Humane and Responsible Use of Laboratory Animals

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http://www.youtube.com/watch?v=NT4IL1DsjGA
Agenda

• History
  – of the use of animals in biomedical science
  – of the regulatory environment as it relates to the use of animals in research

• Definitions & acronyms

• Current regulatory environment
  – Federal regulations
  – Public Health Service Policy
  – AAALAC and the *Guide for the Care and Use of Laboratory Animals*, NRC 2011
  – Canada, the UK, and the EU

• Practical matters
  – IACUC & AV
  – Training
  – Occupational Health and Safety
  – Biosecurity
  – Physical security
  – Records
Early history

- Aristotle (384-322 BC) – Greek philosopher/physician was the first known to have made dissections which revealed internal differences among animals
- Erasistratus (304-258 BC) – was probably the first to perform experiments on living animals and using pigs established that the trachea was an air tube and the lungs were pneumatic organs
- Galen (130-200 AD) – dissected many species to study the anatomy and justified experimentation as a long arduous path to the truth
The Dark Ages

Dogma replaced experimentation during medieval times by ecclesiastical authorities who wanted to prevent acquisition of knowledge about the natural world. Blasphemy was the threat!
Reawakening of Science

• Andreas Vesalius (1514-1564) – considered the founder of modern anatomy, used dogs and pigs

• Sir William Harvey – in 1628 published about the movement of the heart and blood in animals

• Claude Bernard (1813-1878) – known as the founder of experimental medicine stated, in 1865, …it is proper to choose certain animals which offer favorable anatomical arrangements or special susceptibility to certain influences. For each kind of investigation we shall be careful to point out the proper choice of animals. It is so important that the solution of a physiological or pathological problem often depends solely on the appropriate choice of the animal for the experiment so as to make the result clear and searching.
John Call Dalton, M.D. (1825-1889) – spent a year in Bernard’s laboratory in Paris (~1850) and was so impressed with the instructional methods, some of which utilized living animals to demonstrate important physiological principles, that he included such demonstrations in his teaching at the College of Physicians and Surgeons.
Medical Advances Resulting from Animal Research

1700s: Smallpox vaccine (cattle)
1800s: Rabies vaccine (dogs, rabbits)
1900s: Genetics, inheritance (mice)
1910s: Cardiac catheters (dogs, rabbits)
1920s: Insulin therapy (dogs)
1930s: Inhalant anesthesia (dogs)
1940s: Antibiotics (many species)
1950s: Polio vaccine (monkeys)
1960s: Drugs for mental illness (rodents)
1970s: Leprosy Rx (monkeys, armadillos)
1980s: Organ transplant (dogs, livestock)
1990s: Laparoscopic surgery (pigs)
2000s: Genetic revolution (mice)
Nobel Prizes for Physiology & Medicine

• **1901-2009**: 68 of 108 awards were given for research involving animals
  - squids, crab, nematodes, flies, fish, birds, mice, dogs, cats, pigs, cows, chimpanzees, others.
  - immunity, nerve function, nutrition, diabetes, antibiotics, polio, imaging, etc.

• **1996**: 100% of responding laureates agreed that animals were important to their work & would be important in the future.
Public Opinion and Regulations

- Societies for the Prevention of Cruelty to Animals (SPCA) begin to be established. First in England, but by the 1860s in New York, Philadelphia and Massachusetts.

- UK ‘Cruelty to Animals Act of 1876’
  - Supported by scientists
  - Scientists are ‘certified’ based upon the species used and the nature of the experiments
  - Legal regulatory relationship is between the government and the scientist, not the government and the institution as in the US
International Legal Precedents for Animal Research

Nuremberg Code
International Legal Precedents for Animal Research

• **Nuremberg Code of 1947**
  • Post WWII as a consequence of Nazi atrocities
  • Any experiments on humans “should be designed and based on the results of animal experiments”.

• **Declaration of Helsinki**
  • 18th World Medical Assembly, 1964
    • Revised in 1975
  • Medical research on human subjects “should be based on adequately performed laboratory and animal experimentation”
Opponents of Research

“It would be great if all the fast-food outlets, slaughterhouses, these laboratories and the banks who fund them exploded tomorrow.”

