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Animals in NASA Research: Ethical, Regulatory & Biological Challenges

Larry Carbone DVM PhD, D.ACLAM, D. ACAW
Institutional Animal Care and Use Program, UCSF

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Why are you
here today?

Even if you don't use animals in research . . .

If you:

- Vote
- Pay taxes
- Prescribe medications
- Take medications
- Do any sort of life science
- Work for a scientific institute like NASA

This is YOUR issue

Today's agenda

- Basic ethical principles of using animals in laboratories
- Applied ethics: regulatory systems to safeguard animals
- Focus on the Animal Care & Use Committee (IACUC)
- Applying the principles and the standards to NASA animal studies

From the prior sessions in this series (paraphrased)

- Role of individual scientist, the institution, and society in setting research priorities and ethical standards
- Role of scandals (and changing societal norms) in shaping research regulations
- Good science = good data + good ethics
- Scientific publications must be believable to other scientists (and reproducible too)
- Mutual policing and whistleblowing
- Need to estimate extent and likelihood of risks for planned projects

From the coming session in this series (my prediction)

Human Subjects in Science:

- Scandals that led to changed regulations
- Role of Human Subjects reviews (IRB committees)
- Central principles of autonomy, respect for persons and informed consent
- Special protections for vulnerable subjects (for example, children, institutionalized adults, mentally limited patients)
- Need to estimate potential harm to human subjects and volunteers

History: evolving societal views on animals

Wide range of sensibilities, and context and species-specific.

For example:

LIFE magazine in [1961](#) featured Ham, the first chimp NASA sent into space, with no discussion of laboratory animal welfare and ethics.

Five years later, *LIFE* published an [exposé](#) on dog trafficking for laboratories. Along with an [article](#) in *Sports Illustrated*, this led to a public outcry, and passage of the United States Laboratory Animal Welfare Act of 1966

History: 1966

The Animal Welfare Act

- Passed in 1966; first federal lab animal law
- Result of exposés of dog trafficking
- Originally written as anti-pet-theft law
- Covered animal CARE but not scientists' USE of animals

History: 1985

The Animal Welfare Act amendments

- Result of exposés of two monkey labs, [Pennsylvania](#) and [Maryland](#)
- Expands coverage of how animals are USED in labs
- Established rules for IACUCs, psychological well-being, exercise for dogs, & search for alternatives to painful uses of animals

And thus: rules, regulations, guidelines

- Animal Welfare Act
 - Public Health Service Policy/NIH
 - Agency-specific (NASA)
 - *The Guide for the Care and Use of Laboratory Animals*
 - Accreditations
 - United States Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research & Training
 - NASA's 1996 "Sundowner Report": Principles for the Ethical Care and Use of Animals
- and many more . . .

Animal Welfare Act

- Covers all research labs
- Species: less than 1% of research animals (not lab mice, rats, fish)
- USDA vets do unannounced inspections (not of Federal facilities like NASA)

Public Health Service /NIH

- Coverage based on receipt of federal research dollars
- Covers all vertebrate animals
- Self-reporting to the NIH Office of Lab Animal Welfare

BOTH:

Require Committee (IACUC) prior review of research

Require IACUC inspections & oversight of ongoing research

Require involvement of veterinarians

Why talk about **Laws** in a series on **Ethics**?

Laws approximate
society's ethics

The overarching principle:

**Harming animals is
permissible but requires
strong justification.**

Human vs Animal Subjects Protections

Similar structures, dissimilar principles

Human Subjects – the IRB

- Informed Consent
- Risk assessment for subjects
- Protections for institutionalized subjects
- Death as a Harm
- Special restrictions on vulnerable subjects
- Adverse events reporting

Animal Subjects – the IACUC

- No consent (acquiescence?)
- Risk assessment for subjects
- Most research is on caged animals
- Death/euthanasia: Not a Harm
- Animals on projects that will not benefit them (or their species)
- Post-approval monitoring and inspections

Harming animals is permissible but requires strong justification.

What harms?

- Pain? Fear? Loneliness? Death? Captivity?

What animals?

- Monkeys? Fish? Fruit flies?

What Justification?

- Cheaper than human studies? No reasonable alternatives? Medical advances? Safer cosmetics? Space flight? How certain must the benefits be?

