds were taken to the Veterinary Unit at the Massachusetts Agricultural College in Amherst. A follow - up, apparently recommended at Amherst, involved taking exudate from the tracheas of affected hens and using a small brush to get it into the cloacas of the non - infected groups. Birds in the pens adjacent to the ones with laryngotracheitis were treated first, followed by those in other housing facilities. This prevented much spread of disease. Birds used as breeders had to be tested for S. pullorum. I remember putting leg bands on the birds to identify the source of blood used for the serum needed for the tube-agglutination test, in accordance with the 'requirements' set up by Dr. L. F. Rettger. Another health problem, that still exists, was 'prolapse'. As soon as recognized, the affected laving hen was killed and dressed and then taken to a large local family that needed food.

The 4 - H Club meetings included one each year at the Massachusetts Agricultural College in Amherst where judging contests were conducted. I won the cup two times and also at the State Contest at the Boston Poultry Show in 1929. I became interested in going to the Mass. Agric. College but continued to work at the local poultry farm for a year after finishing high school.

As one of two permitted to give an 'Essay' at the high school graduation in 1929, at the age of 16, I concentrated on "Agriculture as a Profession", which was contrary to the ideas of many young people at the time. Included were references to Luther Burbank who had worked on plants, McCormick who invented farm machinery, and Professor Rice at Cornell who was considered "to be the most valuable man in the poultry world".

A year after the 'great depression’ started I did get into the Mass. Agric. College to major in Poultry Husbandry. Entrance into the college required 'certification' for a given number of points for high school courses where the grade earned was acceptable for college admission. If 'certification' was not provided by the Principal, a college entrance examination would have to be taken and passed. I needed three points and so would have had to take the examination for the French language or Latin. But, my acceptance statement from the college included the 3 points for my performance in the 4 - H project, over a period of 5+ years.

The college courses included physiology (human) and serology, both taught by Dr. G. E. Gage, who had worked on the diagnosis of Bacterium pullorum in the domestic fowl back in the early teens. I also took most of the courses in bacteriology and had a part time job in the department washing glassware and setting up the laboratory for the courses.

The great depression created problems. I had only limited savings and so after the first year it was necessary to spend considerable time to make ends meet. Room at the AGR fraternity was covered in part by a 'custodial' assignment, food by washing dishes at a local restaurant, and then work at the College library and later at the Dept. of Bacteriology at $0.25 per hour. Close to 40 hours per week was used to meet these needs. There was little time for social activities. By remaining in the ROTC program there was a small periodic payment during the last two years.

Once college was over (June 1934) there were few jobs available. I had stayed in the ROTC program, that at the college concentrated on Cavalry, because of my interests in horses. After graduation I was able to spend two weeks on military duty dealing with the CCC (Civilian Conservation Corps) program. Thereafter the only available job of interest was at the poultry farm (Rotzel's). Because of the depression and absence of money, my desire to become a poultry farmer could not be met.

Dr. Erwin Jungherr, at the Connecticut Agricultural College in Storrs, was looking for a lab-assistant to do the bacteriology related to his necropsies which dealt primarily with poultry. His request to Dr. G. E. Gage, Head of the Department of Bacteriology at Amherst, yielded my name and the fact that I had majored in Poultry Husbandry. One evening in August I drove to Storrs, Connecticut, about 65 miles, to meet his request for a visit and almost immediately was offered the position in his department.

The year with Dr. Jungherr was wonderful. I did all sorts of things to help, including bacteriology, care of the lab animals (rabbits, guinea pigs, and chickens), help with post mortems, etc. He taught me how to do necropsies, a procedure I never changed!, how to keep records and participate in extension meetings dealing with poultry diseases and necropsies. I also took his course in Animal Diseases.

Things changed in the summer of 1935. Professor Hutt, at Cornell, was looking for someone for a position as Instructor in his department, who would also be able to participate in a graduate program. His request for a name led Professor Graham, Head of the Poultry Department at the Massachusetts State College in Amherst, as it was then known, to cite my training and the fact that I was working for Dr. Jungherr. I had answered Hutt's request for information but shortly after the Poultry Science Association meeting in 1935 at New Hampshire, which Hutt and Jungherr had attended, Dr. Jungherr brought me some papers to sign, so he could begin to search for a replacement for me as a lab assistant. I strongly objected that I was to give up my interesting job. He insisted that I take the opportunity to advance my training and strongly suggested that it include courses at the Cornell Veterinary College.

One day after I arrived in Ithaca (15 Sept. 1935) Prof. Hutt took me to the poultry farm to see some of the chickens he was working with. There were some dead ones and he asked if I could identify the cause. Using a 50 - gallon metal barrel (bottom up) and a pair of scissors I opened several. Most of them had 'neurolymphomatosis' which could easily be recognized when the affected nerve could be compared with the normal one on the other side of the body (brachial or sciatic) or in a non - infected bird. I was

immediately assigned the responsibility for doing necropsies on all dead or sick birds among those used for research or teaching purposes by the department - something that continued for 40+ years.

Under the influence of Prof. Hutt, I became interested in the role of genetics and its effect on disease and defects in chickens. Following the recommendations of Dr. Jungherr I took a minor in animal pathology under Dr. Olafson at the Vet. College as well as courses in histology and organology at the Ithaca pre-med unit associated with the Cornell Medical College in New York City. I also took Dr. Duke's course in animal physiology at the Vet. College.

