

The Use of Animals for Research on Animal Diseases: Its Impact on the Harm–Benefit Analysis

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Summary — The use of animals in scientific experiments is sometimes controversial. Usually, the debate focuses on the advantages or disadvantages of using animals in biomedical research or for testing products for safety or efficacy in humans. This has been the case in the previous World Congresses on Alternatives and Animal Use in the Life Sciences. Such studies can be subjected to a harm–benefit analysis that attempts to assess the expected benefits of the research to be done in relation to the harm done to the experimental animals. This paper suggests that studies carried out in the target species offer a higher level of fidelity and discrimination (confidence in the proper expression of the disease and greater ability to detect the impacts of any treatments under investigation) than do experiments carried out in animal models of a different species. A number of examples are given to show the benefits that have accrued to the welfare of domesticated animals through research on the diseases from which they suffer. These examples suggest that there will be an ongoing need to use animals in research to develop methods for the control or eradication of newly emergent diseases.

Key words: *animal disease, animal research, discrimination, fidelity, harm–benefit analysis.*

Introduction

The advantages and disadvantages of using animals in scientific research are often the subject of controversy and strongly opposing views. The debate usually focuses on the use of animals in biomedical research or for testing the safety and efficacy of pharmaceutical or other products that are to be used in humans. This was the case in the previous World Congresses on Alternatives and Animal Use in the Life Sciences. Such studies can be subjected to a harm–benefit analysis, which attempts to assess the harm done to the experimental animals in relation to the benefits expected to accrue from the research. Without care, these analyses can be rather subjective and lacking in quantifiable input.

Discussion

The harm–benefit analysis

In using animals for research purposes, it is our duty to make sure that we minimise the extent of the welfare compromise and maximise the expected benefits. Mellor & Reid (1) used the “five freedoms” proposed by the Farm Animal Welfare Council of the United Kingdom to develop a system for assessing the impact of a particular animal use by a systematic approach that considered all of the possible sources of welfare compromise. The “five freedoms” are:

- freedom from hunger and thirst;
- freedom from adverse environmental impacts;
- freedom from disease and injury;
- freedom to exhibit normal behaviour; and
- freedom from adverse mental states.

The five freedoms were transformed into five “domains of welfare compromise” (1, 2) and it was suggested that any proposal for use of animals in experiments should be examined in each of the five domains. Scores for each of the first four domains are aggregated into the fifth domain (Figure 1) to give an overall rating of welfare compromise. This is then measured against the expected benefits.

Despite the sort of comprehensive analysis proposed by Mellor & Reid (1), it can still be difficult to make a totally objective assessment because of an inability to accurately determine the true expected benefit of an experiment. This is certainly the case when considering the value of indirect benefits, such as career advancement, kudos and wider community benefits. It is often also the case when considering the direct benefits, such as assigning a value to a potential advance in knowledge, or even to a practical outcome, such as a step toward producing a vaccine against a serious human disease. In the latter case, if an animal model of the human infection is being used, it simply may not be feasible

to assess the outcome in terms of its likely relevance for application in humans. Despite these limitations, many advances in human medicine have been made using “model” systems, and it is often the case that there is simply no alternative. It is also the case that research carried out on animals for the benefit of humans has generated outcomes that yield benefits to animal welfare, e.g. the treatment of arthritis.

The use of animals for research on animal diseases

The use of animals for research on animal diseases falls broadly into two categories. Many studies use “models” of diseases in hosts other than the natural animal host for a variety of reasons. Major factors in deciding which animal species to use in an experiment can be the cost, the availability of appropriate housing and the lack of appropriately trained staff. In some cases, particularly where the same disease occurs in several hosts, it may make little difference, although, even then, the complex host/organism interaction can vary widely between different hosts. So, while important advances have been made with “model” systems, they generally suffer from the same limitations in determining the expected benefits, as does the use of animal models of human disease.

Using the natural host to study a particular disease has important advantages with respect to *fidelity* and *discrimination* and the likelihood of being able to predict the expected benefit of an experiment. Fidelity describes the accurate expres-

