EBOLA VIRUS and PET ANIMALS

American Veterinary Medical Association

Ed Note: With all the interest and concern regarding Ebola virus these days, we have opted to add this article from the American Veterinary Medical Association regarding the risk of Ebola to our pets. While clearly not a research topic, the health and safety of our family pets is just as important as our regular focus upon the health & welfare of our research animals. Informed pet owners are the best defense against Ebola ignorance and paranoia. Be an informed pet owner!

Although there have been human cases of Ebola in the U.S., these cases resulted from direct contact with a person infected with the Ebola virus and showing obvious signs of illness. Ebola is a zoonotic disease, because it can be passed between certain animals and people. Ebola may have originally spread to humans from infected fruit bats, apes or monkeys but is now primarily spread from person to person through direct contact. Although a study has shown that some dogs in Africa have been exposed to the Ebola virus, there is no evidence that they become ill or spread the disease to people or other animals. In the current West African outbreak, animals have not been found to be a factor in the ongoing spread of the disease. Ebola is NOT spread through the air or water or by mosquitoes. You or your pet would need to be exposed directly to the blood or body fluids of a person or animal that is infected with Ebola in order to be at risk for infection.

Just as the risk of you becoming infected with Ebola is very low, your pet’s risk of becoming infected with Ebola is extremely low, especially when you compare this risk to the preventable, yet deadly, diseases like parvo, distemper, and rabies to which our pets may regularly be exposed. The American Veterinary Medical Association, CDC, and the US Department of Agriculture do not believe that pets are at significant risk for Ebola in the United States.

AAALAC is COMING... AAALAC IS COMING!!!

As reliable as any comet coursing through the heavens is the triennial visit from the Association for Assessment and Accreditation of Laboratory Animal Care, International (AAALAC, Intl.). Yes friends, it has been almost three years since the last AAALAC site visit to Duke and we are now in the early stages of preparation for the October 2015 accreditation site visit.

Over the next year you’ll hear AAALAC discussed several times and see many opportunities to educate yourself regarding the actual site visit expectations. What you should know today?

- The Duke Animal Care and Use program has been accredited by AAALAC in 1975.
- The AAALAC site team will probably be here in early October 2015 for 3-4 days.
- They will also spend time reviewing select protocols, maybe in your laboratory, as well as IACUC processes and procedures.
- Preparing for the AAALAC site visit is very similar to preparing for an IACUC semiannual site visit ... only better!

We look forward to another very successful accreditation site visit next fall and appreciate all your efforts to assist the program with this review.

Wishing you a successful research month,
AAALAC PREP IDEAS

As we all prepare for the AAALAC visit next fall, it is time to start thinking and reviewing the core expectations. Below are a few beginning questions to discuss in your next lab meeting:

1. Does our research staff have access to copies of your approved protocols and amendments?
2. Are we following the HUMANE ENDPOINTS listed in our protocol?
3. Are all of the research staff familiar with the protocol approved procedures they are using?
4. Are we using only analgesics / anesthetics that are in our approved protocol?
5. Are our controlled substance licenses current and our controlled substance logs up to date?
6. Can all of the surfaces in our animal use areas be adequately sanitized?
7. Do we sterilize all instruments used in surgery of our animals?
8. Do all of our staff understand (and can they explain) Duke’s veterinary care reporting system?
9. Does our research staff know how to contact a Duke veterinarian after hours if needed?
10. Are our animals observed at least daily, including weekends and holidays?
11. Have our research staff completed the required animal training? Safety training?
12. Are all of our animal cages labeled with the CURRENT PROTOCOL and PI information?

The animal program would like to help your lab be a shining star during the 2015 AAALAC accreditation review. Contact Bill Wade (919.668.6720; w.wade@duke.edu) for suggestions!

WHAT is AAALAC?

Ed Note: Duke University has been continuously accredited by AAALAC since 1975!

AAALAC International is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. AAALAC stands for the "Association for Assessment and Accreditation of Laboratory Animal Care."

More than 900 companies, universities, hospitals, government agencies and other research institutions in 39 countries have earned AAALAC accreditation, demonstrating their commitment to responsible animal care and use. These institutions volunteer to participate in AAALAC's program, in addition to complying with the local, state and federal laws that regulate animal research.

In addition to Duke, a few other institutions that have earned AAALAC accreditation include the Sloan-Kettering Cancer Center, St. Jude Children’s Research Hospital, The American Red Cross, all Department of Defense and VA Medical Centers, and the National Institutes of Health.