— Bruce Friedrich, Campaign Director
People for the Ethical Treatment of Animals (PETA)

“Our nonviolent tactics are not as effective. We ask nicely for years and get nothing. Someone makes a threat, and it works.”

— Ingrid Newkirk, President and Co-Founder of PETA

PETA uses their contributors’ tax-exempt donations to support the North American Earth Liberation Front. This FBI-certified “domestic terrorist” organization was responsible for a $12 million fire in Vail, Colorado. PETA has admitted to giving more than $100,000 to convicted arsonists and other violent criminals.

PETA: As warm and cuddly as you thought?

ConsumerFreedom.com Find out more about PETA.
• Confinement is cruel.

• Science is cruel.

• Research with animals is meaningless: cells, tissue culture, DNA.
Definitions

- **Animal experimentation**: the scientific study of animals for the purpose of gaining new biological knowledge or solving specific medical, veterinary, dental or biological problems

- **Comparative medicine**: the study of the nature, cause and cure of abnormal structure and function in people, animals and plants for the eventual application to and benefit for all living things
**Animal (from the AWA):** any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. **This term excludes:** Birds, rats of the genus *Rattus* and mice of the genus *Mus* bred for use in research, and horses not used for research purposes and other farm animals, such as, but not limited to livestock or poultry, used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs, including those used for hunting, security, or breeding purposes.
**Animal (PHS Policy)**- Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes
Important Acronyms

- **AAALACi** – Association for the Assessment and Accreditation of Laboratory Animal Care, International
- **AWA** – Animal Welfare Act
- **IACUC** – Institutional Animal Care and Use Committee
- **OLAW** – Office of Laboratory Animal Welfare
The "three Rs", first described by Russell and Burch in 1959, are guiding principles for the use of animals in research in many countries:

• **Replacement** refers to the preferred use of non-animal methods or less sentient species, over animal methods whenever it is possible to achieve the same scientific aim.

• **Reduction** refers to methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.

• **Refinement** refers to methods that alleviate or minimize potential pain, suffering or distress, and enhance animal welfare for the animals still used.
Average American Lifespan
(Source: U.S. National Center for Health Statistics, 9/17/2009)
Life, February 4, 1966

CONCENTRATION CAMPS FOR DOGS
US Regulations

- **1966:** The Laboratory Animal Welfare Act was passed by Congress to regulate the care and handling of dogs, cats, non-human primates, guinea pigs, hamsters, and rabbits at licensed research institutions and animal dealer facilities.

- **1970:** The act was, with certain exceptions, expanded to cover all warm-blooded animals in research as well as to cover animals in circuses, zoos, roadside shows, and commercial breeding operations. It was rechristened the Animal Welfare Act.

- **1976:** Congress approved amendments to the act to cover animals in transportation as well as those forced to fight.

- **1985:** Congress passed amendments requiring the use of pain killers; presurgical and postsurgical care; animal care training for personnel who work with animals; and euthanasia of an animal upon completion of an experiment. The amendments, among other things, also required exercise for dogs and a physical environment to promote the psychological well being of nonhuman primates.

- **1990:** Congress passed amendments that imposed longer holding period requirements upon animal dealers.

- **2002:** U.S. lawmakers, as part of the Farm Bill, passed an amendment that closed loopholes in the federal ban on the interstate shipment and foreign export of fighting animals. Congress also passed an amendment that codified into law the USDA’s long-standing exclusion of birds, mice, and rats from coverage as research animals.
US Public Health Service Policy

• 1985 Health Research Extension Act (Public Law 99-158): Congress required compliance to the *PHS Policy on the Humane Care and Use of Laboratory Animals* for institutions receiving funding from any USPHS Agency

• OLAW Categorizes Funding Recipients:
  – Category 1: Accredited by AAALAC, International. IACUC evaluation of all facilities and report prepared every 6 months
  – Category II: Not AAALAC, International accredited. Institution evaluates facilities and programs. IACUC reviews programs every six months and submits report to OLAW.
• Private therefore not subject to the FOIA
• Voluntary
• Peer Review
• **Gold Standard**
• *Guide* Promulgated by ILAR of the NAS
How Important are these to CUMC?

