

Chapter Nine

A History of the Program of Laboratory Animal Medicine, Science and Technology in the Department of Veterans Affairs

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Introduction: Origin of the VA Program

Public concerns about the care and use of laboratory animals in the early 1960s led the Veterans Administration (VA), as it was then known, to create and to fill a position for a veterinarian in the Research Service of the Department of Medicine and Surgery at the VA Central Office, (VACO) in Washington, D.C.

Jules Cass, DVM, MSc, then at the Kettering Laboratory of the College of Medicine, University of Cincinnati, was invited to address an assemblage of VACO officers. He described how veterinary medical specialists in laboratory animal medicine, science and technology could best serve VA's programs of research, development, and education involving animal subjects while also addressing the public's concern about animal welfare. Dr. Cass was offered the position and asked to write the job description to encompass all animal-related matters in the VA. Dr. Cass reported to the VA Central Office in September 1962, and served as chief veterinary medical officer (CVMO) for the VA until September 1983. Dr. Cass brought a rich reservoir of knowledge to the position, derived from 10 years of association with John Nelson, rat pulmonary disease; Liz Kraft, mouse infectious diseases; Phillip Trexler, germfree technology; Sam Poiley, laboratory animal breeding; Henry Foster, commercial production; William Gay, lab animal surgery and technology; Cohrs, Jaffe and Meessen, pathology, (1), as well as others.

To be the first to hold the newly created position of chief veterinary medical officer was a remarkable circumstance. No previous VA Central Office organizational program existed. Dr. Cass relates that when he reported to the office of the director of personnel and having sworn his allegiance to the VA, the

director of personnel turned to him and asked, "What does a veterinarian do in the VA?"

Program Development

Animal programs that existed among the VA Medical Centers in the early 1960s were individually developed and organized. Animal facilities were variously managed as service and study segments of the Research Service, in each center. Dr. Cass received full support from the director of VA Research Services, to initiate and develop policies and procedures that were animal related for VA research. Few of the research staff, at any level, were directly aware of the extent of the biomedical studies involving animal subjects that were being conducted at about 100 of the 135 Veterans Affairs Medical Centers (VAMC)s with programs of research, development, and education.

Dr. Cass spoke at meetings of VA regional directors and their staffs on the importance of animal studies to research and their bearing on the efficiency, effectiveness, and reliability of the VA medical research program. These presentations became a continuing part of the orientation of newly appointed staff leaders at VACO to maintain understanding of the essential need of the program to the VA research, development and education programs, and to gain advice and consent for current initiatives by the Chief Veterinary Medical Officer (CVMO). Early on, Dr. Cass conducted a series of visits to 16 selected VAMCs to meet hospital medical directors and staff investigators who used animal subjects. At these meetings he introduced the program; and discussed appropriateness of selected animal subjects; animal technology and procedural problems; animal research facility (ARF) problems; and the availability of resources and information about laboratory animals. Together with ARF staff, he reviewed: personnel, husbandry, management practices, facilities and equipment, procurement of animals, and health care procedures. From these meetings and visits, Dr. Cass identified overall programmatic needs and where to focus attention. Among the most significant problems were:

1. Problems existed with the quality of animals used. Local and regional sources often provided biomedically undefined animals; the quality of animals was often not considered. The need to condition animals prior to study was often overlooked.
2. Animal research facilities had inadequate maintenance; deficiencies in physical plant and equipment; and inadequate operating procedures.
3. Investigators and their staffs were often responsible for purchasing animals and animal supplies and equipment, animal husbandry, and animal health surveillance.

On the basis of these observations, Dr. Cass determined that the success and reliability of animal studies throughout VA could best be achieved by appointing full-time, part-time, or consultant specialists in laboratory animal medicine to the research programs at VAMCs. Accordingly, position descriptions for veterinary medical specialists were developed for the VA based upon a new federal standard series for veterinarians (DVM, VMD). Dr. Cass succeeded in changing the title for the veterinary medical standard series from "Veterinary Sciences" to "Veterinary Medical Officer," thus paralleling "Medical Officer" (MD). The pay grade for veterinarians who were laboratory animal medicine board eligible was established at GS-13 and for those who were board certified at GS-14.