Why is AAALAC’s role important?

For some, animal research is a controversial topic. But like others in the animal welfare arena, AAALAC endorses the use of animals to advance medicine and science when there are no non-animal alternatives, and when it is done in an ethical and humane way.

When animals are used, AAALAC works with institutions and researchers to serve as a bridge between progress and animal well-being. This is done through AAALAC’s voluntary accreditation process in which research programs demonstrate that they meet the minimum standards required by law, and also going the extra step to achieve excellence in animal care and use.
WHAT INVESTIGATORS NEED TO KNOW ABOUT THE USE OF ANIMALS
(From the NIH Web)

Principal investigators are responsible for the scientific and technical aspects of a grant award and must ensure compliance with Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals when using live, vertebrate animals. PHS Policy incorporates U.S. Government Principles, the Guide for the Care and Use of Laboratory Animals, and the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. Vertebrate animals include traditional laboratory animals, farm animals, wildlife, and aquatic animals. Animal use encompasses research, teaching, or testing. Generation of custom antibodies is considered an activity involving vertebrate animals.

Who Must Comply With the PHS Policy? The PHS Policy on Humane Care and Use of Laboratory Animals applies to extramural and intramural activities supported by any PHS agency, including the National Institutes of Health (NIH), the Food and Drug Administration, and the Centers for Disease Control and Prevention. All funding mechanisms, including research and training grants, cooperative agreements, and contracts, conducted at domestic and foreign institutions, are covered by the Policy.

What is the IACUCs Task? Institutional Animal Care and Use Committees (IACUCs) are local institutional committees with federally mandated oversight responsibilities, including:

- Reviewing animal-use protocols;
- Reviewing significant changes to protocols;
- Evaluating institutional compliance with PHS Policy, U.S. Department of Agriculture (USDA) Animal Welfare Regulations, and institutional policies;
- Monitoring institutional animal care and use programs, including inspecting animal facilities;
- Reviewing concerns about animal care or use;
- Reporting noncompliance and suspensions to the Office of Laboratory Animal Welfare (OLAW).

Institutional and Investigator Responsibilities: The NIH has certain specific and detailed expectations of Duke and each Investigator holding a federally funded grant. These expectations include:

- Describing proposed use of animals in grant applications.
- Obtaining IACUC approval prior to using animals and prior to implementing significant changes.
- Ensuring research is conducted in accord with the protocol.
- Complying with institutional policies and procedures.
- Addressing significant changes to the use of animals in progress reports & amendments.
- Addressing changes in the use of animals that may be a potential change in scope of the grant.

How to Write an Application Involving Research Animals: New investigators, or post docs wishing to learn, can complete the on-line tutorial at the NIH website listed as: http://www.niaid.nih.gov/ncn/clinical/researchanimals/tutoriaUindex.htm While the tutorial differs form the Duke protocol template, the concepts and procedures are applicable to the Duke template.

Applying for Funding: The proposed involvement of vertebrate animals is evaluated as part of the agency peer review process. In addition to providing IACUC approval status, applicants must address five points in the Research Plan of the grant application:

1. A detailed description of the proposed use of the animals, including species, strains, ages, sex, and numbers.
2. Justification of the use of animals, choice of species, and numbers to be used.
3. Information on the veterinary care of the animals.
4. A description of the procedures for ensuring humane treatment (i.e., minimization of discomfort, distress, pain, and injury).
5. The method of euthanasia, the reasons for its selection, and consistency with the AVMA Euthanasia Guidelines.

Failure to address these elements will result in the application being designated incomplete and is grounds for PHS to defer the application or may negatively affect the priority score.

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DID YOU KNOW?

Alcohol alone is not acceptable for skin disinfection. The utilization of a disinfectant (e.g., iodophor or chlorhexidine detergent) in combination with alcohol is required. Exceptions may be approved by the IACUC on a case-by-case basis, following consultation with a Duke veterinarian. For more information, see the Animal Surgery policy for more details.

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Obtaining IACUC Review: IACUC approval is required prior to award except in rare circumstances. The use of animals as described in the protocol approved by the IACUC must be congruent with the description in a competing grant application. Any modification required by the IACUC that affects the content of the application must be submitted to the agency along with the IACUC approval date.

Receiving all Award: To receive an award the grantee organization and every performance site where animal work will be performed must have an Animal Welfare Assurance approved by OLAW. OLAW will contact an organization with specific instructions when an Assurance is required. An Inter-Institutional Agreement (IIA) is negotiated when the grantee does not have its own animal facilities and the animal work will be performed at an institution with an Assurance.

