

Ethical Issues for Life Sciences, and Research Involving Animals as Research Subjects

Dr Dave Lewis

d.i.lewis@leeds.ac.uk  [@lewisd99](https://twitter.com/lewisd99)

 www.linkedin.com/in/dave-lewis-ba927a8/



My 40yr research animals sciences career



UNIVERSITY OF LEEDS



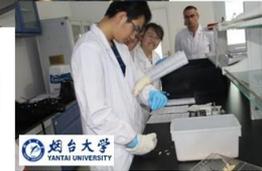
UNIVERSITY OF LEEDS



BRITISH PHARMACOLOGICAL SOCIETY



INTERNATIONAL UNION OF BASIC AND CLINICAL PHARMACOLOGY



MAKERERE UNIVERSITY

@lewisd99

Animal research can raise strong emotions



UNIVERSITY OF LEEDS



Animal Rights Activists Make Off With One Hundred Mutant Mice

Animal rights activists ruined years of important research on diseases such as autism and schizophrenia



(Rick Eh?)



Pensioner's body reburied after animal rights graverobbing



▲ The coffin of Gladys Hammond is carried into St Peter's church, Yoxall, for reburial, nearly two years after her body was stolen by animal-rights extremists. Photo: AP/David Jones.

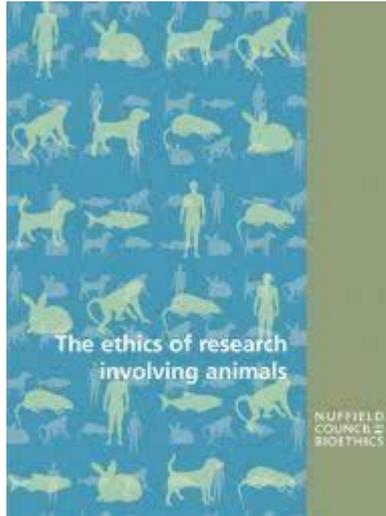


Huge range of stakeholders & opinions

- Public
 - Patients & patient advocacy grps
 - Clinicians
 - Science and scientists
 - Individual researchers
 - Animal care colleagues
 - Veterinarians
 - Animal welfare organisations
 - Animal rights activists
 - Governments
 - Institutions, Organisations & Industry
 - Financially dependant
-
- For many, conditional acceptors
 - Opinions change
 - Influenced by time, events, culture, religion, species, approach, society.....



Four differing perspectives:



- The ‘**anything goes**’ view: value therefore no further ethical justification;
- The ‘**on balance justification**’ view: morally justified if take reasonable steps to minimise costs to animal;
- The ‘**moral dilemma**’ view: will always be wrong by neglecting humans or animals;
- The ‘**abolitionist**’ view: no moral justification for causing harms to animals.

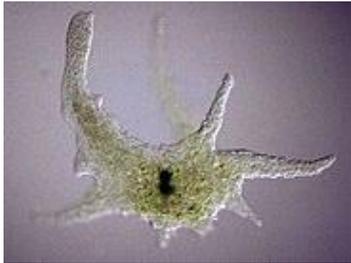
<https://www.nuffieldbioethics.org/publications/animal-research>

- Competing human and animal interests;
- Animal vs human “rights” & moral status;
- Rights of species & sentience;

The principal actors: Research animals



UNIVERSITY OF LEEDS



Chaos carolinense



Rattus norvegicus

**ANIMALS CANNOT
GIVE INFORMED
CONSENT**



Sus scrofa domestica



Canis lupus



Tragelaphus strepsiceros

Eunectes murinus



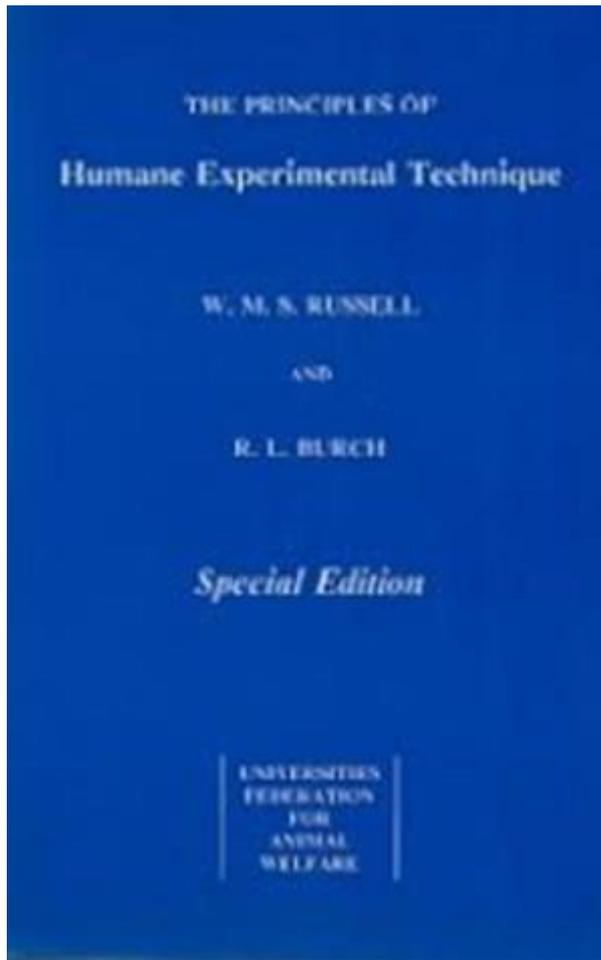
“Practice of performing operations on live animals for the purpose of experimentation or scientific research”