Regional research service conferences were used as platforms to present the program of, and to describe the essential role and

contributions that veterinary medical specialists and animal technicians would make as integral members of VAMC research programs. As a result, veterinarians became full/part-time employees or consultants in approximately 100 VAMCs. For the most part, these professionals were laboratory animal medicine board qualified or certified. In addition, animal technicians were encouraged to further their training and many became certified through the AALAS animal technician certification program.

From this cadre of specialists, as well as other contributors, groups were convened by the CVMO to prepare and publish articles on pain and anesthesia in laboratory animals. These deliberations were published in *FASEB Proceedings* (2), and were widely distributed to the research community. An edited text on the comparative radiology of laboratory animals was prepared and published under the aegis of VA Research Service (3). Dr. Cass also initiated a program to provide VA investigators with reliable sources of defined quality animals through a collaborative arrangement with the National Institutes of Health (NIH). He introduced and promoted accreditation of VAMCs by the American Association for Accreditation of Laboratory Animal Care (AAALAC); and initiated a VACO supported training program for veterinarians in laboratory animal medicine; He also began tele-conferencing with all VAMC veterinary medical officers on selected pre-determined subjects, using experienced individuals as discussion leaders; initiated a program of veterinary medical reviews of all animal related matters in VA investigator submitted research protocols; was a leader in requiring that all distressful experimental procedures be identified and described; and assisted in the design of animal research facilities at VAMCs.

VA Organization

The VA, now the Department of Veterans Affairs, is currently comprised of three primary elements: the National Cemetery System; Veterans Benefits; and Veterans Health Administration. The VA Research and Development program falls under the Veterans Health Administration. Most studies that require animal subjects are funded through the Office of Medical Research Service Research and Development of the Veterans Health Administration, and the CVMO reports to the Director of Medical Services Research and Development.

Although VACO, recently retitled VA Headquarters (VAHQ), in Washington, D.C., maintains administrative oversight of VAMCs, each center operates with considerable autonomy. Virtually all centers with significant medical research are affiliated with one or more university medical centers, and most VA investigators hold joint appointments with the affiliated university medical center. Presently, 83 VAMCs conduct animal related research, and each employs the services of either a full- or part- time veterinary medical officer or consultant. These veterinary medical officers report to the local associate chief of staff for Research and Development, who, in turn, reports to the local VAMC medical director. The VAHQ chief research and development officer and the chief veterinary medical officer exercise their influence primarily through allocation of funds and formulation and promulgation of VA laboratory animal medicine nation wide policy.

Historically more than half of all VA funded studies have included the use of animals. The 1977 Nobel Prize for Medicine was shared by two VA investigators who used animals in their research: Drs. Rosalyn Yalow, Bronx VAMC, and Andrew Schally, New Orleans VAMC. Drs. Andrew Gage and William

Chardack, Buffalo VAMC, were early leaders in the development of open heart surgery and cardiac pacemakers, using dogs as models. Dr. William Starzyl, Pittsburgh VAMC, perfected surgical transplantation of kidneys and liver using cyclosporin and other anti-rejection drugs in animal models. Other notable VA animal research contributions include advances in treatment of tuberculosis, spinal cord injuries, hypertension, kidney dialysis, and psychiatric disorders (4).

Chief Veterinary Medical Officers

Dr. Cass was a fortuitous choice for the first chief veterinarian, and his vision and foresight account in large measure for the success of the program that he developed and nurtured. He was an early leader in laboratory animal science and served as president of the Animal Care Panel in 1957-1958. In 1960 he published an extensive annotated bibliography of the literature on laboratory animal medicine, science and technology (5a) and this was updated in 1963 (5b) and again in 1971 (5c). He was awarded the AALAS Griffin Award in 1983, and in 1984 the Ohio State University College of Veterinary Medicine "Distinguished Alumnus" award in recognition of his achievements.