Working with a foreign (non-US) institution? Foreign institutions provide a Statement of Compliance with Standards for Humane Care and Use of Animals.

Past Award IACUC approval is required at least every 3 years (annually if covered by USDA regulations). Significant changes in animal care and use are to be approved by the IACUC prior to implementation. Check with your IACUC to determine what constitutes a significant change. Conducting research in the absence of a valid IACUC approval or implementing a significant change without IACUC approval constitutes noncompliance.

Investigators also must be aware of and comply with additional institutional policies that may be more restrictive.

For additional information:
♦ http://grants.nih.gov/grantsiolaw/olaw.htm
♦ http://www.nap.edu/readingroom/books/labrats
♦ http://grants.nih.gov/grantsfunding/phs398/phs398.html

IACUC-APPROVED PROTOCOLS & NIH/PHS FUNDED GRANTS
(Adapted from the Institutional Animal Care and Use Committee Guidebook)

In order to approve a protocol that involves the use of animals, the IACUC must review the proposed care and use of animals, and determine that all federal criteria have been met. PHS requires that the project be conducted in accordance with the PHS Policy, the AWA, the Guide, the institution’s Assurance, and all other applicable federal statutes and regulations related to animals. The project should also comply with all institutional policies.

If the IACUC requires changes to the protocol that are not reflected in the grant application, then the PHS funding component must be notified in the follow-up certification of IACUC approval. Duke is required to provide PHS with the date of IACUC approval. There is no provision for providing a contingent approval date; the date provided must signify full approval by the IACUC.

In most cases, the NIH/PHS allows a 60-day grace period following the grant receipt deadline date during which the investigator may secure IACUC approval. If the IACUC review occurs subsequent to the grant submission, then a letter verifying IACUC approval, and stating any modifications required by the IACUC, is submitted to the funding agency.

Note: You can view the entire text of this publication online at http://grants.nih.gov/grants/olaw/GuideBook.pdf

CONGRUENCY REVIEWS

A congruency review is a comparison between the grant submitted to the funding agency and the protocol reviewed by the IACUC. To be congruent, all grant proposals, even if the procedures will not be performed until the 4th or 5th year, must be in an IACUC-approved protocol before the congruency letter can be generated.

Congruency reviews generally require 5-7 business days to complete. Why so long? OAWA or IACUC staff must review the entire grant (except for biosketches or non-animal proposed activity).

The secret to smooth congruency reviews? Submit an electronic copy of the grant at the same time the protocol is submitted (if you have the grant at that time). PLAN AHEAD! If you think you MAY need a congruency review, request it up front, because these reviews cannot be rushed, and do require time to complete.
How to protect yourself and your pets:

⇒ It’s always a good idea to avoid contact with people or animals that are obviously ill, regardless of what may be making them sick. This includes their blood and body fluids.

⇒ Although bats in the U.S. are not known carriers of Ebola, they can carry rabies. Contact with bats should be avoided as a general rule.

⇒ While not a common menu item for most of us, there are people who eat bushmeat (wild animal meat) that may be imported from Africa. This is a potential source of infection, so you should avoid eating any of this meat.

⇒ If you have been exposed to someone infected with Ebola, or if you feel you may be infected, contact your physician immediately.

⇒ If your pet has been exposed to someone infected with Ebola, contact your veterinarian immediately.

⇒ If your pet is ill — regardless of the cause — or if you have questions about your pet’s health, contact your veterinarian.

For additional information:
http://avma.org/ebola
http://cdc.gov/vhf/ebola/transmission/qas-pets.html

SANITATION, STERILIZATION, & DISINFECTION
(Why Do I Care?)

Before we address why we should care, let’s first look at defining terms and understand the differences. Most simply put:

⇒ Sterilization kills all viable microorganisms.
⇒ Disinfection reduces the number of viable microorganisms, but doesn’t kill everything.
⇒ Sanitation picks up dirt and debris, but does not kill viable microorganisms.

Or to be a little bit more scientific:

⇒ Sterilization is the statistical destruction of all microorganisms and their spores (e.g., a 99.9999% reduction <also called a 6-log kill) of the bio-burden.
⇒ Disinfection reduces the number of microorganisms by 99.99% (4-log) to 99.999% (5-log).
⇒ Sanitation … well, picks up a bunch of bugs.

While our choices of agents are many the real question is “When should each be used?” One way to answer this question is:

⇒ Sterilize anything going into animals.
⇒ Disinfect next to or around an animal.
⇒ Sanitize surfaces and rooms.

