mon to the diet of both birds and man or other environmental agents of possible etiologic significance might be identified. (The complete report from The People's Republic of China does, in fact, report on the analysis of food for nitrosamines and precursor compounds, and of food and drinking water for trace elements.) While that report deals with only one type of cancer, the multispecies approach might apply to some other types as well. Thus, chickens, particularly those of advanced age, might be excellent sentinels in agricultural environments for the occurrence of carcinogens that could affect other animals, man included.

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Guest Editorial

Serendipity in Science — Discovery of the B-1 Strain of Newcastle Disease Virus

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Unsought discoveries in research frequently result in significant findings that are more far-reaching than the planned projects from which they arise. These chance discoveries may go unrecognized at times, and unexpected observations should never be dismissed lightly without some attempt to explain their meaning. The discovery of the B-1 strain of Newcastle virus was just such a fortuitous observation, and because of the widespread use of the B-1 strain for vaccination against Newcastle disease and as a strain for research investigation, the history of its discovery should be recorded.

The event took place in 1947 at the Virginia Agricultural Experiment Station, Virginia Polytechnic Institute (VPI), Blacks-

burg, Virginia, where I was employed as an associate professor under the direction of Dr. E. P. Johnson. At that time, Newcastle disease was prevalent in poultry flocks throughout the United States and was of great economic importance to the poultry industry. In 1947 the USDA initiated one of its first regional research projects to aid an agricultural industry, and it was through funds appropriated for this project that the research work on Newcastle disease at VPI was possible. One of my assignments on arriving at VPI was to work on improving the hemagglutination-inhibition (HI) test which was being used as a laboratory aid in research on and diagnosis of Newcastle disease.

This assignment was my first entry into the field of research after graduation from veterinary college followed by a three-year tour of service in the army. I therefore had no accumulation of virus stocks with which to work. Since this was a new field of endeavor for the department at VPI, there were no stocks of Newcastle disease virus there. To acquire some strains to start the project, I contacted Dr. F. R. Beaudette, Poultry Pathologist at the New Jersey Agricultural Experiment Station, New Brunswick, N.J. In my letter requesting the Newcastle strains, I also asked for a strain of infectious bronchitis virus to use as a control of a nonhemagglutinating virus in the HI test.

This story would not be complete without some facts about Dr. Beaudette and my relations with him. Without question he was the foremost authority on poultry diseases and was recognized as such internationally. To his close friends he was known as "Red," a name that fitted the color of his hair, and with the hair was a fiery temperament to match. He was a forceful speaker and was not averse to punctuating his conversation with a few swear words for emphasis. In my educational career I have never experienced a better lecturer. Persons who met with his approval could not hope to find a more generous, kindhearted individual. Woe to those who did not meet with his approval or held opinions with which he did not agree. During my years of acquaintance with Dr. Beaudette, I experienced both ends of the spectrum of his personality.

My acquaintance with Dr. Beaudette began as a student at Rutgers University, where I worked in his laboratory as a part-time assistant. It was through his influence and advice that I decided to pursue avian pathology as a profession. Likewise it was through his kind help and influence that I and two classmates were

admitted to the University of Pennsylvania School of Veterinary Medicine, in the fall of 1939. Therefore, I am deeply indebted to him for directing me into a most interesting and satisfying career. In addition to working as a part-time laboratory assistant during the school year, I had the opportunity of spending the summers at his laboratory through the period that I attended veterinary school. Consequently, during that time I developed a close relationship with Dr. Beaudette and his family.

With such a long-term friendly relation, my request for viruses was promptly filled by his sending eight strains of Newcastle disease virus and one strain labeled infectious bronchitis. Upon receipt, each of the viruses was passed through embryonating eggs to provide stocks for the subsequent trials. To simplify labeling for identification, the Newcastle strains were designated N_1, N_2, N_3, etc., and the bronchitis strain, the first strain of this virus acquired for my collection, was designated B_1. (The subscript was later elevated for ease of typing, and in later publications the strain has been identified as B1, B 1, and B-1.)