A project by Prof. G. O. Hall dealt with trying to improve the quality of egg albumen by selective breeding. This led to my study of the oviduct of chickens and the finding that hens that produced good albumen had higher goblet cells that produce the mucin fibers that control the quality of albumen in the fresh egg [Anat. Rec. 7: 349-361, 1938]. Since the role of genetics in viability is important from the first day after conception, dead embryos should be checked and anything not normal recorded. In the spring of 1936, one of Prof. Hall's matings, which involved a sire and several of its daughters, several abnormal embryos were found. A record of the mating of the same sire, again with daughters the previous year, listed 2 dead embryos with somewhat similar descriptions as recorded by another Instructor, Will Lamoreux. The next year (1937) a hen with low hatchability (42% of fertile eggs) but in a different project, started by Dr. Hutt in 1935, using birds hatched by the Department in 1934 for which egg production data were available, was found to have 4 dead embryos, similar to those in Dr. Hall's mating. The defect, identified as an autosomal recessive character and named the ‘talpid' lethal, proved to be the same in both stocks and could be traced back to a sire hatched in 1927 - as a common ancestor. This lethal gene was eliminated by appropriate testing of the breeders selected to maintain and improve the stock [The Journal of Heredity: XXXIII, 82-86, 1942], The name used for the lethal was chosen because the abnormal foot on the older dead embryos looked like the front feet on moles, which belong to the family Talpidae.

When at Storrs with Dr. Jungherr, he observed (early 1935) a sarcoma, that was somewhat similar to the famous Rous sarcoma, that he could transmit by injection of material from the tumor. The agent could be 'preserved’ by drying tumor material or exudate on glass slides and keeping the material in ‘vacuum-sealed’ tubes.

To determine if heredity played a part in the bird's response to this transmissible sarcoma, subsequent progeny from some of the matings used at Cornell in 1936 and 1937 for the State Project (228), that gave origin to the Cornell C and K strains of White Leghorns, were exposed to the tumor virus by intraperitoneal injection. This was soon changed to the wing-web, for it was much easier to recognize and follow tumor development right from its start. Available non-injected sibs, from the families with the highest or lowest levels of susceptibility, were used to establish both a susceptible and a resistant subline.

The results clearly indicated that heredity played an important role in the response to this sarcoma virus, called the Jungherr sarcoma, but that the use of this procedure as a means to improve resistance to other causes of poultry mortality did not appear effective [Cancer Research 1: 714-729, 1941]. Because of military service (1942 - 1946) this project was not maintained and the ‘virus' preparations disappeared from the laboratory!

Many things were done during the initial years at Cornell in addition to the necropsies, that included bacteriology and histopathology for which there was no help to prepare culture media or prepare, cut, and stain the tissues.

Assistance was given to Dr. Hall in his courses dealing with judging poultry, egg marketing, and dressing poultry. At times very brief reports were given via the Cornell radio system concerning egg prices, etc. in New York State, as part of the Department's extension service.

Other activities, related to the State Project 228, varied with the time of year. In addition to examination of eggs that failed to yield a living chick there was wing-banding of the chicks, recording sex at 6 - 8 weeks with elimination of many males, leg-banding of pullets selected for housing, and recording of any recognized 'abnormality’.

The year of 1939 was of tremendous significance to me. Back in 1936 Dr. Hutt was arranging to hire a statistician to handle records and data for State Project 228 (resistance to disease) and other genetic projects. Lelah Alice Ball, a graduate from the University of Minnesota (1935), where Hutt had been a member of the Poultry Department Staff prior to coming to Cornell in1934, was strongly recommended by the Staff in their Department of Statistics. The information concerning her training, their recommendations, along with a photograph were sent to Dr. Hutt, who then passed the material around to staff members prior to his selecting which person to hire for that position. I was impressed also with the photograph and indicated she would be my 'girl friend'. This proved to be an excellent decision for we were married in early 1939. Because of existing regulations by the College, of which we were not aware, Lelah could not retain her position in the Department because I had one there. It took a few months for the Dept. to find a person, so Lelah could still receive a small salary for a few months.

Since I was to complete my formal graduate training in June 1939, I was pleased that I would be able to continue my position as an Instructor in the Poultry Department. Under such conditions one could continue to take courses to advance one's knowledge, usually only one course at a time which did not interfere with responsibilities to carry out the assignments by the department. I arranged with Dean Hagan at the Vet. College to do so and get 'credit' towards a DVM degree. I had already taken their courses in pathology and physiology. I had also taken courses in comparative anatomy, embryology, histology, and organology that would meet their requirements. Thus, in the fall of 1939 I took Dr. Milk's course in small animal diseases and then, in the following spring, the course in Bacteriology (Hagan & Brunner). But, when appointed to the rank of Asst. Prof in 1940 it was no longer possible to earn credit for a degree at Cornell.

Also, a new requirement had to be met. Each Staff member in the Poultry Dept. had to teach a course dealing with poultry. Poultry breeding and genetics was already presented by Dr. Hutt. I could give a course in poultry diseases but such a course for students in the Agric. College was being given by Dr. P. Philip Levine from the Vet. College. What was to be the subject for me to prepare a course for students interested in poultry husbandry? Hutt's course was given in the spring semester and had to involve information dealing with avian anatomy, since many of the inherited traits Dr. Hutt covered dealt with skeleton, skin, feathers, and various organs. It seemed best to organize a course in anatomy of the chicken and give it in the fall semester so that Dr. Hutt could concentrate on genetics and not have to give so much information on normal anatomy. I believe that this was the first time a course dealing with anatomy of the chicken was given in any Dept. of Poultry Husbandry. There were ten poultry-major students in the 1941 class, two of whom subsequently went to the Vet. College and earned a DVM degree. Drs. Grayson Mitchell and Morris Povar then spent most of their professional careers working with poultry diseases.

