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Animal Welfare 2006, 15: 1-5
ISSN 0962-7286

The application of Russell and Burch's Three Rs in commercial livestock experimentation

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Abstract

The inclusion of Russell and Burch's Three Rs (replacement, reduction and refinement) in guidelines, codes of practice and law reflects their current position as the guiding principles of ethical assessment of research involving animals. This article explores some activities within the contemporary livestock industry that constitute the experimental use of animals on a local and global scale. The elucidation of correlated responses during trait selection in genetic improvement programs provides one example of experiments occurring within the commercial livestock industry. This experimentation is largely conducted without scrutiny of its conformity to the Three Rs. Experimentation to improve the management of the livestock industry is consistent with the principle of refinement, and experimentation to increase productivity per unit of livestock is consistent with the principle of reduction; however, experimentation to increase total livestock production conflicts with the principle of replacement. Some approaches regarding the appraisal of the ethics of research involving animals, which could avoid arbitrary boundaries associated with the location or purpose of experimentation, are considered together with the relationship between experimentation and other anthropogenic impacts on animals.

Keywords: *animal welfare, consequentialism, deontology, experimentation, genetic selection, livestock*

Introduction

Russell and Burch's principles of the Three Rs — replacement, reduction and refinement — have now guided experimental method and assessment of the ethics of research involving animals for almost five decades (Russell & Burch 1959, reprinted 1992). "Replacement means the substitution for conscious living higher animals of insentient material. Reduction means reduction in the numbers of animals used to obtain information of given amount and precision. Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used" (Russell & Burch 1959, reprinted 1992 p 64). In a frequently cited quote from the introduction to their book they note: "…it is widely recognised that the humanist possible treatment of experimental animals, far from being an obstacle, is actually a prerequisite for successful animal experiments. …the intimate relationship between humanity and efficiency in experimentation will recur constantly as a major theme in the present book" (Russell & Burch 1959, reprinted 1992 pp 3-4).

Today the Three Rs provide almost the universal standard ethic for the regulation and review of animal experimentation; the principles have been enshrined in guidelines, codes of practice and law. The Nuffield Council on Bioethics recently reinforced this position in a commentary on the ethical importance of the Three Rs to research involving animals: "…it is crucial that the Three Rs are, and continue to be, enshrined in UK regulation of research involving animals. The principle that animals may only be used for research if there is no other way of obtaining results anticipated from an experiment is also fundamental" (Nuffield Council on Bioethics 2005, p XIX).

It was recently noted that much of commercial agriculture uses animal experimentation in the day-to-day management of livestock (Colditz 2005). This paper explores the relationship between the research conducted within the commercial livestock industry and the Three Rs, and then describes some potential approaches to the assessment of the ethics of research involving animals that could encompass both institutional and on-farm experimentation.

The experimental nature of commercial livestock production

An iterative process of measurement, analysis and refinement of practice underpins most business activities today. In the livestock industry, experimental practices can be used at the level of individual farms to gain local knowledge, and at national and global levels to gain more general knowledge, for example, through breed comparisons and epidemiological studies.

Of the many types of experimentation carried out in the livestock industry, four categories can be readily identified: to acquire knowledge to improve livestock husbandry systems; to improve attainment of breeding goals; to understand epidemiological patterns; and to improve attainment of commercial goals. Interventions to collect samples and data from animals often constitute impositions on their well-being that provide no benefit to the individuals being measured.

Experimentation through genetic practises is very widely used. Quantitative genetics methods are used to identify animals of superior genetic merit for production, disease or welfare orientated traits. Animals selected on the basis of their merit for the traits of interest are used for breeding in order to improve the genetic make-up and performance of the flock or herd. In 1990, data from Interbull — an international dairy genetic evaluation consortium — indicated that 50% of the dairy bulls undergoing genetic evaluation in the global dairy industry were sons of just five sires (Wickham & Banos 1998). The degree of relatedness, or inbreeding, of animals can be used to calculate the effective size of a population. It has been estimated that by 2015 the effective population size for Holstein dairy cattle in the USA will be just 66; this means that the distribution of genes within the Holstein population is equivalent to that which might be found in a population of 66 unrelated animals (Hanson 1995). Furthermore, the international trade in semen has led to a situation where the global Holstein population will not be much larger; in 1998, it was estimated that 50% of all commercial cattle in the global cattle industry were mated by artificial insemination (Thibier & Wagner 2002).

