From the
JAMES A. BAKER INSTITUTE
FOR ANIMAL HEALTH
Cornell University, Ithaca, New York
December, 1976
THE Institute Report is prepared annually for all those individuals whose financial help has made possible our continued operation. Each year we take this opportunity to acknowledge the support of dog owners, kennel clubs, foundations, and colleagues in practice and industry who recognize that further progress in the understanding of animal diseases and in the development of better means of prevention and treatment arises only through vigorous research. The generation of useful knowledge through research and its transfer to others is our prime function.

In last year's Report we paused and indulged in some of the accomplishments of the first quarter-century of investigation that led to the Institute's growth and to its present reputation. This year, as in the past, we sketch the principal activities of the laboratories to illustrate how your contributions are converted into information leading to improvements in the health of animals.

We are fortunate to have attracted to the Institute Dr. Douglas D. McGregor, who assumed his duties as Director in September of this year. Dr. McGregor enjoys an international reputation as a scientist with unusual insight into the mechanisms by which animals defend themselves against infectious diseases. Like his predecessor who came to Cornell from the Rockefeller Institute, a research institute famed for its work in infectious diseases, Dr. McGregor comes with a similar background from the Trudeau Institute, another center of world-renowned excellence located in Saranac Lake, New York. Both institutes share a common philosophy in holding that problems of animal disease can best be solved by studying the animal rather than in test tubes alone. Experience has proved the wisdom of this approach. Dr. McGregor's scientific interests have ranged from his early contributions to the study of renal disease in dogs, to tuberculosis in animals and man, and on to the method by which the immune response deals with *Listeria monocytogenes*, a bacterial organism causing fatal encephalitis in a variety of animals, including man. His recent research interests have been in the field of general immunology to which he has contributed richly. The main thrust of his current scientific effort has been to analyze the mechanisms of acquired resistance to infectious disease agents, with the practical goal of developing more effective methods to prevent diseases. This requires a clear understanding of how the immune system operates and of the many devices used by bacteria, viruses, and other parasites to escape their destruction within the host animal. Many of today's practical problems will remain unsolved until further knowledge is obtained, by the use of modern research tools.
Although trained initially as a physician, Dr. McGregor has sustained a long-time interest in problems of veterinary medicine. He is an avid fancier of dogs, a trait readily apparent to visitors when they first are greeted at his home by a pair of eager Labradors. Moreover, he has carried out collaborative work on viruses and canine brucellosis during the past several years with members of the Baker Institute staff; so he arrives as no stranger.

Dr. McGregor comes to the Institute at a time when we are confronted with the economic problems that face all institutions who must depend in large part on private financial support. In addition, many other worthy causes have been advanced during recent years that seek private assistance from the limited resources available. Nevertheless, through the conservation over the years of a portion of our capital resources and your support we have managed to surmount many of the difficulties that have arisen during the past year. Research scientists have been attracted to the Institute who have provided a portion of their own support, and a new generation of veterinary graduate students have commenced their work. The laboratories are active, and the Institute is in capable hands, positioned to start the second phase of its life and respond to the responsibilities that come with maturity. We are grateful to all of our supporters whose interest and financial help continues to make possible the work in the Cornell Research Laboratory for Diseases of Dogs and the other divisions of the Institute.

We are saddened to report the death of Dr. Hadley C. Stephenson, Professor of Veterinary Therapeutics and Small Animal Diseases, Emeritus, at Cornell who had been an integral member of the staff of the Cornell Research Laboratory for Diseases of Dogs since 1953, when he retired from fulltime teaching and research at the Veterinary College. Dr. Stephenson was instrumental in developing and maintaining a close relationship between the Laboratory and its supporters and had dedicated his career to promote better health for dogs through his unique ability to communicate research information developed within the laboratories to dog owners and veterinarians in the field. His many services to the Institute and to all who sought his advice were greatly valued, and they will be missed.

