Module 19

Welfare of Animals used in Education, Research and Testing

This lecture was first developed for **World Animal Protection** by Dr David Main (University of Bristol) in 2003. It was revised by **World Animal Protection** scientific advisors in 2012 using updates provided by Dr Caroline Hewson.

Free online resources

To get free updates and additional materials, please go to

www.animalmosaic.org/education/tertiary-education/

This module will teach you

Why using animals for education, research and testing is so well established

- Lock-in theory
- Ethics review

The main welfare concerns for animals in education, research and testing

How to improve their welfare

Background

~100 million animals involved worldwide

- Mice and rats are most common

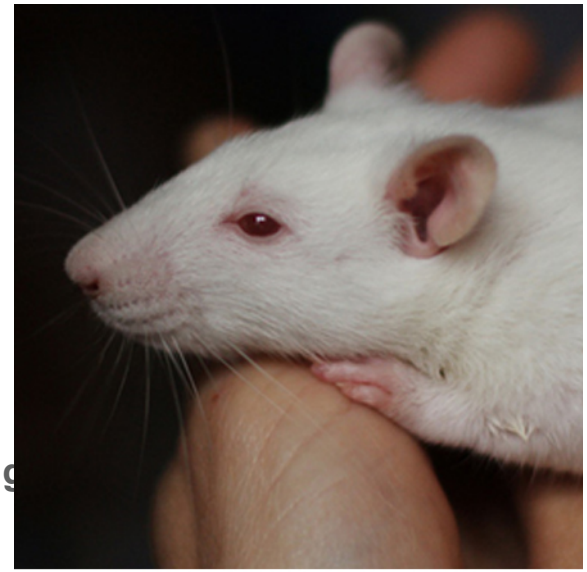
International concern, e.g.

- South America, e.g. Brazil (Filipecki et al., 2011)
- Africa (Nyika, 2009)
- China (Kong & Qin, 2010)
- Turkey and Iran (Izmirli et al., 2010)

Animal Health Code (OIE, 2011)

Causes of concern / moral unease

- Animals are sentient and are often harmed by procedures and
- The benefits to us of using animals for research, testing and education is limited, or can be achieved using alternative methods



Credit: Bulyonkova / flickr.com

Guidelines: OIE's *Terrestrial*

Why animals are used (1)
(Frank, 2005)

Early Christian church forbade research on humans

19th century

- Claude Bernard: imperative to use animals to make medical discoveries, teach, test
- It was the only option then – no statistical methods, computer modelling, etc.
- Entrenched as primary working method

Credit: Wellcome Trust (Painted by Emile-Edouard Mouchy, 1832

Why animals are used (2)
(Frank, 2005)

‘Lock-in’

- **Economic theory: path of increasing returns inflexible behaviours and strongly held assumptions even though a different path might be more beneficial in the long term**
- **Laboratory animal research: big initial investment, but inexpensive production ⇨ increasing returns ⇨ ‘lock in’ likely**

‘Lock-in’ inertia because

- **Huge infrastructure, e.g.**
  - Journals, research labs, private testing companies, cosmetics companies, pharmaceutical production, staff, regulatory bodies, academic departments, funding agencies, etc.
- **Cost of changing buildings, etc.**

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Psychological factors (1)
(Frank, 2005)

Biases, e.g.

- Tendency not to use information that is different from local experience
- Publishing biases
- Confirmatory bias: despite contradictory evidence, persevere in belief
- Internal psychological appeal, e.g. ‘scientific’, ‘controlled’
- Criticism is associated with animal liberation extremism, which can be associated with violence

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Psychological factors (2)
(Frank, 2005)

Cognitive dissonance, e.g.

- **‘Sacrificed’ not ‘killed’**
- **Animals listed by number, not name**

Human–animal bond (Herzog, 2002)

- **Personnel may favour some animals**
- **Affects results** (e.g. Sherwin, 2004)

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Ethical theories (1)
(Sandøe & Christiansen, 2008)

Utilitarian

- Use justified if the benefit to people outweighs the cost paid by the animals
- 3Rs: replace, reduce, refine

Credit: Digital Visions

The 3Rs
(Russell & Burch, 1959; Fenwick et al., 2009)

Russell and Burch: *The principles of humane experimental technique*

- **3Rs: replace, reduce and refine as alternatives to using animals**

3Rs in OIE *Terrestrial Animal Health Code*, Chapter 7.8 (OIE, 2011)

- **Relative Replacement: use cells, tissues, organs**
- **Absolute replacement: use inanimate systems (e.g. computer modelling)**
- **Reduction: use fewer animals**
- **Refinement: minimise pain etc. and enhance welfare, e.g.**
- Use species with less capacity for suffering or distress
- Consider welfare throughout the animal's life – husbandry, transport and death, as well as during the procedures

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Criticisms of utilitarianism
(Sandøe & Christiansen, 2008)

Problems with utilitarian approach, e.g.