The anatomy course was given every other year, save for 1943 and 1945, until 1972. When Prof. Hutt retired in 1965 I then took on the course in poultry breeding and genetics. I also presented his course in Animal Genetics at the Vet. College in 1955 when Dr. Hutt was on sabbatic leave.

Military service (1942 -1946) dealt with police duties, primarily in the USA. Soon after the war in Europe ended (May 8, 1945) and the expansion of activities in the Pacific, a new assignment was indicated (Philippines). A brief 'vacation' led to a return to Ithaca where I became aware of a new book - Diseases of Poultry, edited by Biestor & Devries. Reading it cover to cover provided much entertainment while on board ship (8± weeks) as well as in Manila, since the war had ended by the time the ship arrived there.

Over the years other people sought help in their research projects. Dr. Jacob Furth at the Cornell Medical College in New York had been involved with spontaneous leukemia in mice. The inbred Ak stock had an incidence of 70% while the Rf stock had only 1.6%. He had produced many types of backcrosses and kept records that included age at death and the cause, as recorded. Because of our interests in 'avian leucosis' at the Agric. College, he asked that his records be analyzed to determine the role of heredity. He was already well-known for his work on lymphomatosis, erythroid leukosis, and myelomatosis in chickens. The data from his extensive records were organized and analyzed. The results indicated that this disease was hereditary, due to multiple genes, but influenced by some environmental factors that caused some deaths from other causes. The incidence of leukemia, expressed as a logarithm of the percent, yielded a 'straight line' versus the percent Ak-heredity in the mice [Cancer Research Vol 1:957-965, 1941].

In 1955, Prof. E. Y. Smith, who was breeding and developing the Empire White Turkey, observed some abnormal poults in one of his matings. When the records were checked for these abnormal poults, which closely resembled a lethal condition known as 'congenital loco' in chickens, they were shown to have come from only 3 of the females

in the mating which were closely related to the sire. Early in 1956, these known ‘heterozygous' birds were used to determine if the recessive gene (lo) was present in any of the potential breeders for that year. The given sire, when mated to 4 daughters, showed that 3 of them carried the gene. One of the brothers also had the gene. Further testing, using known heterozygous breeders, revealed that the gene had been present in two of the other 9 sires used in 1955, as well as in some dams. All breeders selected for use in 1956 to maintain and improve the stock were shown, by testing, to be free of the lo gene, hence a solution to the basic problem [Journal of Heredity 48: 173-175, 1957].

The major project (State 228), initially started by Dr. Hutt in 1935, dealt with using genetic selection for resistance to disease as a possible means of helping the poultry industry to control mortality, especially neoplastic for which no other procedure was then known. Selection was not only for resistance (C & K strains) but also for susceptibility (S strain). This was combined with selection for economic traits as a means for ensuring that selection for resistance to disease did not have to lead to poorer egg production, etc. One of the major factors of this project was that every bird was identified as to parents and complete records were obtained, summarized, and maintained for future evaluations. [All of these records are now at the Cornell University Archives under code no. 21-32-2806.]

Some people, including the Dean of the Agric. College, considered this work on the S-strain to be unnecessary and inappropriate, but its increased level of mortality, versus a decrease in the C and K strains, clearly indicated that the improvement was not due to a reduction in the level of natural exposure to disease producing agents or conditions.

Early findings had shown that the environmental factors (closeness to adults) during the first two weeks of brooding did have an effect on subsequent mortality, and so the brooding area for the first two weeks was then limited to that nearer to the adults. After two weeks the chicks were moved to other facilities and then to an 'open range', starting at 8 weeks of age. Subsequently it was shown that if the susceptible S-strain chicks were reared to 150± days of age in an area and by a person that was not in contact with other chickens, mortality was very low and no mortality from what is now known as Marek's disease occurred during the rearing period [Poultry Science 30:205-212, 1951]. Marek's disease began to occur, but at a lower rate, starting at 8± weeks after these birds were returned to the laying house at the Poultry farm and penned with other layers (C, K, and S) that had been reared under the regular procedures.

Later (1962), to ensure a high level of exposure to the Marek's virus, the air used for ventilation of the brooding facility for the first two-week period came via a duct and fan from the building used to house the laying birds. Mortality to 500 days of age from neoplasms (mostly Marek's disease) rose from an average for the previous 5 years of 1.54% to 2.93% for the 5 years following the change in ventilation for the C and K strains, while for the S strain it rose from 43.7% to 63.5%.

The initial State 228 Project, as designed by Dr. Hutt, was to develop four different strains of White Leghorns, with selection for resistance to disease and for economic

traits, to be used for crossing to provide a valuable commercial-type layer that would take advantage of hybrid vigor, as had been done by corn breeders.

One strain (C) was developed from the existing population that had been hatched at Cornell in 1934. A second strain (K) was developed using males from the Kimber farms in California and females from the same families that were used to establish the C strain. Two other stocks came from existing breeding farms in NY State, but these could not be retained because of limited facilities for breeding pens and housing of progeny. A control strain (S), that was selected for susceptibility to disease, came from the initial pedigreed population produced in 1935 that was also the source of the C strain.

The initial test for level of hybrid vigor involved progeny of pedigreed sires, selected on basis of previous tests, mated at the same time to females, selected on basis of 500-day test performances, from both strains in 1948 and 1949. The hybrids began to lay earlier and produced 21.7 more eggs, during the 500 day period, than the pure-strain daughters. Both the egg and body weights were a little heavier. Similar matings were made in 1959 and 1969 that involved the C and K strains following continued selective breeding, during which time improvements had been obtained. The hybrids from these matings, at 10 - year intervals, also laid better (25+ more eggs) than did the pure-strain half-sisters. Thus, a procedure for improving egg production became evident. The use of a good breeding program to improve the performance of the pure (parent) lines was also expressed in the hybrids [Animal Breeding Abstracts 1973, Vol. 41, No. 3].