Not all outcomes of a breeding program are known at the time that the program is implemented. Genes that contribute to traits under selection can also affect traits that are not the object of the breeding program, through molecular processes termed pleiotropism and epistasis. The nature of such pleiotropic and epistatic effects, and of correlated responses during trait selection, often only become evident as the selection process progresses. Rauw *et al* (1998) provide over 100 references to undesirable and negatively correlated responses in metabolic, reproductive and health traits to selection for high production efficiency in pigs, poultry and dairy cattle. Knowledge of these outcomes has arisen largely through the analysis of data collected from animals on farms and is important to the further refinement of breeding practices. To the precautionary principalist, the uncertain outcomes of breeding practices might provide an example of the need for knowledge before implementation; for the livestock scientist and the farmer it is an example of practical experimentation to gain new knowledge for further incremental refinement of hypotheses, experimental designs and commercial practices.

The importance of experimentation on commercial farms to future genetic research in the livestock industry has been highlighted by the recent review of Farm Animal Genomics undertaken by the UK's Biotechnology and Biological Sciences Research Council (BBSRC). The report notes: "...that use of experimental herds should be complemented by more extensive use of normal commercial farm herds to test hypotheses built using experimental animal populations…. Commercial populations provide large numbers that are essential for fine-scale genetic mapping, and whilst logistically ambitious, such measures will contribute greatly towards meeting the challenges of our recommended priority areas, especially farm animal health. Recommendation 7: BBSRC should seek ways to promote greater utilisation of commercial farm animal resources in academic farm animal genomics research. We encourage BBSRC to take an ambitious stance in this matter; to take the initiative and use financial leverage to work with other stakeholders (Defra, SEERAD, industry) towards the formation of a national network of commercial farms collaborating with academic researchers" (BBSRC 2005).

The introduction of electronic, lifetime identification for livestock is likely to increase the scope for experimentation in the commercial livestock industry. For example, in Australia, the implementation of the lifetime identification of cattle is being accompanied by the provision of individual carcass data by abattoirs to cattle producers; the producers can then use these data to refine their livestock management and breeding practices. Failure to utilise the opportunities created by individual animal identification, new data capture technologies, and new analytical methodologies through these global and local experiments would limit the opportunities to refine livestock breeding and management practices, and to improve the welfare outcome for livestock.

Application of the Three Rs in commercial livestock production

If commercial livestock practices do use animal experimentation, to what extent does this experimentation comply with Russell and Burch's principles of replacement, reduction and refinement?

Replacement

Replacement means the substitution for conscious living higher animals of insentient material in experiments (Russell & Burch 1959, reprinted 1992). Although the replacement of livestock as a source of power, affluence, prestige, enactment of tradition, companionship, landscape maintenance, transport, fibre, food and specialised products appears improbable in the short to medium term, not only because of its incongruence with contemporary societal values but also because of economic and humanitarian pressures, the potential to substitute insentient material is increasing. A recent US patent (number 6 835 390) describes a system for producing meat from muscle cells cultured *in vitro*, and it is possible to envisage a method for producing milk from bovine mammary epithelial cells maintained in an *in vitro* continuous culture system; mammary epithelial cells are already cultured *in vitro* to investigate factors such as hormone regulation and gene regulation of milk production (Blatchford *et al* 1999). Such methods would admirably satisfy Russell and Burch's principle of replacement; however, these culture systems are not commercially feasible within today's economy.

Reduction

Russell and Burch described the principle of reduction as applying to individual experiments, by using as few animals as necessary "to obtain information of given amount and precision" (Russell & Burch 1959, reprinted 1992 p 64). Research within the animal sciences and in on-farm livestock production systems has long sought to increase

https://doi.org/10.1017/S0962728600029870 Published online by Cambridge University Press

the productivity per animal. This production goal is in accordance with the principle of reduction by decreasing the number of animals required per unit of product; however, superior genotypes and improved on-farm management systems are contributing, in part, to the massive expansion of the livestock industry, which is occurring around the world. By 2020, the global consumption of meat and milk is predicted to be 160% of that consumed in 1993 (Delgado *et al* 1999). In 2000, the Food and Agriculture Organization of the United Nations (FAO) estimated that global livestock numbers were 20.6 billion animals, of which 14.3 billion were chickens, 1.3 billion were cattle, 1.1 billion were sheep, 0.9 billion were pigs and 0.2 billion were geese.

