Responsible Conduct of Research Seminar:

USE OF ANIMALS IN RESEARCH

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• Why do we need animal models for research and education?
  ◦ What about alternatives like computers or cell lines?
  ◦ Can results from animal studies really apply to humans?

• What have we learned from animal research?

• Are the animals used in research & education protected?
  ◦ Regulations to protect research animals
  ◦ Do scientists care about animals? Do they treat them well?
  ◦ Are lab animals suffering and in pain?

• Opposition to animal research
Why do we need animals for research & education?

- Animals serve as good models to help us understand how living tissues function and the biology underlying disease.
  - The interaction of cells, tissues and organs within the body is very complex, and can often only be studied in the whole animal.

- Only by understanding how disease or injuries affect living organisms can we develop treatments or cures.

- Animal models are used to:
  - Help researchers understand the fundamental ways in which diseases affect living tissue.
  - Develop and test treatments for illness or injury.
  - Train future scientists and physicians.
Can’t Computer Models and Cell Cultures Replace Animal Research?

- Computer models and cell cultures are good for screening and are used frequently.
- Such models cannot replicate complicated interactions in the whole system.
- Final testing depends on studies in animals; sometimes it is required by law.
- Animal and non-animal models used in conjunction achieve the best answer.
Can Results from Animal Studies Really Be Applied to Humans?

- There are many similarities between animals and man. Examples include:
  - Immune function in mice
  - Cardiovascular function in dogs

- Animals provide index of safety.
  - Nuremberg Code mandates that animal studies precede and support human studies.
  - Declaration of Helsinki mandates that medical research on humans must be supported by preceding animal research.

- Nearly all medical advances of the past century started with research in animals.
What have we learned from animal research?

- Animal research has played a major role in nearly all medical advances for both humans and other animals.
- These include, but are not limited to:
  - Angiograms, X-Rays, CAT scans, blood pressure measurement, cardiac pacemaker, hypertension medications, insulin for diabetes, MRI, numerous vaccines, cardiac catheters, kidney dialysis, cataract surgery, burn treatments, heart valve replacements, artificial hips.... The list goes on and on!!
- So what animals have helped which medical advances?
  - Let’s look at some specific examples...
• Polio
  ◦ Landsteiner and Popper proved it infectious; able to transmit disease to monkeys.
  ◦ Salk and Sabin developed their vaccine through work with chickens and monkeys.

• Diabetes
  ◦ Banting and Best showed importance of insulin in dogs.

Animal Models for Research & Disease
- Infant Mortality
  - Studies in sheep and lambs led to use of steroids in treatment of respiratory distress syndrome (formerly hyaline membrane disease), a major cause of death in premature infants.
  - Advances in understanding and treatment of sudden infant death syndrome (SIDS) came from studies in rats, mice, dogs, and sheep.

Animal Models for Research & Disease
Cystic Fibrosis
- A major killer of young adults.
- Mouse models led to understanding role of chloride channels.
- Genetic therapies on the horizon are an outgrowth of work in mice.
• High Blood Pressure (HBP)
  ◦ Goldblatt linked HBP to kidney in rats, cats, and dogs; led to diuretics and angiotensin converting enzyme inhibitors to treat high blood pressure.
  ◦ Cushing linked HBP to brain in dogs; led to understanding sympathetic nervous system influence on blood pressure and drugs to treat it.

Animal Models for Research & Disease
Obesity

- Major risk factor for diabetes mellitus, high blood pressure, heart attack, stroke and certain cancers.
- Epidemic in the United States: 64% of adults are overweight and 25% are obese.
- Mouse models and Zucker obese rats shedding new light on causes of overeating, importance of leptin receptors, and ways that obesity leads to disease.