Dr. Cass retired in 1982. Dr. Charles C. Middleton, of the University of Missouri assumed the role of CVMO in May 1984. While at the University of Missouri, Dr. Middleton gained international recognition as a pioneer in the use of swine in biomedical research. At the VA, Middleton began a program of visitation to VAMCs (6) to identify deficiencies and develop a program for remedial action. Middleton left the VA in August 1985 to accept an appointment at State University of New York at Stony Brook, and the position of CVMO remained vacant until October 1986, when Dr. Donald D. Holmes of Oklahoma State University was appointed. Dr. Holmes had served as part time veterinary medical officer (VMO) at the Oklahoma City VAMC from 1965 until 1978, thus gaining valuable insight into problems and potential solutions at the local VAMC level. During his tenure, he continued initiatives developed by his predecessors. In addition, he instituted an animal facility core equipment request procedure, formalized policies and procedures regarding animal research issues, recruited additional qualified VMOs who would serve as a cadre of laboratory animal medicine specialists to address and advise on system-wide issues, wrote the original VA Manual Chapter M-3, "Animal Subjects in Research," (7) initiated the concept of a system-wide policy on occupational health and safety in VA animal facilities, and developed and published the *VA Veterinary Medical Unit Design Guide* for animal facilities construction (8). He received an Outstanding Career Award from the VA upon his retirement in February 1993.

Dr. Conrad Richter replaced Dr. Holmes in March 1993. At the time, Dr. Richter was professor and director of the Division of Laboratory Animal Resources at Duke University, and served as the veterinary medical consultant (VMC) for the Durham, NC, VAMC (9). He was appointed CVMO through an Intergovernmental Personal Act (IPA) agreement between Duke University and the VA Office of Research and Development. During his tenure, he completed and published the *VA Program Guide on Occupational Safety and Health in the Animal Facility* (VHA Program Guide 1200.5). Recognizing the need to fulfill the federally mandated training of all VA research personnel involved with the use of animals in research, he conceived and awarded a multi-year training grant through a request for proposals and peer review process. He organized and co-sponsored a VA/National Institutes of Health (NIH) training

conference on regulatory oversight of animal experimentation, and served as VA representative on the NIH National Advisory Research Resources Council (9). He retired in May 1997, and was succeeded in June 1997 by Dr. Jack R. Hessler.

Dr. Hessler had served as part-time VMO at the Memphis VAMC from 1975 to 1989 while holding the position of director, animal resource division at the University of Tennessee Medical Center in Memphis. He is highly regarded as an expert in animal facility design and construction, and was an active member of the VA Design Guide Committee. He was faced with the difficult task of reducing funding for VMOs and VMCs, concurrent with budgetary limitations, and also dealt with consolidation and closing of VA animal research programs that no longer met the test of critical animal research mass. He resigned his position as CVMO in January 1998, and resumed his professional career as a consultant in laboratory animal medicine.

Dr. Michael T. Fallon, then serving as VMO at the Atlanta VAMC since 1989, replaced Dr. Hessler. At the time of his appointment he was president of the Association of VA VMOs. With Dr. Fallon's appointment, the CVMO position was changed to 49 percent central funding, with Dr. Fallon based in Atlanta rather than in Washington, D.C. Under this arrangement he travels twice a month to VAHQ, and performs VAMC site visits as needed (11).

In addition to line responsibilities, the CVMO serves as the VA representative or liaison with numerous other agencies and organizations such as the Interagency Research Animal Committee, the NIH National Advisory Research Resources Council, the Interagency Animal Models Committee, AAALAC, the U.S. Department of Agriculture (USDA), the Institute of Laboratory Animal Resources, and the Association of Military Surgeons of the United States. Although each CVMO has had different priorities and strategies for coping with the challenges of the job, all have been committed to facilitating the work of VA investigators, technicians, and animal facility supervisors. Most have been granted extraordinary latitude to achieve their objectives, and all have been equally committed to ensuring adherence to the highest standards of animal care and use.