A good place to review the options for animal use is the Duke animal program web page ‘Guidelines for Disinfection & Sterilization Methods.’

DLAR has also established schedules for reducing microbial load in all animal care facilities. When entering a facility, check and see when it was last sterilized, disinfected, or sanitized. Then assure you are managing your animals to protect their health as well as the health of the facility and other animals being housed within.

For more information on reducing microbial load, contact the DLAR Operations Staff for discussion and advice.
DUKE PRE-VET CLUB SEEKS OPPORTUNITIES

Looking for students to work in your office or laboratory? Want to mentor and teach undergraduates with special interests in animals? The Duke undergraduate Pre-Vet society has many students looking for animal experience, research experience and opportunities to work with veterinarians. These are hard-working future veterinarians are interested in science and committed to preparing for veterinary school. Experience hours are crucial to veterinary school application, but are not always easy to find. Most students qualify for work study. Shadowing opportunities are also of interest.

Currently there are pre-vet students interested in exotics and wildlife, a student interested in exploring the roles of veterinarians at Duke, and a student looking to learn about animal and conservation research over spring break. Help develop tomorrow’s veterinarians by contacting the Duke Pre-Vet society (VML5@duke.edu). If you would like to learn more about the Pre-Vet Society, visit the website at: http://sites.duke.edu/dukeepvs/

THE BASICS OF RUNNING A PI MANAGED HOUSING FACILITY

PI-managed facilities have specific requirements for maintaining these areas, including:

General:
- Initial IACUC approval followed by annual re-approval through inspection by site team & IACUC Semi-inspection.
- Contact person assigned for each lab/facility.
- Twenty-four hour animal environment monitoring.
- Accurate and complete record keeping.
- Training for all lab staff involved in the animal care.

Daily Husbandry Procedures:
- Animal observations (required by federal guidelines).
- Environmental monitoring.
- Provide food and water (check daily to ensure quality).
- Cleaning of the housing area.
- Check live traps (if used) for escaped or feral rodents.
- Document all daily husbandry procedures.
- Cage changing activities.
- Monthly requirements include sanitizing of the room, equipment (caging), feed and bedding containers, etc.
- Report animal health issues or emergencies to DLAR.

Administrative Procedures:
- Cage cards are correctly reflect the protocol, etc.
- SOP describing care practices to the OAWA.
- An Adverse Event Mitigation Plan.
- Records available for site team inspections.
- Lab SOPs and protocol documents available/accessible for all lab staff.

ALWAYS USE A SECONDARY PHYSICAL METHOD OF EUTHANASIA!

Please note this list is not all inclusive and any form of euthanasia used MUST be approved on your IACUC protocol. For more information on methods of euthanasia, consult the Duke animal program website:

⇒ Euthanasia of Rodents
⇒ Euthanasia of Fetuses
⇒ Euthanasia of Finfish, Invertebrates, & Birds
⇒ Euthanasia of Animal Other Than Mice, Rats, or Aquatics

CO2 EUTHANASIA IN MICE & RATS

Performing CO2 euthanasia humanely is a critically important activity for the university and the animal care program. Performing CO2 euthanasia on certain ages of rodents simply will not work. Failure to perform CO2 euthanasia properly requires a federal report to the NIH. The guidelines below applies to laboratory mice and rats:

Gestational age 0 to gestational age 14:
- Euthanasia of the mother; or
- Removal of the uterus/fetus

Gestational age 15 to birth:
- Euthanasia of the mother; or
- Decapitation with surgical scissors
- DO NOT USE CO2 euthanasia on fetus

Birth to 14 days of age:
- Overdose of chemical anesthetics; or
- Decapitation; or
- DO NOT USE CO2 euthanasia

15 days of age through weaning:
- Follow guidelines for adults (below)

Post weaning through adulthood:
- CO2 euthanasia; or
- Overdose of barbiturates

Caution: Animals younger than weaning may not respond to CO2 as full grown adults do, some young animals are resistant to CO2 euthanasia for up to 30 days of age.
Introduction
Less than ¼ of one percent of all laboratory animals needed in the U.S. are non-human primates. Approximately 30 different species are studied by the research community. Many historic scientific breakthroughs, such as the discovery of the Rh factor and the development of a live polio virus vaccine were achieved through research with non-human primates. Today they are considered extremely important models in many areas of medicine because of their close relationship to humans.

