Responsible Conduct of Research: Use of Animals in Research

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Use of Animals in Research

• 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?

- Understanding how disease or injuries affect living organisms is necessary to develop treatments or cures.
- Animals provide an index of safety.
  - **Nuremberg Code (1949)** mandates that animal studies precede and support human studies.
  - **Declaration of Helsinki (1964)** states that medical research on humans must be supported by preceding animal research.
Why do we need animals for research & education?

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

• 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
Species Used in Research

• Mice and Rats ~95%
• Dogs and Cats <0.5%
• Nonhuman Primates <0.25%
• Other species
  • Other rodents
  • Rabbits
  • Fish
  • Amphibians/Reptiles
  • Livestock
    • Pigs
    • Cattle
    • Sheep
    • Goats
Can’t Computer Models and Cell Cultures Replace Animal Research?

- Good for screening
- Cannot replicate complicated interactions in the whole system
- Follow up testing requires studies in animals
  - often required by law
- Animal and non-animal models used in conjunction achieve the best answers.
Can Results from Animal Studies Really Be Applied to Humans?

- There are many similarities between animals and man:
  - Mice – Immune
  - Rats – Nervous system and behavior
  - Dogs - Cardiovascular
  - Sheep – Musculoskeletal
  - Ferrets – Respiratory
  - Pigs – Cardiovascular and skin

- Genetically engineered and “humanized” rodents provide unique models for specific conditions
Can Results from Animal Studies Really Be Applied to Humans?

- Nearly all medical advances of the past century started with research in animals.
- Of the 98 Nobel Prizes awarded for Physiology or Medicine, 75 were directly dependent on animal research.
- In a further 4 instances the discovery relied on crucial data obtained from animal studies by other research groups.
Animal Research Advances

• Pre-1900
  • Smallpox vaccine (cattle)
  • Anthrax vaccine (sheep)
  • Rabies vaccine (rabbits, dogs)
  • Typhoid, cholera, and plague vaccines (mice, rats)
  • Early anesthetics (cats, rabbits, dogs)

• 1900s
  • Cardiac catheters (dogs)
  • Rickets treatment (dogs)
  • Corneal transplants (rabbits)
  • Local anesthetics (rabbits, dogs)
  • Discovery of Vit C (guinea pigs)

• 1910s
  • Blood transfusions (dogs, guinea pigs, rabbits)

• 1920s
  • Insulin (dogs, rabbits, mice)
  • Canine distemper vaccine (dogs)

• 1930s
  • Modern anesthetics (rats, rabbits, dogs, cats, NHP)
  • Tetanus vaccine (horses)
  • Diphtheria vaccine (guinea pigs, rabbits, horses, NHP)
  • Anticoagulants (rabbits, mice, dogs, guinea pigs, cats)
Animal Research Advances

- **1940s**
  - Penicillin, streptomycin (mice)
  - Rh factor discovery (NHP)
  - Kidney dialysis (guinea pigs, rabbits, dogs, NHP)
  - Whooping cough vaccine (mice, rabbits)

- **1950s**
  - Polio vaccine (mice, NHP)
  - Hip replacements (dogs, sheep, goats)
  - Heart valve replacement (dogs, calves, rabbits, rats)
  - Cardiac pacemakers (dogs)
  - Kidney transplants (dogs)

- **1960s**
  - Heart transplant (dogs)
  - German measles vaccine (NHP)
  - MMR vaccine (NHP)
  - Antidepressants and antipsychotics (rats, guinea pigs, rabbits)

- **1970s**
  - CT scans (pigs)
  - Leukemia chemotherapy (mice)
  - Ulcer treatments (rats, dogs)
  - Asthma medicine (rabbits, guinea pigs)
Animal Research Advances

• 1980s
  • MRI (rabbits, pigs)
  • Life support and corticosteroids for premature babies (NHP, sheep, rabbits)
  • Hepatitis B vaccine (NHP)
  • Viral disease treatments (numerous species)
  • Leprosy treatment (armadillos, NHP)
  • Medication to control transplant rejection (mice, rabbits, dogs, NHP)

• 1990s
  • HIV combined therapy (mice, NHP)
  • Meningitis vaccines (mice)
  • Breast and prostate cancer medicines (mice, rats, dogs)
  • Statins to lower cholesterol (rabbits)