Animal Models for Research & Disease
• Bioterrorism
  ◦ Smallpox vaccine from calves
  ◦ “Two animal rule” – FADA mandates that all vaccines must be tested for efficacy and safety in two animals (typically rodent and non-human primate) before introduction in humans
  ◦ Botulinum antitoxin tested in mice and non-human primates
AIDS

- Numerous animal models in studies to understand the disease and how it attacks the immune system.
- Current anti-AIDS treatment developed in animal models have greatly extended life expectancy and quality of life for AIDS victims.
- AIDS vaccines being developed in monkeys.
Stroke

- Stroke kills over 150,000 people in the U.S. each year and causes major disability that can include paralysis, inability to speak, loss of vision and loss of cognitive function.
- Tissue plasminogen activator (TPA), a new treatment for acute stroke, and one that can reverse disability due to stroke was first studied in rats with experimental stroke.
- Other potential treatments, even cures, for stroke are now being studied in experimental animals.

Animal Models for Research & Disease
There are a number of federal and local laws, regulations and institutions, as well as nonprofit organizations, that ensure animals used in research & education are being treated humanely.

These include:

- Animal Welfare Act
- Public Health Service
- IACUCs
- AAALAC

Are the animals used in research & education protected?
Animal Welfare v. Animal Rights

Quiz: Question 2 of 3
Which is more despicable?

a. Experimenter Michel Perin, who surgically implants heavy pipes into monkeys’ skulls in order to study the connection between stress and the menstrual cycle.

b. Columbia University, for paying him to do it.
• Animal Welfare
  ◦ ...a human responsibility that encompasses all aspects of animal well being, including proper housing, management, nutrition, disease prevention and treatment, responsible care, humane handling, and when necessary, humane euthanasia
• Animal Rights
  ◦ ...a philosophical view and personal value characterized by statements by various groups.
  ◦ Animal Welfare and Animal Rights are not synonymous terms
Opposition to Animal Research

- Animal welfare is not the same as animal rights.
  - Animal welfare is fully supported by the scientific community, and says we should treat animals with compassion & provide for their humane treatment.

- Some philosophers argue that animals have the same rights as humans and should not be used even to preserve human life or cure human disease.

- Groups that believe in this philosophy work actively to end the use of animals in research & education.
People for Ethical Treatment of Animals (PETA) advocates abolishing all animal research.

- “Even if animal research resulted in a cure for AIDS, we'd be against it.”
- “I wish everyone would get up and go into the labs and get the animals out and burn them down.” --Ingrid Newkirk, PETA Director
Animal Rights Extremism

- Vast majority of animal rights activists pursue their goals legally, through protests and information campaigns.

- However, there has been a movement towards smaller, underground animal rights groups who believe violence & extreme measures are acceptable methods to achieve their goal.
  - Stop Huntington Animal Cruelty (SHAC)
  - Animal Liberation Front (ALF)
Examples of statement from animal rights extremist groups

• “I think violence is part of the struggle against oppression.” – Jerry Vlasak, spokesperson for SHAC and ALF

• “I don't think you'd have to kill too many [researchers]. I think for five lives, 10 lives, 15 human lives, we could save a million, 2 million, 10 million non-human lives.” – Jerry Vlasak, spokesperson for SHAC and ALF

• "In a war you have to take up arms and people will get killed, and I can support that kind of action by petrol bombing and bombs under cars, and probably at a later stage, the shooting of vivisectors on their doorsteps. It's a war and there's no other way you can stop vivisectors." – Tim Daley, ALF
Laboratory animals

- 1940s and 1950s — Increased public concern about vivisection, especially within the context of pets
- 1954 – Universities Federation for Animal Welfare (UFAW) commissions a systematic study of laboratory techniques in an ethical context
  - William Russell
  - Rex Burch

Emergence of Animal Welfare Science
Emergence of Animal Welfare Science

- Published *The Principles of Humane Experimental Technique* in 1959
- The Three R’s have been adopted as key guiding principles for the welfare of animals in research
  - **Reduction**
    - The number of animals used should be the minimum that is consistent with the aims of the research
  - **Refinement**
    - Use of methods that alleviate or minimize potential pain and distress and enhance animal well-being
  - **Replacement**
    - Involves achieving a given purpose without conducting experiments or other scientific procedures on animals
1965—Brambell Commission appointed

- Farmers, veterinarians, animal protectionists, regulators
- Identified science as a way to work through questions
- First funding for animal welfare science begins to flow
- Principles included that “an animal should at least have sufficient freedom of movement to be able, without difficulty, to turn around, groom itself, get up, lie down, and stretch its limbs” – first statement of the Five Freedoms

