Section V: Research, Development, and Public Health Services

This statue featuring a veterinary laboratory technician working "at the bench" represents one of the major duties of Army military veterinary services: making scientific discoveries at the laboratory bench, often using a microscope to study various samples sent to a US Army laboratory to support the military veterinary research, development, and public health mission. Other US Army veterinary statues, representing other key veterinary service missions, are located side by side outside the US Army Medical Department Museum at Joint Base San Antonio-Ft Sam Houston, Texas.

Photograph: Courtesy of Nolan A. Watson.

Chapter 14

LABORATORY ANIMAL MEDICINE

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INTRODUCTION

The laboratory animal medicine (LAM) veterinary specialist plays a valuable role in all aspects of Department of Defense (DoD) research, development, test, and evaluation (RDT&E) activities, as well as combat trauma and other training using animals. Animals are often the best asset available to support medical advances and train warfighters. This chapter articulates how Army veterinarians act as advocates for both animals and service members in support of DoD missions.

Scope

LAM specialists are those experienced in the discipline of using animals for RDT&E and training. Army LAM veterinarians supporting RDT&E and training missions strive to become board-certified by the American College of Laboratory Animal Medicine (ACLAM) because ACLAM board-certified veterinarians are recognized experts in the humane care and responsible use of laboratory animals. Military veterinarians who are not yet ACLAM board-certified must have extensive training and experience in the specialty in order to work in DoD animal care and use programs.

Because the DoD requires a veterinarian with training and experience in laboratory animal science and medicine to fulfill every RDT&E mission using animals, approximately 50 specialty-trained veterinarians are needed to adequately support these missions, making the DoD one of the largest employers of LAM veterinarians in the world.[1] In order to meet this requirement for highly qualified specialists, the Army established its own LAM residency program for military veterinarians, which has achieved notoriety especially for its exceptional success rate regarding the number of residents attaining the difficult and coveted board certification by the ACLAM. This chapter will overview this residency program as well as document its well-known achievements.

Roles and Goals

LAM veterinarians fulfill many roles within DoD institutes, the most important of which is to ensure that each institute and activity complies with all laws, rules, and regulations regarding animal care and use. LAM veterinarians and trained LAM technologists also play a critical role as animal advocates by promoting animal well-being and proper ethical use of animals in all situations. In addition to being experts on laws, rules, and regulations, LAM veterinarians must possess comprehensive expertise in a number of areas beyond traditional veterinary clinical care of animals, to include providing animal husbandry and environmental enrichment for a wide variety of species, ranging from traditional research species such as rodents and nonhuman primates to unusual species such as bats and dolphins.

Of the DoD personnel working with animal programs, LAM veterinarians and LAM technologists are probably most able to ensure species-suitable environments and security for DoD animals. Because facility design is so important to providing high-quality animal care and supporting the most advanced research, LAM veterinarians often advise engineers, architects, and design specialists on the construction and renovation of animal facilities, paying particular attention to housing systems, sanitation, lighting, and ventilation as appropriate to each species.

Procurement and care of the healthiest animals available are also objectives crucial to DoD research. The LAM veterinarian is the go-to specialist for procuring disease-free research animals and making certain that new animals are properly quarantined before integration with existing colonies or herds.

In addition to being involved with procurement, husbandry, and basic veterinary care of a wide variety of species, a LAM veterinarian provides guidance so that all DoD institutes uphold the standards necessary to remain fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).[1] AAALAC is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. This organization thoroughly reviews all aspects of a comprehensive animal care and use program, including institute policies, animal housing and management, veterinary care, and facilities.

Purpose and Oversight of Activities

The purpose of an RDT&E animal care and use program is to provide the infrastructure and resources needed by principal investigators (PIs). PIs are specialized scientists who develop and execute detailed scientific plans to achieve DoD RDT&E missions. Many of these research plans involve the use of animals. In the DoD, completed research plans translate into the products and information needed to support service members to better accomplish various DoD missions throughout the world. Such products and information improve military readiness and lower morbidity and mortality rates in military operations. Laboratory

animal veterinarians, veterinary technologists, veterinary technicians, and animal care personnel provide the intellectual and technical competence needed for PIs to perform animal work in the conduct of scientific research in the diverse disciplines encompassed by DoD RDT&E programs.

The DoD uses animals for RDT&E and training both within DoD-owned institutes (intramural activities) and via contract or using other agreement mechanisms at various civilian institutes including academia and industry (extramural activities). About one third of the animals are used intramurally, with the remainder of the work performed extramurally, to include locations overseas when appropriate.[2] All animal work conducted by the DoD, whether intramurally or extramurally, requires review by a DoD LAM veterinarian. Three primary oversight offices, one each for the Army, Navy, and Air Force, are responsible for most of the oversight of DoD animal care and use programs both intramurally and extramurally.

Although the DoD continues to adopt animal use alternatives whenever possible, many DoD programs depend on the judicial use of animals in various education and training programs. For example, animals are used in DoD graduate medical education (GME) programs that train physicians to conduct clinical investigations requiring animals; the DoD also uses animals to instruct medical personnel in medical and surgical skills and combat casualty care. After more than 10 years of war in Iraq and Afghanistan, it has become very clear that use of animals to train people on life-saving medical techniques is invaluable and cannot yet totally be replaced by nonanimal training systems such as manikins and other simulation tools.[3,4,5]

REGULATION OF ANIMAL USAGE IN THE DEPARTMENT OF DEFENSE

The US government and the public directly influence how the DoD implements its animal care and use programs and animal use alternatives. DoD organizations using animals for RDT&E or training not only must follow all US laws, rules, and regulations pertaining to animal use, but also must abide by even more stringent requirements set forth by the DoD. The DoD currently endorses the use of animals to advance medicine and science when there are no suitable nonanimal alternatives and when the animals are used in an ethical and humane way.

As noted earlier, all DoD animal research facilities are expected to maintain AAALAC accreditation. The DoD uses three primary standards to evaluate animal care and use programs, which aids in the accreditation process: the National Research Council *Guide for Care and Use of Laboratory Animals* (known as the *Guide*),[6] the Federation of Animal Science Societies (FASS) *Guide for the Care and Use of Agricultural Animals in Research and Teaching* (known as the *Ag Guide*),[7] and the *European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes* (known as *ETS 123*).[8] The *ETS 123* serves as a pivotal guiding document when DoD RDT&E work or training is conducted in foreign countries.[1,8] Any use of animals for RDT&E or training conducted or supported by the DoD must adhere to these standards, or, if in a foreign country, must be evaluated by a DoD veterinarian to verify comparable standards are used.

Moreover, the DoD follows the US Public Health Service (PHS) policy *Humane Care and Use of Laboratory Animals*[9]; the US government's *Principles for the Utilization and Care of Vertebrate Animals in Testing, Research, and Training*[10]; and the DoD's own regulatory guidance consisting of DoD Instruction (DoDI) 3216.01 *Use of Animals in DoD Programs*[1] and Army Regulation 40-33 *The Care and Use of Laboratory Animals in DoD Programs*.[11] At the time of writing, Army Regulation 40-33 delineated the Secretary of the Army as the DoD Executive Agent for Veterinary Services to develop and issue service regulations to implement DoDI 3216.01. This regulation has also been adopted by the Navy, Air Force, Defense Advanced Research Projects Agency (DARPA), and the Uniformed Services University of the Health Sciences (USUHS) to create uniform policies, procedures, and responsibilities among DoD components involved in the use of animals.

All of these guidance documents expand on federal requirements outlined in the Title 9 Code of Federal Regulations (Animals and Animals Products) Animal Welfare Regulations.[12] LAM veterinarians serve as the primary advisors to institutional officials, research directors, and commanders on regulatory issues.[13]

The next section is an overview of the DoD's regulatory history and two oversight agencies' recommended practices regarding animal use for research purposes from the 1960s forward. For more comprehensive texts covering the history of animal care and use laws and regulations, readers should consult *50 Years of the Institute of Laboratory Animal Research* by TL Wolfe[14] or *50 Years of Laboratory Animal Science* by CW McPherson.[15]

Evolution of the Department of Defense Regulatory Documents

In the 1960s, discussions within the federal government were leaning towards regulating the use of animals in research facilities. The DoD established

an internal document, *Policy on Experimental Animals in Department of Defense Research*, in 1961 as a DoDI, in response to social concern about animal use in research.[16] In 1963, the Animal Care Panel, the predecessor to the American Association for Laboratory Animal Science, published an initial version of the *Guide*[14] to disseminate common standards for all research animal facilities to emulate. The DoD also incorporated the common standards articulated by the *Guide* into their 1966 revision of the DoDI. Thus, the professional standards of industry became requirements for the DoD.[17] Today, the *Guide* is a broad-reaching document that has become unquestionably the most influential document in the field of laboratory animal science and has been translated into at least twelve languages.[6,18]

Inspector General Review and Recommendations

During the 1980s through the 1990s, the public became discontented with the state of animal research. Disgruntlement culminated with a congressional hearing before the House Armed Services Committee on April 7, 1992. Representatives from the research community and animal welfare and rights organizations organized a concerted complaint to Congress. Many concerns were expressed, many focused on Institutional Animal Care and Use Committee (IACUC) function and DoD accountability, resulting in the House Armed Services Committee directing the DoD Inspector General (IG) to perform "a review of every program, project, or activity funded by the DoD that conducts any type of live animal research, and report on whether the animals used in each program, project, or activity are handled and treated in accordance with the Animal Welfare Act (AWA), DoD regulations, and rules of basic humaneness that govern live animal research."[19,20(p20)] The outcome of the congressional hearings dictated emphases on the unique requirements of animal care and use programs in the DoD, thereby raising regulatory standards above civilian institution requirements.[20]

The IG's visit to 36 DoD animal research facilities housing animals (as defined by the AWA) resulted in four best practice recommendations that every DoD facility now incorporates into its animal care and use programs: (1) ensure a strong training program for personnel using or providing oversight of laboratory animals, (2) use a formal checklist for IACUC semiannual inspections, (3) clarify requirements of the nonaffiliated member of the IACUC, and (4) develop a standardized protocol format to be used at all institutions.[21] These recommendations formed the building blocks of higher quality DoD programs and are the originating actions for many currently emphasized activities. The impact of these recommendations also has left lasting impressions on how the DoD conducts current animal care and use programs.

First Recommendation. The first best practice recommendation was strong command support for personnel training. During the course of its inspections, the IG found that facilities with the most complete and comprehensive animal care and use programs were those that received the strongest command support—both in time and money—for training all personnel using animals or reviewing animal activities. These facilities encouraged training of key staff to include IACUC members, principal investigators, veterinarians, and animal care staff. Although the type of training varied, the support for continuous education was strongly evident in these facilities.[20,21]

Second Recommendation. The second best practice recommendation was to use a formal, detailed checklist for the IACUC's semiannual inspections. The IG found that those facilities that used a detailed checklist provided the most comprehensive reports while committees that did not have a formal checklist for semiannual inspections produced the least comprehensive reports.

Characteristics of the most comprehensive reports included the following items: a section for every room to be inspected; a list of all policies to be reviewed; a list of animal husbandry factors to be assessed (eg, housing, food and food storage, bedding, water, sanitation, animal identification, and animal records); a list of veterinary care required (eg, preventive medicine, surveillance, diagnosis and treatment, anesthesia and analgesia, surgery, aseptic procedures, euthanasia, and emergency care); a list of what to assess as part of the physical structure (eg, construction, floors, walls, ceilings, drains, lighting and power, temperature, humidity, ventilation, storage, and equipment sanitization); and a section for verification of the qualifications and training of animal caretakers, technicians, and research staff. Additionally, the best comprehensive reports involved all IACUC members in the review process, with documentation of concurrence and minority concerns in each report.[20,21]

Third Recommendation. The third recommendation made by the IG was for the DoD to standardize its approach for meeting the AWA requirement for unaffiliated member representation on IACUCs. The IG had noted that, within the DoD, it was unclear what the expectations were to be for the required number of nonaffiliated IACUC committee members, their professional characteristics, and their eligibility qualifications. On July 16, 1992, the General Counsel, Department of Defense, issued a memorandum entitled *The Institutional Animal Care and Use Committee and the Federal Advisory Committee Act*.[20] The memorandum addressed the issue

of whether the DoD IACUC is covered by the Federal Advisory Committee Act,[20] and, ultimately, the issue of the relationship of the nonaffiliated member to the federal government. In this memorandum, the General Counsel stated that the IACUC does not fall under the definition of advisory committee as is stated in the Federal Advisory Committee Act and therefore is not subject to its requirements, including the one that the IACUC meeting must be open to the public.

The General Counsel further clarified that since the IACUC members do not merely advise but actually perform government functions, a member serving on the IACUC must have the necessary official status. Specifically, an individual who is not affiliated with the facility and is appointed as an IACUC member must be either a full-time federal employee or employed as an expert on the intermittent basis under Title 5, US Code, Section 3109.[20,22] During the inspections, the IG found that the guidance provided by the General Counsel had not been disseminated to all DoD IACUCs, nor had many IACUCs implemented these limitations at the time of the review. Nonetheless, institutes still had trouble filling the nonaffiliated member positions. Most IACUCs had only one nonaffiliated member with no alternate member available if the primary member was unable to attend a meeting. One IACUC had experienced a vacancy for a few months when the nonaffiliated member resigned.[20]

The IG also recommended that the DoD provide clearer guidance with regard to eligibility requirements and professional characteristics of the nonaffiliated member. Additionally, while the AWA allowed for meetings to be held without all members present, the IG believed outside representation was desirable at all meetings.[20] The IG recommended that having alternates to the nonaffiliated member would help meet the goal of having outside representation at every IACUC meeting.[20]

Fourth Recommendation. The fourth recommendation advised that the DoD should develop and implement a standardized research protocol format for use throughout the DoD. Most facilities had developed their own form or format. However, the IG felt that a standardized DoD format would be beneficial, particularly with collection of information required for the annual report to the US Department of Agriculture (USDA).[20]

For example, IACUCs are required to report pain and distress levels in research animals to the USDA, and prior to the IG recommendations, collection of data for such reporting was inconsistent. Some IACUCs would make the determination themselves while other IACUCs considered the pain or distress level assigned by the PIs. However, when the pain or distress codes were defined differently than the pain or distress categories in animal welfare regulations (AWRs), the facility staff had to reclassify the codes to align with those required in the annual report to the USDA. The IG reasoned that a standardized protocol request form using the standardized pain or distress categories as defined by AWRs would serve to eliminate any confusion or misunderstanding when completing the annual report to the USDA, especially when experiments were performed at more than one DoD research facility.[20]

Similarly, some of the institution formats required that literature searches be performed but did not have a place to submit results of the search into the protocol. If a submission place had been a standard requirement, the IG felt the six instances in which literature searches were not complete may have been prevented.[20]

Inspector General Commendable Practices

The IG inspectors also advised all DoD research facilities to obtain AAALAC accreditation and identified seven commendable practices that each facility commander was to consider implementing if they weren't already being used.[21] Sharing and suggesting these commendable practices throughout the DoD animal research program improved the entire DoD program as a whole.[20]

The seven commendable practices are as follows: (1) maintain a transparent animal care and use hotline but allow for anonymous reporting of violations concerning humane treatment of animals; (2) use an animal incident reporting form to describe animal care concerns or suggestions for improvement; (3) provide investigator handbooks; (4) maintain employee training records; (5) use animal facility and room logs; (6) ensure IACUC protocol review by both the DoD facility and contracting facility for any contract work performed extramurally; and (7) require PIs provide assurance statements for adhering to the four Rs (4 Rs) (refinement, reduction, replacement, and responsibility).[21]

Although prior standard practice within most research facilities was to consider the three Rs (3 Rs) identified in *The Principles of Humane Experimental Technique* by WMS Russell and RL Burch (ie, refinement, reduction, and replacement—all means to jointly diminish the level of inhumanity in animal experimentation),[23] one facility also required the PIs to adhere to one more principle—responsibility. The IG felt the practice of expanding the assurance statements to four principles would demonstrate a strong commitment to humane animal treatment and could be incorporated into the standardized protocol form.[20]

The IG felt publishing the name and contact information for the facility commander, the attending veterinarian, and key staff for notification of an animal use concern demonstrated the commander's commitment and support to the animal care and use program. Anonymous written or verbal reporting on the form or via the hotline would ensure that no adverse action would be taken against any person reporting and would reassure staff and others that all animals were to be treated humanely. [20]

The IG also believed certain facility-generated and maintained documents were valuable standardization tools. Some facilities distributed handbooks to the research staff and IACUC members that were filled with information to help investigators prepare protocols, understand and support the animal care program, and serve as a reference text. Handbook categories included laws and regulations; protocol submission requirements; oversight procedures; organizational charts and narrative; procedures for ordering, housing, restraining, and handling animals; noninvasive procedures; surgical procedures; procedures on the use of pain-relieving drugs; procedures on euthanasia and handling of dead animals; and record-keeping requirements.[20]

Several facilities maintained training worksheets on every individual involved in the care and use of animals that detailed required training, training received, training date, and signatures of both instructor and employee. This practice ensured that all employees were provided all levels of training needed for their positions.[20]

Some facilities provided PIs with animal room logs and facility logs. Animal room logs indicated what was checked in the room on a daily basis, and facility logs described how the facility operated and how each room was used. Both logs recorded that the animals in each room were cared for every day.[20]

Finally, the IG found that most protocols indicated that animal work contracted out to extramural facilities was only required to be reviewed by the funding organization for a scientific need. However, at least one commander required that his IACUC perform an animal care and use review in addition to the commander's scientific review. This practice ensured that the federal research facility was actively involved in oversight of research funded by the DoD.