- Is the use of animals necessary?
- Similar knowledge via other means?
- Is all scientific knowledge worthwhile? What would happen if didn't have it?
- Can we do things differently to minimise harms & maximise benefits?
- Who benefits & how?
- Are the benefits realisable & when?
- Do the benefits always have to outweigh the harms?
- Can an economic or career benefit justify using animals?

- Professional obligations & values;
- Is application of the 3Rs or 5Fs sufficient?



1. **Freedom from hunger or thirst** by ready access to fresh water and a diet to maintain full health and vigour
2. **Freedom from discomfort** by providing an appropriate environment including shelter and a comfortable resting area
3. **Freedom from pain, injury or disease** by prevention or rapid diagnosis and treatment
4. **Freedom to express (most) normal behaviour** by providing sufficient space, proper facilities and company of the animal's own kind
5. **Freedom from fear and distress** by ensuring conditions and treatment which avoid mental suffering



Russell & Burch (1959)

R R R

Replacement
Refinement
Reduction

- Societal
- Legal
- Moral

Do we have to use animals at all? (Replacement)



UNIVERSITY OF LEEDS

Complete (*Ultimate aim*)

- Computer models
- Databases
- Human cell cultures and tissues

Partial

- Animal tissues and cultures
- Invertebrates
- Immature/embryonic vertebrates

AltTox.org

RESOURCE CENTER

DATABASES

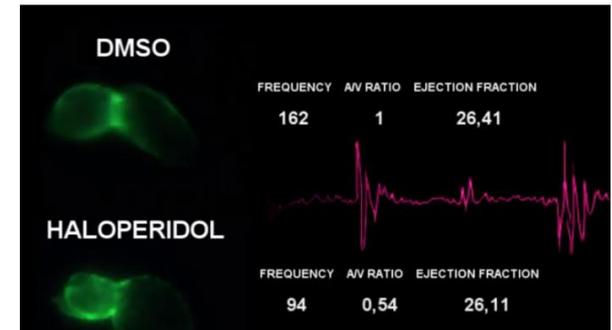
Last updated: February 5, 2018

Alternatives, literature, grants, toxicity data, biomedical, and policy databases containing information of potential use to the development of non-animal alternative methods.

- Alternatives Databases
- Scientific/Technical Literature Databases
- Database Journals
- Chemical Toxicity Databases
- Grants/Awards Databases
- Genome and Other Biomedical Databases
 - Bioinformatics Databases
 - Cell Line Databases
 - Cell Types Databases
 - Genomics Databases
 - Drug Discovery Databases
 - Single Nucleotide Polymorphisms (SNP)
 - RNA and miRNA
 - Proteins and Proteomics
 - Metabolomics
 - Pathway Databases
 - Database Lists
- Pharmacokinetics and Pharmacogenomics Databases
- Biomedical Simulation Projects/Software
- Policy Databases

AltTox Resource Center

AltTox 2018



If do, MUST optimise animal numbers (Reduction)



UNIVERSITY OF LEEDS

- Optimisation of animal numbers
- Robust statistical & experimental design
- Multiple data collection / Longitudinal studies
- Previous control
- Pilot studies



