



4-1-1986

Bovine Leukemia Research

John E. Martin
University of Pennsylvania

Rosettes & Ribbons

Students, staff, and faculty donated 97 pints of blood to the American Red Cross during the fall blood donation drive. This was an increase of 23 pints over the spring drive.

Dr. Lawrence T. Glickman (V'72), associate professor of epidemiology and Chief, Section of Epidemiology, has been awarded a \$426,149 grant for three years from the National Institute of Allergy and Infectious Disease for a study entitled "Canine Model of Selective IgA Deficiency." The grant, awarded jointly to Dr. Glickman and **Dr. Peter J. Felsburg (V'69)**, University of Illinois College of Veterinary Medicine, will permit the two researchers to investigate many of the important clinical manifestations of IgA deficiency in the dog, to begin to characterize the role of IgA in the gut, and to study the mechanisms of inheritance.

Dr. Amy R. Marder (V'79), the first resident in animal behavior at the School, has been appointed to the staff of Tufts University School of Veterinary Medicine.

Dr. Robert C. Hammond (V'48) has stepped down as Associate Dean-Maryland Campus of the Virginia-Maryland Regional College of Veterinary Medicine. Dr. Hammond and his wife have built a retirement home in Earlysville, VA, and he plans to continue his rehabilitative work with the eastern bluebird.

Dr. Mattie J. Hendrick (V'78) has been appointed assistant professor of pathology in

the Department of Pathobiology. **Dr. Michael Kotlikoff (V'81)** has been appointed assistant professor of pharmacology in animal biology. Recently Dr. Kotlikoff received a grant from the University of Pennsylvania Research Foundation for his proposal "Airway Smooth Muscle Cell Culture." **Dr. Dean W. Richardson** has been appointed assistant professor of surgery in Clinical Studies (New Bolton Center). **Dr. Thomas J. Van Winkle (V'75)** has been appointed assistant professor of pathology in the Department of Pathobiology.

Dr. Michael S. Miller (V'79) was awarded diplomate status in the American Board of Veterinary Practitioners. He is a staff consultant in electrocardiography and vice president of Clinical Affairs for the Cardiopet division of ANIMED, Inc., Roslyn, NY. Recently he has authored or co-authored chapters on the treatment of cardiac arrhythmias or conduction disturbance in the *Manual of Small Animal Cardiology*; Current Veterinary Therapy Nine, and a chapter on avian electrocardiography in *Avian Medicine and Surgery, a Clinical Approach*.

Dr. E. Neil Moore, professor of physiology, has been invited to serve on a committee to review computer grant proposals from different schools within the University.

Dean Robert R. Marshak has been named vice chairman of the newly formed Pennsylvania Friends of Agriculture. He also was

appointed to serve on the faculty of the School of Arts and Sciences for the academic year 1985-86.

Dr. William A. Moyer, associate professor of sports medicine, was one of the principal speakers at an equine laminitis symposium, held in January in Lexington, KY.

The January 1986 *American Kennel Gazette* contained an article about a specialty veterinary practice. Featured was a four-specialist practice in Gaithersburg, MD, co-founded by **Dr. H. Steven Steinberg (V'73)**, whose specialty is neurology. **Dr. David K. Saylor (V'76)** is also a member of the practice, as specialist in soft tissue surgery. Another member, **Dr. Ann Chiapella**, the internal medicine specialist, also has ties to Penn; she was a resident here.

Dr. Charles J. Driben (V'65), Moorestown, NJ, was honored by the Congregation Beth El, Cherry Hill, for his service to the synagogue, to the Jewish community, and to the people of Israel. He was presented the Lion of Judah Award.

Dr. Robert J. Rutman, professor of biochemistry, has been appointed chairman of the board of the Ile-Ife Center for the Arts and Humanities in Philadelphia. In February Dr. Rutman participated in a symposium on Vietnam at Gettysburg College. He discussed the "Ecocidal Effects of the Vietnam War." In March he gave a seminar at the Howard Uni-

Bovine Leukemia Research

Bovine leukemia (lymphosarcoma, malignant lymphoma) is the most common neoplastic disease of cattle, affecting animals of both sexes and all breeds. It occurs most frequently in dairy cattle.

The most significant pathological feature of bovine leukemia is the malignant or neoplastic transformation of lymphoid cells. The neoplastic lymphoid cells multiply in an uncontrolled fashion, invading various tissues and organs either diffusely or forming tumor masses. The disease is always fatal. Affected animals die within weeks, or at the most, months after appearance of clinical signs.

Early in the 1960s research on bovine leukemia was initiated at New Bolton Center under the direction of Dr. Robert R. Marshak, and since 1969 this work is continued in the Comparative Leukemia Studies Unit under Dr. Jorge F. Ferrer. Under Dr. Ferrer the Unit has made some outstanding breakthroughs, not only in the area of bovine leukemia, but also in the field of basic viral oncology. Research during the period 1971-1972 established conclusively the existence and identity of a virus as the causative agent of the disease. Since that time Dr. Ferrer's group has contributed a number of important findings about the virus, now known as the bovine leukemia virus (BLV). The virus is a member of the C retrovirus group, the same



A cluster of BLV particles outside of a bovine lymphocyte

group to which all mammalian leukemogenic viruses belong. This group includes HTLV-1, the virus responsible for T-cell lymphomas in humans.

