L. N. (Jim) Payne

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Reflections on a Career in Veterinary Research

I formed the idea that I wanted to become a veterinary surgeon in 1949, when I was 15 years old, living in Oxford, and approaching the English School Certificate examination. I knew that being a vet involved working with sick animals, but I had no direct knowledge of what a vet's life involved. Rather, the career idea followed from my hobbies of fish keeping, collecting aquatic life, and amateur microscopy, and from an interest in medical discoveries. I particularly remember experiencing something of the excitement of the work of scientists and doctors such as Pasteur and Koch from reading 'Microbe Hunters' by Paul De Kruif. After gaining sufficient passes in 'School Cert', I embarked on 3 years of school sixth form studies in botany, chemistry, physics and zoology. I was encouraged by a family friend, Ronald Amoore, a chemist, who invited me to lectures at meetings of the Royal Institute of Chemistry. He also introduced me to a local farm where I worked in the school holidays in order to acquire some knowledge of farming and farm animals. I passed my Advanced level school exams and gained an Open Entrance Scholarship in the Medical Faculty of the University of Bristol. This gave me a place in the new School of Veterinary Science.

Training and early research at the Bristol Vet School

Over the next 4 years I enjoyed the diversity of subjects and disciplines that make up a veterinary course, including 'seeing practice' with veterinary practitioners in the vacations. I also met my future wife, Dinah, who was a veterinary classmate. Perhaps significantly, the course placed rather more emphasis on the chicken and its diseases than was traditionally the case, as poultry were seen as an agricultural commodity of increasing importance. But like most veterinary students, I thought in terms of getting a job in practice on graduating, and I had no particular interest in chickens. However, when I graduated as a Batchelor of Veterinary Science in 1956, I was offered a job in the veterinary school as a Research Assistant in Veterinary Clinical Pathology, which I was pleased to take. By then, I had decided that I was more interested in the science than the art of veterinary medicine.

At that time I met Dr Peter Biggs who had joined the Department of Veterinary Medicine as a Lecturer, and who was completing a PhD on the lymphoid tissue of the chicken in the Department of Veterinary Anatomy under Dr A.S. (Tony) King. Biggs was interested in the avian leukosis complex, which was recognized to be a major disease problem in poultry in Britain. I too became intrigued with the role of viruses in the etiology of cancer, and more specifically in avian leukosis. Peter and I worked together on the graft-versus-host splenomegaly reaction in chickens, which had been recently described by Morten Simonsen, and which we felt was an interesting system for studying lymphoid proliferation. We acquired at the Veterinary School chickens from several of the highly inbred Reaseheath lines, which we thought would be of value in attempts to transmit avian lymphoid leukosis and fowl paralysis (Marek's disease) experimentally. These conditions were regarded as distinct entities pathologically by various British workers although their etiological relationship was uncertain. In 1959 Peter Biggs left Bristol to develop and head a unit at Houghton Poultry Research Station to study the avian leukosis complex, and I continued work for a PhD on the graft-versus-host reaction with Dr Paul Jaffe. At that time, my wife Dinah was working for a PhD with Tony King on the structure and function of the avian lung, receiving her degree in 1960. I received a PhD in 1961 and moved to join Peter Biggs in the new Leukosis Experimental Unit at Houghton.

Work at the Leukosis Experimental Unit at Houghton

Early research projects in the Unit were the experimental transmission of Marek's disease (fowl paralysis) and studies on the cellular susceptibility of the inbred Reaseheath lines of chickens to infection by Rous sarcoma virus. Successful transmission of Marek's disease was achieved by use of blood from cases of the disease as the inoculum, and of a susceptible strain of Rhode Island Red chickens as recipients. From this work, the HPRS-B14 strain of Marek's disease agent was established, which induced fowl paralysis and ovarian lymphomas. The RIF (resistance-inducing factor) test for avian leukosis virus, discovered by Harry Rubin in the USA, was established at Houghton, and the HPRS-B14 agent was found not to have resistance-inducing (interfering) property. For comparative purposes, transmission experiments were also conducted with viruses isolated from field cases of lymphoid leukosis. These viruses were "RIF-positive"; and they induced lymphoid leukosis which differed pathologically from Marek's disease lymphomas. This work was presented at a National Cancer Institute Conference on Avian Virus Tumors held in 1964 at Duke University, North Carolina. It helped to establish that Marek's disease and lymphoid leukosis,

which had formerly been confused by their inclusion under the name 'lymphomatosis', were distinct diseases.