L. E. Carmichael
The Hadley C. Stephenson Laboratory for Study of Canine Diseases. Max J. G. Appel, Dr.med.vet., Ph.D.; David A. Bemis, Ph.D.; Helen A. Greisen, Ph.D.; Patricia A. Barker, B.S.; and Mary B. Metzgar.

The laboratory's primary function is to study infectious diseases of dogs, especially distemper and respiratory diseases, and to develop methods for improved diagnosis, prevention and control. During the past year considerable effort was devoted to the study of distemper virus strains of varying pathogenicity. Marked differences in clinical signs, pathological changes, degrees of immunosuppression and in tissue levels of virus have been observed, but not adequately defined. Some strains cause generalized illness, others cause only encephalitis. All strains studied have been found immunologically the same; therefore, current vaccines protect against all distemper virus types despite differences in their pathogenicity. Other studies included an examination of attenuated strains of distemper virus presently used in vaccines. In some instances, curious field outbreaks of encephalitis have occurred following vaccination which have not been explained. The question whether certain distemper vaccine virus strains can cause disease is under intensive study, for it appears that several factors are involved. Where problems have occurred in the field, and in the laboratory, distemper vaccine virus always was given with infectious canine hepatitis virus (canine adenovirus-1, CAV-1). Current data suggests that field problems would be reduced by substituting CAV-1 vaccine strains with canine adenovirus-2 (CAV-2), which we have shown affords complete protection against both viruses. CAV-2 also has the beneficial attribute of not causing "blue eyes," which may occur with CAV-1 vaccine strains.

Respiratory disease studies continue, with principal attention given to a long neglected bacterium Bordetella bronchiseptica. Methods were developed to establish a uniform infection by aerosol to evaluate the bacteriological and clinical-pathological responses of dogs, and to examine differences in strain pathogenicity. An epidemiological study of respiratory disease in a large breeding kennel clearly established B. bronchiseptica as the problem, for viruses such as parainfluenza (SV-5), CAV-2, distemper and others were excluded. Methods for antibiotic treatment by aerosol exposure were evaluated and published. An outbreak of severe respiratory disease in another kennel revealed SV-5 parainfluenza plus Mycoplasma sp. as the causal agents. The virus or Mycoplasma, given alone, resulted in trivial disease. Such studies further point out the multiple causes of canine respiratory disease, and the necessity of studying mixed or sequential infections.
Research activities:

1. Differences in the pathogenicity of virulent canine distemper strains. M. Appel, H. Greisen, and R. Schultz

2. Differences in tissue culture infectivity with different distemper strains. L. Sihvonen, W. Shek, M. Appel

3. Studies on the immune response of dogs to CAV-2, with respect to safety and immunizing efficacy against CAV-1. M. Appel and L. E. Carmichael

4. Pathogenicity of certain attenuated distemper vaccines for zoo animals (black-footed ferrets and lesser pandas): Fatal distemper following vaccination. M. Appel

5. Isolation of a coronavirus from dogs during outbreaks of acute gastroenteritis. M. Appel and H. Greisen


7. Canine distemper virus: Localization of virus in the central nervous system by electron microscopy. H. Greisen and M. Appel

8. Survey of *Bordetella bronchiseptica* strains by electron microscopy: Relationship between strains with pili and their association with ciliated tracheal cells. D. Bemis and H. Greisen


10. An outbreak of severe tracheobronchitis in a closed colony of dogs caused by dual infection with parainfluenza virus (SV-5) and a *Mycoplasma* sp. D. A. Bemis and M. Appel

11. Attempts to immunize dogs against *B. bronchiseptica* with living and inactivated organisms. D. A. Bemis and M. Appel

12. Encephalitis produced in SPF dogs with subacute sclerosing panencephalitis virus. M. Appel

13. Failure of attenuated distemper virus given intravenously after exposure to virulent virus to alter the course of distemper: Lack of "cell blocking effect" and the failure to provide any experimental basis for this apparently common clinical practice. M. Appel
The goal of this research is to understand why and how abnormal changes occur in the hip joint tissues of dogs that ultimately are manifested as hip dysplasia. A diagnostic test is needed which can be applied to young pups to predict accurately whether they will have either normal or dysplastic hip joints at maturity. Research studies have continued with these goals in mind.