Donald McQ. Shaver of Gait (now Cambridge), Ontario, was in the process of breeding for egg production and had recognized some strains that yielded a good level of hybrid vigor when crossed. He came to Cornell seeking help, especially from Dr. Hutt, also a Canadian. Hurt was already involved in consulting with a poultry breeder in England, and so I was given the chance to help with the breeding program at Shaver Company. Because of the results that were being obtained at Cornell, it seemed best to use a pedigreed breeding plan to improve the performance of his good parent lines that involved selection of breeders on a basis of a test of their progeny, with the expectation that a similar improvement would be shown by their hybrids, to be used as a commercial layer. The project, started in 1956, soon led to a good success. The Starcross 288 ranked first in terms of profit among all the commercial stocks of layers entered in the Random-Sample Egg Laying Tests in the fall of 1964. The reported data from these Tests were analyzed and evaluated by USDA's ARS. The Starcross 288 also ranked first for 1965 and 1966. The ‘Hat-trick’ of Canada dealt with one player making 3 goals in a hockey game. Thus, winning the Poultry Tribune award for 3 years soon led to the Shaver Hat, with a band of chicken feathers, given to those working for the company in North America and around the world. When traveling, it was thus easy to recognize those involved with this excellent layer. In the early 1970s it was calculated by those in the Netherlands, that 650 million of Starcross 288 were being used as layers. After two years when the Starcross did not win first place (but 2nd and 4th), it returned to first place for the next 9 years. The USDA then ceased to analyze the Random Sample Test results due to the reduction in the number of such tests and the number of breeders who would have their commercial layers put to such a test.

The breeding program at Cornell concentrated on resistance to disease, especially neoplastic, economic traits such as egg production, egg and body size, egg-shell quality, and freedom from anatomical defects, as well as reproduction related to fertility and hatchability. Selection of breeders was based on individual performance, that for the family which was very important in the case of young males, and the average performance of the breeder's progeny. A breeder, proven by a progeny test to rank high, was re-used as long as feasible and providing the progeny continued to rank at a high level. Most young males used as breeders came from the very best families, especially those from repeated matings for which the second sample of full sibs again proved to be exceptionally good.

One of the most significant components of the poultry breeding program at Cornell was the maintenance of complete records of performance for each chicken, including its pedigree, date and reason for discarding including the necropsy findings, as well as performance of sibship and progeny.

It was therefore easy to recognize genetic differences when some health problem was observed that affected birds in the C, K, & S strains, since these were kept in mixed-populations, save for the time in a breeding pen.

"Blue comb disease" was recognized in 1949, and Dr. Levine agreed with the diagnosis, in growing pullets (9-17 weeks old) that were being reared on an 'open-range'. Heredity played a significant role as indicated by strain differences: 7.4% in C-strain pullets vs 0.99% in the K strain, while the F-l's had 3.25%. [This was a year that hybrids were produced, using C- and K-strain breeders.]

Mortality following vaccination for Newcastle disease (1955-1956) was much higher in K-strain pullets out on the range. The genetic difference was verified in 1960 by the use of cockerels and the same Roakin strain of vaccine virus. [Avian Diseases V: 205-214, 1961.] Vaccination for this disease started in 1955 and was not used after 1956.

The C strain was more susceptible to coccidiosis and bumblefoot. It was also more susceptible to problems not considered infectious that affected the reproductive system, such as cystic right oviduct and adenocarcinoma. These last two problems, like another (autoimmune thyroiditis for which information is provided elsewhere) became of considerable significance in the mid-1950's. [See Appendix A: for details about them and the possibility of their relation to our solution for a problem of low fertility, during the 1951-1954 period.]

The role of genetics, known to affect almost every trait, was obvious in several other observed differences between the C and K strain which were being selected under the same criteria. Differences in the indicator of sex as seen in the cloaca at hatching time, comb size during the early growing period in males, frequency of stubs, and size of pituitary and pineal glands were also recognized, essentially by graduate students.

The recognition of 3 'abnormal' pullets in the C strain that were obese, small, and showing silkie feathers at 150± days of age, two of which were full sisters, led to an investigation of that trait. By selective breeding it was possible to increase the frequency from 0.3% of 3200 C-strain pullets hatched in 1955-57, but not seen in 450 cockerels, to a level of essentially 100% in 1995, when only one of 680 birds (males & females) classified at 10 weeks of age did not clearly show the symptoms. The trait was shown to be an autoimmune thyroiditis, similar to the Hashimoto disease in humans. Once the nature of the trait was fully established (1970±) effort was limited to maintaining and improving the Obese strain so that it would be available to researchers who were in a position to investigate the biological problem. [Genetics 53: 1021-1033,1996, and Autoimmune Disease Models, A Guidebook, Edited by I. R. Cohen & A. Miller, Chapter 7, 1994.]

A small population of C-strain birds was maintained by mass selection to provide a control, from the original population from which the Obese strain was derived. By blood typing, done by Dr. Larry Bacon, the control population was made homozygous for the B13 haplotype so that it would be the same as was being maintained in the Obese strain. One C-strain hen reacted to three different reagents, used to identify the genes at the MHC-haplotype locus. When the finding was verified by a second test, the hen was checked for a condition (triploid), since such had been reported in the DeKalb stock. Dr. Steven Bloom indicated that this was not present but by chance, he observed three nucleoli per cell, which indicated that this hen was trisomic for chromosome #17 and thus the MHC locus was in that small chromosome. This finding indicated how significant a follow-up of some rare finding can be. It was similar to the results involving the 10 original 'obese' pullets that led to a wonderful laboratory model for a study of autoimmunity.