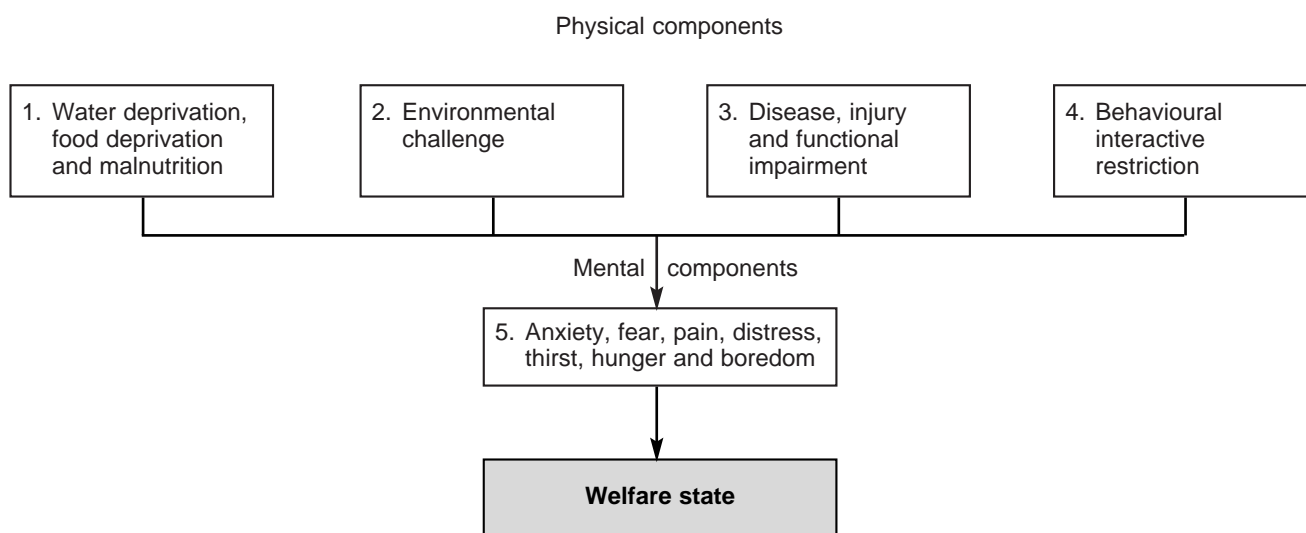
sion of the disease in its natural host and its reproducibility in subsequent experiments. The final expression of a disease is the outcome of a series of often very complex interactions between the infecting agent and the many body systems of the host. With the physiologically normal natural host, the outcome of experimental infection is usually predictable and reproducible. An additional benefit is that the progress of a disease can be followed using a range of known clinical, physiological and biochemical parameters and humane endpoints can be more accurately determined.

Discrimination is the sensitivity and accuracy with which it is possible to detect and measure any effect of modifying the course of the disease by treatment of the host animal, for example by vaccination or chemotherapy. Because the disease is being studied in its natural host, the outcome of the experiments to modify the course of the disease will have direct relevance to other members of the same species, or breed of that species, which is similarly treated. There is therefore a greater likelihood of achieving a practical outcome, which makes it easier to quantify the expected benefit in a harm-benefit analysis than when using model systems. It is also often the case that the total number of animals used to achieve the desired outcome can be less than when using model systems.

The benefits of research on animal diseases

Major benefits have accrued to the welfare of animals through research on the diseases from which

Figure 1: Five domains of potential welfare compromise divided broadly into physical and mental components



From Mellor & Stafford (2).

they suffer. In the Australian context, some examples are:

- 1880s: the development of an attenuated vaccine for anthrax;
- 1920s: vaccines against clostridial diseases of livestock, such as tetanus, botulism, enterotoxaemia and black disease;
- 1960s: the eradication of contagious bovine pleuropneumonia; and
- 1980s and 1990s: the eradication of bovine brucellosis and tuberculosis.

There is a long list of vaccines that have been produced worldwide for use in companion and recreational animals, as well as in wildlife, to protect them from disease. Antibiotics have saved the lives of countless animals infected with bacteria, and chemicals are routinely used to prevent or treat chronic and acute diseases caused by internal and external parasites.

Conclusion

Has science solved all of the problems, and is there any need for ongoing research? Unfortunately, new diseases continue to emerge, and there is concern that this is happening at an increasing rate (3). A classic case of the emergence of a new disease was parvovirus infection in dogs, which first manifested itself in the USA in 1977 (4). The disease was associated with outbreaks of vomiting and diarrhoea in puppies, as well as with myocarditis and a high mortality rate. The disease was highly contagious, and disinfection of infected premises was difficult because of the robustness of the virus.

By 1979, canine parvovirus had spread around the world, causing suffering and death in an untold number of dogs. The first commercial vaccine was available in 1981, and several others are now available and administered routinely to puppies, usually

in combination with vaccines against other common diseases of dogs. Such a rapid and effective response to develop a vaccine against a new infectious disease would not have been possible without the use of dogs in experiments, and it would still not be possible to do the same today without the use of experimental dogs.

A comprehensive analysis of factors promoting emergence of new diseases and why this appears to be increasing has been presented (3). Expansion of the human population into new habitats and the ever increasing mixing of humans, their domesticated animals and wildlife have created increased opportunities for the transfer of diseases from one species to another. Three recent Australian examples highlight this: Hendra virus from fruit bats to horses to man in 1994; bat lyssavirus from fruit bats to humans in 1996; and Menangle virus from fruit bats to pigs to man in 1997.

Whilst the principle of the Three Rs, *reduction*, *replacement* and *refinement*, is a laudable and worthwhile goal to strive for, it is difficult to envisage in the foreseeable future that there will not be a need to use some experimental animals to develop methods to reduce or eliminate the adverse impact of new diseases on the welfare of other members of their species.

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