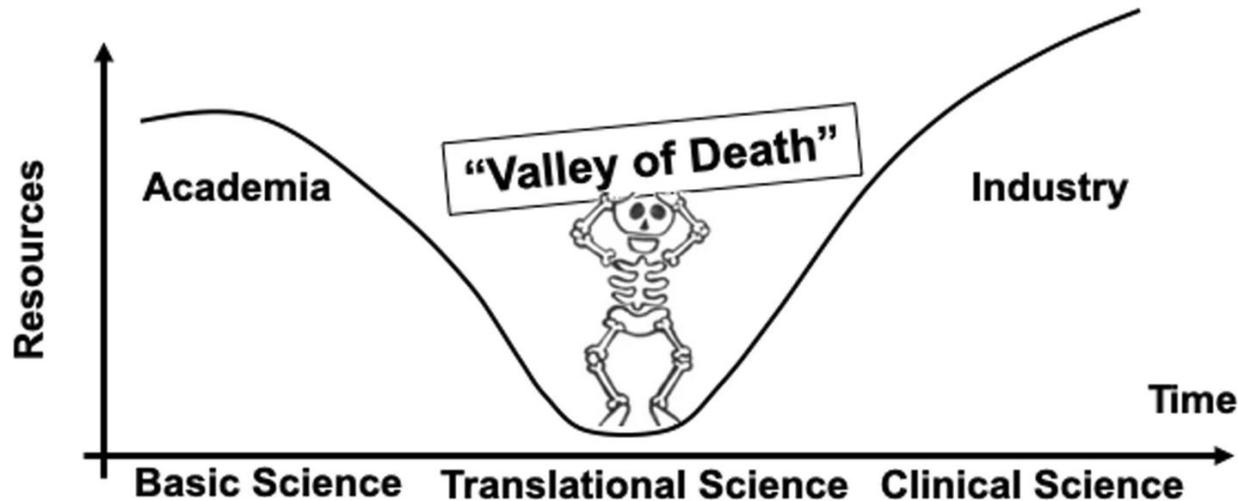
Critical to minimise harms (Refinement)

- Model, species;
- Life-time experience: breeding, housing & husbandry;
- Refined procedures & techniques, including handling;
- Peri-operative analgesia;
- Habituation & training;
- Early recognition & pro-active intervention;
- Robust humane endpoints;
- Afterwards.

Why is welfare so important?



UNIVERSITY OF LEEDS



- Pre-clinical studies neither reproducible, reliable & translatable
- 95% drugs entering Clinical trials fail: efficacy, safety, models
- 100,000,000+ animals p.a.
- Risks
- Costs
- Focus on profit: rare diseases & diseases of the Emerging World

Animal welfare factors affecting reproducibility, reliability & translatability.



UNIVERSITY OF LEEDS

ScienceDirect article snippet: "Early environmental therapy rescues brain development in a mouse model of Down syndrome". Authors: Tatjana Begenisic^{a,1}, Gabriele Sansavero^{a,1}, Laura Baroncelli^a, Giovanni Cioni^b, Alessandro Sale^{a,*,2}. Published in *Neurobiology of Disease*.

ScienceDirect article snippet: "Cage aggression in group-housed laboratory male mice: an international data crowdsourcing project". Authors: Katie Lidster^a, Kathryn Owen^a, William J. Browne^a, Mark J. Prescott^{a*}. Published in *Neurobiology of Disease*.

Nature article snippet: "Missing mice: gaps in data plague animal research". Author: Monya Baker. Published in *Nature*.

PLOS Biology article snippet: "A big-data approach to understanding metabolic rate and response to obesity in laboratory mice". Authors: June K. Corrigan, Deepti Ramachandran, Yuchen He, Colin Palmer, Michael J. Jurczak, Bingshan Li, Randall H. Friedline, Jason K. Kim, Jon J. Ramsey, Louise Lantier, Owen P. McGuinness, Alexander S. Banks. Published in *PLOS Biology*.

Inappropriate animal welfare CHANGES data!
Continuous evaluation & modification of 3Rs

ScienceDirect article snippet: "The Japanese diet from 1975 delays senescence and life span in SAMP8 mice". Authors: Kazushi Yamamoto M.Sc.^a, Shuang E M.Sc.^a, Yu Hatakeyama M.Sc.^a, Yu Sakamoto M.Sc.^a, Taro Homma Ph.D.^a, Yuri Jibu Ph.D.^a, Yuki Tsuyoshi Tsuduki Ph.D.^{a,*,2}. Published in *Nutrition*.

Nature article snippet: "Squeaky clean mice could be reared in pristine conditions, but a few imitations make them a better model of human disease". Published in *Nature*.

PLOS Biology article snippet: "Microbiota and reproducibility of rodent models". Authors: Craig L. Franklin and Aaron C. Ericsson. Published in *PLOS Biology*.