- **Uncritical acceptance of animal usage** (Haynes, 2010)
- **Many new products are unnecessary for human or animal health, only for commercial gain**
- **Non-vital human ailments (e.g. baldness)**
- **Animal data do not predict human data, e.g. polio vaccine**

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Case study: polio vaccination
(Frank, 2005; WHO, 2012)

Viral disease that paralyses children; can be fatal

Vaccine research used ~1 million monkeys, mostly Rhesus macaques from India

Nasal route of infection in monkeys but oral in people

- **Researchers ignored presence of virus in human gut – confirmatory bias?**

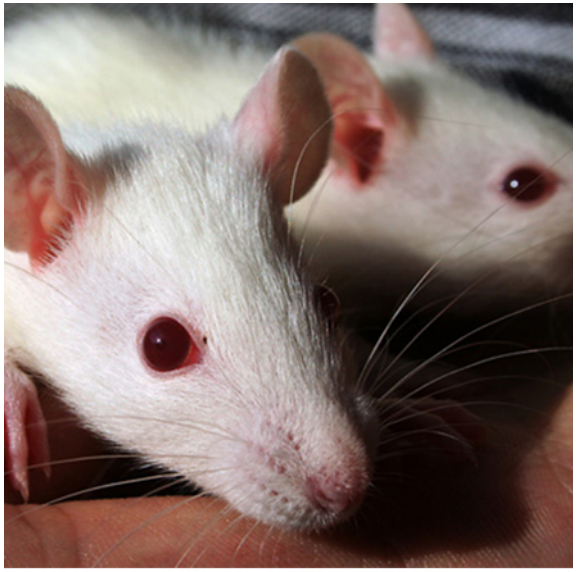
Effective vaccine after cultured virus in human intestinal tissue

- **However, the clinical / observational studies from humans were considered inferior to lab-based animal work**

Ethical compromise
(Sandøe & Christiansen, 2008)

Conditions for animal use:

- **Research issue must be of vital importance**
- What is ‘vital’? Market forces…
- **No other way to study the issue except by using animals**
- **Animals do not have to suffer more than the experiment requires**



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Animals used in teaching
(Balcombe, 2000; King, 2004)

~2–3 per cent of laboratory animals are used in schools and undergraduate teaching

- **Skills, e.g. multiple survival surgeries; rectal palpation**
- **Knowledge, e.g. to visualise effects of drugs; to see anatomical structures (dissection)**

Concerns include

- **Utilitarian: diminishes respect of life and sentience (NB: veterinary training)**
- **Efficacy: no more effective than alternatives**
  (e.g. Patronek & Rauch, 2007)
- **Animal welfare: housing, pain relief, etc.**
- **Lack of data, e.g.**
  - Numbers of animals killed for the purposes of dissection, etc. are not recorded
  - Relatively few controlled comparisons of the learning outcomes using traditional methods vs. alternatives

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Animals used in veterinary teaching (1)

Conscientious objectors:

- **Constructive solutions – 'win-win'**

3Rs (Martinsen & Jukes, 2005; Hart et al., 2005)

- **Animal Care and Use Committee within the university**
- **Conferences, e.g. InterNICHE**

Replacement (absolute)

- **Haptic Cow, UK: bovine abdominal anatomy and rectal palpation (Kinnison et al., 2009)**
- ***Foal in Mare* DVD in 3D, Belgium: equine obstetrics (Govaere et al., 2012)**

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Animals used in veterinary teaching (2)
(King, 2004; Martinsen & Jukes, 2005)

Replacement (relative)

- Plastination of organs to preserve for longer

Reduction

- Donation of cadavers by clients: Educational Memorial Programmes
- New preservatives so cadavers' tissues are flexible for surgical practice (Silva et al., 2007)
- Rectal palpation of cows at abattoirs? (Lopes & Rocha, 2006)
- Mentorship: seeing practice / field experience, with owner consent