Secretary of Defense Reports and Congressional Hearing Revisions

The Fiscal Year 1993 House Armed Services Committee Report, 102-527, included a request to the Secretary of Defense to provide a comprehensive annual report on animal care and use programs.[24] This report was prepared in accordance with a specific requirement to record all animal research conducted by the DoD including education, training, and testing both in DoD laboratories and by extramural projects funded by the DoD. Yearly data was prepared in an annual report from 1993 to 2002, then in a biennial report since 2004. The structure of the reports is comprised of indepth discussions of publicly accessible information on DoD research, policies, and procedures for oversight of DoD animal care and use programs, DoD animal use profiles, and DoD initiatives to promote alternative methods that replace, reduce, or refine animal use.[25]

During the 1994 Congressional Hearings, in which Congress heard the report from the IG on the DoD animal research program, the DoD indicated that revisions to the DoD Directive 3216 on the use of animals in research were already in progress. The new version, published in 1995, contains the following six significant changes, compiled in direct response to congressional involvement: (1) DoD facilities should apply for and maintain continued AAALAC accreditation; (2) the DoD is prohibited from purchasing or using dogs, cats, or nonhuman primates to (*a*) inflict wounds from any type of weapon, (*b*) conduct training in surgical or other medical treatment procedures, or (*c*) use in research conducted for developing biological, chemical, or nuclear weapons; (3) DoD standards for IACUC composition must include an alternate to the nonaffiliated member; (4) specific oversight requirements must be established for extramural research to include review and approval of animal use protocols, review of facility inspections by the USDA, and site visits by DoD veterinarians under certain circumstances; (5) channels for reporting noncompliance must be established; (6) a more formal structure for oversight, particularly for extramural research, had to be established; and (7) a special dual-hatted position—that of Commander, US Army Veterinary Command, and Director, DoD Veterinary Services Activity (a field-operating agency of the Army), Office of The Surgeon General, who would serve as a consultant to the Assistant Secretary of Defense for Health Affairs and the Director, Defense Research and Engineering, for technical and professional matters—would need to be established.[26]

The DoD also implemented *Department of Defense Policy for Compliance with Federal Regulations and DoD Directives for the Care and Use of Laboratory Animals in DoD-Sponsored Programs*.[27] This 1995 policy memorandum specified training requirements for nonaffiliated DoD IACUC members and implemented a standard format for animal use protocols, a standard checklist for IACUC inspections, and a standard reporting requirement for all animal use research to support the Biological Research Database (BRD). Through the

use of the BRD, the DoD required all animal research projects, to include those involving clinical training or investigations, to be reported.[27] The BRD became publicly available, whereas the former reporting system, the Defense Technology Information Center database, had restricted public access.[28,29]

In 1995, House Report 103-499, issued by the House Armed Services Committee in its consideration of the National Defense Authorization Act for Fiscal Year 1995, directed the US Government Accountability Office (GAO) to examine several issues related to the DoD's administration of its animal research programs, specifically, how the DoD was addressing unnecessary duplication of research done elsewhere and how it incorporated the commonly known and accepted 3 Rs.[30] Upon completion of this evaluation, via the GAO Report to Congressional Committees entitled *DoD Animal Research: Improvements Needed in Quality of Biomedical Research Database*,[31] the GAO recommended that the Secretary of Defense continue to take steps to improve the BRD; changes were suggested to ensure public accountability.

The GAO reported that the data collection and reporting procedures should be modified to ensure that the BRD contains accurate, detailed information about individual animal research projects, including information on the number and species of animals used in each project, the research goals and justification, and the pain categories for each project. The GAO also recommended that a uniform reporting format be used for all projects.[31]

Ongoing Department of Defense Regulatory Revisions

While Congress continues to assess and reassess the status of the DoD animal research program, and the DoD repeatedly modifies procedures to address concerns, the public and animal welfare groups still raise questions about whether the DoD uses animals appropriately, which prompts further government evaluations. In 1999, the GAO produced another report, *DoD Animal Research: Controls on Animal Use Are Generally Effective, but Improvements Are Needed*.[32] In this report, the GAO again addressed potential unnecessary duplication of research.

Two other specific recommendations, which were adopted by the DoD, were to (1) amend the DoD standard protocol format requiring researchers to identify refinement alternatives that were considered but not adopted (and to explain why they were not adopted) and (2) make another change in the literature search requirement, necessitating a search of the BRD and either the Federal Research in Progress database or the Department of Health and Human Service's Computer Retrieval of Information on Scientific Projects database.[28,33,34]

A significant 2005 revision to the DoD Directive 3216 was the requirement for all DoD institutions housing animals for RDT&E or training to attain and maintain AAALAC accreditation. What was a recommended practice became a required action. In 2010, the DoD Directive 3216 was updated and became DoD Instruction 3216.01 (DoDI), which requires institutions to have a quorum including at least one veterinarian and one nonaffiliated member (or his or her alternate) to be present at all IACUC meetings. Until this time, the attendance of nonaffiliated members was highly encouraged but not required. These standards exceed regulatory requirements and industry standards, indicating the DoD's dedication to humane care for animals used in research and training.[1]

In 2009, a bill to promote the Battlefield Excellence through Superior Training (BEST) Practices Act was introduced in Congress, which, if enacted, would have required a similar annual report to Congress and would have prohibited use of animals in combat-trauma training no later than October 2016. Although a phase-out date for animal use in combat-trauma training did not make it into the National Defense Appropriations Act for Fiscal Year 2013, the BEST Practices Act directly influenced its language by directing the DoD to report on their strategy to address transitioning away from animal use in certain medical training scenerios.[35,36]

Continued animal welfare group pressure on Congress to limit the use of animals in combat-trauma training led to further DoD direction to implement a strategy "to refine, reduce, and when appropriate, replace the use of live animals in medical education and training."[35(p188)] Congress requested an initial report be submitted by the Secretary of Defense by March 2013 and an additional annual report on the development and implementation of human-based training methods (such as use of simulators that better replicate human anatomy, moulage, simulated combat environments, and human cadavers) be submitted beginning in 2014.[35]

TRAINING OF MILITARY LABORATORY ANIMAL VETERINARIANS

The Army is estimated to be one of the top three largest employers of laboratory animal veterinarians in the world (e-mail communication from Melvin Balk, Executive Director, ACLAM, to Lieutenant Colonel Brett Taylor, chapter author, October 2012). Consequently, its residency program has significantly impacted the training of laboratory animal veterinarians throughout the entire United States.

In 1999, reportedly 32.7% ACLAM Diplomates (208 of the 636) had received training or experience while on active duty in one of the uniformed services (e-mail communication from Lieutenant Colonel [Retired] Susan Goodwin, former Director of the US Army LAM Residency Program [USALAMRP] to Lieutenant Colonel Brett Taylor, chapter author, September 2012).

As of 2012, the total number of ACLAM Diplomates increased to 872, and the percentage of these Diplomates who were trained in the uniformed services decreased to 11.5%.[37] This change reflects an increase in the number of civilian LAM residency programs and candidates across the nation during this period while the uniformed services' program (currently composed only of Army candidates) has remained largely unchanged in size, making the DoD's contribution proportionately smaller.

History of the Army's Laboratory Animal Medicine Residency Program

For an aspiring VCO, the transition from Area of Concentration code 64A (field Veterinary Services officer) to 64C (veterinary LAM officer) begins upon selection for the Long-Term Health Education Training (LTHET) program, generally at about the 5-year point in his or her career.[38] A major recruitment venue for all of the veterinary research advanced training programs is the Army's Research and Development Short Course. Instituted in the mid-1990s, this 1-week course invites prospective candidates to the Washington, DC, area and is designed to introduce VCOs to the specialties of pathology, laboratory animal medicine, and comparative medicine. The course provides candidates with a more indepth view of these specialties before they decide to apply to a particular LTHET program. The LAM Consultant to the Army Surgeon General (typically the specialty's most senior officer) is responsible for recruiting junior VCOs into the specialty.

The first formal training program for civilian veterinary specialists in this field was developed in 1960 at Bowman Gray Medical School.[39] This civilian program was followed closely afterward by the establishment of the first uniformed services' training program in 1961, under the auspices of the US Air Force School of Aerospace Medicine (USAFSAM) at the former Brooks Air Force Base in San Antonio, Texas. This program, developed by Air Force Colonel Robert Hummer, occurred in consultation with the faculty and staff of Texas A&M University. The 2-year program included coursework at the university, along with 15 months of instruction, residency training, and thesis research at USAFSAM. Upon completion, the student was awarded a Master of Science degree in LAM from Texas A&M and a residency certificate from USAFSAM. The program was discontinued in 1975 when the Air Force determined it was more economical to send students to other established civilian universities. Thirty-nine individuals completed the USAFSAM Texas A&M program; the last residents of the program graduated in 1977.[40]

In the US Army, veterinary-supported research was in place as early as the 1950s, and by the 1960s, a more structured but still informal, on-the-job-type training program existed at Ft Detrick, Maryland. This program was mentored by one of the ACLAM "founding fathers," Dr Melvin Rabstein, a 1937 graduate of the University of Pennsylvania veterinary college. In 1966, a more formal program was proposed by Dr Robert Whitney while assigned at Edgewood Arsenal, Maryland; Dr Whitney would later serve as Acting Surgeon General of the United States from July to September 1993.

In 1968, the Edgewood program became the first program officially sanctioned by a US Veterinary Corps Chief (Colonel Wilson Osteen). Dr Harry Rozmiarek and Dr Bill Cole were the first graduates of the official Army Edgewood program in 1971. Dr Rozmiarek immediately took over as director upon graduation from the program and served in this position from 1971 to 1972 (e-mail communication from Dr Harry Rozmiarek, former Director of the US Army Edgewood LAM training program to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Edgewood remained the primary location for LAM training in the Army until 1974 when Walter Reed Army Institute of Research (WRAIR) began a LAM training program of its own. Dr Robert Beattie, Kansas State University veterinary college graduate, class of 1964, was the original director of this program, and he was later joined by Dr Cole to fully implement the program. The centerpiece of the program was the special topics seminar series, which remains in existence today.

Dr Rozmiarek went on to establish an additional formal training program at Ft Detrick in 1976, which combined the core seminar series with clinical and administrative training conducted at the Army's premiere biodefense laboratory: the US Army Medical Research Institute of Infectious Diseases (USAMRIID). The program also established a liaison with Pennsylvania State University; residents spent 12 to 18 months doing university course work at Pennsylvania State and then spent the remainder of the 4-year program at Ft Detrick (e-mail communication from Dr Harry Rozmiarek, former Director of the US Army Edgewood LAM training program to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Because of the physical proximity of Ft Detrick, WRAIR, and Edgewood, a joint program, designated the Combined Laboratory Animal Medicine Program, was established in 1984. Core and special topics seminars were presented by residents and board-certified mentors once weekly each academic year. This 4-year LAM residency remained in effect from 1984 to 1995.[40]

Starting in 1996, the Army residency was converted to a 3-year joint curriculum with the PHS at the Uniformed Service University of the Health Sciences (USUHS), which also awarded a concurrent Master of Public Health (MPH) degree. However, since didactic work for the MPH option consumed one full year of the program, residents had to maintain an accelerated pace of study in the practical application of LAM throughout the second and third years, in order to complete the joint curriculum. Complicating matters further, from 1996 to 2000, the MPH was sometimes considered a 2-year program by the PHS but a 3-year program by the Army. Because of very low participation by PHS students and confusion about program management, the US Army dissolved the joint curriculum program between 2000 and 2002 (email communication from COL [Retired] Terry Besch, former Army Consultant to The Surgeon General for Laboratory Animal Medicine to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

In 2003, the Army provided separate options for the residents: pursue a university curriculum (combined MPH and LAM residency) or pursue the traditional model (LAM residency only). Also since 2003, residents have been assigned to one of the local DoD laboratories for 1 to 2 years of practical on-the-job training experience, which is required for candidates to achieve board eligibility status by ACLAM.[41]

In keeping with the traditional view of the early, long-established program, this year of experience is still referred to as the "fourth year" of the program because officers do not go on to post-residency assignments until the year of experience is complete, and they have (ideally) passed the ACLAM board examination. Residents in this final year typically form a weekly study group to prepare for the board examination. (See also Chapter 15, Veterinary Pathology, for information about the veterinary pathology residency program.)

Current Army Laboratory Animal Medicine Residency Experience

Upon acceptance into the LAM LTHET program, the LAM resident is assigned to one of five residency sites, all of which are located in the greater Washington, DC, area. In order of size from largest to smallest in terms of daily animal census, these five residency sites are as follows: WRAIR, USAMRIID, USUHS, the Armed Forces Radiobiological Research Institute (AFRRI) in Bethesda, Maryland, and the US Army Medical Research Institute of Chemical Defense (USAMRICD) at Edgewood. The total number of residents assigned to these sites at any time does not exceed 20 candidates, and the minimum ratio of one boarded Diplomate per every three residents is maintained at each location.[42]

There is an overall director of the USALAMRP, and each location also has its own USALAMRP site director. The program incorporates a Laboratory Animal Medicine Residency Advisory Committee (LAMRAC), which meets quarterly to discuss program issues and review student progress. The LAMRAC is comprised of the USALAMRP director, deputy director, and individual site directors. The LAM consultant (discussed in more detail later in this section) is invited to the LAMRAC in an advisory capacity.

Both of these training programs (MPH and non-MPH options) are 36 months in length. During this period, the residents meet (and in many cases exceed) the requirements set forth by ACLAM.[41] They are exposed to 340 to 380 hours of didactic training via the US Army LAM seminar series, journal reviews, and reviews of the various ACLAM-authored laboratory LAM textbooks (the "blue books," so called because of their historically blue covers); they work 2,400 to 3,600 hours under the supervision of ACLAM Diplomates in a facility accredited by the AAALAC; and they design and conduct a research project for first-author publication in a peer-reviewed journal.[42]

Additionally, residents are encouraged to attend a variety of educational seminars and continuing education conferences offered by organizations such as the Association of Primate Veterinarians, the American Association for Laboratory Animal Science, the CL Davis Foundation, and many others. Certificates denoting successful completion of the program are conferred to the residents once residency program site directors are satisfied that candidates have met all requirements: didactic training, practicum experience, and research project.

While details of the residency experience vary from site to site, year one is typically a very intense time for new residents. From the very beginning, they are encouraged to begin after-hours study of the core regulatory and veterinary medical references while spending their days learning and performing a variety of medical and surgical techniques. Weekend and evening on-call duty is typically shared among residents at each site.

Responsibilities increase as officers progress through years two and three and become more integrally involved in ongoing research missions at their institute. Duty positions rotate among the residents each year and are typically distinguished by area of responsibility. Most residents are given the title Officer

in Charge (OIC) of a subdivision within the Veterinary Medical Department or Division. Examples include OIC of Nonhuman Primate Section; Surgery and Radiology; Small Animal (Rodent and Rabbit) Section; Large Animal Research Facility; or Research Protocol Support. Specific assignment titles vary by institute, depending on the organizational arrangements at a particular location.

A 2006 estimate reported that ACLAM candidates spend an average of 1,100 hours total in preparation for the board exam, including review of textbooks and study notes,[43] although as the basic body of laboratory animal medicine knowledge continues to expand over the years, the typical number of study hours required to pass the exam may expand as well. One method of board preparation that has proven to be effective in any setting is the previously mentioned study group.[44]

The weekly Army-sponsored study group has produced an exceptionally successful board-exam pass rate. As far back as current records exist (approximately 1971), 78% of candidates from the uniformed services' training program have successfully passed the board exam on their first attempt (e-mail communication from Lieutenant Colonel [Retired] Susan Goodwin, former Director of the USALAMRP to Lieutenant Colonel Brett Taylor, chapter author, September 2012), and 90% of these candidates passed on their second attempt. Since 1971, an impressive 96% of candidates from the Army have passed the board exam at some point, whether on their first or subsequent attempts. When comparing these success rates to the national average over the period of 2008 to 2012 (only about 55% percent of this group were successful on the first attempt), the military percentages loom even larger (e-mail communication from Melvin Balk, Executive Director, ACLAM, and former US Army Veterinary Corps officer, to Lieutenant Colonel Brett Taylor, chapter author, October 2012).

Additionally, between 1996 and 2012 (17 years), nine winners of the prestigious ACLAM Henry and Lois Foster Award for Academic Excellence were Army veterinarians who used study group resources. This award is presented each year to the board candidate with the highest exam score (e-mail communication from Lieutenant Colonel [Retired] Susan Goodwin, former Director of the USALAMRP to Lieutenant Colonel Brett Taylor, chapter author, September 2012).[37]

Assignments Following Laboratory Animal Medicine Residency

Following the successful completion of the USALAMRP, 64Cs (veterinary LAM officers) serve in a variety of utilization assignments. Currently, there are 30 different assignment locations around the globe, with 48 officer authorizations between them (Figure 14-1).

Many new graduates of the residency program head to clinical investigations programs. Clinical investigations programs are part of the military Graduate Medical Education program for medical doctors, typically at large military medical treatment centers: William Beaumont Army Medical Center (El Paso, Texas); San Antonio Military Medical Center (formerly, Brooke Army Medical Center, San Antonio); Tripler Army Medical Center (Honolulu, Hawaii); Eisenhower Army Medical Center (Ft Gordon, Georgia); and Madigan Army Medical Center (Joint Base Lewis-McChord, Washington).

These assignments are ideal positions for the newly boarded veterinarian as they are small programs but still require all the components of an AAALAC-accredited animal care and use program (ACUP). The medical management and leadership skills of these new 64Cs are tested as they become the attending veterinarians, responsible for the well-being and clinical care of animals used in RDT&E and training, with a much smaller staff of ancillary experts (eg, laboratory animal technicians, IACUC members, and facility engineers) than they are accustomed to from their residency experiences.

Other small programs ideally suited for newly boarded veterinarians include the US Army Public Health Command (Aberdeen Proving Ground, Maryland), Navy Clinical Investigations Services (San Antonio; Portsmouth, Virginia; and San Diego, California), the Keesler Air Force Base Clinical Research Laboratory (Biloxi, Mississippi), Wright-Patterson Air Force Research Laboratory (Dayton, Ohio), US Army Research Institute of Environmental Medicine (Natick, Maryland), and Joint Special Operations Medical Training Center (Ft Bragg, North Carolina).