A similar potential laboratory model for the study of articular gout was developed by a follow-up of a finding of articular gout, without any visceral gout or kidney pathology, in a small population of sex-linked dwarfs. The affected birds had high blood levels of uric acid that could be partially controlled by dietary restriction of protein. Essentially 100% of the birds developed high uric acid levels when given a diet with higher levels than normal of protein [Poultry Science 59:952-960, 1980]. Unfortunately this stock was discarded by the Dept of Poultry & Avian Science.

In the 1950's Dr. Hutt was attempting to find some 'markers' that could be easily identified early in the life of a pullet that might be linked to genes related to economic traits. Crosses of White Leghorns with Houdans and Anconas eventually yielded birds heterozygous for various traits that were to be tested for reproduction traits. Pedigreed chicks from 4 different sires were being raised in a 'colony' house that was heated by a coal-burning stove. At one time the caretaker entered the house to check the brooder, feed, and water and noticed a few birds that appeared to be dead. They were picked up and put aside, for subsequent pickup and submission for necropsy. Later, when these 'dead' birds were to be picked up for delivery to the Rice Hall necropsy room, those from this colony house were not found. The next day I went to that brooding house and observed some pullets lying on the floor and showing limited movements but they recovered in a short time. A follow up of the pedigree for these pullets showed that they

all came from one of the four sires, as well as from each of the 16 dams involved in the mating. Affected pullets would die following a showing of these symptoms, called paroxysm, by 14 to 15 weeks of age. Some birds showed the symptoms many times before death. The location of this sex-linked lethal gene (px) was established [Journal of Heredity 52 46-52, 1961].

In 1938 Dr. Burns, from New Zealand, who had finished his graduate training in England, came to Ithaca (? for post-doc. activity) and stayed at Gamma Alpha for a short time. He then married a gal from Ithaca and went back to New Zealand, where he became president of Lincoln College, close to Christchurch.

In 1960 they wanted someone to help their poultry industry. Dr. Burns knew of my interests in poultry and that I was at the Cornell Poultry Department. I therefore accepted the opportunity to take advantage of a Fulbright Grant, for a six-month period, January through June of 1961. In those days a position of Cornell was for nine months per year, which started April 1st. Salary payments were made bimonthly for only nine months per year. A staff member could use one of the extra 3 months for vacation but had to do something in the other 2 months that would improve his ability to serve on the faculty. Most people continued their activity at Cornell, especially those involved in agriculture since research with animals or plants went on during the summer when teaching was not normally a requirement. Thus the last 3 months of the year ending Mar. 31st along with the first 3 months of the year starting April 1st were combined to provide the time to go to New Zealand.

Travel across the USA via train from Syracuse to Long Beach, California was followed by a 2-week boat trip across the Pacific, with a stop at Honolulu. Prof. C. M. Bice, who did extension work with the poultry industry, had come to Cornell about 10 years earlier for a year of extension service for our Poultry Department in exchange for a similar service by Prof. Weaver who went to Honolulu. Unfortunately he was in a hospital and could not be seen but on the return trip, 5+ months later, we could visit Mrs. Bice. Prof. Bice had not survived.

I had a wonderful time in New Zealand where I visited many poultry farms and participated in poultry meetings all over the country. Because of concerns about poultry diseases which they did not think were present they prohibited the importation of chicks or hatching eggs. One person did bring 2 dozen eggs which he tried to get someone who had a hatchery to incubate for him. This person would not accept the eggs but did inform the authorities, who quickly confiscated them. At the meetings I was asked many questions which I tried to answer.

After one such meeting, a news report of it raised the question of how I could give an answer regardless of what the subject was. In the early 50's I had prepared an index, covering papers published in the Poultry Science Journal for a period of 10 years. Thereafter, through 1961, I prepared the annual Index. This required the reading of each of the papers and hence I was knowledgeable of current information related to poultry, regardless of the science or management details involved.

Another interesting lethal (ametapodia) came from a single White Leghorn chick that was observed by Dr. Robert and Marion Ball at their commercial hatchery in Owego, NY. Both of these people had been in the Poultry Department before the war. Marion brought the defective chick to the laboratory at Rice Hall when I and Dr. Hutt were having lunch, a practice followed for 4 days each week over many years (1946-1965+). Neither of us had ever seen such a chick, with obvious defects in the lower leg region. At the end of the short visit, I was asked to get rid of the chick. Instead, I put an electric light over the box to provide some heat, and exposed the chick to water by dipping its beak and then putting the wet beak into some chick mash. The next morning the chick was still alive and eating, hence kept. It was a female that reached maturity and laid quite well. From 72 fertile eggs resulting from artificial insemination, all embryos were still alive on the 20th day of incubation. Of those 38 with normal embryos, 34 yielded healthy chicks. There were 28 chicks showing the defect in the metapodial region of the leg and wing, which was similar to that expressed by the mother. Of the 10 eggs that did not hatch 4 had normal and 6 had a 'chick' showing the defect. This was obviously an autosomal dominant trait, later shown to be lethal when homozygous [Journal of Heredity 58: 141-146, 1967].