Emergence of Animal Welfare Science
• Ideal welfare = five conditions met
  ◦ Freedom from hunger and thirst
  ◦ Freedom from discomfort
  ◦ Freedom from pain, injury, and disease
  ◦ Freedom to express ‘normal’ behavior
  ◦ Freedom from fear and distress

• Generally not possible to fulfill all five simultaneously
• **The dream**
  ◦ All animal welfare decisions are science-based
    • Look at inputs and outputs and arrive at a scientific solution
      ◦ Biological function—is homeostasis maintained?
      ◦ Health—absence/presence of disease/injury
    • Behavioral/social function
      ◦ Adaptation
      ◦ Emotional states
      ◦ Cognition/awareness
      ◦ Choices
  ◦ We know this is the best way to assure that the welfare of the animal is protected
The reality

- Animal welfare decisions are social decisions
  - Integration of culture, ethics, and science
  - Science didn’t even really play a role until 1950s
- Science isn’t black-and-white or value-free
- Science can be used to help resolve disputes
- Science may not exist, may be used selectively, or be ignored
- Science is used by both sides in policy debates
- If societal perception is that something is ‘wrong’ then science is unlikely to change that perception

Science can determine what type or level of risk exists
Science cannot determine what type or level of risk is acceptable
1946 Post WWII boom in public funding of science
1950 “Chicago Five” Animal Care Panel
1963 Guide for Lab Animal Facilities and Care
1966 Lab Animal Welfare Act
1973 PHS Policy
1985 PHS Act
1991 PHS Act Amended
Who Enforces Standards?

- USDA (regulations)
- OLAW (regulations)
- AAALAC, Int. (voluntary accreditation standards)
- States (statutes)
- Local Municipalities (laws)
- Institutions (policies)
- Local IACUCs (policies, procedures)
- Attending Veterinarian/Institutional Animal Care Personnel
Animal Welfare Act

“The AWA is a Federal law that Congress passed in 1966 and amended in 1970, 1976, 1985, 1990, and 2002 to protect warm-blooded animals used in research, bred for commercial sale, exhibited to the public, or commercially transported. The law requires minimum standards of animal care to be established and enforced.”

--USDA Animal & Plant Health Inspection Service

Administered by the United States Department of Agriculture

The Animal Welfare Act applies to dogs, cats, primates, guinea pigs, hamsters, and farm animals;

- mandates institutional review, care and feeding, licensure of facilities, and annual report by USDA to Congress.
The Public Health Service Policy on Humane Care and Use of Laboratory Animals (updated 2002) requires compliance with federally mandated standards of care in use of laboratory animals for any work funded by the National Institutes of Health.

Mandated by law, Health Research Extension Act of 1985. Administered through the Office of Laboratory Animal Welfare (OLAW) at the U.S. Dept. of Health & Human Services. Covers the vast majority of animals used in medical research, including rodents.
• Includes mandatory surprise inspections of animal research facilities.
• These federal laws & regulations are in place to ensure that all research animals receive:
  ◦ Good veterinary care
  ◦ Appropriate housing
  ◦ Feeding
  ◦ Humane handling
  ◦ Sound sanitation and ventilation

AWA and PHS policy
Animal Welfare Program

Institutional Leadership

PI Cooperation

Animal Welfare

Quality Animal Care

Healthy IACUC
Institutional Leadership

- Institutional Official provides leadership, promulgates campus research policies, sets “tone”
- Provides adequate resources (money, space, equipment, and staff) for quality animal care, healthy IACUC
- Appoints IACUC members
Institutional Animal Care & Use Committees (IACUCs)

- Required at all research institutions by both AWA and PHS policy.
- Committees consist of veterinarians, scientists, members of the public.
- Without IACUC approval no research using animals may proceed.
- Among IACUC considerations are the measures used to control potential pain and avoid distress as well as the potential value of any scientific outcome from the proposed studies.
IACUC (What is it?)

- The IACUC is the institutional body with responsibility for review and oversight of the institution’s program for the humane care and use of animals.

- The IACUC supports, facilitates, and promotes ethical and humane use of animals by upholding the standards set forth in all applicable laws, policies & guidance.

