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# THE WISDOM OF RUSSELL AND BURCH

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## 15. Comparative Substitution

Michael Balls

*The scientifically-justifiable choice of species is a crucial issue in animal experimentation, which should not be based on ignorance and habit, or on slavish compliance with political expectations and regulatory requirements*

*The Principles of Humane Experimental Technique*<sup>1</sup> was published a year after it was written, and Russell and Burch added an *Addendum*, because they felt that year had “seen much activity in several parts of the field”.

One point they made in the *Addendum* was that “the comparative substitution of lower for higher animals raises difficult issues”, but, “where great severity is concerned ... we must be glad to see lower forms substituted for mammals”. Unfortunately, they said nothing more about the “difficult issues” to which they referred, and I wish I had asked them about it, while I had the chance to do so.

The discussion on comparative substitution in the chapter on *Replacement* in the main part of the book focuses on the use of non-sentient material (plants, micro-organisms), degenerate metazoan endoparasites and free-living metazoan invertebrates. They regarded such use as a “limited gain”, and considered that “to shed obsessional tears over the fate of these organisms would bring the whole concept of humanity into contempt”. They preferred to concentrate on “the wholly desirable progress and prospects of replacement proper”, i.e. the use of any scientific methods which “replace methods which use conscious living vertebrates”.

Russell and Burch considered that not enough was being done with lower vertebrates, and saw the predominant use of mammals as “yet another expression of the high-fidelity fallacy”.<sup>2</sup> Here, Russell’s experiences as a zoology student at Oxford came to the fore, since “our ignorance of the behaviour of common laboratory mammals is offset by a wealth of knowledge about that of numerous lower vertebrate species”. He had worked on mating behaviour in *Xenopus laevis*, the South African clawed toad, alongside the Nobel-prizewinning work of Tinbergen and his colleagues on the behaviour of birds and fish.

In a section on *The Choice of Species*, Russell and Burch argued that, in terms of humanity, the “subtle matching of procedure to species, and species to

objectives, is more significant that it appears at first sight”. They said that “a formal or informal training in zoology has again and again proved its value in the progress of medical research”, and lamented attempts to “correct the mistaken choice of a wrong species by forcing it to conform to the requirements of the investigation”.

They marvelled at “the present large-scale choice of laboratory species”, but regretted that, “out of the almost astronomical number of vertebrate species, only a minute selection are employed ... this includes about 20 mammal species, three bird species, about four reptile species, half a dozen or so amphibians, and half a dozen or so fish”. Of the mammalian species, they said, “only about half the species are used in numbers over 1,000 *per annum*, the overwhelming bulk being made up of the four chief species (mouse, rat, guinea-pig and rabbit), and, of these, more than two-thirds are mice”.

Lack of sufficient understanding of the animals used for experimental purposes is still rife today. For example, the customary feeding *ad libitum* of caged rats and mice fundamentally alters their endocrinological, neurological and behavioural status. In real life, they spend most of their time searching for food, not eating it, while keeping alert because of the threat of predators. Also, the feminisation of male fish and amphibians by so-called endocrine disruptors, was taken as a warning of threats to human masculinity, whereas it is a normal part of the adaptability of these lower vertebrates. Even worse are attempts to genetically humanise laboratory animals, in order to make them better models for humans, without sufficient understanding of the cascade of complications likely to result from the consequent distortions of the very nature of the animals concerned.

Russell and Burch said rather little about choosing between the higher mammals, except to say that they were pleased to note that the Indian Government had “imposed salutary regulations” on

the shipment of monkeys to provide kidney cells for vaccine production, and that the Medical Research Council had “issued recommendations on humane shipment”, which had been “adopted by all the British airlines concerned with livestock transport”. They welcomed “such action being taken on behalf of animals, which, although our near relatives, receive none of the privileges accorded by the Home Office to cats, dogs and the *equidae*” (the commonest animals to be encountered in Victorian England, when the *Cruelty to Animals Act 1876* became law).

Over the years, I have had many discussions with veterinarians about whether there should be a hierarchy of laboratory mammals in the terms of the need to justify their use, with rats and mice near the bottom, and dogs and non-human primates at the top, or whether all the species should be afforded the same standards of consideration and care. I take the former view, and that is the position laid down in the *Animals (Scientific Procedures) Act 1986*, as amended to comply with *Directive 2010/63/EU*.

But what about the substitution of one species high in the hierarchy with another species high in the hierarchy. This point arose when somebody occupying a high position in the Three Rs movement, commenting on our study on the use of tests in dogs for predicting human toxicology and drug safety,<sup>3</sup> warned us that “dropping the dog on the basis of your existing evidence could result in an increase in the use of non-human primates”. That would present advocates of

the routine use of a second, ‘high-fidelity’, non-rodent species in toxicity testing with a dilemma and a challenge. How could they justify replacing point-less tests in one highly-protected species with point-less tests in another highly-protected species?

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## References

- <sup>1</sup> Russell, W.M.S. & Burch, R.L. (1959). *The Principles of Humane Experimental Technique*, xiv + 238pp. London, UK: Methuen.
- <sup>2</sup> Balls, M. (2013). The wisdom of Russell and Burch. 3. Fidelity and discrimination. *ATLA* 41, P42-P43.
- <sup>3</sup> Bailey, J., Thew, M. & Balls, M. (2013). An analysis on the use of dogs in predicting human toxicology and drug safety. *ATLA* 41, 335-330.

*The Principles of Humane Experimental Technique* is now out of print, but the full text can be found at [http://altweb.jhsph.edu/pubs/books/humane\\_exp/het-toc](http://altweb.jhsph.edu/pubs/books/humane_exp/het-toc). An abridged version, *The Three Rs and the Humanity Criterion*, can be obtained from FRAME.

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