A major project, dealing with genetic resistance to disease, came as a consequence of some interesting findings by Dr. Marty Sevoian (University of Massachusetts). He was able to transmit lymphomatosis by the use of tumor tissue, soon proven to involve a filterable agent, hence a virus. Since he had been at Cornell, he knew of our work on selection for resistance and susceptibility to the "leucosis complex" and so obtained K-strain and S-strain hatching eggs to provide chicks for his testing. He soon came back to Cornell and told us how important the S-strain chicks were for his research. They were very susceptible, while those from the K strain were quite resistant. He soon found that the non-inoculated S-strain chicks became infected when raised in the room used for his inoculated chicks. At that time, when S-strain chicks were raised at Cornell under conditions of natural exposure to pathogens, 44.5% of the S-strain chicks vs 1.7% of the K-strain chicks died from neoplastic mortality (43-500 days of age), of which most was neurolymphomatosis. Sevoian named his agent as JM, now known to be a Herpes virus that causes Marek's disease.

At that time it seemed better to use a 'standardized' level of exposure to the etiological agent than relying on natural, but uncontrolled, level of exposure when using genetic selection to improve resistance to this very important disease. Marty provided some 8± week old S-strain birds from his laboratory, some of which were showing evidence of neurolymphomatosis. Back at Cornell these birds soon developed tumors, especially of the gonad, which were used as material for inoculation of some very young S-strain chicks.

A source of the virus was maintained by frequent inoculation of groups of S-strain chicks but the material used for inoculation came from different sources of gonadal tumors. Thus, there was no assurance that the quantity of the infectious agent per unit of inoculum was the same for each experiment.

Initial tests confirmed Sevoian's findings related to high susceptibility of the S strain. It was also possible to test the chicks from several different strains of White Leghorns, used commercially for egg production, as well as from families within the Cornell K, C, and S strains. It was very clear that differences among families (sire & dam) existed and that there was a tremendous difference in susceptibility among the commercial strains of chickens. The effectiveness of the breeding program for resistance to disease at Cornell became obvious. Of the 33 different strains of male chicks tested in 1964, the most susceptible was the Cornell S strain (96%) while the most resistant was the Cornell K strain that was only 18%. The 28 strains of commercial male chicks were hatched at Cornell in connection with a New York State Random Sample Test conducted by the Poultry Department. The susceptibility of each strain, based on 50 male chicks, was released only to the specific source of the hatching eggs and the primary breeder involved. The 27 different commercial strains varied from 28 to 78%. One strain had two entries for which the susceptibilities were 30 and 34% [see Avian Diseases XII: 9-28, 1968].

These findings suggested that the use of inoculation with a standard amount of virus might be more effective than relying on 'natural' exposure in a breeding program concentrating on a method for controlling this very important disease.

A new project, funded by the USDA ARS unit at East Lansing, was set up to determine how effective the use of inoculation with JM-virus containing material would be to increase resistance to Marek's disease. Using the Cornell Randombred stock because it included genetic material from several of the important commercial stocks available in the early 1950's, selection based on progeny-test results soon led, after only two generations, to the marked differences between the N-line (resistant) and the P-line (susceptible). Dr. Philip Levine objected to the initial use of JM-R and JM-S to identify these lines, hence N (for negative) and P (for positive) were used. The N line had an incidence of lesions, by 8 weeks after inoculation, of 12.4% (ex 1248 chicks) while 90.7% of the 1299 P-line chicks were shown to have Marek's disease.

The paper published in Avian Diseases XII: 9-29, 1968, that covered all my studies done with the JM-virus containing material until then, was honored in 1969 by the Tom Newman Memorial International Award for Poultry Husbandry Research. Another report [1972, Oncogenesis and Herpesviruses, Int. Agency Res. Cancer, Lyon; Editors - O.M. Biggs, G. De-The, and L.N. Payne] involved the use of the N line as a parent, when crossed with other strains, to evaluate its effect on hybrid progeny. Both sexes had a significant effect on susceptibility to Marek's disease. Samples of chicks from the 3rd and 4th generations of the N and P lines were used.

Since data from most of the subsequent research were never published, it seems appropriate to cite it here. The records are included in the material listed under Code 21-31-2806, boxes 23 & 24, at the University Library Archives.

Further improvement had been made in the N and P lines, following continued testing and selective breeding, based on a test of progenies. For Generations 3, 4, and 5 the

susceptibility for the N line was 7.3% (ex 1287), 3.6% (ex 1057) and 5.0% (ex 860). For the P line the susceptibility rose to 94.4% (ex 1364), 96.8 % (ex 1113) and 97.7% (ex 899).

Because of the question of the level of virus in the tumor material used for inoculation, how could the preparation used in various tests be made uniform? In 1968, Lloyd Spencer, then a graduate student at Cornell, played a significant role in making it possible to 'standardize' the level of exposure for all subsequent tests. Tumor material, mostly gonadal, was obtained from 40± S-strain birds in a group previously inoculated with JM-tumor material. A ground-up mass of these tumors was mixed with sterile saline and then put into small tubes for subsequent freezing in liquid nitrogen. For each subsequent test the inoculum came from a standardized quantity of JM material from one of these vials. The dosage, related to the quantity of tumor material, was only 1/10± that used previously when not frozen.

Material from this supply was made available to others involved in the NE-60 Regional Project, which was then starting to concentrate on genetic resistance to diseases. It was also used for the testing of Generation 4 of the N- and P-line chicks.