More senior officers (ie, majors who have been recently promoted) tend to serve as department chiefs at larger institutes such as USAMRIID, WRAIR, or the Tri-Service Research Laboratory in San Antonio or in deputy director positions at smaller institutes such as AFRRI, USUHS, or USAMRICD. Follow-on assignments provide a continual increase in the officers' scope of responsibility and may include any of the following job opportunities: (*a*) overseas and joint billets such as the Naval Medical Research Units in Cairo, Egypt, or Lima, Peru, and the Armed Forces Research Institute of Medicine in Bangkok, Thailand; (*b*) assignments focused on oversight and regulation of programs or contracts such as positions at the Office of the Army Surgeon General, US Army Medical Depart-

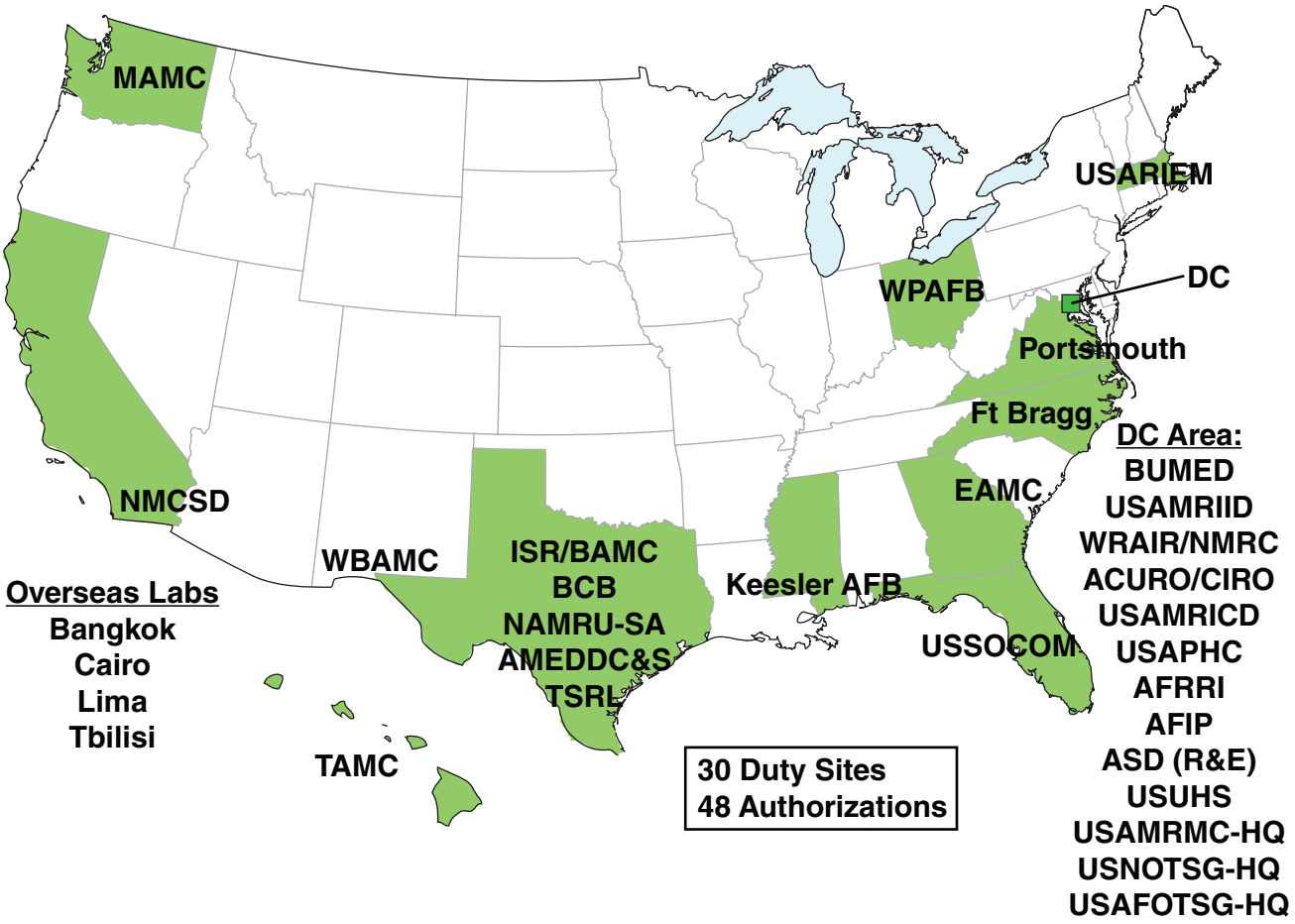

Figure 14-1. US Army Laboratory Animal Medicine Duty Sites and Authorizations.
Data courtesy of Colonel Brian Ketzenberger, Consultant to the Army Surgeon General for Laboratory Animal Medicine.

ment Center and School, Health Readiness Center of Excellence (AMEDDC&S, HRCoE), or US Army Medical Research and Materiel Command Animal Care and Use Review Office.

After one or two assignments following board certification, most officers are senior majors or lieutenant colonels with experience in a variety of programs. Lieutenant colonels are then typically assigned as directors of smaller programs such as USAMRICD, USUHS, AFRRI, or the US Army Institute of Surgical Research or Naval Medical Research Center (co-located with WRAIR). By the time officers have 18 to 20 years of service, they are usually either senior lieutenant colonels or colonels capable of serving in the most challenging positions in the field that include Consultant to the Navy, Air Force, or Army Surgeon Generals; directors of Veterinary Medicine Divisions at large institutes such as WRAIR or USAMRIID; or Director of the Army's Animal Care and Use Review Office (ACURO) under USAMRMC.

The consultant and ACURO positions are highly engaged in regulatory oversight activities for both intramural and extramural ACUPs. As the Army has been historically responsible for oversight of 70 to 80% of all funding used by ACUPs across the DoD,[45] the ACURO is a key assignment. Its director is often dual-hatted as the director of the USLAMRP.

The Consultant to the Army Surgeon General, typically one of the most senior and experienced LAM officers in the Army, is appointed by the Army Surgeon General (as compared to being assigned as a matter of course to the Air Force or Navy consultant positions). The Army Consultant is responsible for recruitment of officers into the specialty and recommending assignments for all officers from residents to the most senior officers to LAM duty positions. When making such recommendations, the Army Consultant attempts to put the right officer in the right place at the right time within the constraints of the available inventory of officers. The Army Consultant is also the DoD's senior advisor for all laboratory animal matters.

ANIMAL CARE AND USE IN THE DEPARTMENT OF DEFENSE

Laboratory animal veterinarians are responsible for clinical care and promotion of animal well-being at all times and during all phases of an animal's life, which requires an indepth understanding of physical, physiological, and behavioral indicators of health, all of which vary considerably across the species commonly used in research.[6] At times, their role as advocates for the animals may place laboratory animal veterinarians at odds with investigators and research staff in pursuit of scientific discovery or therapeutic developments, but, ideally, research scientists and the laboratory animal veterinarian work together to ensure appropriate and humane care and use of animals.

It has been said that the reliability of research data is only as good as the least reliable link in the chain of procedures used to derive it,[39] and the laboratory animal specialist's role in ensuring the health and well-being of the animals used in research is an absolutely critical link in that chain.

The role of the attending veterinarian (ie, the individual within an institute or program with the responsibility and the authority to ensure appropriate animal care, handling, and humane use) is specifically defined and mandated by federal law[12] and is a position generally held by the senior laboratory animal specialist in each of the DoD's institutes and programs. There may be many veterinary specialists working together in larger DoD facilities, but overall responsibility for the veterinary care program rests solely with the appointed attending veterinarian at each location. The individual in this position provides guidance and training to ensure appropriate procedures are followed throughout the procurement, transportation, husbandry, handling, medical treatment, immobilization, sedation, analgesia, anesthesia, surgical care, and euthanasia of animals within a particular institute or program.

Historically, Army laboratory animal medicine veterinarians have had unique opportunities to influence and shape the practice of animal research across the globe. For example, as the Director of the Veterinary Medical Department at USAMRIID in the late 1970s, Colonel Harry Rozmiarek helped establish the Laboratory Animal Use Review Committee with a structure and function that closely resembled what would later be described as an Institutional Animal Care and Use Committee (IACUC) in the 1985 PHS policy (e-mail communication from Colonel [Retired] Harry Rozmiarek, former Director of the US Army Edgewood laboratory animal medicine training program, to Lieutenant Colonel Brett Taylor, chapter author, April 2013).[40] In 1984 and 1985, Colonel Rozmiarek, along with several other 64Cs, also gave presentations at regional workshops conducted by the Scientists Center for Animal Welfare on consensus recommendations for effective animal care and use committees.[46]

Other contributions made by the Army include the assistance Colonel (Retired) Clifford Roberts, a former LAM veterinarian with the Walter Reed Army Institute of Research, provided to the nation of Kenya in developing modern animal research regulations in the early 1990s (e-mail communication from Colonel [Retired] Clifford Roberts to Lieutenant Colonel Brett Taylor, chapter author, April 2013). Additionally, Colonel Roberts assisted in developing the first breeding colony of cynomolgus macaques (*Macaca fascicularis*) in the country of Malaysia.[47] More recently, chapter author Lieutenant Colonel Brett Taylor had the opportunity to train laboratory animal scientists in the former Soviet Republic of Georgia and assisted them in standing up their own Georgian Association for Laboratory Animal Science, a new scientific member organization of the International Council of Laboratory Animal Science Associations as of 2016.[48]

Animal Care Considerations of Special Concern to the Department of Defense

Animal Mission Challenges

Several animal care challenges evolve from the types of research conducted by the DoD. In many cases, these challenges are unique to the missions of the institutes designed to conduct such studies, but some of them are consistent to the DoD as a whole. For example, personnel turnover is one of the pressing DoD-wide challenges. Military laboratory animal veterinarians and enlisted animal care technicians must rotate duty assignments approximately every 3 years,[38] which results in occasional periods of personnel underlap and a consistently recurring threat to institutional memory. Additionally, the execution of classified research projects at some facilities necessitates considerable security clearance procedures for all IACUC members as well as specially designed secure areas for the review of classified protocols and the execution of classified research.

Some examples of mission-specific challenges relate to the use of highly lethal chemical warfare agents at USAMRICD. One such challenge has been the modification of caging for larger animals (ie, swine and nonhuman primates) to fit inside a chemical

hood. This equipment must pass rigorous industrial hygiene monitoring for maintaining proper laminar flow inside the hood to meet occupational health and safety standards. Ensuring appropriate animal welfare while conducting experimental manipulations inside biological safety cabinets such as blood collection under pole and collar restraint is also difficult to accomplish (e-mail communication from Lieutenant Colonel Richard Probst, Chief, Research Support Division, USAMRICD, to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Additionally, since chemical agent exposure of animals entails increased risk to the personnel who must handle them for biosampling or examination, a chemical surety team carefully manages the chemical agent and provides training to agent users and safety orientation to all personnel granted access to agent use areas. Methods for handling the animals are very clearly described in stepwise fashion and thoroughly reviewed at multiple levels within the organization. Personnel authorized to work in a room with an open agent keep an M-40 protective mask at arm's reach in the event of power or ventilation failure. The chemical surety team also closely monitors these operations and tracks room usage on a board that is visible to all who come and go. Agent use and storage areas have considerable security measures in place as well (e-mail communication from Lieutenant Colonel Richard Probst, Chief, Research Support Division, USAMRICD, to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Similar to the procedures in place at USAMRICD, USAMRIID uses a closely monitored surety program to ensure the safety of the general public and the reliability of workers engaged in all studies involving use of highly pathogenic biological agents and toxins.[49,50] For example, access to the biocontainment suites at USAMRIID requires a considerable amount of background training, immunizations for relevant pathogens, and a lengthy period of interviews and observation of personnel, all of which require months to complete. The military's relatively short 3-year assignment cycle thus causes occasional challenges in maintaining veterinary officers with full biocontainment access, along with biocontainment-qualified technicians and caretakers.

Additional challenges arise periodically as new technology and items of equipment are introduced for use in conventional animal housing and husbandry, which must then be adapted for biocontainment use. Because of these ongoing challenges and the need for constant innovation, USAMRIID has remained at the forefront of a wide variety of advances in biocontainment procedures and technology since its inception (e-mail communication from Colonel Pedro Rico, DVM, Director of Veterinary Medicine Division, USAMRIID, to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Another category of mission-specific challenges exists at the AFRRI that relates to the use of ionizing radiation in research protocols. In addition to maintaining worker safety in this environment, the two most challenging aspects of animal care are performing post-irradiation blood draws and maintaining animal food intake and hydration. Since much of radiobiology work is geared towards finding novel biomarkers or measuring known markers in blood samples, multiple blood draws are critical. However, as platelet counts fall because of a compromised hematopoietic system from radiation exposure, stopping the bleeding caused by even minor blood draws from superficial veins becomes difficult. Given these circumstances, even minor, superficial scratches can become opportunities for sepsis. Following radiation exposure, animals also may lose their desire to eat and have decreased ability to digest and absorb what is being eaten (e-mail communication from Lieutenant Colonel Rebecca Holt, Head of the Veterinary Sciences Department, AFRRI, to Lieutenant Colonel Brett Taylor, chapter author, April 2013). Critical nursing care of such animals is paramount under these conditions.

Animal Procurement and Transportation

Since it is rarely economically feasible for the DoD to maintain its own breeding colonies (historical exceptions include the Strain 13 guinea pig colony at USAMRIID and various small rhesus macaque colonies worldwide), the DoD relies heavily on commercial vendors to provide animals. Thus, the animal procurement process typically begins with an evaluation of the quality of potential vendors' animals. Vendors of purpose-bred research animals (USDA Class A dealers) provide information to DoD veterinarians and other prospective buyers, describing the pathogen status of colonies or individual animals, along with any relevant clinical history. The laboratory animal veterinarian's responsibility and area of expertise in this process is the development of specific requirements for the animals to be purchased (eg, genetic background, specific disease-free status, preimplanted telemetry devices, and other requirements specified by investigators for a particular project).

The responsibility for writing contracts, placing them out for public bidding, and handling any contractual actions lies with trained DoD contracting officers who are advised by LAM veterinarians. Once

animals arrive at an institute, LAM veterinarians become responsible for animal receipt and quarantine and ensure that vendors meet all contract specifications for animals purchased. (The subsequent section of this chapter covers quarantine and other receipt responsibilities.)

The vendor typically arranges transportation of animals purchased by the government. These vendors are required to comply with a number of US regulatory agencies and international bodies, including the USDA, International Air Transport Association, US Fish and Wildlife Service, and Convention on International Trade in Endangered Species of Wild Fauna and Flora.[12,51,52,53]

The DoD also must comply with these same laws on the rare occasions when it moves animals using government transportation assets. Typically, this type of DoD transport occurs only for small numbers of animals for short distances (eg, collaborative research between the five DoD institutes located in the greater Washington, DC, area). However, in the event of an emergency affecting DoD animal facilities, each institute typically has the capability to transport large numbers of animals specified as part of its internal disaster management plan. The attending veterinarian has the responsibility to oversee all of these processes and ensure that procurement and transportation of research animals are performed in accordance with all applicable laws, rules, and regulations.

Quarantine and Acclimation

Within the setting of a facility performing RDT&E or training using animals, the word "quarantine" refers to the separation of newly received animals from those already present in the facility, and quarantine is performed in order to prevent the spread of any infectious contaminants that may be harbored by new animals and potentially spread to animals already housed in the facility. Veterinary personnel evaluate the general health and pathogen status of all newly received animals using procedures that reflect acceptable veterinary medical practices, along with all federal and state regulations applicable to zoonoses.[54] Like their civilian counterparts, military veterinarians obtain information from vendors before or during procurement in order to define the potential risks to personnel and animals in the colony, establish an appropriate quarantine period and procedures, determine whether any therapeutic intervention is required during quarantine, and, in the case of rodents, may even determine whether special procedures (eg, cesarean rederivation or embryo transfer) are necessary to secure animals free of specific pathogens.[6]

In addition to an appropriate quarantine period, newly received animals are given a period of time for physiologic, behavioral, and nutritional acclimation before use.[55] The length of this acclimation period is dependent upon the species, the duration of their transportation, and their intended use. The need for such acclimation has been demonstrated in a wide variety of species and serves to ensure that the animals have recovered from any distress experienced during transit.[6]

Even after completion of quarantine and acclimation periods, most species are kept physically separated from others present in the facility in order to avoid interspecies disease transmission and eliminate the potential for anxiety and physiologic changes due to interspecies aggression.[56] This is most often accomplished through the use of separate rooms for different species; however, cubicles, laminar flow units, and cages with filtered air or separate ventilation may be equally as effective and are often used to accomplish species separation.[39]

Husbandry and Enrichment

As is true for civilian organizations, all species maintained in each of the DoD's animal facilities are provided with appropriate food, housing enclosures, husbandry techniques, and environmental enrichment that takes into account their physical, physiologic, and behavioral needs. Given the large numbers of individual animals and the wide variety of different species maintained at each facility and across the DoD as a whole, this is a considerable effort that would be difficult without the assistance and expertise of dedicated animal caretakers and veterinary technicians. Many animal caretakers, along with the majority of veterinary technicians working in the field of laboratory animal science across the DoD, are certified by the American Association for Laboratory Animal Science. This certification recognizes the animal caretakers' and veterinary technicians' special skills and establishes them as among the most competent animal care professionals in their field.[57]

In the course of their duties, caretakers and veterinary technicians become very familiar with individual animals and are often the first to notice subtle changes in appearance or behavior that may indicate illness or injury. Thus, their involvement in the performance of daily rounds enhances the quality of care provided to each animal. Additionally, their assistance in developing environmental enrichment programs and in performing procedures to Good Laboratory Practices (GLP) standards is critical to the excellent quality of DoD research.