Veterinary Medical Services at VAMCs

The small size of the animal research unit at most VAMCs has made arrangements for the provision of adequate veterinary medical care a challenge. In only a handful of the larger programs can employment of full time VMOs be justified, unless the individual employed assumes additional responsibilities such as research beneficial to the VA. Most part time VMOs and VMCs hold positions in the affiliated university medical center. Much of the success in recruiting qualified VMOs and VMCs is attributable to the early steps taken by Dr. Cass. He convinced officials in the Office of Research and Development in Washington that compensation for VMOs and VMCs should be funded as a VACO budget line item, reducing the negative effects of local VAMC research budget perturbations. For many years VMOs held the title of chief, research in laboratory animal medicine, science and technology (Chief, RILAMSAT), as designated by Dr. Cass. In the early 1990s the titles were changed to chief, veterinary medical unit (VMU), and the animal research facility became the veterinary medical unit.

In 1963 Dr. Donald G. Devalois was appointed chief, at the Los Angeles VAMC and Dr. Robert F. Locke was appointed chief, at the Hines VAMC. In 1964 Dr. Donald Clifford was appointed chief, at the Houston VAMC. In 1965 Dr. Don Holmes was ap-



FIG. 1. VA veterinary medical officers, the chief veterinary officer and other VA officials meeting—1969. Those mentioned in the text are Dr. Donald Holmes (extreme left), Dr. Donald Devalois (2nd from left), Dr. Donald Clifford (6th from left), Dr. Jules Cass (10th from left), Dr. Joseph E. Wagner (11th from the left), and Dr. Robert Locke (2nd from right).

pointed to a VMO position at the Oklahoma City VAMC with a concurrent appointment at the University of Oklahoma Health Sciences Center. These were interesting and exciting times for the four VMOs. They were periodically summoned to Washington, D.C., by Dr. Cass, attended annual VA Research Conferences, and were detailed to other VAMCs to provide guidance in the animal study programs. The visitors were usually well received; however, occasionally their expertise was not fully understood. Later, Dr. Joseph E. Wagner was appointed VMO at the Kansas City VAMC, and joined his four colleagues in working with the CVMO on VA issues of national significance.

The VMCs play a vital role in providing veterinary services to VAMCs, and many of the most highly respected laboratory animal specialists in the country either currently serve as consultants, or have served in the past. Many of the early leaders of AALAS and other laboratory animal organizations also provided guidance to VAMCs. The list included such luminaries as Bennett Cohen, Sigmund Rich, Orland Soave, Douglas McKelvie, Steele Mattingly, C. Max Lang, Gerald Van Hoosier, Steven Pakes, and James Fox. Since the early years, under Dr. Cass's leadership, VMOs and VMCs have met during annual meetings of AALAS and the AVMA to discuss relevant programs, ideas, and problems. For several years these were conducted as informal breakfast meetings, but in the late 1960s this group organized as the Association of VA Veterinary Medical Officers with Dr. Holmes elected the first president (4). This organization serves as an active network for VA veterinarians across the country. In more recent years, annual luncheons, as well as business meetings have been held during the AALAS meetings. The Association serves as an important resource for the CVMO in formulating new guidelines and policies that affect VA's program of laboratory animal management, and regularly communicates with its members through a newsletter.

Supervisors of VA Animal Research Facilities

Animal research facility supervisors serve a critical role in the VA. Recognition of the importance of trained supervisors led to the establishment of a nationwide supervisory training program at the Los Angeles VAMC in 1971 under the direction of Dr. Devalois (12). In 1974 the program was transferred to Oklahoma City, where it was co-directed by Dr. Holmes and Dr.

Gary White from 1975 to 1978. The course was structured with morning lectures, afternoon laboratories, reading assignments, and weekly examinations. The success of the program resulted in all trainees becoming certified by AALAS at the technologist level. In 1988 the supervisor's training program was placed at the Little Rock VAMC, which had the advantage of on-site housing for trainees. In 1989 the program was again moved to Oklahoma City, and the emphasis was changed to "exportable" training material because of the high cost of on-site training. In 1990, Dr. Larry Peters became the director, assisted by Mary Dittmar as the coordinator. A privately owned correspondence course was purchased to serve as a basis for the exportable training material. The training material was adopted by a local community college as part of an associate degree in laboratory animal science, and ownership of the material was transferred to the community college when training was discontinued by the Oklahoma City VAMC in 1995 (13). AALAS has included some of this material in a correspondence course for technicians preparing for certification examinations (11).