Current work is focused on the identification of specific metabolic changes responsible for the initiation of the degenerative process that become manifested as hip dysplasia. Biochemical analyses and cell cultures from explants of hip joint tissues are evaluated and compared with environmental, nutritional, clinical, and radiologic procedures. The overall research plan perhaps is best described in terms of two general subdivisions; namely, (a) understanding the theoretical, mechanistic reasons for the initiating events of the disease at the cellular level and (b) developing diagnostic procedures that may be useful in clearly identifying the presence of the disease early and, additionally, devise therapeutic procedures that may prevent or improve the condition.
The second, practical aspect of this research focused on a useful, accurate diagnostic procedure for predicting degenerative hip joint disease early in the life of individual pups at risk. This work involves definition of a test which assays the abnormal levels of protein metabolites in the hip tissues of pups genetically at risk. We have found repeatedly that biochemical abnormalities were present when the joints still were radiologically normal. This led us to adapt a novel procedure to identify these abnormal stages in dogs. Results from a non-invasive procedure, called radionuclide joint imaging, using radioactive pertechnetate or phosphate to identify degenerative changes in joints are encouraging. In results to date this method has been more sensitive than the radiographic techniques in detecting joint abnormalities. Standardization of this procedure is in progress now.

Additionally, studies are in progress to test a therapeutic compound which might ameliorate or prevent the degenerative process and improve the functional capacity of the hip joint. Another approach to control the disease may require dietary restriction of pups at critical times in their development. In a previous study from our laboratory, results clearly indicated that pups at risk for hip dysplasia raised at a slower than normal rate of growth — restricted dietary intake — manifested a significantly reduced incidence of hip dysplasia.

The significance of this research program will be to contribute to the identification of specific gene products that are involved in the pathogenesis of hip dysplasia in dogs. It will permit the identification, early in life, of those individuals who carry a substantial risk factor for development of this widespread and important disease of dogs. It will define the nature of the critical events in its development and eventually should form the basis for controlling the disease in a population of dogs, and for ameliorating the condition or reversing its progression in an individual dog. Correlation at all stages with pelvic radiographic evaluation also will enhance radiologic diagnosis as well as provide a method of accurate, early diagnosis.

Research activities:

1. Development of degenerative hip joint disease (hip dysplasia) in dogs. G. Lust and R. Meier

2. Collagen metabolism in ligaments of normal and degenerative canine hip joint tissues and in cell cultures. D. R. Miller and G. Lust

3. Effect of environmental conditions on the expression and development of hip dysplasia in dogs. G. Lust, R. Meier and B. E. Sheffy
4. Therapeutic measures for amelioration or prevention of the degenerative processes that result in hip dysplasia. G. Lust, R. Dueland and D. Swann (Harvard University Medical School)

5. A rapid, enzymatic assay for measurement of inorganic pyrophosphate in biological samples. G. Lust and J. E. Seegmiller (University of California, San Diego, Medical School)

6. An ultrastructural investigation of canine articular cartilage: Comparison of normal and degenerative samples from hip joints. H. Greisen and G. Lust

_The Oswald R. Jones Laboratory of Immunology._ R. D. Schultz, B.S., M.S., Ph.D.; E. F. Bloch, B.S., M.S.; Janet Smith, B.S., M.S.; L. Adams, B.S.; Lynn E. Perko, A.A.S.

This laboratory was created in 1973 to augment the scientific capabilities of the Institute by introducing contemporary methods in applied and basic immunology. In concert with the desire to examine presently unresolved problems with new approaches, studies have focused on the role of cellular and humoral immunity in canine distemper virus infection and on characterizing the profound immunosuppression associated with this disease that allows certain secondary infections caused by agents not normally pathogenic for the dog that cause severe manifestations such as pneumonia, a condition not observed in germ-free dogs. The mechanisms of suppression are currently being investigated.