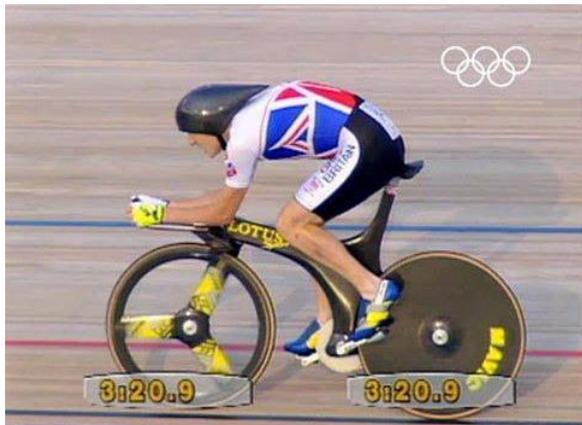
Nature article snippet: "Male researchers stress out rodents". Author: Alla Katsnelson. Published in *Nature*.

PLOS Biology article snippet: "A big-data approach to understanding metabolic rate and response to obesity in laboratory mice". Authors: June K. Corrigan, Deepti Ramachandran, Yuchen He, Colin Palmer, Michael J. Jurczak, Bingshan Li, Randall H. Friedline, Jason K. Kim, Jon J. Ramsey, Louise Lantier, Owen P. McGuinness, Alexander S. Banks. Published in *PLOS Biology*.

Nature article snippet: "Microbiota and reproducibility of rodent models". Authors: Craig L. Franklin and Aaron C. Ericsson. Published in *Nature*.

<https://youtu.be/GB5BSzPsLsw>

Single large step



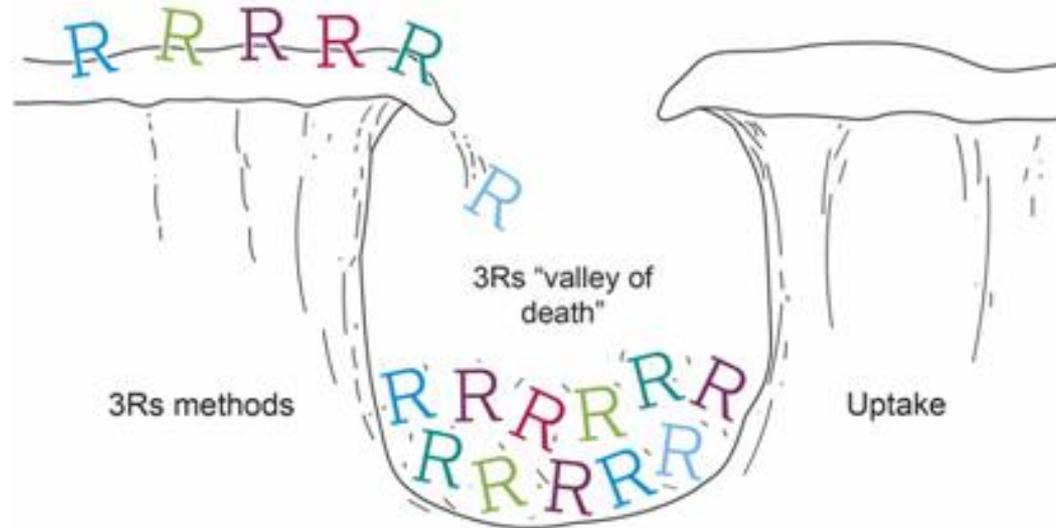
Multiple small steps

- Redesign saddle
- Lighter tyres
- Aerodynamic helmets
- Suit design
- Nutrition
- Psychological support
- Heat pads between races
- Physiotherapy/massage gel
- Own comfortable pillows
- Hand washing

Limited Global uptake & application of 3Rs



UNIVERSITY OF LEEDS



- Varying legal & ethical requirements
- Knowledge & understanding
- Historical knowledge
- Own previous research

Emerging Topics in Life Sciences (2019)
<https://doi.org/10.1042/ETLS20190061>

Perspective

Animal experimentation: implementation and application of the 3Rs

David I. Lewis
School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, Leeds LS2 9JT, U.K.
Correspondence: David I Lewis (d.i.lewis@leeds.ac.uk)

PORTLAND PRESS

© 2019 Portland Press

- **Animal**, Institution & public voice
- Active & inclusive participation- different roles & responsibilities
- Is it necessary?
- All steps to minimise harms & maximise benefits
- Application of 3Rs
- Appropriately resourced
- Appropriate experimental & statistical design
- Application of learning from previous studies

➔ Institutional Culture of Care

Commitment of EVERYBODY to:

- Providing highest quality of animal welfare & application of 3Rs;
 - Scientific quality;
 - Care of Staff;
 - Transparency for stakeholders.
-
- Appropriate attitudes and behaviours
 - Institutional expectation- top down
 - Shared & individual responsibility
 - Pro-active approach
 - Empowered animal care staff & vets
 - All voice and concerns listened to

Questions or comments?

Please get in touch

Email: d.i.lewis@leeds.ac.uk

Twitter: [@lewisd99](https://twitter.com/lewisd99)