Regulations, Policies, and Practices

No instance is known of a VAMC research facility having been the primary target of a public demonstration by animal rights activists; furthermore, unfavorable publicity in the news media has been uncommon. Animal rights groups may hesitate to challenge research designed to benefit veterans, but perhaps equally important, the policies and practices adopted by the VA to ensure proper care of animal subjects has been an effective preemptive measure.



FIG. 2. VA Supervisors Training Class in 1976. Left to right are J. Nelson, J. Sporn, A. Gauthier, J. Roberts, and G. Smith.

The VA has been a leader among federal agencies in this regard, and the lines of communication between the VA and animal welfare groups such as those established by Dr. Cass with the Animal Welfare Institute, have undoubtedly been beneficial (14). Several important measures established by Dr. Cass were significant in this regard. These include the review by laboratory animal medicine specialists of all VA investigator proposals in which laboratory animals serve as subjects. Such reviews were instituted in the mid-1970s and were originally conducted in Washington by six to eight veterinary medical specialists meeting in marathon review sessions. Dr. Middleton adopted a modification of the process whereby the animal component forms for proposed research are mailed to selected qualified veterinarians, both VA and non-VA,

for review and return to the CVMO (6). The veterinary medical reviewer may recommend that the proposal be approved; recommend that the proposal be reviewed and approved with changes by the local Subcommittee on Animal Studies (SAS), counterpart of the Institutional Animal Care and Use Committee; or recommend that the proposal not be funded until identified animal related problems are resolved. If the CVMO concurs with the latter recommendation, funding is not released until the identified problem is satisfactorily resolved.

To further instruct VAMC personnel and codify VA policy on animal research, Dr. Holmes wrote and the VA approved an official policy document, *Manual Chapter M-3, "Animal Subjects in Research"* in 1987. Revised in 1989, M-3 remains the official policy of the VA in this important matter (7). Dr. Holmes also began to address the problem of occupational health and safety in VA research facilities in 1991. Under his guidance, Dr. Michael Fallon, Atlanta VAMC, working with personnel at the Center for Disease Control and Prevention (CDC) prepared a full color pamphlet on this subject which received wide distribution inside and outside the VA. Holmes and later Richter expanded and revised the initial document, and in 1996, the official *VA Occupational Health and Safety for Veterinary Medical Units Program Guide* was published as *VHA Program Guide 1200.5*, and distributed throughout the VA.

Early in his tenure, Dr. Cass worked with VA architects and engineers to devise standards for animal facility design, material, and traffic flow in animal research facilities (14). Dr. Middleton refined these standards by bringing to VAHQ laboratory animal veterinarians with animal facility construction experience to work with VA architects, engineers, and specification writers. This panel produced standards for floors, walls, ceilings, construction finishes, floor drains, light fixtures, barrier facilities, and heating, ventilation and air conditioning (HVAC) which were adopted by the VA (6). This effort was continued by Holmes with a Field Advisory Committee of laboratory animal specialists and representatives of the VA Office of Construction Management, and culminated in publication of the *Veterinary Medical Unit Design Guide* in 1993 (8).

Continuing Education

From its inception, the VA laboratory animal medicine program assigned high priority to continuing education. Dr. Cass made arrangements for VMOs to attend Armed Forces Institute of Pathology courses in laboratory animal disease and pathology, and in 1965 a residency program in laboratory animal medicine was established at the Hines VAMC, with participation of other institutions in the Chicago area. The program was initially directed by Dr. Robert F. Locke, and later by Dr. Charles L. Holmes and Dr. Fred A. Buddingh (15)(16). The program trained 14 residents before being discontinued in 1973. Drs. Alvin Moreland and Cass collaborated in presenting continuing education to VMOs via videotapes and teleconferences in the 1980s. Moreland received VA funding for preparation of videotapes and a syllabus to be viewed by selected VMOs. This was followed by teleconferences, originating from VAHQ, to discuss the material. When the program was completed, copies of the material were placed in the VAHQ library and made available to the AVMA and AALAS for use at the audiovisual sessions of annual meetings. The videotapes continued to be used at AVMA annual meetings through 1996 (17).