Justification: must meet these conditions

- **Speciesism** : it must be acceptable to use animal subjects to benefit people in ways we would not use human subjects
- **Utility/Usefulness** : data from animal studies must actually produce reliable useable knowledge that is relevant to human well being
- **No Reasonable Alternative** : Using (especially, harmfully using) animals is only allowable if that is the only realistic way to obtain the data
- **Animal Harms must be kept to the Minimum** : No “unnecessary” suffering

U.S. Government Principles
for the Utilization and Care of
Vertebrate Animals Used in
Testing, Research, and Training

II. Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.

IV. Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.

- V. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia, or anesthesia. Surgical or other painful procedures should not be performed on unanesthetized animals paralyzed by chemical agents.

- VI. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.

IX. Where exceptions are required in relation to the provisions of these Principles, the decisions should not rest with the investigators directly concerned but should be made, with due regard to Principle II, by an appropriate review group such as an institutional animal care and use committee. Such exceptions should not be made solely for the purposes of teaching or demonstration.

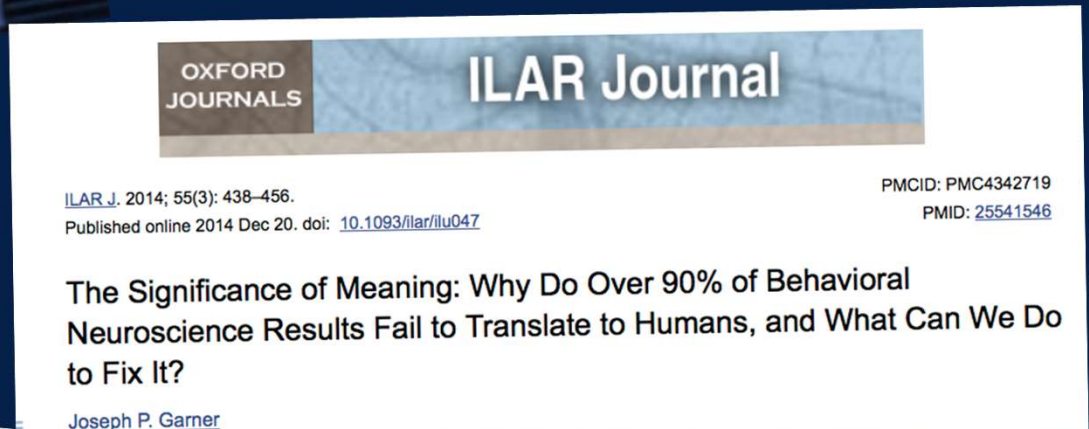
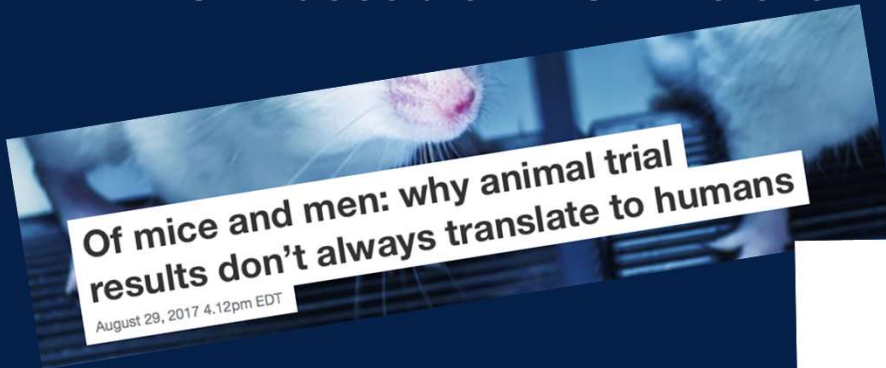
Speciesism

- People are more important than animals
- Different treatment of different animals
- Treated differently because of different needs/capacities, or for arbitrary reasons?

Utility/Usefulness :

data from animal studies must actually produce reliable useable knowledge that is relevant to human well being ---

HOW useable? HOW relevant? Can it be MISLEADING?



Are there **Reasonable Alternatives**?

The 3Rs/Alternatives framework to limit animal pain and distress (“inhumanity”) Russell & Burch, 1959

- REPLACE Sentient Animals (SAs)
 - Computers, humans, cells, non-sentient animals
- REDUCE numbers of SAs in Pain/Distress
 - Better stats, less variable study groups
- REFINE to reduce pain/distress for SAs
 - Pain management, vet care, better housing, less invasive procedures, humane endpoints

Alternatives Case: Guinea Pigs & Tuberculosis

- Russell & Burch: Guinea Pigs were third most numerous laboratory animal in the UK
- Screen milk for TB and diagnose human TB by inoculating material into Guinea Pigs
- Propagate TB organisms in Guinea Pigs (no good culture methods)
- Then euthanize the Guinea Pigs weeks later and look for abscesses and other disease

- Refine?