An immunodiagnostic laboratory to evaluate the immunologic disorders in various domestic animals, including the dog, was established and more than 2,000 clinical samples were studied. Numerous tests for cell-mediated and humoral immune functions were developed for both clinical diagnostic and experimental purposes. Disorders of special interest were immunodeficiencies, principally those secondary to other factors, and certain autoallergic conditions like rheumatoid arthritis.

**Research activities:**


2. Characterization of the immunosuppression associated with canine distemper virus. R. D. Schultz, M. Appel and L. Adams

3. The mode by which measles virus protects dogs from distemper: A study of the mechanisms for failures to satisfactorily immunize very young pups from distemper-immune bitches. R. D. Schultz

5. Immunologic and therapeutic aspects of canine generalized demodetic mange. R. D. Schultz and D. Scott (Small Animal Clinic, NYS College of Vet. Med.)

6. Demonstration of the immunocompetence (cellular and humoral) of pups at birth, and earlier. R. D. Schultz and L. Adams


8. The role of Group-G streptococci in neonatal puppy death and the establishment of diagnostic tests to identify streptococcal infections. E. Bloch and R. D. Schultz

9. The effect of nutritional deficiencies on cellular and humoral immunity in the dog. R. D. Schultz and B. E. Sheffy
10. Effects of attenuated viral vaccines on the fetus: Severe fetal disease para-influenza caused by attenuated hepatitis and the Rockborn strain (attenuated) distemper, and SV-5 virus occurring in pups inoculated prior to birth. R. D. Schultz

11. The role of milk lymphocytes in protective immunity. Janet Smith


13. Ultrastructural studies of in vivo stimulation with mitogens and antigens in the dog. R. D. Schultz and H. Greisen


The Daynemouth Laboratory for Canine Nutrition. Ben E. Sheffy, Ph.D.; C. A. Banta, M.S., Ph.D.; Alma Williams, M.S.; Sue Fei Fan, M.S.

"We are what we eat" was a frequent quote of Nancy Day, wife of Colonel Day and co-founder of the Daynemouth Division. Her consuming interest was in the definition of a scientific basis for non specific resistance to infection with special reference to nutrition. This represented one of the early research objectives of the Daynemouth Division.

With the development of new techniques and approaches in immunology and their application, a better understanding and evaluation of nutrition on the immune responses both cellular and humoral, is now possible. Studies are currently under way to redefine the influence of certain specific nutrients on the host response to infection. In addition to specific cellular and humoral events, correlations are being made with clinical, biochemical and hisopathological changes in the dog both during the development of a specific nutrient deficiency and during the period following antigenic exposure, and after the host has been repleted nutritionally. In concert with the above studies, a continuing study to reevaluate the principal nutrient requirements of dogs has been initiated. Several biological parameters are being considered in the determination of optimum requirements.

Research activities:

1. Gastrointestinal function in the dog: Mechanical and physiological parameters of the canine gastrointestinal tract. C. A. Banta, E. T. Clemens and B. E. Sheffy
2. Protein and amino acid requirements of dogs. C. A. Banta, B. E. Sheffy and A. J. Williams

3. Carbohydrate requirements of dogs: Evaluation of growth and reproductive performance of dogs fed diets with similar protein calorie to total calorie rations from protein and fat sources only and from combinations of protein, fat, and two different levels of carbohydrate. B. E. Sheffy, M. M. Krinsky, A. J. Williams and C. A. Banta

4. Trace mineral and vitamin requirements of dogs: Manganese, cobalt, B12, selenium and vitamin E. B. E. Sheffy and A. J. Williams


6. Chronic Vitamin D toxicity in dogs. B. E. Sheffy, A. J. Williams, L. T. Pulley and J. Bentinck-Smith

7. Nutritional adequacy of fortified all-meat and commercial dry dog food. B. E. Sheffy, A. J. Williams, M. M. Krinsky, and C. A. Banta


Principal activities in the Brucellosis Laboratory have been directed toward a critical evaluation of existing canine brucellosis diagnostic methods and the development of more accurate means for serodiagnosis. Other areas of investigation dealt with further definition of all possible ways by which Brucella canis is spread, and the exploration of various treatment methods that may prove more successful, especially as regards infected males. Only with additional knowledge will we be able to offer dog owners rational alternatives to current measures of control.