• 2000s
  • Cervical cancer vaccine (rabbits, cattle)
  • “Bird flu” vaccine (chickens, ferrets)
  • Deep brain stimulation for Parkinson’s dz (NHP)
Animal Models for Research & Disease

- Obesity
  - Major risk factor for
    - Diabetes mellitus
    - High blood pressure
    - Heart attack
    - Stroke
    - Certain cancers
  - Epidemic in the United States
    - 64% of adults are overweight
    - 25% of adults are obese
    - Over 1/3 of all children are overweight or obese

- Mouse models and Zucker obese rats shed new light on causes of overeating, importance of leptin receptors, and ways that obesity leads to disease.
Animal Models for Research & Disease

- Infectious Diseases and Bioterrorism Agents
- Animals are used to study the pathogenesis of disease and vaccine/treatment efficacy.
  
  - “Two animal rule” – FDA mandates that all vaccines must be tested for efficacy and safety in two animals (typically rodent and NHP) before introduction in humans.
    - CFR Title 21, Chapter I, Subchapter D, Part 314

- Smallpox vaccine (cattle)
- Anthrax vaccine (sheep)
- Plague vaccine (rodents)
- Botulinum antitoxin (mice, NHP)
Animal Models for Research & Disease

- HIV/AIDS
  - Many animal models are used to understand the disease and how it attacks the immune system.
  - Current anti-HIV therapies developed in animal models have greatly extended life expectancy and quality of life for AIDS victims.
  - AIDS vaccines and therapeutics still being developed in NHP
Animal Models for Research & Disease

- **Breast Cancer**
  - Tamoxifen (rats)
  - Aromatase inhibitors (mice)
  - Herceptin (rats)

- **Cervical Cancer**
  - Viruses can cause cancer (rabbits)
  - Vaccine (rabbits, dogs, cattle)

- **Leukemia and other blood cancers**
  - How cancer develops
  - Chemotherapy, bone marrow transplants, monoclonal antibodies, stem cell treatments
Animal Welfare vs. Animal Rights

• Animal Welfare
  • Humans have moral obligations to provide for the well-being of animals
  • Establish humane care and use standards for animals in research, testing, teaching, and exhibition

• Animal Rights
  • Based on the viewpoint that animals have similar (or the same) rights as humans
  • Humans do not have the right to use animals at all including for food, research, clothing, in zoos or as working animals and pets
Animal Rights Groups

• 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

• The vast majority of animal rights activists pursue their goals legally, through protests and information campaigns.
Animal Rights Extremism

- Smaller, underground animal rights groups believe violence and extreme measures are acceptable methods to achieve their goal.
  - Stop Huntington Animal Cruelty (SHAC)
  - Animal Liberation Front (ALF)
- “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
Animal Welfare Science

• **Laboratory animals**
  • 1940s and 1950s — Increased public concern about animal research, 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
    • *Principles of Humane Experimental Technique* (1959)
  • 1965 - American Association for Accreditation of Laboratory Animal Care (AAALAC) founded
    • Private, non-profit organization
    • Now called Association for Assessment and Accreditation of Laboratory Animal Care International
3 Rs

- **Replacement** – replacing higher animals with lower animals or non-animal models (e.g. computer models, cell culture)

- **Reduction** – maximizing the information obtained per animal and minimizing the number of animals needed to obtain statistically significant results

- **Refinement** – improving protocols to minimize pain and distress and enhance well-being

Animal Welfare Science

• Laboratory animals
  • 1966 - The Laboratory Animal Welfare Act (P.L. 89-544) is signed into law.
    • Amended several times to expand protections for laboratory and other animals
    • Now called the Animal Welfare Act
    • Enforced by the United States Department of Agriculture
    • All Public Health Service funded research using animals must comply with the PHS Policy
    • Enforced by the Office of Laboratory Animal Welfare
Are the animals used in research & education protected?