Preventive Medicine and Biosecurity

Effective programs in preventive medicine and biosecurity enhance the research value of animals in an institute by minimizing disease-related sources of variation between study groups. Preventive medicine consists of all the various policies, procedures, and equipment related to the quarantine and separation of animals by species, source, and health status. Animal biosecurity consists of the measures taken to identify, contain, prevent, and eradicate known or unknown infections that cause clinical disease or alterations in animal physiology or behavior.[6]

Biosecurity practices are applicable in all instances when animals are used in research, but these practices become critically important when large numbers of animals are maintained in a single facility. However, some DoD-specific factors necessitate even higher levels of preventive medicine and biosecurity practices, particularly those in the context of studies designed to develop new therapeutics against biological warfare agents.

Surveillance, Diagnosis, and Treatment of Disease

All DoD-owned animals are observed by trained personnel at least daily for signs of illness, injury, or abnormal behavior in accordance with industry standards[6] (veterinarians, animal caretakers, and veterinary technicians all contribute to these evaluations). Observations are performed even more frequently when animals are ill, recovering from a surgical procedure, or approaching a study endpoint. Unexpected deaths and signs of illness or distress are investigated promptly, and animals displaying signs of contagious disease are isolated from healthy animals. However, if an entire room or housing enclosure is believed or confirmed to be exposed to an infectious agent (eg, *Mycobacterium tuberculosis* in nonhuman primates or *Syphacia* infestation in rodents), the group is generally kept together throughout the treatment and eradication procedures.[6]

The principal methods for detecting microbial infections in animal populations are serologic assays, but many other methods (eg, polymerase chain reaction, microbial culture, clinical chemistry, and even histopathology) may be used to make or confirm a diagnosis. Laboratory animal veterinarians must be subject matter experts on infectious diseases for each species, along with the constantly evolving methods used to identify and treat such diseases. In the event that a disease or infectious agent is identified within the animal colony, the veterinarian must make therapeutic decisions in coordination with scientific investigators in order to maintain a balance between the requirement for healthy animals and the requirement for minimization of adverse or unexpected effects on the RDT&E or training program.

Clinical and Emergency Care

Treating and maintaining the health of laboratory animal species often requires specialized skills and knowledge beyond those of veterinarians in traditional companion animal settings. Two examples are the treatment of bite wounds in primates housed under Animal Biosafety Level 3 biocontainment and the placement and maintenance of telemetric implants and indwelling vascular catheters in small rodent species.

Because a wide variety of differences exists between veterinary care programs among the various DoD facilities that use animals (which correspond to the DoD's wide variety of institutional missions and species used), LAM veterinarians also must be skilled at providing veterinary care to a wide spectrum of animal species undergoing diverse RDT&E or training methodologies. Similar to practices at civilian institutes, the attending veterinarian must institute procedures to ensure that animals are provided emergency care both during and outside of regular business hours.[6]

Restrictions on the shipment of animals or tissues due to the Convention on the International Trade in Endangered Species of Wild Fauna and Flora and benefits sharing contract requirements with host-nation governments (such as those in place at the AFRIMS facility in Thailand) may impact the ability of veterinarians to send biopsies and tissue samples from overseas laboratories to the United States for definitive diagnoses of disease. Consequently, some overseas facilities are forced to breed their own animals for use in research. Maintaining a high-quality research animal breeding colony is an expensive and labor-intensive method of acquiring research animals when compared to purchasing them from specialized and established dealers—and one that presents its own set of requirements for the clinical and emergency care of the animals used in such colonies (e-mail communication from Lieutenant Colonel Robin Burke, Chief, Department of Veterinary Medicine, Armed Forces Research Institute of Medical Sciences, to Lieutenant Colonel Brett Taylor, chapter author, April 2013).

Procedures to Reduce Pain and Distress

The alleviation of pain and distress associated with procedural and surgical protocols is an integral component of veterinary medical care in the laboratory setting. Unrelieved pain leads to unacceptable

levels of stress in animals, making the proper use of anesthetics and analgesics in research animals an ethical and scientific imperative. Animal species vary considerably in their responses to pain; thus, pain assessment criteria differ accordingly.[6] The DoD adheres to the PHS policy, *US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, which is comprised of nine principles, one of which asserts that (in the absence of evidence to the contrary) procedures which cause pain in humans should be considered to also cause pain in other species.[10]

"Distress" is generally described as an aversive state in which an animal fails to cope or adjust to the various stressors it encounters.[6] In the absence of immediately observable pathologic or behavioral alterations, distress can be challenging for the veterinarian to definitively recognize. Both duration and intensity of the inciting stimuli are important considerations when trying to prioritize the attention to and treatment of animal distress. For example, an injection requiring brief immobilization may produce an acute level of distress lasting only seconds while the long-term individual housing of a social species in a metabolic cage may produce chronic distress. As in the case of veterinary intervention to treat infection, veterinarians should make any decisions regarding the relief of pain and distress in coordination with investigators to maintain the balance between the requirement for healthy animals and the requirement for minimization of adverse or unexpected effects on the RDT&E or training program.

Figure 14-2. Researcher using a powered air-purifying respirator (PAPR). Ausculation of animals using a stethoscope is not possible while wearing a PAPR.
Photo courtesy of the US Army Medical Research Institute of Infectious Diseases, Ft Detrick, Maryland.

The assessment of both pain and distress in animals is further complicated by reduced-access environments such as those necessitated by the use of biological, chemical, or radiological exposure in research animals. The auscultation of heart or lung sounds is impossible in a powered air-purifying respirator or PAPR hood, much less in a BioSafety Level 4 "blue suit" such as those worn in biocontainment suites at USAMRIID (Figures 14-2 and 14-3). Additionally, the ability to palpate animals is impaired by the multiple layers of gloves worn in these environments. Direct observation and intervention for animals during the process of their exposure to radiation (such as in research performed at AFRRI) or chemical warfare agents (such as in research performed at USAMRICD) can be extremely challenging. All such considerations

Figure 14-3. Another view of a powered air-purifying respirator. Researchers also use BioSafety Level 4 "blue suits" (not pictured). Ausculation of animals using a stethoscope is also not possible while wearing a "blue suit."
Photo courtesy of the US Army Medical Research Institute of Infectious Diseases, Ft Detrick, Maryland.

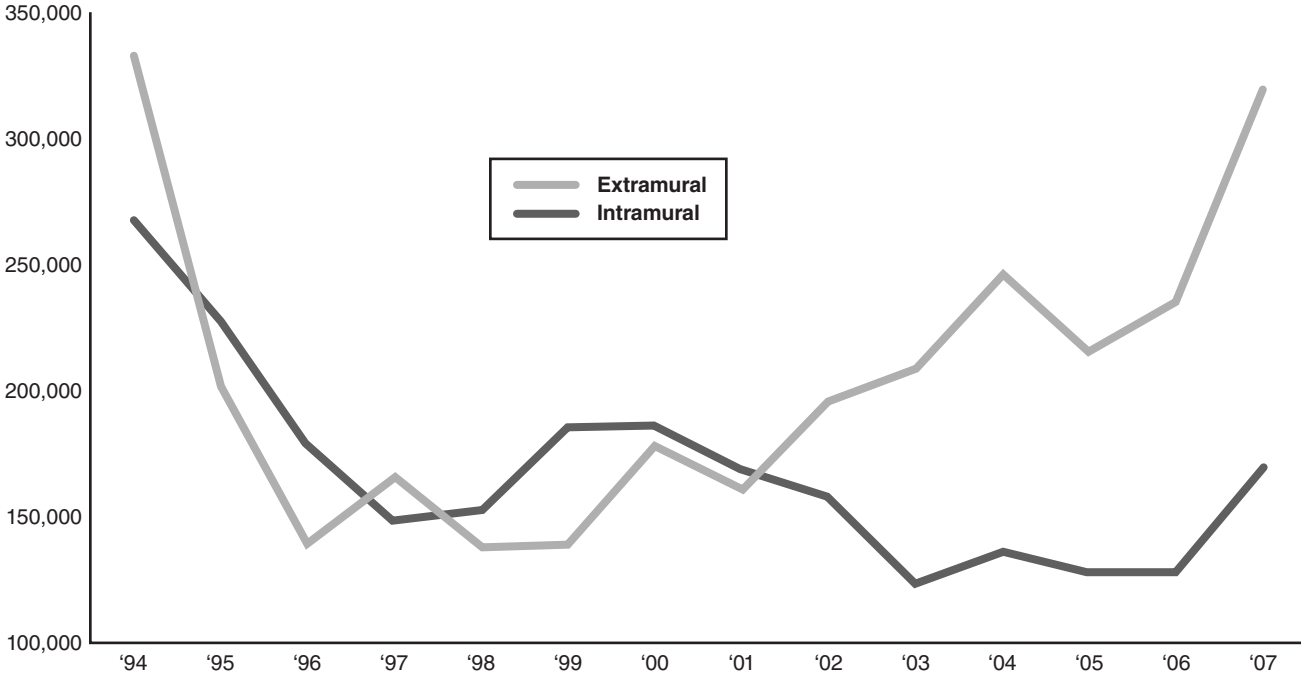

Figure 14-4. US Department of Defense Animal Usage, 1994-2007.
Data courtesy of the Assistant Secretary of Defense for Research and Engineering, Human Performance, Training, and Bio-Systems. http://www.dtic.mil/biosys/au.html. Accessed April 9, 2013.

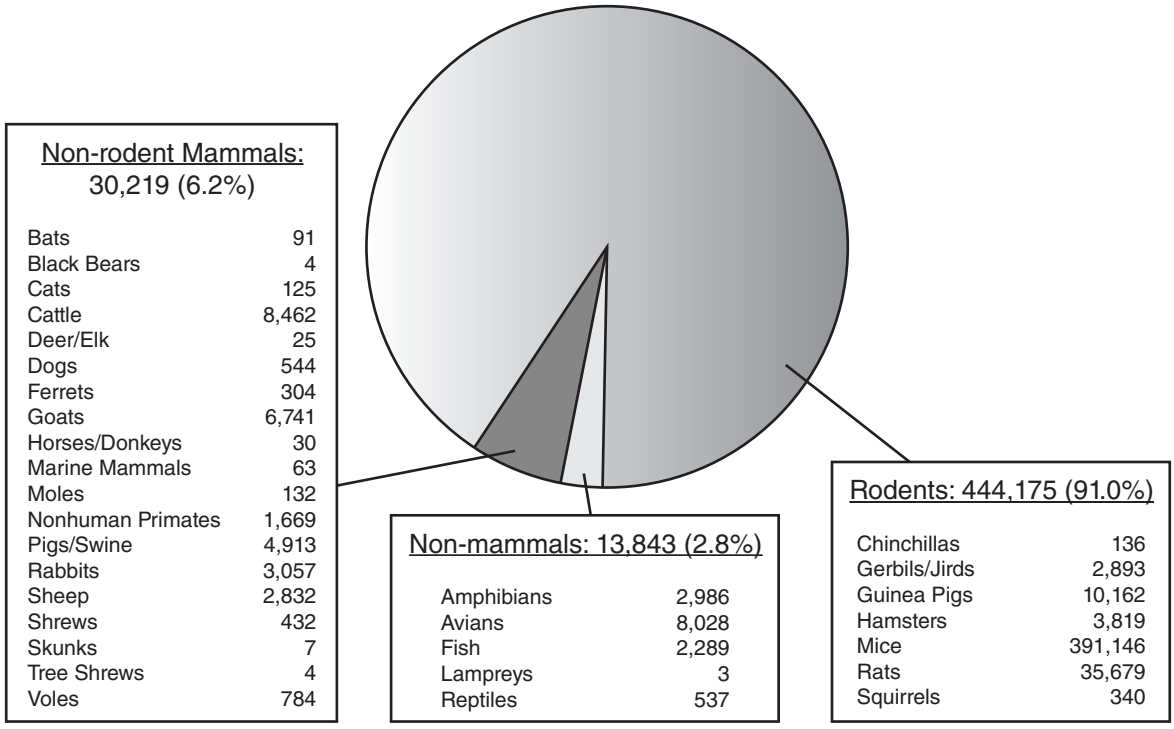

Figure 14-5. US Department of Defense Animal Usage by Species, 2007.
Data courtesy of the Assistant Secretary of Defense for Research and Engineering, Human Performance, Training, and Bio-Systems. http://www.dtic.mil/biosys/au.html. Accessed April 9, 2013.

relating to the monitoring and reduction of pain and distress must be specifically addressed in the animal use protocol.

Euthanasia Procedures

Euthanasia may be directed by the veterinarian to relieve animal pain or distress that cannot be alleviated by analgesics or other treatments. Euthanasia may also be planned in advance as part of a protocol-specific endpoint (such as a defined point of tumor size or disease progression). As with civilian organizations and in keeping with the American Veterinary Medical Association guidelines on euthanasia, all methods of euthanasia employed within DoD facilities must predictably induce rapid unconsciousness and death while minimizing the distress and anxiety experienced by the animal.[58] The specific selection of agents and methods for euthanasia are dependent upon the species involved, the age of the animals, and the research objectives of the protocol.[6]

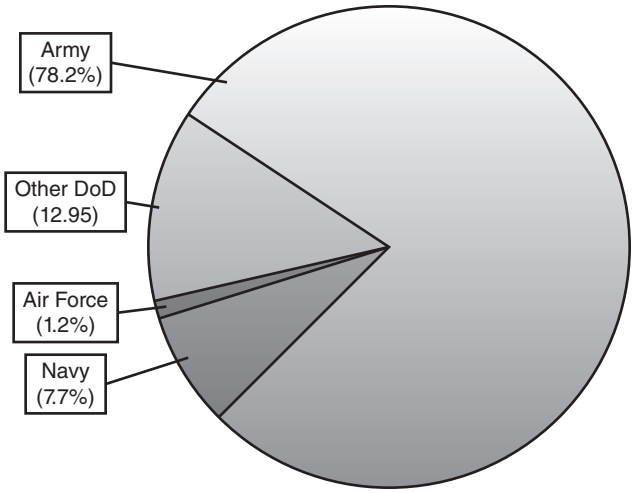

Figure 14-6. Animal usage by Department of Defense Service, 2007.
Data courtesy of the Assistant Secretary of Defense for Research and Engineering, Human Performance, Training, and BioSystems. http://www.dtic.mil/biosys/au.html. Accessed April 9, 2013.

Animal Usage Within the Department of Defense

Intramural animal use in the DoD is reported to the USDA on an annual basis. Since approximately 2002, more DoD work has been conducted in extramural programs than intramural. Figures 14-5 and 14-6 provide a summary and overview of all animal use for the purposes of research, development, testing, and evaluation and training from each of the branches of service. Although extramural animal use has been generally increasing since 1999, trends in intramural animal usage remain stable over that same period (Figure 14-4). The significant decline in both categories of animal usage from 1994 to 1996 is only the tail end of a trend of sharply decreasing numbers that started in at least 1987.[45]

Interestingly, the breakdown of the individual species used by the DoD has remained very similar over this same period of time. The most recent species-specific numbers available are depicted in Figure 14-5 and display a very clear preference (91%) for the use of rodents. In fact, mice alone account for approximately 80% of the total of all the animals used by the DoD in the year 2007.[45] Although the numbers differ slightly from year to year throughout the period from 1994 to 2007, the general percentages represented by each category (rodents, nonrodent mammals, and nonmammals) are similar.

Another pattern that has remained relatively unchanged across the past 14 years is the percentage of the DoD's total animal use that is performed by each service. Overall, the Army has a much more robust research and development program than the other services. In 2007 alone, the Army used more than three times as many animals as all other branches combined (Figure 14-6).[45]

The majority (92.1%) of the DoD's intramural animal use in 2012 consisted of animals such as reptiles, fish, rats, birds, or mice (primarily mice) that are not required to be reported to the USDA. Of the USDA-reportable animal use that was conducted in 2012, the majority occurred at four different facilities: USAMRICD (26.9%); USAMRIID (22.6%); AMEDDC&S, HRCoE (15.3%); and WRAIR (10.5%).[59]

DEPARTMENT OF DEFENSE ANIMAL CARE AND USE PROGRAMS AND COMPONENTS NECESSARY FOR PROGRAM SUCCESS

As with civilian organizations, trained personnel, excellent facilities, and strict regulatory compliance are all integral parts of any complete, successful ACUP. This section describes some other necessary attributes and common program requirements of military ACUPs that help these programs operate effectively and achieve excellence in animal care and use within the DoD.

Adaptable and Comprehensive Programs and Functional Areas

Throughout the world, ACUPs are unique to their particular institutes, which is also true in the DoD. Although many program components are common among various organizations, each institute's ACUP is tailored to its own research and accompanying missions. ACUPs must also be dynamic. As personnel and missions change; as standards and regulations evolve; and as research facilities, equipment, and methodologies advance, the ACUP is modified and adapted to support current operations utilizing up-to-date information and best practices.

Furthermore, an ACUP is comprehensive and includes the policies, procedures, standards, organizational structure, staffing, facilities, and practices adopted by an institution to achieve the humane care and use of animals by an organization.[6] ACUPs include all activities conducted by and at an institute that have a potential impact on the well-being of animals. Activities include animal husbandry and care, veterinary care, institutional policies and procedures, personnel and program management and oversight, occupational health and safety, IACUC functions, and animal facility design and management.[6] These activities are common to all ACUPs, including DoD programs; however, the extent and complexity of each specific functional area is determined by the size and scope of the individual institute and its particular research and mission focus. Large DoD biomedical research institutes (eg, USAMRIID, WRAIR, and USAMRICD) have more extensive animal care and use programs to cover their broader missions and a greater number of research and support personnel and functional areas than a smaller DoD clinical investigations facility supporting a military hospital's GME program for physicians. At larger institutions with more complex programs, responsibility for the day-to-day operations of program activities may be delegated to various departments or staff members. However, at smaller institutes, the attending veterinarian may primarily be responsible for most or all program activities.