• **Scope of CUMC activity**
  - >250 Principle Investigators
  - >1,000 Active Animal Use Protocols
  - >$850M in sponsored research
  - >$150M of those projects use animals

• **AAALAC can revoke accreditation**

• **OLAW can revoke funding to noncompliant institutions**

• **USDA can levy fines for violations and/or revoke license**
Canada, UK & EU

- Canadian Council on Animal Care
- Animals (Scientific Procedures) Act
- European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (ETS 123)
Painful procedure (as defined by the USDA)

... as applied to any animal means any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is, pain in excess of that caused by injections or other minor procedures.

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USDA Categories of Pain or Distress

• Category C – teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs;

• Category D – experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used;

• Category E – teaching, experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results or interpretation of the teaching, research, experiments, surgery, or tests.
• **IACUC:**
  - Requirements for composition vary, but common are:
    • A veterinarian
    • A scientist
    • A community member
  - Responsible for oversight of the institutions animal program, procedures, and facilities to ensure compliance with the triad
  - Authorized to approve, disapprove and **suspend** animal activities

• **Attending Veterinarian:**
  - Advise research personnel on the humane use of animals compatible with scientific endeavors – **required for procedures that may cause pain or distress**
  - Responsible for the husbandry, sanitation, zoonotic disease control and hazard containment
IACUC Responsibilities

• Must review the program and inspect the facilities at least every 6 months
  – Must write a report and send it to the Institutional Official
  – Deficiencies must have a specific plan, with timeline for correction
  – Failure to correct deficiencies must be reported to the USDA and OLAW

• Reviews and approves or withholds approval of animal use proposals (protocols)
  – Rationale and purpose for the use of animals
  – Justification for the species and number of animals
  – Consideration of less invasive procedures ‘3Rs’ – aka consideration of alternatives to painful procedures
  – Training and experience of personnel
  – Special housing or husbandry considerations
  – Use, or lack thereof, sedation, analgesia, and anesthesia
  – Duplication of experiments – literature search and justification
  – Major operative procedures – approval for multiple surgeries must meet additional criteria
  – Criteria for timely intervention (aka endpoints)
  – Post-procedural care
  – Euthanasia and/or disposition – IAW AVMA Guidelines on Euthanasia
  – Safety of working environment
Minimal Training Requirements

• Humane methods of animal maintenance and experimentation
  – Basic needs of each species
  – Proper handling and care for the species to be used
  – Proper pre-procedural and post-procedural care
  – Aseptic surgical methods

• The concept, availability, and use of research or testing methods that limit the use of animals or minimize animal distress

• Proper use of anesthetics, analgesics, and tranquilizers for species used

• Methods whereby deficiencies in animal care and treatment are reported

• Utilization of services (NAL, NLM) available to provide information:
  – On appropriate methods of animal care and use
  – On alternatives to the use of live animals in research
  – That could prevent unintended and unnecessary duplication of research involving animals; and
  – Regarding the intent and requirements of the Act

9 CFR Ch.1
Occupational Health & Safety

• Allergies

• Zoonotic Diseases

• Research related hazards:
  – Physical
  – Chemical
  – Biological
Biosecurity

• Standardization of animals is a prerequisite for reproducible experiments

• Microbiological standardization aims to produce animals that meet preset requirements, commonly called Specific Pathogen Free (SPF)

• Biosecurity programs include:
  – Procurement of animals that meet standards
  – Husbandry and research practices to maintain those standards
  – Sentinel program(s) to detect inadvertent introduction of undesired agents
  – Physical security to prevent vermin or transfer of diseased entities by man
Physical Security

• CUMC vivaria all have restricted access

• Control of access is used to ensure all of the aforementioned parameters have been met, including:
  – Safety of personnel
  – Biosecurity for other researchers
  – Compliance with federal law and policies

• Providing access to non-authorized personnel may result in revocation of your access and privileges
• Laboratory notebook?
• Sedation, analgesia, and anesthesia!!!
• Surgical
• Euthanasia
• Controlled substances!!
http://www.youtube.com/watch?v=LAkq2wtE4VA
To Protect and To Serve

• The IACUC, the Attending Veterinarian, the staff at the IACUC office, and ICM exist to facilitate your research. Use them!

• Get to know the veterinarians!

• The IACUC & AV must also protect the animals, the institution, and the staff.