- Institutions follow federal and local laws and regulations to ensure animals used in research and education are being treated humanely.
  - Animal Welfare Act (AWA)
  - Public Health Service (PHS) Policy
    - The Guide for the Care and Use of Laboratory Animals
    - 2013 Report of the AVMA Panel on Euthanasia
  - AAALAC International – voluntary
AWA and PHS policy

- Ensure that all research animals receive:
  - Good veterinary care
  - Appropriate housing and surgery facilities
  - Feeding
  - Humane handling
  - Adequate sanitation and ventilation
  - Pre and Post-operative monitoring

- Requires each institution to have an emergency plan

- Requires that for all proposed animal research:
  - A protocol is reviewed and approved by the IACUC
  - Any serious or continuing noncompliance is reported to the federal government and funding agency
AWA and PHS policy

• Animal Welfare Assurance is filed with NIH Office of Laboratory Animal Welfare (OLAW) when we accept federal grant dollars for animal research
  • NIH inspects for cause unannounced
• Registered research laboratory with USDA
  • Subject to an annual unannounced inspection by the USDA
AAALAC International

- Association for Assessment and Accreditation of Laboratory Animal Care

- Private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs

- Endorses the use of animals to advance medicine and science when there are no non-animal alternatives when it is done in an ethical and humane way

- Conducts formal site visits at three-year intervals
  - Ensures that animal care and use programs maintain high standards
Reporting Concerns

• If you have a concern regarding the health and safety of animals at Tulane University, you are encouraged to contact:
  • IACUC Chair – Sheila Garrison
  • Director of the DCM – Dr. Georgina Dobek
  • Executive Director of the DCM – Dr. James Blanchard
  • Associate Vice President for Research – Dr. Laura Levy
  • Any member of the IACUC committee

• Your identity may remain anonymous
• Employees are protected from reprisal as guaranteed by law
Animal Welfare Program

Institutional Leadership

PI Cooperation

Animal Welfare

Quality Animal Care

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, a healthy IACUC, and high level research
- Appoints IACUC members
- Reports to USDA and OLAW
Institutional Animal Care & Use Committee (IACUC)

• Required by AWA and PHS policy at all research institutions using animals
• Supports, facilitates, and promotes ethical and humane use of animals by upholding the standards set forth in all applicable laws, policies & guidance.
• No research using animals may proceed without IACUC approval.
• Committee members:
  • Veterinarians
  • Scientists
  • Non-scientists
  • Non-affiliated members of the public
Role of IACUC

- Reviews of the institution’s animal care and use programs semiannually
- Inspects facilities, laboratories, and animal use areas semiannually
- Evaluates protocols for the humane use of animals
  - Justification – animals, species, numbers
  - Personnel training
  - Consideration of alternatives
  - Alleviation of pain and distress
- Investigates concerns regarding the care and use of animals
- Suspends animal activities in cases of non-compliance
Animal Care

• 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 Veterinarian

- Monitors the care and use of animals
- Manages animal housing facilities, including space allocation
- Provides technical assistance and training to personnel involved in animal activities
  - 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
  - euthanasia
Attending Veterinarian

• Assists investigators with protocol preparation

• Halts 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

• Reports animal welfare concerns and/or possible non-compliance to the IACUC
Animal Care Duties

- Housing
- Daily Health Checks
- Pathogen Control
- Feed, Bedding
- Enrichment & Socialization
- 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
Animal Care Duties

- Cares for animals 7 days a week, including weekends and holidays
- Essential Personnel and will stay through emergency closures
- Veterinarian on-call during weekends and holidays
PI Responsibilities

• Obtain IACUC approval prior to commencement of any live vertebrate animal care or use activity

• Purchase animals to be used 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 related to the care and use of animals

• Comply with an IACUC decision to suspend or withdraw its approval for an animal activity
PI Responsibilities

• Obtain continuing approval prior to the expiration date of the original study approval

• Ensure all personnel having direct live animal contact are trained in applicable humane and scientifically acceptable procedures for animal handling, procedures, and euthanasia

• 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

• Enforce requirements for study personnel participation in the institution’s occupational health program
Occupational Health and Safety

• Risks for personnel with animal contact
  • Allergies
  • Asthma
  • Animal bites and scratches
  • Skin Rashes
  • Burns, cuts, needle sticks
  • Chemical exposures
  • Infectious agents
  • Repetitive stress, overexertion
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Resources

- AAALAC International
  - http://www.aaalac.org/

- AALAS - American Association for Laboratory Animal Science
  - http://www.aalas.org/

- AMP - Americans for Medical Progress
  - http://www.amprogress.org/

- FASEB - Federation of American Societies for Experimental Biology
  - http://www.faseb.org/

- FBR - Foundation for Biomedical Research
  - http://www.fbresearch.org/

- NABR - National Association for Biomedical Research
  - http://www.nabr.org/

- Understanding Animal Research
  - http://www.understandinganimalresearch.org.uk/