A large centralized research facility may include all of the various functional areas as separate departments within the same institute. A decentralized program may spread the functional areas out among multiple facilities with each individual facility relying on others to perform those functions they lack internally. Smaller programs may utilize services of their parent organization or may contract out some functional areas to civilian entities. For example, a DoD Clinical Investigation Program with a Department of Clinical Investigation (DCI) supporting a military medical center may rely on the military hospital to provide certain services or a portion of various functional area services (eg, logistical, pharmacy, and pathology services or facility and medical equipment maintenance), or they may establish contracts with outside agencies to perform some of the more specialized services.

Furthermore, outsourcing services is not an all-or-nothing approach. There are different degrees of functional area services that may be provided by a supporting institute or by civilian vendors. As an example, the DCI may be able to perform certain blood analyses in-house such as complete blood counts and serum chemistry panels with its own equipment, but they may rely on the hospital's clinical laboratory to run other tests; specialized tests that neither the DCI nor the hospital laboratory is capable of performing would be sent out to a contract reference laboratory.

Flexible and Qualified Attending Veterinarians

To uphold appropriate oversight of these activities in accordance with relevant regulations, policies, and guidelines, the attending veterinarian needs to be adequately trained and experienced in laboratory animal science and medicine[6] and have direct or delegated authority over all animal activities. Regardless of how the attending veterinarians obtain their LAM training and experience, each veterinarian must be familiar with the species that fall within their scope of responsibility. As noted earlier in this chapter, because animal species may vary according to the institute, the mission, the research underway, and a particular period of time, the range of species-specific knowledge required to be a LAM veterinarian is extensive.

LAM veterinarians may be responsible for the health and well-being of common companion and agricultural species covered in most veterinary college curricula (ie, dogs, cats, horses, cattle, swine, sheep, goats, and poultry); traditional laboratory animal species (ie, mice, rats, hamsters, guinea pigs, rabbits, and nonhuman primates); more novel and specialized laboratory animal species (eg, laboratory fish, amphibians, transgenic rodents, miniature swine, and immunocompromised animals); exotic animal model species (eg, dolphins and sea lions); and even wild animals (eg, fish, wild birds, bats, and deer, as in the case of disease surveillance studies and field research).

Also, as previously highlighted in this chapter, just being familiar with the species is not enough. The attending veterinarian needs to understand proper husbandry and care standards; special regulatory requirements; appropriate handling and restraint procedures; suitable anesthesia, analgesia, and therapeutics;

and how various manipulations may or may not affect research data collection for any particular animal species specified by each RDT&E or training activity.

Specified Animal Care and Use Program Management and Oversight Responsibilities

The attending veterinarian plays a key role in managing the DoD ACUP and shares this responsibility with the institutional official and IACUC; all work together to ensure the program remains current and effective in supporting an institute's mission and humane use of animals. The attending veterinarian is primarily responsible for the health and well-being of all animals used in RDT&E and training by an institution.[6] This responsibility goes beyond just animal husbandry and veterinary care to include all aspects of the ACUP that have a direct or indirect impact on the lives of animals.

The institutional official is ultimately responsible for the overall ACUP and has authority to allocate resources necessary to support the program and is the signature authority for official documents and reports attributable to the institute's program.[6]

The IACUC is the local body responsible for oversight of the institution's ACUP. In addition to meeting frequently enough to effectively and efficiently carry out committee duties, the IACUC is also responsible for conducting semiannual reviews of the ACUP to include inspecting facilities that have an impact on animal care and well-being.[6] In addition to these local management authorities (ie, the attending veterinarian, institutional official and IACUC), DoD ACUPs fall under additional supervision from DoD component oversight offices. The primary DoD component oversight offices are those of the Army (Animal Care and Use Review Office, US Army Medical Research and Materiel Command); the Navy (Bureau of Medicine and Surgery, Veterinary Affairs); and Air Force (Office of Research Oversight and Compliance, Animal Use Program). DoD institutions must submit required documents and reports to their respective oversight office; in return, they receive correspondence, guidance, staff assistance visits, and compliance site visits from their respective oversight office.

Organizations that do not fall specifically under the Army, Navy, or Air Force include joint commands such as the US Special Operations Command (USSOCOM) or various geographic combatant commands (CCMDs) such as the Southern Command or Northern Command. With the exception of USSOCOM, little to no RDT&E or training occurs within the CCMDs. Historically, CCMDs have typically had one of the three primary oversight offices (Army, Navy, or Air Force) conduct animal use oversight activities under a memorandum of agreement or understanding. In 2016, the USSOCOM added a permanent 64C (LAM veterinarian) to its joint manning document and established a component oversight office within the Office of the SOCOM Command Surgeon.

Depending on the type of program and research, additional (both DoD and non-DoD) agencies may examine a particular DoD ACUP or a portion of that program. For example, institutions utilizing biological select agents or toxins (BSATs)[60] (as determined by the US Department of Health and Human Services and USDA) or institutes that utilize chemical agents in research receive additional inspections from DoD biological and chemical surety agencies (eg, the Army Medical Command and Department of the Army Inspector General)[49,50] or other governmental agencies (eg, the Centers for Disease Control and Prevention [CDC]). Institutions working with radioactive materials may be inspected by the Nuclear Regulatory Commission (NRC); programs performing GLP studies are inspected by the Food and Drug Administration or Environmental Protection Agency.

Regardless of the size of the institute and its accompanying ACUP or the type of RDT&E and training conducted, a multitude of requirements exist that must be adhered to; oversight occurs within the institute and by DoD oversight offices, nonmedical DoD entities (eg, the Inspector General), and extramural agencies (eg, the CDC, Nuclear Regulatory Commission, and AAALAC) as described above. Thus, the program's attending veterinarian must not only be trained and experienced in laboratory animal science and medicine,[6] but must also be well-versed in the various regulatory requirements, to include knowing which ones apply to their particular program.

Other Common Animal Care and Use Program Requirements

Attempting to cover how the DoD meets all potential requirements that may be encountered in managing the many DoD ACUPs would be very extensive and still fail to cover all possibilities. However, certain requirements are more universal than others; the following section highlights some of the more common ACUP essentials.

Animal Health Monitoring

The LAM veterinarian manages staff execution of a military ACUP's animal health monitoring, which involves routine health testing and review, identification of potential infectious diseases, and effectively containing and eradicating any disease outbreaks

that occur. Sentinels (additional animals utilized specifically for disease surveillance) are often housed within rodent colonies to be available to regularly test for subtle diseases without having to test and potentially stress the actual animals on study. Maintaining healthy research animals, verified through routine sentinel testing, is especially important because some diseases are subclinical but recognized to adversely affect research results.

A significant risk to overall research animal health is the use of improperly screened biologics (eg, mouse serum) purchased from outside sources. Such materials may harbor and transmit infectious agents to study animals, which, in turn, may spread disease to many other facility animals in a short period of time. Unfortunately, complete colony depopulation is sometimes the only way to eradicate certain infectious agents or stop an epidemic. The LAM veterinarian must maintain visibility and control of the potential introduction of agents from biologics or animals into the vivarium by ensuring that proper testing and quarantine is conducted before permitting entry.

Despite best efforts, animals sometimes experience unexpected, nonstudy-related health issues, and addressing these is another basic component of the general health monitoring program. Animal health monitoring in DoD research facilities is not significantly different from that done in civilian ACUPs.

Budget and Resource Projection

Also similar to civilian organizations, management of DoD animal research facilities includes projecting resource requirements for upcoming years as well as managing use of incoming resources throughout the year. Animal care resources typically account for a sizable percentage of an organization's total budget. Costs associated with animal facility management and veterinary research support may include animal purchases, feed, bedding, enrichment items, waste disposal services, basic personal protective equipment, veterinary medical supplies, various medications and pharmaceuticals, animal caging, and sanitation equipment and supplies.

Military research organizations obtain funding through a variety of sources and funding agencies that may limit how the funds can be spent and the period of time in which the funds remain effective (eg, 1-year versus 2-year money), making resource projection and management unique to each duty site. Projecting and managing funds accurately requires an indepth understanding of categories of expenditures, accurate historical tracking of expenses, and ability to monitor and summarize purchases in an ongoing manner throughout the year. While seemingly not directly related to humane animal care and use, failure to appropriately project and manage resources can lead to shortages of food, supplies, personal protective equipment, or other critical materials, which can result in mission stoppage. Animals must be checked, fed, and cared for every day, a fact that makes a shortage in critical items—for even 1 day—unacceptable.

Personnel Management

The military LAM veterinarian is typically given responsibility for managing all components of the organization's animal research support team. This team may include animal caretakers, veterinary technicians, additional veterinarians, and administrative staff. Animal caretaking involves all daily care of animals and maintenance of animal housing areas to include proper feeding, watering, and maintenance of housing and environmental conditions appropriate to the species in question, and the prompt resolution of any problems on-the-spot or through coordination with other members of the animal research support team. The animal caretaking staff is usually made up of civilians who may or may not possess any veterinary-specific training prior to first employment within an organization.

Veterinary technicians within DoD intramural programs may be either military or civilian; the proportion of each type of employee depends on the organization and whether or not specific support contracts are in place. Civilians are required to possess certain experience, training, and, in some cases, formal veterinary technician licensure or certification. Exact requirements are based on the organization's mission, species used, and complexity of animal manipulations conducted (eg, whether work is conducted in biological or chemical containment areas or whether nonhuman primates are used).

The requirement for military LAM veterinarians to manage both the animal facility and the animal care staff can be notably different from some civilian institutions. Although many civilian laboratory animal veterinarians serve as facility and staff managers, others may be more typically involved only with direct veterinary support (eg, positions in contract research organizations or pharmaceutical companies) or in conducting their own animal research (eg, many academic positions).

Disaster Planning and Emergency Preparedness

All animal facilities, military and civilian, should have contingency plans in place to help mitigate the effects of any potentially unexpected conditions

that could interfere with normal facility operations, including equipment failures, fire, and man-made or natural disasters. Power failures are probably the most common unexpected occurrences, and facility disaster plans should include emergency generators or backup power sources to maintain proper environmental conditions for animals and essential equipment.

In the event of a power failure, an institute that houses animals under biocontainment or barrier conditions needs a backup power system to immediately take over and maintain the proper airflow and pressure differentials to those areas. Similarly, essential equipment such as ventilated animal racks, biosafety cabinets, fume hoods, freezers holding agents or tissue specimens, intensive care units and surgical suite equipment, and security systems need automatic transfer to secondary power sources to prevent the loss of animal life and the compromise of animal health, personnel safety, research work, and facility security.

Each facility should also have detailed plans for those situations that are most likely to occur in their particular location and circumstances. As noted above, most facilities list actions to take in the event of a power failure, facility fire, or flooding in their emergency preparedness plans; however, only those facilities located in areas prone to hurricanes or earthquakes need to formulate plans for these natural phenomena.

Some portions of disaster plans may be generalized to apply to multiple situations, and the planning and preparedness requirements are generally the same for both civilian and DoD institutions, with some variations. For example, both civilian and DoD plans are usually required to designate essential personnel who may need to shelter within the facility to care for animals and keep the institute functioning when circumstances prevent the regular staff from accessing the facilities.

In civilian facilities, all essential personnel are civilians. However, in DoD facilities, active duty military personnel are typically designated essential personnel; which civilians are given what designations varies widely from institute to institute; and civilian staff (eg, DoD government civilians, contracted civilian staff, and foreign nationals working in DoD overseas laboratories) may be considered nonessential personnel. Situations limiting access to the institute include road closures due to winter storms, floods, vehicle accidents, chemical spills, and other incidents; curfews enacted following natural disasters or due to civic unrest, protests, or riots; a pandemic disease outbreak; or even a government furlough or budget crisis which prevents civilian staff from reporting to work.

It is important that the DoD institute's contingency plan is incorporated into the parent organization's (eg, the military installation's) disaster plan and that the plans complement each other. Since the institute is a member of a local community, too, such integral planning must go beyond just installation personnel. Even a relatively small incident such as a chemical spill, a fire, or an act of vandalism contained to a single DoD laboratory may require assistance from the local authorities. Thus, the installation should be involved in the local community's disaster planning, and reciprocally, the installation should involve the local authorities in their own planning. Plans also must be understood by all key players, including first responders, law enforcement, and nonfacility emergency personnel.

Institutes authorized to work with the US Department of Health and Human Services or USDA BSATs are required to regularly conduct emergency drills or exercises to evaluate the responsiveness and effectiveness of disaster plans. Some of these exercises necessitate involving the local community responders as well (eg, the fire department and HAZMAT teams). DoD laboratories or activities conducted in foreign countries must coordinate disaster plans through their military chain of command as well as with US Embassy assets of the host nation, especially with respect to security and evacuation procedures in the event host nation relations become strained.

Security

Security and access control are important components of all ACUPs to avoid complications due to the intentional or accidental introduction of factors that could interfere with operations or the reliability of the research conducted. Work involving BSATs (eg, anthrax spores, Ebola virus, and ricin toxin) inherently includes enhanced regulatory requirements for security and documentation such as storage requirements, key control, intrusion detection, emergency response capability, biological or chemical personnel reliability and surety programs, and other control measures.[49,50] However, all ACUPs must consider and implement measures to protect the health and safety of animal subjects and personnel and safeguard research work, information, and data storage. Such measures go beyond just managing entrance onto an installation or into an animal facility to prevent vandals or domestic terrorists from disrupting operations. Measures may also include restricting access to animal rooms and investigator laboratories to only those individuals who require admittance and maintaining information technology security measures to protect data and intellectual property from theft or computer hacking incidents.

Controlling access to animal rooms may be as simple as limiting access into the vivarium through door locks, key pads, or card readers or as high tech as biometric

fingerprint or retina scanners. Controlling access to a barrier room maintaining an immunocompromised animal species to properly trained personnel wearing the appropriate personal protective equipment (PPE) and working in accordance with established laboratory procedures helps prevent introduction of infectious and adventitial agents and protects the health of the animals and the integrity of the research conducted in such rooms.

Conversely, controlling access to Animal Biosafety Level rooms that maintain infectious animal species to properly trained personnel wearing the appropriate PPE and working in accordance with established laboratory procedures will help prevent spread of the infectious agent outside of the biocontainment rooms, protecting the health of other susceptible animals within the facility and the health of other personnel if the agent is zoonotic. Any breakdown in security measures or biosecurity practices can introduce variables into research studies, which may interfere with results, invalidate work already accomplished, or lead to catastrophic events impacting the health or safety of research animals and personnel.

Security concerns apply to all ACUPs—DoD and civilian. With the potential threat of animal rights extremists attacking enterprises using animals, any institute utilizing animals to conduct RDT&E and training can become a target. However, in the aftermath of the terrorist attacks of September 11, 2001, DoD facilities may have an advantage over some of their civilian counterparts in that all DoD research institutes are now located on closed military compounds with access controlled through security guards manning the installation gates. Most academic institutions and even many civilian contract research organizations lack this level of peripheral protection.

Additional measures within the civilian or DoD facilities themselves (eg, building security guards, cameras, x-ray scanners, and metal detectors at screening checkpoints) depend upon the nature of the RDT&E and training being supported and the level of security required. Such measures are particularly important for institutes working with chemical agents and BSATs that must follow regulations pertaining to chemical and biological agent safety (ie, safely handling agents under study) and agent surety (ie, ensuring defense against loss or theft of agents that could potentially be used as weapons).[49,50]

Occupational Health and Safety

Facilities must maintain a safe and healthy workplace environment for their employees through an established comprehensive occupational health and safety program that operates in accordance with all federal,[61] state, and local regulations. DoD facilities are fortunate in that they are usually either part of a military medical center (eg, Clinical Investigation Program) or operate as a tenant organization on an installation that has a medical treatment facility or clinic with professionals trained in occupational health and safety. Many non-DoD organizations that are not affiliated with a medical facility either have to hire their own medical staff and occupational health and safety professionals or contract out such services.

Though it requires significant coordination and continual communication, DoD research institutes generally utilize local military occupational health and safety assets because these trained professionals possess the knowledge and equipment necessary to perform required health and environmental surveys, conduct testing, and provide preventative vaccinations and treatments while properly protecting patient information (eg, maintaining Health Insurance Portability and Accountability Act Privacy Rule requirements).[62]

An institute's occupational health and safety program should encompass all personnel working with animals or accessing areas utilized for animal RDT&E and training to include personnel who enter animal facilities but who are not considered routine animal husbandry, veterinary, and research staff (eg, facility maintenance workers, IACUC members, training attendees, student hires, and visitors). Occupational health and safety professionals perform risk assessments to determine the proper health and safety measures required for all personnel as well as differing personnel categories. These categories may vary based on the person's expected level of animal exposure, any pre-existing conditions, and the facility areas that the person may be required to access.

Some DoD institutions experience difficulty providing similar occupational health and safety protection measures to divergent personnel because of existing situational contradictions: only some of the various categories of personnel covered by an institute's occupational health and safety program may actually be authorized care through the allied military medical facility. For example, active duty military personnel receive their healthcare through the installation medical facility. However, government civilians working side-by-side with the military in the same research facility may or may not be authorized care at the DoD medical facility, and contract employees usually are not authorized care at military medical facilities. It is imperative that all employees regardless of status (ie, military, government civilian, or contract civilian) receive the same risk assessment and are offered the same occupational health and safety protection

measures, even if the nonmilitary employees have to receive their healthcare through a separate provider. Often the military will register nonmilitary employees into their department's occupational health and safety program to conduct risk assessments, but they may rely on contract healthcare providers to conduct health screenings and provide preventative vaccinations and treatment for civilian or contract employees.