The work on genetic resistance revealed differences between the different Reaseheath lines in susceptibility and resistance patterns to several strains of Rous sarcoma virus. Test cross matings between lines over the succeeding years revealed the existence of different loci controlling responses to the B, C and E envelope subgroups of avian leukosis/sarcoma viruses. This work was done with a view to developing techniques for the selection of genetically resistant stock, which were adopted by commercial poultry breeding companies as a means of controlling leukosis.

A year in Michigan

In 1965 I was fortunate to be awarded an Eleanor Roosevelt International Cancer Fellowship to work for a year at the USDA Regional Poultry Research Laboratory, at East Lansing, Michigan, under the Director Dr. Ben Burmester. This involved an exchange with Dr Graham Purchase who came from the East Lansing lab to work at Houghton. My wife, our three small children, and I moved into a Michigan State University apartment and became accustomed to the snow and the American way of life. At the lab I continued to work on genetic resistance to leukosis with Dr Lyman Crittenden and Dr Bill Okazaki, and on the pathogenesis of lymphoid leukosis with Dr Max Cooper and Dr Peter Dent from the University of Minnesota Medical School. This latter work led to the recognition of early pre-neoplastic transformation of bursal lymphoid follicles in the pathogenesis of lymphoid leukosis. I also met Dr. Dick Witter who had joined the East Lansing lab. This year was a very good experience from the viewpoint of work and play, establishing enduring friendships and work relationships, and providing me with research ideas and procedures that I took back to Houghton.

Back to Houghton

I returned to the Leukosis Experimental Unit in 1966. Roger Chubb had joined the staff in 1963 and A.E. (Tony) Churchill in 1966, strengthening the immunological and virological expertise. 1966 saw the big breakthrough in Marek's disease research, when Churchill and Biggs isolated a plaque-forming herpesvirus from tumour and bone marrow cells from affected chickens. I was involved with Churchill and Chubb in showing that the Marek's disease herpesvirus could be attenuated by tissue culture passage and used as a live virus vaccine to prevent Marek's disease, and field trials were carried out by Biggs and the rest of the group. This work brought considerable recognition from the national, scientific and agricultural press for Biggs and his team.

At this time also, Roger Chubb and I were investigating the occurrence, nature and genetic inheritance of an avian leukosis virus-like antigen present in 'normal' chick embryos. This work provided early evidence for the occurrence of 'endogenous' leukosis viruses in poultry, which has subsequently become of considerable fundamental and practical significance.

The wider scene

The decade from the mid-1960s to mid-1970s was one of tremendous activity and excitement in the tumor virus field generally. Many important discoveries were being made particularly by medical research groups in the USA and elsewhere who used Rous sarcoma virus especially as a model of viral

carcinogenesis, leaders in the field including Harry Rubin, Peter Vogt, the Hanafusas, and Howard Temin. The finding of endogenous retroviruses stimulated the 'virogene' cancer hypothesis of Robert Huebner and George Todaro, who thought retroviruses were the origin of oncogenes. Based on such ideas, and on the evidence that viruses could cause cancers in various animals, the US Congress provided hundreds of millions of dollars to the Special Virus Cancer Program (1965-1978) to find viruses presumptively causing human leukemias and other cancers. In the end, the goal was not found, but a lot of useful work was done which added to understanding of viral oncogenesis. Much knowledge of retroviruses was gained, which was of relevance when HIV appeared, and basic work with Rous sarcoma virus led to the discovery of the cellular oncogenes, starting with *src*, which, rather than viruses, lie behind oncogenesis.

On the herpesvirus front, the Epstein-Barr virus had been discovered associated with Burkitt's lymphoma in humans. Here, the existence of a chicken lymphoma caused by a herpesvirus and preventable by vaccination was of obvious comparative interest. In 1972, Peter Biggs, Guy de The and I organized a symposium on Oncogenesis and Herpesviruses in Cambridge which was very successful and spawned later ones.