The accuracy of on-farm research to improve the genetic selection of superior animals, the development of improved management systems, and estimates of disease prevalence and spread is generally increased by including the largest number of animals available in the population-based studies; the analysis of relatedness of the global Holstein population provides one such example (Wickham & Banos 1998). But does this trend towards the inclusion of all available animals within such analyses represent a trend away from the principle of reduction? If the increased precision obtained from using larger numbers of animals in population-based studies is viewed as necessary for the acquisition of new knowledge and the further improvement of livestock production then the expanding number of animals used may remain in accordance with the principle of reduction as described by Russell and Burch (1959, reprinted 1992 p 64).

Refinement

Refinement of practices within the livestock industry to improve the welfare outcomes for animals is an area of intense research. Many improvements have been achieved, though often with little direct quantification of their positive impact on welfare; for example, selection for polledness (the absence of horns) (Albright & Arave 1997) and the modification of weaning practices in cattle (Colditz 2004). These examples represent two types of refinement: the former arises from matching the genotype of animals to a production environment; the latter arises through the modification of the production environment, which also includes human interventions, such as husbandry practices, to minimise the environment's impact on livestock. A further example of refinement of genetic practices is the measurement of birth weight and ease of calving in cattle genetic evaluation programs (eg see Breedplan [http://breedplan.une.edu.au, accessed 1 November 2005]). These data are used through multi-trait selective breeding programs to reduce the incidence of dystocias (calving difficulties) while increasing the growth rates and mature body weights of cattle.

As well as providing refinements, the development of new genotypes and production systems can also create new threats to the welfare of livestock, which can emerge if the welfare outcomes of changes in genotypes, production systems and environmental variables are not monitored, if new diseases emerge or if disease risks increase as a consequence of the changed production system. Therefore a steady state of optimal welfare is unlikely to be attainable and there is likely to be a requirement for the continual refinement of practices. The scale of the commercial livestock industry is a major source of welfare concern for researchers (eg Rollin 2000) and advocates, such as Compassion in Word Farming; however, rapid advances in technologies for electronic monitoring of individual animal performance and welfare may provide a refinement that reduces the risk of compromised welfare resulting from decreased contact between the stockperson and the animals in large scale enterprises (Rowe & Atkins 2004).

The refinement of methods for the production of livestock, through contemporary husbandry and management systems, is currently being pursued and is amenable to ongoing improvement, while reduction is being achieved through increased production per animal; however, replacement is unlikely to be achieved without global revolutions in ethics, economics and values.

Towards a framework for the assessment of the ethics of experimental use of animals in agriculture

If we accept the argument that at least some commercial farming practices do constitute experimental use of animals, and that this use occurs outside the current framework for the assessment of animal experimentation, then we may wish to consider a new framework for assessing the ethics of these experimental uses of livestock. Several approaches are considered here. The primary aim is to ensure that the most humane management of livestock possible is practiced for the efficient and successful acquisition of knowledge from such experimentation. The viewpoints that are commonly applied in order to determine whether practices are right or wrong have been outlined in detail in the Nuffield Council on Bioethics report on *The Ethics of Research Involving Animals* (Nuffield Council on Bioethics 2005). These viewpoints include consequentialism, deontology and virtue ethics, and the reader is referred to this source for a detailed account of the application of these viewpoints to the ethics of research involving animals; the viewpoints are also expanded on below. Briefly, consequentialism focuses on the impacts and outcomes of a practice; deontology considers actions to be intrinsically right or wrong irrespective of the outcomes they create; and virtue ethics draws guidance from the way a virtuous person might behave in the circumstances under consideration.

In considering potential approaches to the assessment of experimentation involving livestock, two types of experiments that might need to be accommodated can be proposed. (1) The acquisition of local knowledge regarding a production system. For example, a farmer may collect data over a series of years on the percentage of lambs weaned from ewes accommodated in paddocks, which have shelter belts composed of differing floral species. This knowledge could then be used to design appropriate shelter belts for the remaining paddocks on the farm and to improve shelter belts already present in some paddocks. Within a research institution, the equivalent experiment might involve the collection of data on mouse pup survival rates in three commercial mouse boxes, to determine which type of box leads to the highest pup survival rates within the environment and management system of that animal house for each strain of mice used in the institute. (2) An experiment to acquire more general knowledge regarding the genetics of growth and production of an animal species. For example, a farmer may collect data on calving ease, birth weight and growth rate, which they supply to the cattle breed society for the estimation of genetic parameters and the breeding merit of sires for the measured traits. The equivalent experiment in a research institution might be the study of the quantitative genetics of selection of mice for weight and growth rate, such as the work described by Bishop and Hill (1985).