- Reduce?

- Replace?

Journal of
Clinical Pathology

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BMJ

[J Clin Pathol](#). 1983 Jun; 36(6): 719–720. PMID: PMC498360

Is guinea pig inoculation ever justified for the diagnosis of tuberculosis?

[C A Morris](#) and [B W Barton](#)

Ans: Sometimes

Justified:

- Ethically?
- Financially?
- Scientifically?

- Replace: Culture
- Reduce: Culture; Guinea Pigs only for certain cases
- Refine?

Refinement: focus of the IACUC and the Vets Reduce animal pain and distress

- Requires knowing the animals, identifying the welfare challenges, strategizing ways to refine and mitigate them.
- IACUC's job does not stop with trying to minimize animal harms, but somehow "weigh the objectives of the study against potential animal welfare concerns." *2010 Guide* p.27

Refinement --- what is the Goal?

REFINEMENT:

- Refine away the “incidence and severity of inhumane procedures... and pain and distress.”
- Unnecessary pain
- Significant distress
- Suffering
- Welfare
- Well-being
- Health status
- Happiness
- Enrichment
- Thriving

Birth-to-death Inventory of pain & distress

- Identification and genotyping methods
- Spontaneous Infections & Illness and Injury
- Phenotype illnesses
- Fights & accidents
- Isolation stress vs. social stress
- Collections & Administrations
- Restraint & Handling
- Surgery
- Conditions created by the procedure (wounds, infarction, fracture,etc.)
- Subacute to chronic conditions (cancers, inflammation, degenerative diseases, infectious diseases, toxicology)
- Euthanasia / killing
- Denied Enrichment

The Evolving **Ethic**: Aim for Positive states. Don't stop at preventing Negative States.



GREAT !!!

Thriving, happy,
enriched, good
welfare, positive well-
being

Okay,
Can't complain

Humane

Birth-to-death Inventory of pain & distress

- Determine how scientist or vet will recognize or diagnose each of these welfare issues
- Review potential treatments and care (refinements) to reduce the level of harm
- What makes Research Animal ethics so challenging:
 - Assess effects of those refinements on data outcomes
 - Assess effects of unalleviated pain and distress on data outcomes

Inventory of pain & distress

- Isolation stress vs. social stress
- Collections & Administrations
- Restraint & Handling
- Conditions created by the procedure: tuberculosis infection in various organs. Clinical progression from sub-clinical to fatal
- Euthanasia / killing – timing and methods

Model-specific refinements:

Will these help? Will they invalidate the study?

Antibiotics

Oxygen therapy

Other nursing care

Early euthanasia

At NASA:
Unique Research
Institutional Culture and Practices

Case: Rats and Mice as models of osteopenia/osteoporosis associated with reduced weight-loading.

Model: Chronic tail suspension removes weight-bearing of hind limbs

Model: Chronic tail suspension removes weight-bearing of hind limbs

Discuss:

Importance of the questions (how much is it worth to do this?)

Scientific Merit: Does this model produce true and useful data applicable to people?

Welfare costs/harms to animals: Three Rs analysis

Closer to home : Animals in NASA research (thanks to Drs. Ruth Globus & Joe Bielitzki, NASA)

- Two IACUCs, one specifically for in-flight studies
- Animal Welfare Act: covered, but no USDA inspections

Vertebrate Animal Scientific Review (VASR)

A. Vertebrate Animal Scientific Review (VASR)

If vertebrate animals are to be used, the following five points must be addressed completely by applicants in the VASR worksheet of their proposal:

1. Detailed description of the proposed use of the animals, including species, strains, ages, sex and number to be used
2. Justification of the use of animals, choice of species and numbers to be used, and proposer's assessment of potential benefits and knowledge to be gained.
3. Information on the veterinary care of the animals
4. Description of procedures for ensuring discomfort, distress, pain and injury is minimized
5. Method of euthanasia and the reasons for its selection

https://www.nasa.gov/sites/default/files/atoms/files/hrp_vertibrate_animal_scientific_review.pdf

How some things differ for animals in space

Animal Care:

Zero gravity

No on-site veterinarian

Studies in parallel on earth
and in space