To acquaint myself with the hemagglutination (HA) reaction of Newcastle virus and to test the HA ability of the stock preparations, doubling dilutions of each of the eight Newcastle strains were prepared and mixed with a preparation of washed chicken red blood cells (RBC's). It is recognized that infectious bronchitis virus does not cause HA of chicken RBC's, so the bronchitis virus B-1 was used in the same dilutions as the Newcastle viruses as a non-hemagglutinating virus control. When it came time to read the results of the test, the dilutions of the Newcastle viruses performed as expected. A uniform pattern of agglutinated RBC's was observed on the bottom of the tubes with the higher concentrations of virus, eventually disappearing to a solid button of RBC's in tubes with the lower concentrations. However, upon reading the results with the infectious bronchitis virus, I could see no significant difference between the hemagglutination pattern of the B-1 virus and those of the eight Newcastle strains.

At that stage of our knowledge of Newcastle disease, all strains were regarded as highly lethal for young chicks. It was postulated, therefore, that if this B-1 strain was a Newcastle virus, it should cause considerable signs in the central nervous system and mortality when inoculated into baby chicks. To test this point, a small group of fully susceptible day-old chicks were inoculated by placing

a drop of the infected embryo fluids of the B-1 virus into the nostril of each chick. The chicks, along with uninoculated controls, were observed for 19 days but developed no nervous signs or mortality. This 'failure' seemed rather strange. To try to clarify why nothing had happened, one of the Newcastle strains was then used to inoculate intranasally the same group that had received the B-1 virus and also the uninoculated control group. In a few days things began to happen, the results of which would have delighted a seasoned research scientist, and needless to say it was gratifying to a novice. The uninoculated controls began showing nervous signs and, as the expression goes, died like flies, while the group inoculated with B-1 appeared to remain healthy.

During this stage of the epizootiology of Newcastle disease in the United States, many day-old chicks being placed in Newcastle-infected areas did not have the maternal-antibody protection that is passed through the egg from the immune dam to the chick. It was immediately obvious that if a strain of virus was so mild that it could be given to day-old chicks without adverse effects and could immunize birds against subsequent exposure to a virulent virus, it had good potential as a vaccine strain. To make sure the results were repeatable, another trial was made with the B-1 strain, with the same spectacular results.

Shortly after making those observations and verifying that the bronchitis sent me contained a hemagglutinating virus, I had the opportunity of informing Dr. Beaudette of my results. Because of his international reputation, his ability as a dynamic speaker, and the fact that he was deeply involved in research on methods of controlling Newcastle disease, he was very much in demand during this period as a speaker at meetings of the poultry industry. It was at such a meeting in Roanoke, Virginia, that I had lunch with Dr. Beaudette and told him of my experiences with the presumably infectious bronchitis strain he had sent me. I shall never forget the big ear-to-ear grin he gave me when I told him of my results, and although he didn't say it, I could read his thoughts in that big grin, that here was a young greenhorn in the business who already had his virus strains all mixed up.

I was somewhat surprised that he did not show more interest in the vaccine potentialities of this strain, because at that time he was a consultant to the Vineland Poultry Laboratories, Vineland, N.J., and actively participated in supervision of their poultry vac-

cine production. The only explanation I can give for his lack of interest in the strain was that he was already deeply engrossed in research to develop his own vaccine strain and method of Newcastle disease control. It was his hypothesis, developed from extensive review of the literature (1,2,3), that Newcastle disease could be controlled by live-virus immunization of birds at 4 to 5 weeks of age. Immunized parent flocks would transmit maternal antibodies through the egg which would supposedly give the chicks protection against Newcastle infection during the first four weeks of life prior to vaccination. With this concept in mind, he systematically screened 105 virus isolants in 4-to-5-week-old birds to select a strain that could be used with safety as a vaccine (3). At the time of my discussion with him, he was well along on this project, and had selected the Roakin strain as the desirable candidate. Perhaps it was because he was nearing the completion of field trials with the Roakin vaccine that he ignored the potentialities of the B-1 strain, plus the fact that a relatively avirulent virus that could be used on day-old chicks did not fit his preconceived method for the control of Newcastle disease.