The existence of all this biomedical research benefited the poultry tumor work at Houghton, East Lansing, and other locations, very considerably. It resulted in much more rapid progress than would otherwise have been the case, it extended the body of expertise and knowledge, and added to the excitement of working with avian tumor viruses.

Work on Marek's disease and leukosis at Houghton and East Lansing followed similar lines of interest but with differences in emphasis and detail, and the two groups have remained in close contact ever since. At Houghton much was done during the 1970s on the pathogenesis and nature of vaccinal and genetic resistance in Marek's disease. Drs. Patrick Powell, Judith Frazier and Alan Lawn contributed especially to this work. Work on genetic resistance to Rous sarcoma virus was continued by Dr Prafulla Pani. In the late 1970s we started work on the epidemiology and eradication of avian leukosis virus, an area where the East Lansing group were making important advances.

Organizational changes

In 1974 I became Head of the Leukosis Experimental Unit when Peter Biggs became Director of Houghton Poultry Research Station. This involved me in administrative duties in addition to keeping my research going. In the early 1980s the administrative side became more demanding. This was a time when UK government research was put increasingly under the spotlight in terms of accountability, relevance and funding. Money and staff numbers were reduced, and the research institutes which were supported by the Agricultural and Food Research Council (AFRC), which included Houghton, were restructured. The Leukosis Experimental Unit became the Department of Experimental Pathology, and embraced research on several non-oncogenic poultry diseases. In 1986, Houghton joined up with three other animal disease research institutes to form the Institute for Animal Health, and in 1992 the Houghton Laboratory was closed and the poultry disease work and staff were moved to the Compton Laboratory of the Institute. Here research was reorganized on a disciplinary rather than a commodity basis. The AFRC itself was renamed, and with a wider biological remit, as the Biotechnology and Biological Sciences Research Council. I reviewed these changes in my Gordon Memorial Lecture entitled 'Problems and crusades: a history of poultry disease research in the

United Kingdom' (Payne, 1994). The 1980s were thus a very unsettled and unsettling period, with many changes and consequences. From 1986 to 1992 I was Acting Head of the Houghton Laboratory, which involved even more administrative work. Even so, I and my group managed to find a new avian leukosis virus - ALV-J!

Born again - work on ALV-J and a move to Compton

In 1988, we identified an avian leukosis virus belonging to a new envelope subgroup, designated J, occurring in meat-type breeders and causing myeloid leukosis (Payne, 1998). Against the background of arrangements for closing Houghton, we continued work on this virus, and in 1992 I moved with other staff to Compton and continued there. At first, as I have described in my article on the 'History of ALV-J' (Payne, 2000), this virus appeared to be of UK and European occurrence. But in the early 1990s it appeared in the USA and by 1997-98 it had spread throughout the world and become a major disease problem to the poultry meat industry. At the time of writing (October, 2000), following the introduction of ALV-J eradication programmes by breeding companies, myeloid leukosis has greatly decreased as a global problem.

The ALV-J story has been interesting, as this new virus, which apparently arose as a result of genetic recombination involving exogenous and endogenous avian retrovirus sequences, has provided a microcosm of avian retrovirology. Most of the principles and techniques of avian retrovirology that have been elucidated over the past 50 years have been found to apply, so that it was possible to make good progress in tackling the problem. The episode underlines the need to maintain knowledge and expertise in areas which might be considered to be no longer of practical importance. Retro viruses mutate!

Retirement

In 19971 retired from the Institute for Animal Health, but since then have continued with part-time consultative work, mostly related to ALV-J. This work has resulted in visits to meetings in quite a number of countries that were new to me, including China, Colombia, Jordan, Peru and South Africa. For many years I have also been involved in various capacities with scientific societies, particularly with the World Veterinary Poultry Association, and also with scientific publishing, as an Editor of the journal *Avian Pathology*. These activities have been useful in widening my knowledge of poultry diseases and the poultry industry, and interesting too. Some of my research has been done in collaboration with the industry. I have had no regrets about my area of work, which has provided much scientific stimulation. It has been fascinating too to follow the evolution of the poultry industry, with its pace-setting application of science and business methods to the production of cheap food.

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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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