To test if the 8-wk period was adequate, chicks from Generation 4 were handled a little differently than had been done earlier. Among the birds alive and free of any symptoms at the end of the test period (8 wks) those that had odd-numbers on the wing-band were sacrificed and necropsied to determine if development of lesions was in progress, thus susceptible to the disease. Chicks with even-numbered bands were kept until they died or showed symptoms. For the N line, the mortality at the very end of the 8-wk test period was 1.1% and 1.3% for the 'odd' and 'even' wing-band number groups. Necropsies of those of the odd-numbered group showed 13 with lesions of Marek's disease, hence susceptibility was at a level of 3.6%. For the even-numbered group mortality from Marek's disease reached 3.6% at the end of the 14th week. For P-line chicks, the levels were 83.8% and 86.9% for mortality, with 96.0% for the odd-numbered group following necropsies at the end of the test period. Those of the even-numbered group reached 97.5% mortality at the end of the 14th week.

During the 15-18 week period mortality more than doubled in the N line, with involvement of the visceral organs but none of the nerves. Thus, the remaining birds were discarded and necropsied at the end of the 18th week. Of the 458 N-line birds, 209 had gross lesions but only one of the birds had nerve lesions. Thus, the susceptibility of the N line reached 49.8%, but was not due to Marek's disease. Of the birds necropsied 100 had gross tumors of the bursa of Fabricius, 98+ had osteopetrosis, and 29 had nephromas.

For the P line, only 8 birds survived the 18-week period, of which only one did not have any lesions. Three had bursal involvement while only one had lesions related to Marek's disease (vagus and gonad).

When the frozen material was used another problem arose. Among birds free of symptoms but sacrificed at 8 weeks, some had small (1 to 2 mm.) lymphoid nodules on the heart, liver, or kidneys. Were they due to the Marek's virus? When shown slides of the nodules, in 1970±, Drs. Biggs and Payne agreed that they might be listed as 'positive'. The subsequent finding of bursal tumors in birds kept for a longer time indicated that the leukosis virus was present in the inoculum. Thus, these small foci represented early lesions of leukosis, rather than of Marek's disease. These small lesions had not been cited, nor obviously observed, for birds dying during the 8-week test period nor for those examined at the end of the period because they showed symptoms of the disease.

An extremely interesting finding was made by Briles, and others, who found that my selection for resistance or susceptibility to the JM virus had involved different alleles at the MHC locus, something I was not aware of at the time! The N line (resistant) had become almost homozygous for the B21 allele while the P line became almost homozygous for the B19 allele. This finding clearly explained why it had been possible to develop these lines so quickly.

Since a uniform source of inoculum was now available, a second attempt was made to check the value of genetic selection as a means to control Marek's disease. The N2 line was established and involved testing more breeders and, to prevent inbreeding, used about twice as many parents for the next generation than was done for the N line. Another sample of Cornell Randombred stock was obtained as hatching eggs from Purdue University in early 1968. The pedigree matings, to produce chicks for testing, involved 25 males and 125 females. The best 10 males and 50 best females, based on tests of progeny, were then used as parents to produce the next generation of potential breeders, which were not exposed to the JM virus. Using these numbers of potential (progeny-tested) and selected breeders was continued for 3 generations, except that only 40 females were used for the 3rd generation.

The results were essentially the same as had been obtained for the N line. Susceptibility declined from 44.2% (ex 2133) Gen.-O chicks to 12.6% (ex 2194), 8.8% (ex 2271) and 7.9% (ex 2130) for Gen.-3. Controls, from non-tested parents (Cornell Randombred stock), were used in fair-sized populations (232-355) for the three generations of the N2 line. The susceptibility for these samples varied from 39.7% to 42.9% vs 44.2% for the large population of tested chicks for the Gen.-O breeders. These data, when compared with the initial test in the N- & P-line project (51.1%) indicated that the level of virus in the inoculum was somewhat less, but for the 185 S-strain chicks used with the N2-Gen.3 test, susceptibility was 98.4%. [See attached appendix B.]

Another question arose as to whether the use of birds that could survive the challenge, without the need for pedigree breeding and selection, would be effective as a help to the industry. The initial test involved 280 non-pedigreed chicks, ex a population of Cornell Randombreds (originally obtained from Purdue) that had not been tested for survival to an inoculation with the virus-containing material, were given the same inoculum as used for the test of the chicks for Generation 3 of the N and P lines. Mortality in the 8-week test period was 50.3% and the survivors were retained as potential parents for the first

generation. By 7 months of age only 19± were on hand, hence the small population of potential breeders was discarded.

A second attempt to produce a N3 line involved, as Gen.-O parents, the same non-inoculated birds that had been used to produce the Gen.-O chicks for the N2 line. From that inoculated population of N2 chicks some males and females, that were free of any symptoms at the end of the 8th week, were kept as potential parents for Gen. I of the N3 line. Survivors, when mature, produced 668 chicks that were inoculated. By the end of the 8th week mortality from Marek's disease had reached only 6.0%. The population was reduced to 80 males and 256 females for subsequent use as parents of Gen.II. The other birds (256 males & 35 females) were discarded and necropsied. Based on those findings, it was estimated that 16.4% of the population would have been considered as susceptible, if all birds had been necropsied at the 8th week. The susceptibility of the Randombreds, as controls (118), was 48.8%.

The 50± males and 176± females that survived until 11± months of age were mass-mated and produced 496 male and 493 female chicks that were tested, as Gen. II, for resistance to the JM virus. Susceptibility, based on mortality from and or lesions of Marek's disease by the end of the 8th week was, by sex, 14.3% and 17.0%, thus an overall level of 15.7%. The Randombred controls had a susceptibility of 52.2% (50.0% ex 106 males & 52.2% ex 92 females), based on postmortems of all birds.