Dr. Beaudette was sufficiently concerned about my report of finding a hemagglutinating virus in the infectious bronchitis sample sent me that upon his return from the Roanoke meeting he reviewed the passage data on the bronchitis virus from the time that Newcastle disease was first recognized in New Jersey. Shortly thereafter he sent me a letter detailing each of those passages to verify that, according to his records, no errors of virus identity had occurred.

With the endorsement and encouragement of my colleague, Dr. E. P. Johnson, investigations were continued on the vaccine potentialities of the B-1 strain. Field trials carried out on day-old chicks demonstrated the safety and lack of pathogenicity of the virus. Vaccination trials were also conducted in adult laying flocks, again proving the mild nature of the strain. In laying flocks the B-1 strain caused a negligible or very slight drop in egg production, in contrast to the complete cessation of egg production that occurred in flocks infected with other Newcastle strains. The results of those preliminary studies with the virus were published in 1948 (6).

Publication of the results stimulated the interest of commercial poultry-vaccine companies and other investigators. Re-

quests for samples of the strain came from Salsbury Laboratories of Charles City, Iowa, and Lederle Laboratories (now American Cyanamid) of Pearl River, New York. Research investigations on the B-1 strain were carried out at each of those companies, with the results confirming my own studies as to its possible use for a vaccine (7). A license was issued in the spring of 1950 to each of these companies for commercial production of a Newcastle vaccine containing the B-1 strain of virus. Several other vaccine companies soon followed suit in marketing such a Newcastle vaccine. In fact, the demand for the B-1 vaccine prior to its licensing was so great that some unlicensed laboratories were established to produce it, not unlike the recent situation with Marek's vaccine.

Despite acceptance of the B-1 strain by the poultry industry and by other commercial vaccine laboratories, Dr. Beaudette and the Vineland Poultry Laboratories refused to recognize its legitimate role in a program for control of Newcastle disease. This caused him considerable embarrassment in engagements around the country advising poultrymen on the control of the disease. Invariably the question would come up: What about use of the B-1 strain? I never attended any of those meetings, but reports filtered back to me from colleagues that this question would spark vehement tirades about the uselessness of the B-1 strain in the control of Newcastle disease; that when that virus left his laboratory it was infectious bronchitis virus, etc. My colleague Dr. Johnson occasionally appeared on the same program with Dr. Beaudette and kept me advised of my standing on the Beaudette scale of invective. Dr. Johnson was quite good at passing out sly quips, and I only wish I could have been a hidden bystander at some of those meetings.

It was quite natural that because of Dr. Beaudette's association with Vineland Poultry Laboratories they also took up the campaign against the B-1 strain of virus in their promotional literature. Also, quite naturally, they produced and promoted the Roakin strain of virus as the preferred method of controlling Newcastle disease. The Roakin-strain vaccine performed close to Dr. Beaudette's anticipation as to vaccination reaction and immunity. However, the portion of his control program that was not fulfilled was the protection afforded the young chick by maternal antibodies until four weeks of age. Because of highly variable antibody levels in parent flocks, chicks were hatched with variable levels of protection, and many were in need of vaccination before

four weeks of age, the youngest age at which it was considered safe to use the Roakin strain. Consequently, because of its safety in young chicks, the mild B-1 strain vaccine became more and more in demand.

The reality of the situation finally forced Vineland Poultry Laboratories and, I presume, a reluctant Dr. Beaudette to admit to the need for a milder strain of virus in the Newcastle control program. After all the damnation the B-1 strain received from both parties, pride would not permit them to add that strain to their line of vaccines. However, a strain was eventually added to their line which closely approached the B-1 in many of its characteristics (currently known to most workers as the LaSota strain).

