The 3Rs and animal welfare – conflict or the way forward?

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Summary

- What are the 3Rs?
- What are the drivers and blockers?
- Why are the total numbers not coming down?
- Conclusion.
Focus on alternatives: The 3Rs

- “Principles of Humane Experimental Technique”
- Published by UFAW in 1959
- Introduced the 3Rs
  - Replacement
  - Reduction &
  - Refinement

William Russell & Rex Burch
Focus on alternatives: What are the 3Rs?

- **Replacement:**
  - Using totally non-animal methods e.g. *in silico*, *human data* (absolute)
  - Using cells, tissues, organs of animals *in vitro* (relative)

- **Reduction:**
  - Using fewer animals, often through good experimental design
  - Obtain same information from fewer animals or more information from the same number of animals

- **Refinement:**
  - Using methods which minimise pain or distress
  - Using species which we believe have less capacity to feel pain
  - Includes improvements in housing and care e.g. enrichment
Focus on alternatives – Drivers and Blockers

- **Drivers:**
  - Better science
    - Utilising new technologies e.g. non-invasive imaging, stem cell options, sophisticated *in vitro* and *in silico* options
  - Faster science
  - More cost-effective science
  - Funding for quality proposals (NC3Rs, DHT, MRC, etc.)

- **Blockers:**
  - Regulatory inflexibility
  - Conservatism in peer review
  - Getting funding
Why are the numbers not coming down?

- Increased funding for biomedical R&D?
UK R&D (real) expenditure compared with total numbers of animal procedures.
Why are the numbers not coming down?

- Increased funding for biomedical R&D?
- Movement down the phylogenetic scale?
Procedures (all species) 1995-2011

Scientific Procedures on Living Animals 1995 - 2011

Millions of procedures

- Mouse
- Rat
- All other rodents
- Rabbit
- Cats, dogs, ferrets and other carnivores
- Ungulate
- Primate
- Other mammal
- Bird
- Reptile/Amphibian
- Fish
Procedures (exc. mice, rats & fish) 1995 - 2011

Scientific Procedures on Living Animals (excluding mice, rats & fish) 1995 - 2011

Numbers of procedures

- All other rodents
- Rabbit
- Cats, dogs, ferrets and other carnivores
- Ungulate
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Why are the numbers not coming down?

- Increased funding for biomedical R&D?
- Movement down the phylogenetic scale?
- Significant numbers counted are breeding?
Separate breeding from procedures

Animal procedures (thousands) showing breeding separately since 1995
So what about the future?

Will the veterinary profession be a driver of future changes?
Science led uptake of the 3Rs

In 20 years:

- Regulatory toxicology will focus on mechanisms of toxicity using *in vitro* and *in silico* predictive models – almost no animals!
- e.g. “Lung-on-a-chip”: [http://wyss.harvard.edu/](http://wyss.harvard.edu/)
- Scientists in basic research will be striving with enthusiasm for alternatives - to improve their science
- Total numbers may remain level or may rise - but more will be fish, invertebrates and other lower species – explore mechanisms rather than models

Challenge: How will the veterinary profession support this trend?
Housing designed for needs

- Current housing standards for most species are not based on scientific evidence of their needs.
- In 20 years we will have:
  - Extensive scientific data allowing us to describe optimal house shapes & sizes, environments etc.
    - Based on performance standards and sustainable approach
  - Understanding of needs of species and individual strains
  - Evidence base to support complexity designed into an animal’s environment

Challenge: How will vets contribute to this evidence base?
Use of human material

- In 20 years time we will:
  - Increasingly be using ACHM and human tissue banks to cross the boundary between animals and humans
    - E.g. personalised cancer models; ‘humanised’ immune systems in mice etc.
  - Be technically able to do things which raise ethical issues
    - Culture functional human gametes and brain tissue in animals
    - Develop animals with human characteristics e.g. skin, speech
  - Need ethical access to diverse sources of human tissue for research
    - Will require public confidence for informed consent

Challenge: What role will vets play in this ethical debate?
Greater Transparency

- Public confidence is diminished by ‘closed doors’ image
- Lack of public trust feeds extremism – but extremism drives ‘closed doors’
- Increased use of Freedom of Information laws is overwhelming both scientific community & regulators

➢ In 20 years we will have:
  ➢ Defined and agreed what must be kept confidential
    ➢ e.g. intellectual property, personal identities, etc.
  ➢ Openly publish everything else and have open access databases allowing private individuals to mine published information
  ➢ Open house policies encouraging visits to facilities

Challenge: What role can vets play in delivering public trust?
Conclusions

- The 3Rs are being increasingly driven not as an ethical imperative but as:
  - Better science;
  - Faster science; and
  - Cheaper science

- Blockers exist, which will require global action, in:
  - Regulatory testing;
  - Acceptance by peer review

- In 20 years, the 3Rs will be visible through:
  - Widespread uptake by scientists and regulators (Replacement, Reduction);
  - Better housing conditions (Refinement);
  - Greater use of human material – target species;
  - Greater transparency – and public trust

Is the veterinary profession ready to play its role in this challenge?