Another potential predicament for DoD programs is related to the temporary nature of military assignments. Institutes with Animal Biosafety Level-3 and -4 laboratories in particular may have a very lengthy schedule of protective vaccinations and antibody titer checks of personnel, plus extensive training regimens that must be completed prior to gaining access into biocontainment suites. These preventive vaccine schedules, which may take 18 to 24 months to complete, severely limit the utility of these military personnel before they are eligible to move on to their next assignments. Such issues may be mitigated by extending the typical tour length for these particular military assignments or by relying to a greater degree on the already cleared, and more permanent, civilian staff to perform work in these specific areas.

Personnel Training and Qualifications

The AWRs federally mandate that personnel involved in animal care and use—to include husbandry, veterinary, research staff, and IACUC members—need to be qualified to perform their duties. These regulations stipulate that the research facility is responsible for ensuring qualifications are met and that the institute should provide necessary training and instruction. Required training includes the following seven subject areas: (1) humane animal care and handling; (2) experimentation methods and techniques; (3) basic surgical techniques; (4) proper use of anesthetics, analgesics, and tranquilizers; (5) infection control; (6) methods for reporting animal welfare concerns; and (7) instruction on how to perform appropriate literature searches for animal use alternatives.[12]

DoD instructions and regulations echo these training requirements and expand upon them by recommending continuing education and training commensurate with a person's duties and responsibilities and encouraging certification for personnel involved in the care and use of animals in RDT&E or training.[1]

None of the aforementioned regulatory documents delineate how the required training must be accomplished to qualify personnel. Therefore, a variety of training options are available, including both didactic and hands-on methods, and most programs incorporate a combination of training methods. For example, basic information may be provided through printed material, online training modules, and lectures while species-specific techniques may be learned through instructional workshops (provided in-house or through off-site sources) or via on-the-job training with experienced staff or designated instructors.

If an institute lacks an established training department, then the responsibility for training and determining personnel qualifications often is delegated to the IACUC and veterinary staff. Given the wide variety of species used in DoD research, the military LAM veterinarian typically expends significant effort in ensuring a thorough training program is established and managed to achieve requirement mandates. Properly trained personnel not only maximize safety of the people and animals during interactions, but also minimize stress to both. One of the most important aspects of training involves understanding the previously discussed 3 Rs concept[23] (modified by the DoD to 4 Rs by adding responsibility to the previous 3 Rs: refinement, reduction, and replacement.) Incorporating the 4 Rs principles into all DoD animal RDT&E and training justifies the animal use and warrants the most humane treatment.

The military LAM veterinarian also is often responsible for developing and training staff on the animal facility disaster plan as veterinarians typically manage the animal facility and possess subject matter expertise with respect to disposition of all institutional animals. Depending on location, number of animals on-site, and health status, plans to evacuate and transport animals to other locations must be developed, as well as appropriate stock levels for emergency supplies such as feed, water, and bedding. If evacuation or transport is not feasible, mass euthanasia plans must be in place for potential use. Given the recent increased attention on animal care disaster plans, most institutes host training events during which such plans are exercised.

Emergency plans have long been an important component of all Army activities, but such training events have only relatively recently attained a similar priority in civilian facilities.[63] For the most part, the increased emphasis on this civilian training was in reaction to several high-visibility events involving various institutions and their ability, or lack thereof, to effectively respond to several natural disasters, specifically major hurricanes causing power outages and flooded animal rooms.[64]

Training for personnel performing RDT&E or training using animals in DoD institutions is very similar to training personnel working in non-DoD organizations. However, turnover of personnel in DoD facilities is often more frequent due specifically to active duty

military staffing and typical 2- or 3-year assignments. Therefore, with military personnel regularly rotating in and out of DoD programs, the required training activities must recur almost continuously in order to train new incoming personnel.

The frequent turnover rate at military institutions affects the training needs of enlisted military personnel (eg, technicians) and the number of available experienced staff members at each military institution even more. Not only are newly arriving military technicians usually less experienced, but they are also probably stationed at their first RDT&E assignment, likely experiencing their first exposure to working with laboratory animal species. Training must begin at the most basic level for these personnel, and they will not become eligible for American Association for Animal Laboratory Science certification until they satisfy the 6 months to 1 year minimum laboratory animal experience requirement, which often leaves them little time to put their training to use before they are replaced by another set of inexperienced arrivals.

In contrast, civilian organizations may possess a more seasoned technician staff when compared to most DoD facilities, especially the smaller military institutes. Civilian institutes can make laboratory animal technician certification a prerequisite for hiring, allowing them to always have more experienced employees. Furthermore, civilian technicians have a greater opportunity to remain in place longer, even indefinitely, while they continue to increase their knowledge and technical skills, achieve greater levels of certification by American Association for Animal Laboratory Science, and progress to positions of higher responsibility. As noted earlier in this chapter, because of their broader missions, larger military institutes have the advantage of having both an experienced, stable civilian technical staff as well as new and more senior military veterinary technicians.

RESEARCH SUPPORT TO INVESTIGATORS

Properly executed ACUPs provide the essential tools by which DoD investigators achieve scientific progress in animal-based research supporting the warfighter.[11] These programs provide for the selection of appropriate animal models; safe, humane, and legally compliant use of selected species; and animal research support infrastructure and resources necessary for investigators to safely and efficiently execute research. In addition to administering ACUPs, laboratory animal veterinarians are an important part of research teams who lend medical and surgical expertise across the spectrum of laboratory animal species to principal investigators. The veterinarian's knowledge of species-specific anatomy, physiology, behavior, and husbandry synergizes well with other scientists' knowledge concerning specific animal models of human diseases or conditions. LAM veterinarians, therefore, often advise principal investigators on appropriate animal model development and selection relative to a scientist's research goals, as well as providing or developing veterinary surgical and other technical support to scientists.

LAM veterinarians also have many opportunities to conduct independent or collaborative research in addition to their roles as clinical veterinarians and ACUP program managers. Similar to civilian institutions, the degree to which DoD veterinarians perform collaborative or independent research, or to which they are involved in animal model or technique development with principal investigators, will vary from institute to institute, depending on the organization and goals of institute leadership, the type of research underway, and the time available to the military LAM veterinarian.

Research Model Selection and Other Prestudy Consultation

The military LAM veterinarian's role as an integral member of the research team begins well before the start of a research study. The AWRs mandate that all principal investigators consult with the attending veterinarian prior to conducting research to develop any plans for anesthesia, analgesia, surgery, and related activities. In most cases, prestudy consultation extends beyond these precursory plans to include research model selection, methods to minimize animal use, and even the possibility of using nonanimal models (ie, implementation of the 3 Rs to reduce, refine, and replace overall animal use).[11] AWRs require an explanation of the chosen research model and why nonanimal models are not suitable for use. As noted throughout this chapter, LAM veterinarians are uniquely qualified to assist principal investigators in answering these questions, given the research objectives at hand.

Technical Veterinary Support

Because of the vast array of species, many areas of research supported, and periodic rotations to different research organizations, the military LAM veterinarian must remain ready to learn or develop new techniques when needed to support the research goals at their

assigned institute. Every project must be assessed independently based on the current research objective, state-of-the-art concepts and techniques, animal model involved, data required, and personnel and equipment available to perform procedures. Rarely will the LAM veterinarian perform the same procedure for years on end. Similar to civilian laboratory animal veterinarians, DoD veterinarians more commonly develop a procedure, refine it, and then train qualified research staff to perform that specific procedure for follow-on studies while moving on to the next research challenge.

Some of the complex procedures laboratory animal veterinarians have helped to develop include a myriad of surgeries for telemetry implantation permutations (from rodent intraabdominal implants to swine intracarotid devices), intracranial electrode emplacement for neurobiology studies, and related animal instrumentation procedures.[65,66,67] The telemetric procedures have the important benefit of making data collection less invasive and, therefore, less stressful for animals on study.

Less complex procedures must also be developed to suit the specific research goals and species in use and are just as essential for accurate and humane data collection. Such procedures, developed with the help or lead of laboratory animal veterinarians, include the following three examples: (1) safe but frequent blood collection from species in biocontainment requiring long-term emplacement and maintenance of indwelling jugular catheters[68]; (2) maintenance of long-term anesthesia, possibly up to days, in large animal models[69]; and (3) chronic blood sampling over a 14-day period of nonhuman primates weighing less than a kilogram (this type of sampling requires new phlebotomy techniques be developed, intensive staff training initiated, and constant health monitoring of animals conducted to minimize any associated animal stress or adverse health effects).[70]

One of the most important missions the LAM veterinarian performs in direct care of animals is making expert judgment calls on when animals should be removed from study. Typically, this is done in consultation with the principal investigator. However, in the absence of such communication, AWRs grant the institute attending veterinarian the authority over all animal activities within the facility, including authority to remove an animal from study through euthanasia or other approved methods.[12]

Independent and Collaborative Research

During their specialty residency training—in order to qualify to sit the ACLAM's board certification examination—both military and civilian laboratory animal veterinarians are required to fulfill the role of principal investigator in developing and executing an original, hypothesis-driven research project and to publish this research in a peer-reviewed journal.[41,71] Through this process, veterinarians gain experience developing research models, writing original research proposals, interacting with the IACUC for proposal approval, and executing actual research, all from the perspective of the principal investigator. Such experience provides first-hand knowledge concerning the challenges faced by investigators conducting animal-based research as well as providing skills needed to develop additional research projects, either alone or in collaboration with other investigators within or outside the organization.

Since the primary mission for military LAM veterinarians is to manage execution of the military organization's ACUP, any independent or collaborative research following board-certification eligibility is conducted as a supplemental mission based on time available and needs of the organization. Topics for independent or collaborative research range from areas directly related to the organization's primary research goals to more peripheral topics focusing on refinement of the research process or use of animals (eg, development of new surgical techniques in a specific species to support other research, comparison of stress responses to different modes of animal housing that could impact data results, comparison of different methods for obtaining blood samples at various frequencies in a particular species, or comparison of analgesics specific to a species used in any given study). Given the wide variety of species used, the extensive variety of research occurring within the DoD, and the continuing obligation to minimize pain and distress and seek nonanimal alternatives to still achieve scientific objectives, the cumulative list of potential independent or collaborative research topics is virtually unlimited.

Because LAM veterinarians are the only military veterinarians who receive both training and experience in comparative veterinary medicine and surgery for all commonly used research species, principal investigators often utilize this expertise to review in-study clinical animal data, in light of experimental goals, known species-specific background lesions, and other relevant species-specific data. Collaboration between experts in various species anatomy, physiology and research uses, and principal investigators allows for the most accurate and comprehensive picture of animal health status changes during the course of a scientific study. Moreover, this review not only sheds significant light on direct treatment effects, but also identifies clinical markers that may reliably predict experimental outcomes at earlier time points, allowing for significant refinement of follow-on studies.

Based on their understanding of animal anatomy, physiology and husbandry requirements, civilian and military LAM veterinarians are uniquely qualified to assist investigators with developing a plan for humanely accomplishing the logistical aspects of data collection. A common misconception among investigators is that procedural logistics can be extrapolated across species. However, both collection sites and volumes of blood that can be realistically and humanely drawn may vary dramatically among species. For example, phlebotomy in dogs is wildly different than it is in 1-kilogram monkeys or 25-gram mice, as is evidenced by the numerous textbooks and handbooks devoted to detailing the differences among them.[72]

LAM veterinarians also provide advice on the amount of postsurgical or postprocedural recovery time an animal needs either during or prior to a study's inception. Species (not to mention age, gender, and health status), anesthetic agent, type of procedure, and length of time to complete the surgery or procedure all impact time to full recovery and, therefore, impact the personnel and equipment needed for postanesthesia monitoring; because of the complexity and variance across species, textbooks are devoted to the recovery process.[73] Veterinarians review published literature as well as use their own training and experience to properly advise investigators on a myriad of other practical topics, all of which can make the difference between success and failure of data collection efforts.

Support Challenges

The wide variety of research areas and multitude of species used ensure that each research assignment a laboratory animal veterinarian holds is demanding. In addition to inherent veterinary technical support challenges, there are also more peripheral aspects of research support that consume as much time as actual direct veterinary support during the laboratory animal veterinarian's day. These veterinary medical and logistical issues may be a result of the research site's location, its physical facility structure, the nature of the research involved, or the ever-changing staff available for support.

Neurologic and Behavioral Studies

Neurological and behavioral studies in the DoD include research seeking to characterize the genetic, anatomical, and physiological mechanisms of the nervous system related to warfighter performance and resiliency before, during, and after military operations. Since much of this specialized research requires sampling and analysis of various structural and biochemical components of the nervous system both ante- and postmortem, it is critical that any pharmacologic interventions, to include sedation, anesthesia, or antibiotic therapy, preserve brain chemistry and anatomy as much as possible.

Virtually all anesthetics impact brain chemistry and can affect learning, memory, and pathologic analysis,[74] but there are also notable differences in these effects on animal welfare that must be considered, reviewed, and approved by the IACUC. One example is in the use of various euthanasia methods for rodents used in neuroscience research. Although both microwave irradiation and guillotine decapitation preserve brain chemistry, AWRs require training, documentation, and inclusion of details and justification within the animal use protocol for use of these specialized equipment and procedures.

Other behavioral studies restrict food intake to stimulate motivation. Such situations require close animal monitoring and recorded measurements of feed intake and body weight to ensure adequate nutrition of animals. LAM veterinarians work closely with principal investigators to meet both the regulatory and humane aspects of animal care while still ensuring valid scientific outcomes. Behavioral studies also have the potential to be derailed by environmental variables, which are often controllable but overlooked.

Routine sanitation activities are one important example of an environmental variable that can disrupt normal animal behavioral rhythms, cause animal discomfort and/or stress, and therefore impact data validity.[75] Conducting sanitation on a standard schedule with consistent personnel or allowing research staff to perform sanitation activities can minimize this impact. In addition, cleaning schedules normally conducted at frequencies mandated by the AWRs may be modified to achieve a balance of appropriate cleanliness and minimization of personnel and material movement into and out of containment areas; any such exceptions must be justified and approved by the IACUC. Pretraining and handling of rodents is known to reduce stress and increase their ability to learn how to operate in various tests of behavior and is, therefore, considered a benefit rather than a distracter to behavioral research.[76] However, whenever sanitation schedules or personnel performing sanitation are changed additional time is required; this is because changes require increased veterinary oversight and communication with the research staff to ensure sanitation continues to be executed to standard.

Feed enrichment, toy enrichment, and human interaction also may cause significant changes in behavior because of their impact on various neuronal

pathways.[77] Similarly, pair-housing in nonhuman primates has been shown to affect memory and learning (pair-housed animals, not surprisingly, are not as motivated to learn as their single-housed counterparts).[78] Such findings do not mandate rejection of enrichment schemes outright but, rather, a collaborative review of the research objectives in light of AWRs to determine modifications of traditional systems that might meet goals of both.

Unfortunately, one of the greatest impacts on behavioral research is difficult, if not impossible, to control: the amount of vibration, noise, and other sensory stimuli detectable by animals. The LAM veterinarian, civilian or military, can mitigate noise and vibration as much as possible by locating behavioral study animals in less-affected areas, housing them near species not likely to cause olfactory or other sensory stress, or renovating or retrofitting rooms with soundproofing or other measures when necessary.

Of significant interest in the past decade, given the military mission and the number of service members affected by the wars in Iraq and Afghanistan, posttraumatic stress disorder and traumatic brain injury research provide special challenges for military and civilian laboratory animal medicine veterinarians. Military research goals in these two areas of research often require highly specialized facilities that replicate trauma scenarios faced by warfighters. Such facilities are often located remotely because of the space needed for simulated explosions or other high-impact events. Animal transport to and from such sites introduces numerous logistical challenges for the veterinary staff who may be required to transport sedated or anesthetized animals as well as deal with potential cross-contamination caused by transportation of animals through nonanimal areas, both indoors and outdoors. (Cross-contamination can lead to transfer of various opportunistic infectious agents back into a research facility.)

Infectious Disease Research

Infectious disease research makes up a large part of all DoD research conducted for two main reasons: (1) weaponized biological agents continue to pose a serious threat to US forces, and (2) infectious diseases remain a significant cause of nonbattle injuries, causing temporary incapacitation of military personnel deployed around the world. One of the largest military animal-based research programs is the biodefense program at the USAMRIID. All of the animal work in this institute is conducted in biocontainment facilities ranging from Biosafety Level 2 (BSL-2) through BSL-4 (the highest possible level of containment).

Working with animals at BSL-3 and BSL-4 presents significant challenges for the veterinary staff. Support to animal research in a biocontainment environment is subject to an intricate framework of facility infrastructure, institutional policy, DoD regulations, United States law, and actual direct health risks (to both animals and humans) posed by the select pathogenic agents and toxins under investigation. The military LAM veterinarian must, therefore, be knowledgeable of these logistical and veterinary medical factors when designing appropriate support so that optimal times and places for staff monitoring can be identified or intervention is conducted to ensure that critical scientific, regulatory, safety, and AWRs are met.