Soon after identifying BLV, it was found that it differs in certain important immunological, biochemical and biological properties from the other known C-type retroviruses. For example, it was found that cattle continuously infected with the virus have antibodies against the major internal BLV protein. This finding established the fact that BLV is an exogenous virus, and further studies have confirmed this. It is now known that BLV is transmitted horizontally, almost always after birth. For several years the

significance of these and other differences shown by the BLV system was not appreciated by other authorities in viral oncology. However, in 1980 HTLV-1, the first C-type human leukemia virus was discovered, and it was soon found that it shares all of the differential characteristics of BLV. It is now clear that BLV is the prototype of a special family of C-type retroviruses. The unique relationship with HTLV-1 is one of the main reasons why BLV is now considered as one of the most important animal models to study viral leukemogenesis.

Once an animal becomes infected with BLV it remains infected for life, regardless of whether or not it develops leukemia. It is estimated that probably no more than 5 percent, and certainly less than 10 percent, of cattle infected with the virus ever develop leukemia. Thus, 90 percent or more of BLV infected cattle are asymptomatic virus carriers. BLV carriers can serve as a source of infection for other cattle, and they may have subtle abnormalities that are important. For example, they may have immunodeficiencies that, although not clinically apparent, favor the development of other infectious processes.

The fact that only a small proportion of BLV infected cattle develop leukemia indicates that, in addition to the virus, other factors are involved in the development of leukemia. Studies in the Comparative Leukemia Studies Unit have shown that one of these factors, probably the most important, is the host's genetic

versity Cancer Center, Washington, on "Re-evaluation of Liposomes as Biological Modulators." At the end of the month he attended a science conference at Hampton University for the purpose of interviewing science minority students. He also was Visiting Scientist for one week, lecturing on molecular biology.

Dr. Marc A. Rosenberg (V71) stars in a television series, *People, Pets and Dr. Marc*, produced by New Jersey Network, a public television station. The series is being aired by 128 public television stations.

Dr. Susan Donoghue (V76), assistant professor of nutrition, has been installed as president of the American Academy of Veterinary Nutrition.

The University of Pennsylvania Research Foundation has awarded grants to the following faculty members: **Dr. Urs Giger**, assistant professor of medicine, for his proposal "Canine Phosphofructokinase Deficiency"; **Dr. Debra Deem Morris**, assistant professor of medicine, for her proposal "Leukocyte Transfusion Therapy for Bacterial Septicemia in Neonatal Foals: Granulocyte Function in Equine Neonates, before and after Leukocyte Transfusion"; **Dr. Stephen P. Schiffer**, assistant professor of laboratory animal medicine, for his proposal "Characterization of Organic Aciduria in Substrains of Balb/c Mice"; **Dr. M. Raja Iyengar**, professor of biochemistry, for his proposal "Biophysical Studies on N-Phosphoryl Creatinine, a Newly Characterized High Energy Compound."

Dr. Sydney M. Evans (V77), lecturer in radiology, is a diplomate of the American College of Veterinary Radiologists.

Dr. Darryl Biery, professor of radiology and Chairman, Department of Clinical Studies, Philadelphia, received the AAHA Northeast Region Award. ALPO, Inc. recently made a \$1,000 gift to Dr. Biery. It will be used to place

X-ray view boxes in some of the VHUP examination rooms. **Dr. Biery** and **Dr. Gail K. Smith (V74)** received a grant from the Morris Animal Foundation for their project "Hip Dysplasia—Biomechanical and Radiographic Correlations."

Dr. Mark W. Allam (V32), former dean, and professor emeritus of surgery, was awarded the Thomas L. Holmes Community Service Award, the top community award given by Media, PA.

Dr. William S. Chalupa, professor of nutrition, contributed to a National Research Council Report on "Ruminant Nitrogen Usage."

Dr. Robert E. Davies, Benjamin Franklin and University Professor of Molecular Biology, taught a course "Are We Alone in the Universe" in the University's Gifted Program.

Dr. Roy D. Hoffman (V31) was named "Veterinarian of the Year" at the Pennsylvania Veterinary Medical Association meeting in October. Recently Dr. Hoffman was named Bedford Elk's Citizen of the Year. Dr. Hoffman lives in Bedford, PA, and has practiced veterinary medicine for 55 years.

Dr. James S. Reid (V62), Vienna, VA, received the American Animal Hospital Association's Regional Practitioner of the Year Award.

Dr. Elizabeth Atwood Lawrence (V56) has written *Hoo!beats and Society: Studies of Human-Horse Interactions*, published by the Indiana University Press.

Dr. William Medway, professor of clinical laboratory medicine, completed a three-year term as a member of the Marine Mammal Commission's Committee of Scientific Advisors on Marine Mammals.

Dr. Charles W. Raker (V42) has been named The Lawrence Baker Sheppard Professor Emeritus of Surgery.