Hepatitis B and C
Chimpanzees are uniquely susceptible to human hepatitis virus infections and serve as an important study model for this global public health problem. Research with chimpanzees has virtually eradicated hepatitis B and C infections acquired through blood transfusions, a landmark achievement in the control of viral hepatitis. Commercially available hepatitis B vaccines have prevented the development of cirrhosis and liver cancer in millions of people. Because no vaccine for hepatitis C infections is yet available, scientists continue to study the pathogenesis of this disease in chimpanzees to gain a better understanding of the infection process, to improve current treatment modalities, and to pave the way for the development of an effective vaccine.

AIDS — Acquired Immune Deficiency Syndrome
Scientists face major challenges in their quest to develop a vaccine for human immunodeficiency virus (HIV), the agent that causes AIDS. Having no human model of protection to guide them, medical researchers depend heavily on monkeys for the development of promising strategies to protect people from this disease. Vaccines containing various strains of a simian immunodeficiency virus (SIV), a closely related virus that follows a disease course similar to HIV, or a hybrid human/simian immunodeficiency virus (SHIV) are being tested in macaque monkeys, and several research groups have successfully vaccinated monkeys with viral preparations that reduce viral load and halt disease progression.

Malaria
Researchers are beginning to overcome some of the enormous obstacles in developing a vaccine against malaria, a disease that affects millions of people annually. New-world monkeys and chimpanzees are the only species suitable for vaccine evaluation because they are susceptible to the same strains of the parasites that cause human malaria. Unlike simpler organisms, the malaria parasite has many chromosomes, thousands of genes, and a four-stage life cycle as it passes from mosquitoes to humans and back again. A number of promising vaccines that attack the organisms at every vulnerable point in its life cycle are being tested. Some of these have successfully stimulated protective responses in animals and may soon be ready for human trials.

Acute Respiratory Disease
Respiratory syncytial virus (RSV) can cause life-threatening respiratory infections in infants, young children and the elderly. Since there is no effective therapy, an RSV vaccine is a high medical priority in the U.S. Researchers are designing vaccines containing live, weakened viruses that are suitable for applying with nose drops. These vaccines are being tested for their ability to protect chimpanzees, the only animal that is naturally infected by RSV and develops an illness with symptoms similar to those seen in humans.

Periodontal Disease
Microbial infection of the tissue supporting teeth is the most common cause of bone and tooth loss in humans and may be an important risk factor for cardiovascular disease. Periodontitis is also a health problem for captive primates, making these species excellent models for studying the connection between chronic oral infections and systemic disease. Several groups of researchers have shown that immunizing monkeys with a vaccine contain-
ing a killed oral bacterium can halt infection and suppress bone loss.\(^7\)

**Aging and nutrition**

Scientists are currently studying the effects of long-term calorie restriction (CR) on the biology of aging in macaque monkeys. They have learned that a reduction in calories over a period of several years lowers body temperature, slows metabolism, lessens the risk of cardiovascular disease, and reduces predisposition toward diabetes. Long-term studies of CR have increased the lifespan of monkeys.\(^8\)

**Brain biology**

Because they share many features of brain biology and structure with humans, non-human primates are extremely valuable models for studying normal brain function and brain-related diseases, including mental, neurological, and addictive disorders. Many of the functional regions of the cerebral cortex that are present and identifiable in nonhuman primates have provided a precise map of the brain circuitry involved in visual and auditory perception, learning and memory deficits, and brain and spinal cord injuries.\(^9\)

**Alzheimer’s disease**

The decline of memory and other mental functions in patients with Alzheimer’s disease (AD) is associated with the loss of or damage to cholinergic nerve cells that use the chemical acetylcholine to transmit messages to other cells in the brain. Age-related reduction in the functions of these nerve cells also occurs in primate species. Scientists have shown that grafting genetically modified cells to produce nerve growth factor (NGF) directly into the brains of macaque monkeys is a safe procedure that enhances the survival and function of the cholinergic nerve cells. Such studies are now being extended to humans in an attempt to slow the loss of memory in patients with AD.\(^10\)

**Parkinson’s disease**

Parkinson’s disease (PD) is a slow, progressive disease, generally found in the aged and characterized by tremors. Scientists know that the disease is associated with degeneration of brain cells that produce a chemical (neurotransmitter) called dopamine. Recently, they found a new method to deliver the gene that produces GLNF (a factor that protects brain cells) directly into the brains of monkeys. The treatment successfully prevented the progression and reversed the symptoms of PD. Clinical testing to forestall human disease is under consideration.\(^11\)

**References**