The third generation of the N3 line involved 355 females and 365 males. Because funding for the project was not to be continued, all of these birds were necropsied at the end of the 8-week test period and susceptibility was 7.6% for females and 6.0% for males. The 193 Randombred controls had a susceptibility of 46.6% for females vs 27.8% for the males. The incidence of the small lymphoid nodules (not Marek's) was 2.25 vs 5.7% for the two sources of chicks tested. The small population of S-strain chicks (35) had an incidence of Marek's of 97.1%, but no "small nodules" were recognized. See Appendix C.

Following retirement in April 1973, the Cornell K, C, & S strains were maintained by mass matings until my replacement on the Staff could be obtained. The initial person did little and was kept only 3 years. By the fall of 1977 Dr. Rodney Dietert [now at the Dept. Microbiol. & Immunology in the Vet. College] joined the department and still maintains the K strain, which has been used for considerable basic biological research in the USA and elsewhere. Although specific funding was not available, I was allowed to maintain and improve the Obese strain, its C-strain control, and also the HUA line (Articular gout) and its control (LUA line) of sex-linked dwarfs so that these special types of chickens would remain available for others to use for research. Permission was also given to retain a small population of autosomal dwarfs, that had been hatched in 1971. Fortunately, the N and P lines had been accepted and are still maintained by the USDA Avian Disease and Oncology Lab. (East Lansing, Michigan) and also by the Dept. of Avian Diseases at the Cornell Vet. College. The C and S strains were soon discarded but the S strain had been provided to the Dept. of Avian Diseases and is still maintained by them.

The HUA and LUA lines were subsequently turned over to Dr. Austic, who eventually had to discard them. Dr. Marsh had used the LUA line to establish a sex-linked dwarf stock for use in his basic research on dwarfism. He still maintains this stock. The HUA line could have served as an excellent lab-model for research dealing with gout, a serious human disease.

In 1979 it was possible to use the very few remaining autosomal dwarfs to re-establish a strain of chickens wanted for research purposes.

When the Dept. of Poultry Science was eliminated by the College of Agriculture & Life Sciences in 1991, Dean D. L. Call gave me permission to maintain the Obese strain, its control (C-strain B13's), and the autosomal dwarfs. This was continued until Jan. 1996 when office space was eliminated at Rice Hall. In 1991, without any consultation or knowledge, I was transferred, on paper, to the Dept. of Animal Science. Since the late 1960's I had maintained close contact with the Vet. College Dept. of Avian Diseases and participated in their weekly discussions of diseases of poultry and fish. In 1994 Dr. Bruce Calnek wanted me to be transferred to his department (Vet. College, Avian Diseases), which I fully accepted and was soon approved by Dean R. D. Phemister. In Jan. 1996, when office spaces, etc. at Rice Hall were assigned for other purposes, those involved with chickens had to leave. Since the new Veterinary Medical Center building was just completed and the Dept. of Avian Diseases had to be combined with the existing Dept. of Microbiology & Immunology, I was assigned to an office, also used by Prof. Emeritus Julius Fabricant, which is close to those of others involved in avian medicine.

Drs. Wick and Dietrich at the Medical School, Innsbruck, Austria, where the Obese strain had been used as a laboratory model for the study of autoimmunity for over 25 years, wanted to prepare a report covering the history of the Obese strain. Dr. Dietrich came to Cornell in the fall of 1996. Data dealing with the origin and breeding of this stock which started in 1956 were available in the records stored at the University Archives. These data were summarized in detail for each generation so that they would be available for Hermann Dietrich. He organized and prepared a manuscript dealing with the 40-year history of this research-model of autoimmune thyroiditis. (Poultry Science 78: 1359-1371, 1999).

The autosomal dwarf stock, used for research by Dr. Marsh, was improved by selective breeding for 13 generations. Because maintenance of this stock was not to be approved its elimination was obvious. Attempts to preserve special types of chickens have increased. Before the stock at Cornell was discarded, hatching eggs were sent to Dr. Delany at University of California, Davis and to David Caveny in Douglas, Arizona. Some details about the origin and breeding of this stock were also sent to those now concerned. David wanted an expansion of the material dealing with the origin and breeding data. He helped print the tables used in the manuscript. The 30-year history of the autosomal dwarf is available in Poultry Science 79: 1507-1516, 2000.

Because data for a number of the other interesting findings have not been published, it seems appropriate to provide them in the attached appendices. *(The appendices are available in the AAAP archives)*

Obituary

Dr. Randall K. Cole, Cornell professor emeritus, died January 26, 2006 at Hospicare in Ithaca at the age of 93. He was predeceased by his wife, Lelah; and is survived by their three children, Randall Jr. (Valerie) of Albuquerque, NM., Russell (Sally) of Ormond Beach, FL., and Mary Smith (Eric) of Freeville, NY; also six grandchildren and four great-grandchildren. He is also survived by a sister, Caroline Pineo and her husband, Frank of Ithaca, NY.

Dr. Cole was born in Putnam, Connecticut, and attended the University of Massachusetts at Amherst. He received his Ph.D. from Cornell University, under Dr. F.B. Hutt, and worked there for many years as a professor of poultry anatomy and genetics in the College of Agriculture, until retirement in 1973. He followed a lifelong interest in poultry, particularly in painstaking selection for useful traits. Dr. Cole's guidance of the genetic selection program at Shaver Poultry Breeding Farms in Ontario, Canada, produced some of the most productive laying hens ever marketed commercially. His strains of chickens with resistance or susceptibility to Marek's disease and with immune-mediated thyroiditis and obesity were invaluable tools for other researchers studying animal and human diseases around the world. He was a member of the Poultry Science Association and never fully accepted the closure of the Poultry Department at Cornell. He served as a major in the U.S. Army during World War II, later reaching the rank of Lieutenant Colonel in the reserves.

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:

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