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Animals used in veterinary teaching (3)

Refinement (OIE, 2011)

- General husbandry: enriched housing that maximises welfare
- Transport
- Euthanasia
- Teaching procedures: analgesia; humane handling; restricted number of uses per teaching session

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Animals used in research
(Richmond, 2010)

Exploratory models

- Practical application not yet known
- Utilitarian ethic therefore problematic
  (Sandøe & Christiansen, 2008)

Explanatory models

- Discover mechanisms, e.g. disease; drug action
- Genetically modified animals, e.g. cancer gene

Predictive models

- Make decisions: efficacy, potency, safety

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Veterinary vaccines
(Stokes et al., 2011)

Each batch must be tested for:

- **Safety – no adverse effects**
- **Purity – no additional substances that might cause adverse effects**
- **Potency – enough of the antigen to stimulate immune response**
- **Efficacy – adequate immune response**

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The 3Rs and veterinary vaccines
(Stokes et al., 2011)

Potency testing

- Serial dilutions of vaccine given to groups of animals + one unvaccinated control
- Challenged with pathogen – if vaccinated animals become sick and die, potency at that dilution is inadequate
- Welfare concern: inhumane end-point

Humane end-point (OIE, 2011)

- Point when experimental animals suffering is terminated by, e.g. analgesia, euthanasia, removing from the study

Refinement of potency testing

- Research to identify clinical signs that predict death
- Training personnel to recognise this
- In vitro alternatives – not all regulatory authorities have accepted them

Reduction of potency testing

- Minimum numbers per group
- Combination testing

Similar concerns with fish vaccines (Midtlyng et al., 2011)

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Other product testing – safety

Veterinary and human drugs: acute and chronic toxicity

Household products

Cosmetics

- Draize test

Shellfish toxicity (Guy & Griffin, 2009)

- HPLC better than mouse bioassay, but not always used for logistical reasons

Credit: R.Beggs / ADI

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The 3Rs and explanatory research: Parkinson's disease (Manciocco et al., 2009)

Background

- Neurodegeneration dopaminergic neurons ⇨ tremors, weakness and depression
- Cause unknown – genetics and environment?
- Rodent models – pesticides, other chemicals, genes

3Rs

- Replace: in vitro studies; invertebrate models, e.g. fruit fly, flatworm
- Reduce: design and statistics
- Refine: transgenic mice? Researchers' awareness of suffering, e.g. end-points; husbandry

Conflicts between the 3 Rs, e.g.

- Refine (lower dose of toxin ⇨ less suffering) conflicts with reduce (may need to use more animals)
- Refine – not all transgenic mice may develop the disease – what to do with the unaffected ones?

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Genetically modified animals

Manipulating genes

- Within species or
- Between species – transgenic animals, e.g. human gene in mice

Problems include

(Christiansen & Sandøe, 2000; Kues & Niemann, 2011)

- Suffering from the induced condition of interest, e.g. Parkinson's in transgenic mice
- Unexpected effects, e.g. eccelerated growth rate in transgenic farm animals; tumours
- 'Wastage'

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Uses of genetically modified animals
(Kues & Niemann, 2011)

‘Bio reactors’: production of therapeutic proteins in milk

Livestock / agriculture, e.g. routines in fish farming

Transgenic animals as models of human diseases

Xenotransplantation: production of compatible organs for transplantation into humans

Pigs – disease free – Caesarean delivery, reared in sterile environments

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Greater use of the 3Rs

Discussion of them in scientific papers?

- Few researchers do
- Huntingdon's disease papers
- (Olsson et al., 2008): 3/51 mentioned adapting the housing; 6/14 mentioned euthanasia of moribund animals

Make it an absolute requirement, e.g.