In 1990, Dr. James Henderson, Milwaukee VAMC, produced an orientation videotape that was made available to all VAMCs

with programs of animal research. These served to familiarize personnel engaged in the care and use of animals with VA policies and practices. In 1995, Dr. Richter addressed the need to respond to regulatory mandates to provide continuing education to VA investigators, research technicians, and SAS members. He developed a request for proposals to design and produce a multimedia continuing education program to be funded at the level of \$500,000. A peer review committee composed of VMOs and media specialists was convened to review submitted proposals. A five year grant for preparation of this material was awarded to Dr. Michael Fallon (PI) and Kathy Laber, Charleston, SC, VAMC (Co-PI). Shortly after the VA grant was awarded, Drs. Kenneth Boschert, Nicole Duffee, and Michael Talcott, Washington University of St. Louis School of Medicine, received a three year grant for training material production from a private foundation. These two independent projects were merged into a single collaborative endeavor in 1997. The training materials, consisting of 13 modules, will be released as a series entitled "Working With Laboratory Animals." The authors will assign the copyright for the training materials to AALAS, which will distribute them for a reasonable fee, manage archives of original material, and oversee the production of updated versions in the future (18).

AAALAC and the VA

Dr. Cass encouraged VAMCs to request accreditation visits soon after AAALAC was organized. The New Orleans VAMC, the first VAMC to achieve accreditation, was fully accredited in 1970 (9). While serving as chairman of the Council on Accreditation for AAALAC, Dr. Moreland proposed that additional steps be taken to encourage all VAMCs to become accredited. Since full accreditation for all VAMCs was Dr. Cass's goal, he concurred in this suggestion, and a contract was negotiated between VAHQ and AAALAC whereby costs of accreditation site visits and annual fees were paid by VAHQ (17). In addition, the Office of Research and Development allocates funding annually for renovations and repairs to research facilities. Funds necessary to improve animal research facilities, particularly those necessary to meet or achieve accreditation status, receive a priority second only to those necessary to protect human health at VAMCs. In the late 1980s, the VA established a separate committee to review animal research facility equipment requests with special emphasis placed on accreditation needs. By 1992 most VMUs were either accredited or had applied for accreditation. At that time, VAHQ issued a directive that provided a three year phase-in period for all VAMCs to achieve accreditation. By 1999 all VAMCs housing animals on their premises had achieved accreditation, and VA research funding for animal studies is now provided only when such studies are conducted in AAALAC accredited VMUs or affiliated accredited universities.

Trends in VA Animal Research Programs

After several recent years of inadequate funding, the VA Office of Research and Development experienced a significant increase in FY98 and FY99, including increases for support of VMUs (11). The secondary veterinary medical review program is now used as a tool to not only ensure sound biomedical study use in all animal related matters and regulatory compliance by individual investigators, but also to identify weak Subcommit-

tees on Animal Studies. In the near future, the reason for holds on research grants will be tracked as a means of identifying specific areas for increased training emphasis (11).

Although the use of dogs and cats in research has declined nationwide, the VA appears not to follow the trend toward greater use of rodents as strongly as most institutions. Small VAMC research programs face sharp declines in funding, and several are either discontinuing animal research studies, or are merging with an affiliated university program.

The multimedia training program now under development will be linked to an Internet-based VA examination server which will permit VA research staff to choose tests covering the modules required by the institution. This testing program is expected to be adopted as a pre-condition of SAS approval for animal studies across the VA system. It is hoped that AALAS will eventually host the exam server and provide inexpensive testing services to institutions across the country (11).

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