- Per PHS Policy, must consist of no fewer than five members, including a Veterinarian, one practicing scientist experienced in research involving animals, one member whose primary vocation is in a non-scientific area, and one member unaffiliated with the institution.
IACUC Charge

- Review institution’s animal care and use program 2x/yr.
- Inspect institution’s animal facilities, laboratories, and other areas where animals are used 2x/yr.
- Provide IACUC program evaluations and facility inspections to the IO.
- Review and approve, require modifications in (to secure approval) or withhold approval of proposed and continuing animal activities.
- Review and approve, require modifications in (to secure approval) or withhold approval of all proposed changes (modifications) to approved protocols.
- Notify investigators in writing of its decision to approve, require modifications in (to secure approval) or withhold approval of proposed animal activities.
- Investigate concerns involving the care and use of animals.
- Suspend animal activities that are not being conducted in accordance with applicable requirements.
- Make written recommendations to the IO regarding any aspect of the institution’s animal care and use program.
• Attending Veterinarian

• Animal Care Staff: vet techs, husbandry techs, procurement staff, transport staff, cagewash personnel, etc.

• Compliance/post-approval monitoring (may reside with IACUC)
Attending Vet’s Duties

- Monitor the care and use of animals
- Provide technical assistance and training to personnel involved in animal activities, including selection and procurement of animals, husbandry and care, handling and restraint, identification and records, animal health and welfare, employee safety and health concerns, specific experimental and surgical techniques and euthanasia
- Assist investigators with protocol preparation pertaining to animal housing, requirements for surgery, proper use of anesthetics, analgesics, and tranquilizer drugs, methods of euthanasia and other animal health and welfare issues
- Manage animal housing facilities, including space allocation
- Halt any animal activity if the safety or welfare of an animal is at risk or if the work being performed is not in accordance with an IACUC approved animal use protocol
- Report animal welfare concerns and/or possible non-compliance to the IACUC
Animal Care Duties (ARC)

- Housing
- Daily Health Checks
- Pathogen Control
- Feed, Bedding
- Transport
- Monitoring of Surgery/Other Procedures
- Necropsy
- Physical Plant Upkeep
- Equipment Maintenance
- Scientific/Clinical Input on IACUC Review
- IACUC’s “eyes and ears” in the Field
PI Responsibilities

- Obtain IACUC approval prior to commencement of any live vertebrate animal care or use activity
- Purchase any animals to be used at through approved means
- Make no changes to the approved protocol without first having submitted those changes for review and approval by the IACUC
- Provide the IACUC with any information requested relative to the care and use of animals
- Comply with an IACUC decision to suspend or withdraw its approval for an animal activity
- Obtain continuing approval prior to the expiration date approval of the study
- Ensure all personnel having direct live animal contact have been or will be trained in applicable humane and scientifically acceptable procedures for animal handling, administration of therapeutic drugs and euthanasia
- Enforce requirements for study personnel participation in institution’s occupational health program
- Maintain and make available for inspection by the IACUC, Attending Veterinarian and federal agency inspectors all IACUC protocol and animal care and use records in accordance with federal regulations
What is AAALAC?

AAALAC, International is a private, nonprofit organization that promotes the humane treatment of animals in science through a voluntary accreditation program.

Formal site visits are conducted at three-year intervals and are a method of ensuring that animal care and use programs maintain high standards.
• AAALAC site visitors evaluate all aspects of an animal care and use program, including conformance with established procedures and overall performance in the area of animal care and use in research, education, testing or breeding.

• The basic components of a program that are evaluated include (but are not limited to) institutional/IACUC policies, animal husbandry, veterinary care, and the physical plant.
Worker Protection & Employee Health
Risks for Animal Users?

- Allergies
- Asthma
- Skin Rashes
- Burns, cuts, needle sticks
- Chemical exposures
- Infectious agents
- Repetitive stress, overexertion
Worker Protection Program

- Employee Health Clinic
- Brochure
- Health History Questionnaire
- Tutorial on risks for animal users and bystanders
- Access to hazards limited pending assessment/tutorial
- Consultation and referral to specialist
- Case management for Worker’s Compensation claims
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