Details of biocontainment levels and minimum requirements for each are published in the CDC Manual 21-1112, *Biosafety in Microbiological and Biomedical Laboratories*[79]; US military, as well as civilian organizations, must comply with these requirements. The DoD has several additional regulations and policies concerning biosafety, biological surety, biosecurity, safeguarding and inventorying of BSATs, and biological (and chemical) personnel reliability programs.[80,81,82]

For example, BSL-1 practices, safety equipment, and facility design and construction are appropriate for laboratories in which work is done with defined microorganisms not known to consistently cause disease in healthy adult humans. For BSL-1 work, standard microbiological laboratory practices are used. BSL-2 containment is required for work done with a broad spectrum of indigenous moderate-risk agents that are present in the community and associated with human disease of varying severity. BSL-3 containment is needed for work with indigenous or exotic agents that may cause serious or potentially lethal disease as a result of exposure by the inhalation route. BSL-4 containment is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal and for which there are no vaccines or treatments or for work with an agent with an unknown risk of transmission.[79]

Facilities for biocontainment work are designed with clear physical separation of containment and noncontainment areas. Areas designated as BSL-3 and BSL-4 require a number of added procedures for entrance and exit of animals, personnel, equipment, and supplies. Such entry procedures include, but are not limited to, donning specialized positive-pressure protective, completely self-contained suits; using positive-pressure respirators; and wearing extra layers of standard PPE. Exit procedures require personnel to shower out, with decontamination of PPE, and sterilization or chemical decontamination of all materials and equipment prior to exit.[79]

Intensive, detailed training is required for personnel to wear specialized protective equipment, given the severe consequences that could occur in the event of a breach in such equipment. Because of the design of this protective equipment, even routine procedures in BSL-3 and BSL-4 take longer and often require modification to prevent breach of protective gear. Needle sticks, animal bites, or sharp objects can all lead to protective gear puncture.

To minimize these risks, venipuncture procedures may be modified to prevent the needle from coming anywhere near an individual's protective suit or gloves; safety needles (retractable needle heads) are typically used; animals may be anesthetized instead of manually restrained (even for simple procedures such as peripheral small volume blood collections); and in all cases, procedures are done in a slower, more methodical manner to minimize human error. The specialized equipment and procedures required for work in BSL-3 and BSL-4 make entry and exit of personnel and materials and actual work in these areas much more time-consuming than work in other areas. All of these constraints must be considered by the laboratory animal veterinarian when arraying available personnel against the required support mission and scientific and animal welfare needs.

The movement of animals into and out of BSL-3 and BSL-4 areas and ensuring humane care and use of animals while in these areas pose perhaps the most difficult veterinary and logistical challenges to the laboratory animal veterinarian and staff. A key role for military LAM veterinarians is conducting risk assessments to identify those areas most likely to allow cross-contamination of infectious agents into noncontainment areas. Traffic patterns of humans and animals, available PPE, and routes of exposure typical for a particular agent all must be considered. Another key veterinary role is advising investigators on whether certain biological materials may pose risks to other animals within a facility. For example, some replication-competent viruses used as vectors to introduce infectious agents into test subjects may also contaminate other materials moving into and out of a room and possibly infect nonstudy animals or even humans.[83]

Because of the significant risk to human health posed by BSL-3 and BSL-4 infectious agents, as well as the risk of spreading contaminants from containment areas to the rest of the facility, institutes seek to minimize staff time spent working inside these areas as well as the amount of material traffic into and out of containment. Through the use of in-room, continuous cameras, monitoring of activities can be accomplished from noncontainment areas.

However, should problems arise, the ability to respond immediately is necessary, and advance consideration of all potential impacts on animal environmental conditions is needed. For example, environmental enrichment needs must be met at all times (as mandated by the AWRs, especially for nonhuman primates) regardless of the biosafety level. Since human contact is a critical component of animal enrichment programs, and biocontainment at BSL-3 and BSL-4 protective gear and equipment significantly limit this contact, other enrichment strategies must be enhanced to compensate for the lack of human interaction. These additional strategies may, and often do, require significantly more time to accomplish.

Since pair-housing, an excellent enrichment strategy now mandated as the default for nonhuman primates and many other species,[6] can increase the human safety risk of certain animal manipulations when done in containment areas, pair-housing may have to be discontinued during data collection periods. Of special concern are animals participating in long-term studies that, therefore, must be singly housed for extended periods. When there are few or no other animals in the room, isolation stress is a very real issue for animals, one that requires specific attention and mediation through other enrichment methods.[84]

Manipulation of animals within biocontainment areas also often requires modification of procedures to ensure desired data collection is achieved with minimal human intervention and minimal distress for animals. A common monitoring technique well-suited for containment use involves surgically implanted telemetric devices that can monitor a variety of physiologic parameters from outside the biocontainment suite.

Difficulty sometimes arises, however, when postsurgical complications require readjustment or removal of devices. In such cases, all corrective work must be executed within containment areas while within the confines of cumbersome protective suits or equipment. Similarly, central venous catheters are popular for certain studies because they obviate the need for repeated needle use for serial phlebotomy in containment, making collection much safer for humans and more comfortable for animals. Yet, when these same catheters lose patency and require removal or replacement, it is more difficult to accomplish in containment areas.

Additional requirements occur when certain agents are used, specifically, those listed as select agents and toxins by the National Select Agent Registry, which lists biological agents and toxins that have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. This list is developed

and maintained jointly by the CDC and the USDA's Animal and Plant Health Inspection Service. These agents are so identified because they have the potential to be used as weapons or in other ways harm public or animal health.

The select agent regulations (9 CFR Part 121, 7 CFR Part 331, and 42 CFR Part 73) define requirements for ensuring physical security of these agents during storage, use, transport, and disposal.[85,86,87] To meet these requirements, all personnel having access to these agents at any time must be enrolled in a biological personnel reliability program (BPRP). (A similar program exists for working with chemical agents.)

The BPRP requires personnel to obtain and maintain security clearances, continuously report to management any factors that might impact their security clearance or reliability to work with dangerous biological (or chemical) agents to include medical conditions that may arise while employed for such work. Not everyone on the veterinary staff will qualify for the BPRP, making this requirement another management challenge to ensure that only BPRP-enrolled personnel are scheduled to work on studies requiring BPRP enrollment. (See Chapter 15, Veterinary Pathology, for more information about biocontainment levels and military biomedical and chemical research.)

Environmental Toxicology

On the surface, military environmental toxicologists address the same issues as their civilian counterparts: the effects of environmental compounds (naturally occurring or artificially deposited) that negatively impact human or sentinel animal species' health. However, military research often focuses on environmental toxicants produced by military activities such as ammunition by-products found on firing ranges or components of other military weapons systems that, given their use, might cause chronic toxicity in service members operating those systems (eg, depleted uranium residues or aviation fuels).

In this field of study, a variety of animal models, to include many nontraditional ones, are often used, including birds, reptiles, New World rodents, amphibians, fish, and invertebrates. Success in maintaining these species can be achieved only through specialized training of the veterinary care staff, who must not only be knowledgeable in direct care and handling of the species used, but also in maintaining required species-specific environmental conditions for each. For example, optimal reptile housing provides a thermal gradient, allowing them access to both warmer and cooler areas in order to ensure proper body temperature regulation. Moreover, quail eggs require high temperatures for proper incubation and hatching, but adult birds need access to much lower temperatures to maintain normal health, similar to other bird species.[72]

Wild species do not easily adapt to a laboratory environment, so approaching environmental enrichment creatively for each species is also important. Facility stressors that might not harm more traditional laboratory animal species could lead to severe stress or even death in wild species, so minimization of these stressors and the ability of the veterinary staff to identify subtle species-specific signs of disease is critical.

Like other specialized studies, environmental toxicology studies require special equipment for housing and testing, to include inhalation chambers and incubators. The veterinary staff must be able to sanitize these items thoroughly without leaving cleaning material residue that could later influence the response of animals housed therein.

Additionally, many civilian and military studies submitted for acceptance by environmental regulatory agencies must adhere to GLP regulations. GLP regulations require meticulously controlled environmental conditions and documentation of all factors that could impact collected data integrity. Appropriate GLP compliance is possible only through implementation of rigorous administrative oversight of all test articles, animal handling technical methods, equipment maintenance, and environmental factors.

Because GLP regulations mention general standards for animal care but do not replace the AWRs that must be followed by all DoD research entities,[11] a major challenge within GLP-focused facilities is ensuring that compliance with both GLP and AWRs is achieved while still meeting scientific objectives. One example of overlap, where clear and standardized collaboration between the scientific and laboratory animal staff is critical, is the documentation required to make animal use protocol changes—since requirements differ slightly between the GLPs and AWRs.[12,88,89]

Another example of an area requiring close coordination is maintenance of facility conditions. The laboratory animal veterinarian must ensure careful monitoring of facility heating, ventilation, and air conditioning to ensure appropriate standards are met for both GLP and AWR requirements. Finally, the AWRs and the *Guide* specifically address the need for group housing whenever possible,[6] whereas certain GLP study designs may be determined by environmental regulatory standards that mandate single housing.[90] This duly noted, the challenges of meeting GLP and AWR requirements affect any area of research operating under GLP conditions, not just environmental studies.

Certain environmental carcinogen toxicity studies require long-term (12–24 months) housing of rodent species. GLP compliance requires strict oversight of measurement of both the test article and the food or water used as the vehicle for administering test material. While the investigative staff may conduct the test article administration, the veterinary staff must ensure that adequate animal nutrition is maintained, as well as ensure that care activities do not inadvertently confound strictly controlled feeding and watering regimens.[91] Another challenge of long-term studies is that, during this time, animals may develop age- and housing-related medical issues unrelated to test article or study design. In these cases, the laboratory animal veterinarian must work with investigators to determine what effect, if any, these background issues have on specific data or overall study results.

Field Research and Field Studies

Field research and field studies are used to assess animals in their "field" or natural environment, *with* or *without* invasive manipulation (field research or field studies, respectively) of the animals under study.[1] Whether field observations or sample collections are executed by military or civilian organizations, laboratory animal veterinarians must ensure that the AWR requirements for lawful procurement of animals is followed, typically through the investigator's proper securing of permits for work with, or collection of, desired species.

There is an additional military application of field studies in which animals are tested for certain zoonotic diseases of interest occurring within a military area of operations (combat or otherwise). When such military zoonotic testing occurs internationally, the host country's requirements must also be met, as well as all applicable US and DoD requirements. Further, the LAM veterinarian must appropriately advise the investigator on proper personnel protection for exposure to zoonotic disease since field animals are wild, not purpose-bred and, therefore, risk of exposure to disease is increased.

Capturing, anesthetizing, or euthanizing animals as well as appropriately collecting and storing samples is a significant challenge in field research and studies, particularly for military personnel operating in overseas combat zones far from established laboratory facilities. For example, certain controlled substances are difficult to legally transport to nonlaboratory areas or across international boundaries. Necessary equipment may be damaged or rendered inoperative when used outside the laboratory, and in all cases, procedures are rendered far more difficult when done in the field.

The DoD veterinarian also must specifically ensure that even deployment animal trapping plans take into account humane containment, handling, and release of animals. Traps should be checked often enough to ensure animals are not stressed by the inability to obtain food or water or exposure to excessive heat or cold.

Radiobiology Research

The DoD is concerned with radiation exposure of service members both in garrison environments (eg, health care facilities) and in deployed environments where service members may be exposed to radiation as a result of nuclear plant accidents (eg, Fukishima Daiichi nuclear power plant accident in Japan, March 11, 2011)[92] or intentional use of nuclear weapons by enemy forces.

Whole (ie, total) body irradiation of animals and other radiobiology research techniques require working with hazardous equipment and radiation-emitting substances that pose occupational health risks to military personnel. The LAM veterinarian is the primary advocate of, and responsible authority for, ensuring that veterinary staff members are appropriately prepared for and protected when performing such work.

Working with depleted uranium or other radioactive substances poses significant logistical hurdles. For example, test substances are often excreted in animal urine or feces, requiring radiation safety officials to ensure that the waste products are free of radioactive material prior to its removal from animal rooms. Radioactive bedding disposal creates a unique waste disposal challenge for the staff because this bedding must be disposed of in accordance with Nuclear Regulatory Commission or state requirements.[93] In many institutes, radioactive materials must be fully accounted for before animals are removed from that animal room. Work spaces may also be segregated based on presence of radioactive materials as well as on the type of radiation emitted (eg, beta-emitters require different protections than gamma-emitters).

Other logistical challenges of radiobiological research include collecting serial blood samples over extended time periods. In large animals, this is both time-consuming and labor intensive, and for rodents it is technically challenging because of limited total blood volumes and collection sites. When total body irradiation is combined with injury research, additional considerations related to trauma medicine come into play, such as how to create controlled radiologic and traumatic injuries, and whether such controlled injuries adequately replicate real-world scenarios (both a scientific and ethical question). Determining when full-spectrum post-injury supportive care may be

applied, which still allows collection of valid data, versus when modification of post-injury supportive care is needed, with the potential for compromised scientific objectives, is another difficult yet unavoidable question faced by the IACUC and attending veterinarians. The LAM veterinarian is uniquely qualified to provide clinical perspectives on when supportive care may interfere with certain clinical outcomes necessary to meet desired research objectives.

Similar to what occurs in other areas of research, defining and implementing consistent and humane animal endpoints can be problematic. This is because, at the present time, previous work for some areas of radiobiological research is often absent, and the rapidity of onset of clinical signs can make timely identification of optimal endpoints very difficult. It is therefore incumbent upon the LAM veterinarian to advise the investigator and IACUC on those clinical signs, within a potentially rapid progression of clinical effects, that can best be used to assess whether research objectives have been met, at the earliest time point possible.

Diving Research

Because the DoD—in particular, the Navy—conducts a variety of underwater activities in support of military combat and training operations, understanding the physiology of diving effects on service members in this unusual military environment is a high priority for naval research organizations.

Currently, military diving research utilizes hyperbaric chambers in which animals are either conscious or anesthetized, depending on study objectives. Delivery and monitoring of anesthesia during hyperbaric procedures and general animal monitoring without direct human contact are major support requirements for the laboratory animal veterinary staff. Setting up vital sign monitoring equipment, which remains accurate for extended periods of time; staffing the equipment with trained personnel; and maintaining the capability to appropriately address problems promptly are key factors in success for this type of research.

When animals are recovered from dive procedures, postdive decompression becomes another important phase of such studies; this phase must be carefully controlled lest significant abnormal conditions arise. Such conditions include acute decompression sickness that may lead to death or prevent normal recovery, spinal cord decompression sickness in which limb paralysis is seen, or combinations of these conditions in a variety of species.[94,95,96] These conditions must be proactively considered and prevented by the veterinary staff to ensure animals recover appropriately. Preventing loss of animal life, not to mention loss of valuable data and resources invested in the animal, require trained and ready veterinary monitoring during the postdive period. (For more information about US Army veterinary support for naval programs and military marine mammal care and missions, see Chapter 7, Marine Mammal Program.)

Overseas Research Sites

The DoD currently operates three research facilities located outside of the continental United States (OCONUS) that utilize animals: the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand; the Naval Medical Research Unit Number 3 (NAMRU-3) in Cairo, Egypt; and the Naval Medical Research Unit Number 6 (NAMRU-6) in Lima, Peru.

The mission of all of these institutes is to conduct medical research and disease surveillance and develop and evaluate medical products for militarily important infectious and tropical infectious diseases of the particular region. AFRIMS is the largest DoD OCONUS laboratory animal facility that includes a large nonhuman primate breeding colony of Indian-origin rhesus macaques. An additional unit, NAMRU-2, and its various detachments have been located in a variety of places since its inception, to include Guam, Taiwan, Manila, and Jakarta.

The Jakarta facility closed in 2010 at the request of the government of Indonesia. The unit was then relocated to Pearl Harbor, Hawaii, and officially opened as NAMRU-2 Pacific in June 2010. However, the unit in this location was then disestablished in 2013 and relocated to Phnom Penh, Cambodia.[97]

OCONUS facilities that conduct DoD animal-based biomedical research are often located in countries that may be less developed or less politically stable than the United States. Local nationals are frequently hired for some or nearly all of the veterinary support staffing needs, which significantly impacts the daily challenges faced by the military laboratory animal staff in many ways. First, local national staffing can provide a stable and reliable workforce to optimize standardization and continuity of animal care and handling, two extremely important factors desired by investigators. Second, in many cases, work at a local US research site pays more and holds a higher social status than many other local jobs; therefore, US-hired local nationals are extremely dedicated to doing their best to maintain employment at the research site. Finally, in some countries (eg, Thailand), the predominant religious and cultural mores include a deep respect for animal life and welfare, so there is an inherent desire by the local national staff to ensure that animal care and use regulations are followed closely.

Procuring animals for OCONUS sites is challenging because the microbiological status of animals procured locally is often unknown. Other challenges of overseas locations include the lack of available high-quality feed and appropriate animal enrichment items. Consequently, many animals and supplies must be imported, adding expense and layers of importation requirements, quarantine challenges, and additional complicating procedures on top of the normal procurement process. Overall research costs are also increased because of importation taxes not normally incurred by continental US laboratories.

To avoid procurement issues, some sites choose to create and maintain breeding colonies to produce required animals in-house. Development of such breeding systems is costly, requiring specialized facilities as well as special training and experience of the veterinary support staff. In countries where governmental stability has been compromised, the military LAM veterinary support staff are considered essential personnel and have not only been required to take the lead on conducting research animal evacuation or euthanasia (when dictated by local regulations and institutional policies), but have also been required to act as part of the general veterinary force to execute evacuation of pets owned by the DoD or other US personnel.

A contemporary case exemplifying this duty is the uprising that led to the ousting of Egyptian President Mubarek in January 2011; the rapid evacuation of thousands of Americans resulted in a large number of unattended pets being left in the country, many of which were owned by embassy and DoD personnel. A US military veterinarian remained in-country to ensure care, safekeeping, and evacuation of these animals, in addition to providing care for the research animals housed at NAMRU-3 (e-mail communication from Lieutenant Colonel Nancy Merrill, Attending Veterinarian, US Naval Medical Research Unit No. 3, Cairo, Egypt, January 2011).

CLINICAL INVESTIGATION SITES

Upon completion of medical school, the military physician typically matches into a residency program at a major military medical center, and the doctor's training continues in a specialty area such as surgery, obstetrics, or neurology. The Accreditation Council of Graduate Medical Education (ACGME) stipulates research and training requirements be fulfilled in order to maintain accredited residency programs. Clinical departments supporting residents for up to 7 years have recognized the value of adding a research rotation to the residents' curriculum so they may learn about the science behind their chosen craft. To that end, military medical centers offering ACGME-accredited residency training programs in the United States have a Department of Clinical Investigation (DCI).