- Animal Care and Use Committees
- Funding bodies
- Journal guidelines, e.g. *Animal Behaviour* (Anon, 2012)

Other reductions:

- Clinical research on client-owned animals
- More observational 'real world' data, to reduce reliance on lab animals
- Translational research, e.g. osteoarthritis in dogs (Vainio, 2012)

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Summary so far

Why use animals for education, research and testing

- Lock-in theory and inertia
- Ethics review

Main welfare concerns with the procedures in education, research and testing

- Application of the 3Rs
- Non-animal tools, e.g. computer simulations; serological tests
- Humane end-points
- The role of journals

Next: Refinement – husbandry, handling, pain management

Regulations

Refinement: housing and environmental enrichment (EE)

(Patterson-Kane, 2004; Simpson & Kelly, 2011)

Barren environments

‘Environmental enrichment’

- Alteration of environment of captive animals in order to increase their behavioural diversity and so to improve their welfare (Young, 2003)
- Shelters, bedding and nesting material, group housing
- OIE guidelines recognise it (OIE, 2011)

Effect of barren housing on research data – reduces validity (Sherwin, 2004)

- Effect of rearing on cognitive processes and visual acuity: behavioural tests, e.g. swimming, maze
- Routine handling vs. additional friendly handling

Refinement: social effects
(Olsson & Westlund, 2007)

Rodents and primates

- Pre-weaning experience
- Group housing vs. isolated: groups must be compatible and stable – kinship, etc.
- Tests: results if tested in group vs. individually – validity of data

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Refinement: feeding regimens

(Kasanen et al., 2010; Kyriazakis & Tolkamp, 2011)

Ad libitum food delivery

- Can result in excess adipose tissue (obesity)
- Obesity → diabetes mellitus, musculoskeletal disorders, reduced longevity

Dietary restriction to limit calorie intake

- Quantitative vs. qualitative
- Feelings of hunger
- Kept in isolation to ensure correct amount fed

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Refinement: pain management

Pain in laboratory animals has historically been poorly recognised and treated

Different species show different behaviours

- **Poor recognition of pain in rabbits by vets, personnel and researchers**
  (Leach, 2010)

Importance of analgesia and pain pathway

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Refinement: assessment of welfare

Animal Welfare Grading (Mellor et al., 2009):

- Developed to assess impact of procedures on research animals
- Assesses level of welfare compromise, but not positive experiences

Five domains

- Each graded A to E according to specific criteria, and one overall grade then assigned

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Example of Animal Welfare Grading
(Mellor et al., 2009)

Under-fed animals exposed to severe cold for 24 hours

1. Nutrition: food intake restricted to cause loss of 20 per cent of body weight	GRADE: C
2. Environment: low temperature – at the limit of the animal's capacity to adapt	GRADE: C
3. Health: mild impairment	GRADE: B
4. Behaviour: mild restriction	GRADE: B
5. Mental state: severe distress from under-feeding and cold	GRADE: D
	OVERALL GRADE: D

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Protection of animals used in research, testing and education (1) (OIE, 2011)

Competent authority

- Sets standards – national + / – international laws (EU)
- Registers institution
- Checks compliance
- Overseen by national or local committee / officers

Centralised, e.g. UK, Brazil (Filipecki et al., 2011)

- Licences for researchers, projects and institutions
- Inspectors consider licence applications, inspect institutions, give expert advice
- Ethical review committee

Protection of animals used in research, testing and education (2)

Enforced self-regulation, e.g.

- **Australia:**
- No federal legislation but code of practice
- State laws; local committees, containing qualified and lay staff, enforce code
- **Turkey (Izmirli et al., 2010):**
- Law passed in 2004 mandating ethical review committees – 1 central, 73 local

Self-regulation, e.g. USA

Overall: becoming standard internationally

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Concluding remarks

Why using animals for education, research and testing is so well established

The main welfare concerns for animals in education, research and testing

- 3Rs
- Humane end-points

How to improve animals' welfare

- Environmental enrichment (EE)
- Social issues
- Pain management
- Regulation, e.g. ethics committees

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Feedback:
Please let us know what you think

- **How have you used this module?**
- **What did you like about it?**
- **What did you not like?**
- **Do you have any tips to share?**

Please take part in our 10 minute survey here:

https://www.surveymonkey.com/s/BKP3D6H

Your feedback will help other teachers like you

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Websites about alternatives to animals in laboratories or education

www.interniche.org

www.eurca.org

http://oslovet.veths.no/NORINA

www.HumaneLearning.info

www.pcrm.org

www.navs.org/site/PageServer?pagename=index

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Websites about the 3Rs

www.nc3rs.org.uk

www.frame.org.uk

http://caat.jhsph.edu

http://ecvam.jrc.it/index.htm

http://iccvam.niehs.nih.gov

www.ardf-online.org

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