It has been 10 years since B. canis was first isolated and described in our Laboratory. During this period a great deal has been learned, but the successful control of a very difficult disease such as brucellosis requires sustained and vigorous effort. It is imperative that we address the practical problems of diagnosis, prevention and treatment; however, it also is important that the study of fundamental immune mechanisms be carried on, for trial-and-error tests of immunization methods using traditional approaches have not proved adequate. Many basic questions regarding our understanding of the Brucella-host interaction remain unanswered, and they require clarification before practical benefits can be realized. For example, we don’t yet know which properties of the
bacterium allow it to multiply and persist within the host animal, nor the means by which the organisms damage parasitized cells. Mononuclear phagocytic cells probably are critical in determining the outcome of *B. canis* infection. Recovery from infection and the development protective immunity will depend on our understanding of how the immune system cooperates to increase the ability of these phagocytic cells to destroy the bacteria within the infected dog. These are the problems currently under study in the Brucellosis Laboratory. The current status of canine brucellosis was reviewed in a recent Laboratory Report (Series 2, Number 7, September 1976) from the Cornell Research Laboratory for Diseases of Dogs, and is available to all who wish to know more about this disease.

Studies on canine herpesvirus (CHV) infection also have continued. The canine herpesvirus has been reported by others to cause respiratory and genital disease; however, long-term studies of kennels with endemic CHV infection have not confirmed these observations. The virus causes occasional death of young pups, generally those 1 week to 1 month of age. They generally occur in pups from susceptible females that had been introduced into a kennel where CHV persists. Losses have not been observed in litters from females that had acquired the infection at a time prior to breeding. Pups infected when older
than a few weeks of life usually appear clinically normal; however, immuno-suppression by corticosteroid drugs or antithymocyte serum favors generalization of CHV within animals at an age (1 month old) where the infection normally remains localized. Current studies focus on the use of immunosuppressants to probe sites of viral persistence in latently infected dogs. Variant strains with reduced virulence for pups, and suitable for a vaccine, also have been developed in the laboratory. Should the need for a vaccine be recognized, candidate strains now are available.

Research activities:

1. Evaluation of several antibiotic treatments for canine brucellosis using Rifampin, Declomycin, Tribriessen, Disulmethoxine, Minocycline hydrochloride, and Dihydrostreptomycin in various combinations, dosage rates, and times of treatment. R. Flores-Castro, P. Barker, and L. E. Carmichael

2. Comparative study and evaluation of the rapid slide agglutination test (Pitman-Moore), tube agglutination test, 2-mercaptoethanol tube agglutination test, and immunodiffusion test for canine brucellosis. R. Flores-Castro and L. E. Carmichael

3. A study of B. canis isolates from Brazil. L. E. Carmichael and P. Barker

4. Antigenic comparison of non-smooth, gram negative bacteria with B. canis. R. Flores-Castro

5. Effect of immunopotentiating agents on the response of dogs to B. canis. R. Flores-Castro


8. Canine herpesvirus: Epidemiological studies of CHV in an endemically infected kennel and failure to associate the virus with respiratory illness. L. E. Carmichael, D. A. Bemis and P. Barker

9. Host-response to a microplaque variant of canine herpesvirus. L. E. Carmichael

FINANCIAL SITUATION

To assure donors of funds for research for dogs that their funds will support such research, currently or in the future, the Cornell University Board of Trustees made a provision for disposal of excess income as follows: "The Institute's income is in excess of its operating expense, and the balance of the funds is added to the Institute's Endowment."