The overarching mission of most DCIs is to provide the tools, training, and expertise required to develop clinicians and scholars who engage in intellectually rigorous, safe, and ethical conduct of research that advances the science of medicine. The DCI provides excellent opportunities to train many in the medical and ancillary services using animal models. Trauma training is especially available at several DCIs, with an emphasis on validating physicians' skills as first responders.

Of the twenty plus DCIs in the DoD, only two Air Force, two Navy, and five Army medical centers have animal care and use programs supporting preclinical research and training. Military laboratory animal veterinarians play a pivotal role at the following nine locations: Mississippi (Keesler Air Force Base Medical Center-KMC), Ohio (Wright-Patterson Air Force Base), California (Naval Medical Center San Diego-NMCSD), Virginia (Portsmouth Naval Medical Center-PNMC), Hawaii (Tripler Army Medical Center-TAMC), Georgia (Eisenhower Army Medical Center-EAMC), Texas (William Beaumont Army Medical Center-WBAMC and San Antonio Military Medical Center-SAMMC), and Washington (Madigan Army Medical Center-MAMC).

LAM veterinarians are assigned to one of the nine aforementioned DCIs and serve as the attending veterinarians for the institute's overall animal care and use program. Training initiatives and research focus are unique to each location and fluctuate with the medical needs of warriors, both on and off the battlefield, and other populations served by the medical center (military retirees, DoD family members, or government civilians).

The principal roles of the attending veterinarian at a DCI include the following six duties: (1) provide adequate veterinary care; (2) serve as a voting member on the IACUC; (3) use appropriate methods to prevent, control, diagnose, and treat diseases and injuries; (4) provide guidance to principal investigators and other personnel in the care and use of animals; (5) maintain the program's AAALAC accreditation status; and (6) exercise professional judgment to facilitate the science in the context of animal welfare.

Military veterinary roles at DCIs also may expand to cover unique circumstances. For instance, at EAMC, studies assessing methods to promote nerve healing in

traumatized limbs require veterinary input to create formulations to provide maximum bioavailability in nervous tissue. At MAMC, limb reattachment studies in rats involve training animals to walk on a track after having the hind paws inked to leave prints for measurement. Another institute uses the new DigiGait analysis system (Mouse Specifics, Inc., Framingham, Massachusetts) for similar studies. Veterinarians must be familiar with methods of proper conditioning of animals for such behavioral tests.

One way to maximize the use of a DCI animal care and use program is to create long-standing animal models of disorders or wound conditions that may be studied in perpetuity by a succession of new clinician-scholars. In this manner, short-duration studies may be crafted to fit into the timeframe of a very busy resident and help keep a central research focus for the clinical department. The senior staff of such departments may then guide the residents in the choice of how to use the established model based on current issues, challenges, and injuries/conditions facing warriors.

LAM veterinarians work closely with physicians who have treated patients on the battlefield or who have implemented solutions to clinical problems based on research conducted in the DCI. While some physicians have had some exposure to animal research, many are unaware that animal models exist or can be developed to support research on a variety of clinical conditions. Outreach to department leaders within a medical center by DCI staff, including the LAM veterinarian, helps ensure maximum involvement by medical staff and residents, which serves to strengthen the training program of the medical center. The LAM veterinarian can also help identify animal model options not yet considered for use in training and research, thereby enhancing the quality and depth of DCI research or training programs.

Forging a strong collaboration between the new physician scientist and the LAM veterinarian is also a good long-term investment. Many residents understand the process of the institutional review board (IRB) for human-use studies, but few are aware of the IACUC process for animal studies or fundamental differences between these two committees. Training residents on the role of the principal investigator, coaching them on writing an animal care and use protocol, and mentoring them through the steps of data collection in animals can bring a much greater understanding of what lies behind a valid and useful scientific publication. Whether or not the military physician continues on active duty, this type of training also helps mold a scientific mind, which, in turn, enhances the physician's capabilities and expertise such that he or she may be able to contribute to research programs throughout his or her career as a scientific mentor or even as an IACUC member or consultant.

COMBAT TRAUMA TRAINING

Animal models of human combat trauma have been used for decades as an adjunct to training provided to military medical personnel (unpublished data, LTC Chad D. Foster, chapter author and [former] attending veterinarian, US Army Medical Department Center and School, based on experience reviewing multiple past DoD policies and protocols related to animal use in human medical training from May 2003 to July 2016). This training, commonly referred to as combat trauma training (CTT), live tissue training, or animal-based medical readiness training, involves the creation of simulated combat injuries in an anesthetized live animal model, followed by the administration of emergency interventions by medical personnel. The purpose of such training is to teach medical personnel how to independently manage critically wounded patients at the point of injury on the battlefield and during the first few hours afterwards.

Prior to September 11, 2001, this training was limited to a small number of select military service members and often utilized as a component of the US military's Advance Trauma Life Support courses. However, the nature and severity of the injuries encountered on the battlefield during more than a decade of war in Iraq and Afghanistan have made CTT a critical component of predeployment training for all medical personnel who might be called upon to treat combat casualties. In fact, Headquarters, Department of the Army Executive Order 096-09 (HQDA EXORD 096-09) mandated predeployment trauma training for all physicians, physician assistants, oral surgeons, dentists, nurses, nurse anesthetists, and combat medics deploying on or after October 1, 2009.[98]

The mandatory predeployment training is provided by the US Army Medical Department's Center for Predeployment Medicine. Each of the predeployment courses involves use of animals for CTT. The Army, Navy, and Air Force all utilize CTT to some extent in training medical personnel as a supplement to extensive didactic, simulator, and buddy-aid training. The current combat trauma management training methods have contributed to the greatest survival rate in history for military personnel wounded in action—greater than 90%.[99]

Regulations and Oversight

Similar to the use of animals in biomedical research, the use of live animal models in CTT requires an IACUC-approved protocol and is governed by the Animal Welfare Regulations, DoDI 3216.01, and AR 40-33.[1,11,12] These requirements include, in most cases, that institutions conducting CTT be AAALAC accredited. Each of these regulations mandates the involvement of veterinarians in all aspects of animal use. In accordance with the DoDI 3216.01, *Use of Animals in DoD Programs*, headquarters-level oversight of CTT programs is provided by board-certified, military LAM veterinarians in each respective component oversight office.[1] These veterinarians conduct compliance inspections and administrative reviews of IACUC-approved protocols and provide consultation services to CTT programs, just as they do for biomedical research institutions under their purview. Although many CTT programs utilize clinical (nonlaboratory animal medicine) veterinarians to provide veterinary care and anesthesia support during the conduct of CTT, three of the largest CTT institutions in the DoD (ie, AMEDDC&S, HRCoE; Joint Special Operations Medical Training Center; and Madigan Healthcare System) have permanent positions for LAM veterinarians. While these positions involve the traditional responsibilities associated with LAM veterinarians, they also present challenges that are unique to CTT programs.

For example, the LAM veterinarians at the AMEDDC&S, HRCoE, and the Joint Special Operations Medical Training Center may be the only persons at these institutions who have any outside training or experience with regulated animal care and use programs. This is an important consideration, given that each institution's leadership may have little or no knowledge of the regulatory requirements associated with the use of live animals. To ensure regulatory compliance, the LAM veterinarian must work closely and communicate effectively with the institutional official, IACUC, public affairs officer, and individual unit commanders and instructors when providing expert consultation and guidance.

Program Development

The LAM veterinarian in CTT programs must be actively involved in developing all institutional policies and standard operating procedures related to animal use. Development of institutional policies and procedures is complicated by the fact that many animal use regulations and standards were developed with research institutions (and their fixed facilities), not CTT programs, in mind. For example, federal regulations require that all animal use areas be inspected semiannually and approved by the IACUC.[12] While this is not difficult for CTT programs that utilize permanent facilities for training courses, it can be exceedingly difficult for programs that conduct CTT at field-training exercise sites (eg, the Brigade Combat Team Trauma Training [BCT3] course is conducted on training ranges).

BCT3, the mandatory predeployment trauma training course for combat medics that involves the incorporation of CTT into realistic battlefield scenarios, is an exportable course conducted by trained dedicated staff. For each iteration of this course, temporary animal housing, as well as animal preparation areas, are constructed at field-training sites 1 to 2 days prior to animal delivery. These constructions are taken down immediately after conclusion of the training event. However, because the animals used in BCT3 CTT are housed for greater than 12 hours, they still must comply with AWRs.[12] Furthermore, in accordance with DoDI 3216.01 and AR 40-33, the temporary animal facilities used for CTT, which may only exist for 2 to 3 days, must comply with the animal housing requirements of the *Guide*.[1,6,11]

Developing compliant plans for animal housing and processes to ensure proper veterinary and IACUC oversight and approval may require creativity and ingenuity. Moreover, when these courses are conducted outside of the United States, the DoD organization conducting the training is responsible for ensuring strict adherence to both host country and US laws and regulations.[1]

Occupational Health and Safety Program

Another challenge encountered in CTT programs is the development of a comprehensive Occupational Health and Safety Program. Students attending CTT courses are unlikely to have received a medical evaluation and clearance specifically for animal contact. This is especially true for students attending exportable courses where students are not covered by the CTT program's Occupational Health and Safety Office. Since the animals used in CTT programs are generally USDA Class B dealers (ie, these dealers are licensed by the USDA to purchase and resell animals, as opposed to Class A dealers who are licensed to sell animal bred on their own premises),[12] the animal's background and previous exposures will likely be unknown. Therefore, it falls to the veterinarian and the IACUC, in cooperation with occupational health professionals, to ensure that occupational risks, namely zoonotic diseases and allergies, are mitigated to the greatest extent possible.

For example, if the animal model used in the CTT course is a goat, the veterinarian might require that only male castrated goats be used in order to minimize the likelihood of receiving animals with brucellosis or Q fever, both of which can be contracted by humans from contact with female goats that are lactating or giving birth. Vaccination and health screening requirements for animals to be purchased should also be developed and incorporated into contracts, and animals should be inspected upon delivery by a veterinarian for contract compliance (including any indications of zoonotic disease).

The veterinarian must also provide consultation regarding the use of PPE to mitigate any residual risk from animal exposure. The PPE selected must balance the principal instructors' need for realistic training (ie, gloves, masks, and lab coats are not typically worn on the battlefield) with the necessity to ensure the welfare of the students. Moreover, it generally falls to the veterinarian to provide a pretraining briefing to all CTT participants. In addition to regulatory requirements, this briefing should include information on the risks associated with use of the animal model, steps to be taken to reduce that risk, and clinical signs of allergic reactions and zoonotic diseases associated with the species in use.

Protocol Development

The LAM veterinarian must also be consulted during the development of a CTT animal use protocol.[12] Although the veterinarian reviews and provides consultation on all areas of the protocol, the primary role in protocol development relates to model selection and development of an appropriate anesthetic regimen. The model selection should be based primarily on the principal instructor's training goals.

The two most commonly used animal models in CTT programs are goats and pigs, each with their own advantages and limitations. Goats are commonly selected for use because of their anatomical similarities to humans with regards to subcutaneous fat thickness, blood vessel size and location, abdominal wall thickness, rib and intercostal space size, and tracheal diameter (which allows for instrumentation with human medical devices). Furthermore, goats not only possess a temperament and husbandry requirements that make them easily exportable to a field environment, but they are also readily available in and outside the United States. However, on the negative side, goats often require partial shearing and shaving prior to use.

Pigs may be selected as the CTT model of choice because of the similarity of their skin and internal anatomy to that of humans, which may be important if the CTT will focus on surgical interventions. Whichever model is used, the veterinarian will likely be responsible for providing appropriate training to students, instructors, and anesthesia support staff.

Development of an appropriate anesthetic regimen is the single most important way in which the LAM veterinarian serves as an advocate for animals used in CTT programs. The regimen must ensure that the animals are maintained at a surgical plane of anesthesia for the duration of the training, which is generally 2 to 5 hours. A wide variety of anesthetic approaches are used in support of CTT.

When deciding upon an anesthetic regimen, the veterinarian and the principal instructor must consider how the CTT will be incorporated into the overall training event. For example, if CTT is to be conducted in a fixed facility or an environment that simulates a battalion aid station or combat support hospital, then inhalant anesthesia may be appropriate. However, if the CTT will be conducted in the field where there is no suitable inhalant anesthesia equipment necessary for inhalant anesthesia, another approach may be necessary. In these situations, a constant rate infusion of intravenous anesthetics may be a better choice. If the training will involve significant patient movement (eg, evacuation), then the risk of dislodging endotracheal tubes and IV infusion sets may necessitate the use of intermittent parenteral injections of anesthetics.

In all cases, the animal must be closely and continuously monitored for appropriate anesthetic depth to avoid any pain or distress to the animal, which can be quite complicated. In order to better simulate combat scenarios, many CTT courses are conducted in austere environments that limit visibility and hearing, including the dark (simulating nighttime operations), heavy fog (simulating smoke), and noise (simulated gunfire and pyrotechnics). The veterinarian must be aware of these impediments to patient visualization and handling and have a plan for patient monitoring under such conditions. The veterinarian must also ensure that animals are humanely euthanized at the conclusion of the training event and carcasses are disposed of in accordance with local laws and regulations, which vary depending on where the training event takes place.

Future of Combat Trauma Training

CTT has contributed to what is currently believed to be the lowest battlefield fatality rate in military history, and the use of animal models is an essential component of that training.[99] The live animal patient, generally integrated into a culminating training event,

presents students with realistic, unpredictable, physiological responses that hone rapid decision-making skills and expertise in providing life-saving interventions. Students experience the pressure associated with providing care to a critically wounded, actively bleeding patient.

For some students, it is their first time working on a live trauma patient. When successful, they gain confidence in their ability to save lives. In fact, 97% of students who completed the Tactical Combat Casualty Care course at the Madigan Army Medical Center reported that the training significantly improved the confidence they had in their ability to manage combat casualties. Furthermore, of those who completed the course and then deployed for 1 year to Iraq, 99% reported that it helped with their management of battlefield casualties.[100]

The DoD is committed to providing effective realistic training while ensuring compassionate and humane animal use. However, responsible animal use requires institutions to continually consider the use of nonanimal models which can potentially replace or reduce the number of live animals used. In September 2008, the Under Secretary of Defense (Acquisition, Technology and Logistics) formed the Use of Live Animals in Medical Education and Training Joint Analysis Team (JAT) to "address the technology maturity and readiness of medical models and simulations to replace the use of live animals in DoD medical education and training venues."[101(p3)]

In July 2009, the JAT published a review on the use of live animals and nonanimal alternatives in medical training across all services, which concluded that simulation technology was widely being used to augment medical training but could not be used to fully replace live animals used in training. Furthermore, the JAT noted that three of the nine critical or high-stakes medical procedures could not be taught with current simulator technology. They also reported disadvantages in current simulation technology, including a lack of realism, limited real-time physiologic feedback capability, and lack of the intangible sense of urgency associated with caring for a living model.[101]

On the recommendation of the JAT, the DoD is working to develop methods to assess training effectiveness and make scientific comparisons between the live-animal and simulation teaching modalities. Additionally, the DoD is striving to identify gaps in simulation technology in order to facilitate targeted development to meet its training needs. The DoD is highly committed to completely replacing animal-based training methods with alternatives, as long as doing so will not adversely affect the provision and quality of care for injured warfighters. Until such simulation is validated and determined to be as effective as use of the live animal model, the training, experience, and confidence gained by the use of animals in teaching life-saving tactics, techniques, and procedures is critical and must remain intact.[99] Therefore, LAM veterinarians will continue to provide critical support and oversight.

SUMMARY

US Army LAM veterinarians have proven themselves essential to ensuring the humane care and proper use of animals in support of the DoD's worldwide RDT&E and training programs. Since the LAM training program's beginnings in 1961, the program has evolved to become a rigorous, successful training program that continues to produce an indispensable, uninterrupted source of highly trained LAM specialists (military occupational specialty 64C) to sustain the DoD's numerous RDT&E and training missions.

The LAM veterinarian position encompasses many responsibilities; the foremost is ensuring that the DoD complies with all laws, rules, and regulations regarding animal care and use. Acting as an animal advocate by promoting animal well-being and proper ethical use at all times, the attending veterinarian has the additional task of managing an institute's ACUP with its many functional areas. Military LAM veterinarian's duties are very similar, if not identical, to those of civilian LAM veterinarians. However, there are situations and challenges that are unique to the military and to the specific types of research and training missions the various DoD units perform. These challenges demand a VCO who is a creative thinker who can readily adapt to ever-changing research missions, equipment, technology and methodology advances, and evolving standards, policies, rules, and regulations.

In addition to abiding by all international, federal, state, and local laws, rules, and regulations governing the use of animals in RDT&E and training, DoD institutes must also adhere to the DoD's own instructions and regulations, which are often even more stringent. The military LAM veterinarian must be well versed in all of these regulatory requirements (including foreign regulations for work conducted overseas) and must ensure that programs attain and maintain AALAC accreditation.

Whether LAM veterinarians are assigned to a large specialized research institute such as USAMRIID or to a smaller DCI at a military medical center, military

LAM officers must be the primary subject matter experts who assist scientific and clinical investigators with writing research or training protocols, supporting these investigators in the conduct of animal use studies. Similarly, LAM veterinarians are also best suited to assist units utilizing animal models to conduct CTT for deployable medical personnel because of the LAM veterinarians' knowledge of the many rules and regulations required for animal care and use and their extensive experience with a wide variety of animal care and use programs.

As the standards of animal care progress, and as animal rights groups continue to pressure the DoD and others to discontinue using animals for various endeavors, military LAM veterinarians play a critical role to ensure that all DoD RDT&E and training activities involving animals are conducted in accordance with all pertinent rules, regulations, and industry standards; that animal alternatives are considered and incorporated where appropriate; that proper justification exists for the animal use; and that animals are cared for to the highest possible ethical and humane standards.

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