Even during the early period in which Dr. Beaudette was damning the B-1 strain at public gatherings, I maintained friendly personal relations with him; at least it appeared that way to me. I would occasionally see him at scientific meetings, at which time he was very cordial. I also stopped in New Brunswick in June, 1949, at the time I was moving from Blacksburg to a position at the University of Massachusetts, and again I had a friendly visit with him. Unknown to me at that time, that was to be my last cordial meeting with Dr. Beaudette. That fall we both attended a meeting in New York City, at which time he walked by me without recognizing my presence, and our relations stayed at that level for several years. What prompted the silent treatment I received, I shall never know. If I had published the information without first advising him of my observations, then I would have felt there was some justification for it. However, he was one of the first to know the full details and was given first opportunity to use the B-1 strain, but chose to ignore it. Shortly before his death, his attitude toward me did soften to the point where he would recognize me at meetings and exchange a few words in casual greeting.

To my knowledge, the exact origin of the B-1 strain is not known. The most revealing clue to the mystery appeared in a publication by Beaudette and Hudson in 1956 (4) entitled: "Evidence of Newcastle disease in the Eastern United States as early as 1938." That was a report on five virus isolations that had been made and maintained in his laboratory, but no prior attempt had been made to classify them completely. Later studies revealed that those strains had the capability of hemagglutinating red blood cells. No mention of the B-1 strain was made in the text until the last para-

graph of the Conclusions and in the Summary. The Summary, in full, stated: "Strains of virus isolated from flocks in New Jersey in February, 1938, in Illinois in December, 1938, in Delaware in October, 1942, and in Pennsylvania in 1943 produced changes in embryonating eggs at one time or another resembling those of the B-1 strain of NCD. All strains agglutinate chicken red blood cells and at present are relatively apathogenic for young chickens, which develop hemagglutinating inhibiting antibodies."

When the USDA sponsored that research project on Newcastle disease at VPI, little did they realize the far-reaching impact that the results would have throughout the world. I would hesitate to estimate the billions of doses of B-1 strain that have been used in the control of Newcastle disease in the United States since it was licensed, in 1950. In addition, I believe it would be correct to say that it has been used in every country where poultry are vaccinated for the control of Newcastle disease. Since its discovery, other mild lentogenic strains, such as the LaSota and F strains, have been recognized and added to the vaccine armamentarium of the poultryman, but the B-1 strain is still considered the type strain for lentogenic Newcastle viruses. Besides its use as a vaccine, it has been studied widely in research laboratories around the world in investigations on paramyxoviruses.

In presenting these events for the historical record on the discovery of the B-1 strain, I in no way wish to detract from the great tribute paid to Dr. Beaudette at his death, on January 17, 1957, that is so fully documented by Dr. W. R. Hinshaw in the first issue of *Avian Diseases* (5). He was a brilliant scientist, as is verified by his list of accomplishments. My only claim to fame comes through being the recipient of serendipity in science. I regret that among the honors attributed to Dr. Beaudette there was not included the statement that his laboratory was the source of the B-1 strain of Newcastle virus.

It is said that experience is a great teacher. I learned a number of lessons from this experience which I would like to pass along to budding scientists:

1) Keep your eyes and ears open and the wheels of your brain constantly turning. There are untold discoveries in science waiting for your recognition.

2) Never discard an unexpected or unexplained result without questioning the reason.

3) Don't let your mentors in research quell your initiative.

They hold no special keys to the gates of the frontiers of science. Unlock your own doors.

4) Scientists are human beings subject to the frailties of the race. Don't expect them to act otherwise.

5) If you have a fellow scientist whose friendship you cherish, don't work in the same area of research if you wish that friendship to endure.

6) Don't be afraid to make errors. If you make a mistake, admit it and carry on. Eating crow is not fatal and can be nourishing to the soul.

7) There is nothing sacred about a hypothesis. It should be formulated only as a guide. Don't hesitate to desert it if the facts prove it wrong.

Serendipity in science does occur and can be productive. It should not be expected to supplant the well-planned research program, but it can be a fringe benefit to any research project. It is regrettable that the federal government chose to infuse millions of dollars into a program to conquer cancer at the expense of numerous training grants and small research projects in a variety of fields. The appropriation of money to research does not ensure answers. If I had to wager on where the answer for the control of cancer will be found I would place my money on some chance observation by a young scientist laboring on some problem project whose title contains no reference to cancer or its control.

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