Financial situation July 1, 1975–June 30, 1976

Funds Available

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Expenditures

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Reserves used to balance budget: $29,324.00
THE INSTITUTE REPORT

JAMES A. BAKER INSTITUTE FOR ANIMAL HEALTH STAFF

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Publications for the first ten years were listed in the Institute Report for 1960. Those for each following year were listed in its annual report. Since 1960, articles have been numbered consecutively. Some of the following numbers were listed in previous years' reports as "accepted" or "in press." They are repeated this year, with their original numbers, to record the volume and page references. Articles numbered 339–365 were completed during the past year.


(335) SCHULTZ, R. D., with BARRETT, R. E., and POST, J. E.: Chronic relapsing stomatitis in a cat associated with feline leukemia virus infection. Feline Practice, 1975, 3, 34-38.


(345) CARMICHAEL, L. E., with HOUSE, C., and BADAKSL, F. F.: Review of current aspects of canine brucellosis testing. AAVLD Proceedings, 18, 1975, 121-133.


ACKNOWLEDGMENTS

The Cornell Research Laboratory for Diseases of Dogs gratefully acknowledges gifts received from our contributors since September 1, 1975 in support of our research program.

In Appreciation: For their exceptional interest in the Institute, we should like to express appreciation to the following: Mr. and Mrs. Gaylord Donnelley, Mrs. Priscilla M. Endicott, Mr. and Mrs. Alexander Feldman, Miss Gladys Freeman, Dr. Kenneth I. Gumaer, Mr. and Mrs. E. Roland Harriman, Mr. and Mrs. John Lafore, Mr. James A. Moffett, Mr. C. Edward Murray, Jr., Mr. W. L. Newhall, Mr. John M. Olin, Dr. Niel Pieper, and Mr. Robert W. Woodruff.

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(In Honor of Dr. Victor Sancho)
Marion K. Wilcox, a well-known breeder of Gordon Setters and a dog lover in general, died on September 21, 1975. Mrs. Wilcox left a most generous legacy to the Gordon Setter breed in the form of the many lovely specimens she produced under the Afternod prefix. She not only produced excellent dogs but was also a tireless worker for the Gordon Setter Club of America as well as the Farmington Valley Kennel Club, an all-breed club.

Mrs. Wilcox was a firm believer in research directed toward the promotion of better health care for dogs and consequently contributed substantially over the years to the Cornell Research Laboratory for Diseases of Dogs. It is with sadness that we note the passing of one so interested in the welfare of dogs.
Dr. Hadley C. Stephenson was a life-long friend of dogs, a veterinarian's veterinarian, and a vanishing breed of Cornellian. If there was a better life than that of Doctor of Small Animal Medicine at Cornell University, Dr. Hadley C. Stephenson or Steve, as everyone knew him, did not recognize or acknowledge it.

He was the eternal teacher both in and out of the classroom who firmly believed that progress was possible only through research and its application in the field. "Everything I was ever taught was somebody's research" was more than just another expression to Steve, it was his creed. He used it as a spear to prod and to inspire his colleagues and all dog lovers as well.

"If we are to know the answers we must ask the dog." This was his advice to us at the Cornell Research Laboratory for Diseases of Dogs. What greater honor can we pay to Doctor Stephenson than for all of us to rededicate ourselves to research and teaching directed to the improvement of the health of animals.
In establishing the Institute, of which the Cornell Research Laboratory for Diseases of Dogs is a part, the Board of Trustees authorized the Treasurer’s Office of Cornell University to act as custodian of all funds given in support of the Institute. Donors, therefore, are assured of maximum benefits from their gifts by means of this supervision by Cornell University officials. Cornell welcomes any gifts or bequests that will help the work of the Institute. The Legal Department of Cornell University suggests the following provision in making a bequest for dog research:

“I hereby give, devise and bequeath (description of property) to Cornell University, an educational corporation located at Ithaca, New York, for the uses and purposes of the Cornell Research Laboratory for Diseases of Dogs.”

All checks should be made payable to Cornell University and should be mailed to:

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