Dr. Dudley E. Johnston, professor of surgery,

taught a post-graduate refresher course on "Soft Tissue Surgery of Dogs and Cats" and two "Soft Tissue Workshops" at the University of Sydney, Australia, in February.

Biomedical Research Support Grants were awarded to **Dr. Urs Giger** for "Canine Phosphofructokinase Deficiency: An Animal Model for Glycogen Storage Disease Type VII;" **Dr. Joan Hendricks (V79)**, assistant professor of medicine, for "Sleep-disordered Breathing in Pups and Adult Dogs with Upper Airway Obstruction;" **Dr. Gert Niebauer**, assistant professor of surgery, for "Immune Reactivity in Canine Cruciate Ligament Rupture."

Dr. Gerhard A. Schad, professor of parasitology, has been appointed to a three-year term as a member of the Graduate Group in Biology. Recently Dr. Schad made a presentation on parasite biology at the Park City meeting of the MacArthur Consortium on the Biology of Parasitic Diseases.

Dr. James B. Lok, assistant professor of parasitology, has been appointed a member of the NIH-NIAID Ad Hoc Study Section for Tropical Medicine and Parasitology.

Dr. Alan M. Beck, adjunct associate professor of animal ecology, was interviewed by Italian television for "Italia Sera," a national talk show, and he discussed the studies conducted here by the Center for the Interaction of Animals and Society. Dr. Beck also participated in the conference "Zoonoses in New England: A Conference for Veterinarians and Physicians," at the University of Massachusetts. Dr. Beck spoke on the human/animal bond.

Jamie Quackenbush, the social worker at VHUP, and **Denise Graveline**, former editor of *Pet Care Report*, have just completed a book, *When Your Pet Dies: How to Cope with Your Feelings*. The volume is published by Simon and Schuster.

composition.

While basic studies on BLV continue, Dr. Ferrer's group is also working on the development of tests to detect the presence of BLV in cattle, and of vaccines to prevent BLV infection.

An important consideration in the development of a reliable test to detect the virus in animals is the fact that cells infected with BLV do not synthesize virus particles and viral antigens *in vivo*. This means that cattle infected with the virus do not exhibit a viremia and, therefore, the disease cannot be identified by tests based on the direct detection of BLV in the plasma.

All cattle infected with BLV have antiviral antibodies, and procedures aimed at the detection of these offer the best, and most practical, approach for diagnostic tests. The presence of the antibodies provides an accurate indication of active rather than past infection.

Until recently, the radioimmunoassay (RIA) procedure was the most specific and sensitive technique for the detection of antibodies to BLV. However, this test is impractical for routine use because it requires specialized personnel and equipment.

Because of its simplicity, the agar gel immunodiffusion test (ID) has been the most widely used serological test. This has been marketed under the name Leukassay B. After some use in the field this test lost its popularity because it is now recognized that it frequently gives false negative results, particularly with animals in the early stage of infection. Under certain condi-

tions the ID test may give false positive results. Also, the ID procedure does not lend itself to automation, and is therefore not practical for large scale use.

The Comparative Leukemia Studies Unit has directed its efforts to the development of a reliable, inexpensive and practical test that can be automated or semiautomated and used for large scale seroepidemiological studies. With support from the Edgewater Corporation, Dr. Ferrer's team has developed a test based on the enzyme-linked immunosorbent assay (ELISA) procedure. The basic ELISA procedure itself was found not to be suitable, but with modifications it has been developed into a highly sensitive and specific test now designated as the ELISA NBC test. The test is simple to perform, does not require special equipment, and it can be conducted by an individual with minimal training and skills. Further, it is inexpensive (less than ten cents/sample) and it uses reagents that are commercially available and stable. A patent for the ELISA-NBC procedure has been applied for in the United States and in a number of other countries with sizeable cattle and dairy industries.

Immediate applications of the ELISA-NBC test include seroepidemiological surveys to determine the prevalence and distribution of BLV, the testing of cattle in eradication and control programs, the selection of cattle for exportation, the testing of cattle at import stations, and the selection of breeding stock.

Epidemiological studies indicate that about 30 percent of dairy cattle in the U.S. are infected with BLV, and approximately 70 percent of dairy and beef herds in this country contain infected animals. Since BLV is readily transmitted, epidemiologists have estimated that unless control measures are instituted the number of animals and herds infected with the virus will double arithmetically every three years.

Since most cattle become infected with the virus at about 1½ years, there are two main approaches to eradication and control. One is the isolation or removal of infected animals from a herd. The other is immunization of uninfected animals. Vaccination would provide the most practical and economically realistic approach to the eradication of BLV infection.

Dr. Ferrer's group, with support from the Edgewater Foundation, is engaged in a major effort to develop a suitable vaccine and has, in fact, developed a vaccine which is suitable to immunize certain cattle populations. However, this preparation, known as Vaccine I, cannot be used for cattle that are to be tested for BLV infection by means of serological tests (e.g., cattle for export) since it would give false positive results because of the antibodies produced in response to the vaccine. Researchers at the Comparative Leukemia Studies Unit are now engaged in work to produce a vaccine which will not interfere with the serological diagnosis of BLV infection.

—John E. Martin, V.M.D.