(1) Rigorously apply the current framework and processes for the assessment of research involving animals in research institutes to experimentation within the commercial livestock industry

In this approach, the Three Rs could be applied, through instrumentalities such as Animal Ethics Committees and the Home Office, to regulate animal experimentation in commercial agriculture. Commercial livestock practices can be very dynamic: small scale experimental modifications to practices on individual farms can be implemented at short notice and high frequency. Furthermore, the fact that experimentation has occurred may only become evident retrospectively when data over a number of years are examined and related to, for example, weather patterns or, using the earlier example, changes over time in the floral composition of wind breaks. It is likely that regulation within this framework would require a mechanism that did not require prior approval of each activity in order to avoid excessive bureaucracy.

(2) Formalise a distinction on the basis of the location of animal experimentation

In this approach, which is similar to the current circumstances, a criterion would be established that the need for the assessment of animal experimentation would not apply to research involving animals on farms. This criterion ignores many of the moral and ethical concerns regarding the use of animals in experiments.

(3) Create a distinction on the basis of the purpose of animal experimentation

Most assessments of applications for the use of animals in experimental research require justification for the use of animals. This justification is used to balance the cost, in terms of pain and suffering to the animals, against the potential benefit, in terms of new knowledge and the potential outcomes for both humans and animals. In this approach, an *a priori* decision might be made that research undertaken for the purpose of improving the livestock industry be exempt from ethical scrutiny; this approach faces similar moral and ethical limitations to approach (2).

(4) Formalise a suite of acceptable experimental practices that do not require assessment each time they are used

Acceptable standards for most commercial livestock production practices are set by legislation, guidelines or codes of practice. Interventions for data collection, which form part of on-farm experimental research, largely comply with these standards; therefore, it could be argued that these standards already provide a mechanism to ensure the humane use of livestock for experimental purposes. If not, these standards could be extended to include specific methods for the collection of data, as an industry best practice. However, unless the same provisions are also applied to animal experimentation within research institutions, approach (4) becomes equivalent to approaches (2) or (3), by creating a distinction between animal experiments on the basis of location or purpose. Therefore, the logical extension of approach (4) would be for certain practices, within research institutions, to be formalised and subsequently exempt from assessment each time they are used. The criteria used for determining which standard practices could be formalised and removed from assessment, could include the potential severity of the procedure on the animal, in accord with a schema, such as that developed by Orlans (1987): (a) experiments on animals that are expected to produce little or no discomfort; (b) humane killing of animals for tissues; (c) experiments on completely anaesthetised animals with non-recovery; (d) experiments that involve minor distress, discomfort or short-duration pain and; (e) experiments that involve severe pain in conscious animals. The potential impact of a procedure is influenced by the environment in which an animal is managed, and by its genotype, age, nutritional status, reproductive status and prior experience. Therefore, a challenge for this approach would be to define the genotypes and environments to which an exempt status could be applied. A further limitation of approach (4) is its failure to provide an assessment of experiments using animals for its compliance with the principles of reduction and replacement.

(5) Extend concern regarding research involving animals to include all anthropogenic impacts on animals

An assumption of the present-day approach to the ethics of the use of animals by humans is that the use of animals in experiments forms a special class of animal use that deserves its own assessment criteria, which includes the Three Rs. It is generally accepted that the basis for concern regarding the use of animals in experiments is their status as moral subjects. The view of the consequentialist judges the merit of the experiment in terms of its impacts and outcomes for the animal; negative impacts include pain and suffering, and compromises to naturalness and to the telos of the animal. The deontological viewpoint considers some experiments as intrinsically right or wrong independent of their outcome. The current boundary in ethical concern between the experimental use of animals on farms or in research institutes is therefore largely a deontological one. The consequentialist

https://doi.org/10.1017/S0962728600029870 Published online by Cambridge University Press

view leads to an evidenced-based approach for assessing the impacts on animals of various procedures and practices. If we focus on outcomes, we can then ask whether comparable outcomes should be judged to be of comparable merit. An affirmative answer could lead to the development of uniform criteria for the assessment of anthropogenic impacts on animals, irrespective of the proximate anthropogenic cause of these outcomes. However, in the deontological view, animal experimentation may always remain a special case that deserves unique criteria for its assessment. If we look at research involving animals in these terms, the Three Rs appear to be part of a deontological framework for assessing the merits of animal use.

(6) Extend concern regarding research involving animals to include anthropogenic impacts on all biota

Humans and animals need ecosystems to survive; however, a focus on pain and suffering initially leads to a focus on the individual. From a consequentialist viewpoint, the significance of this outcome needs to be viewed not only in terms of the individual but also as an outcome for the population and for the ecosystem in which the individual and its population participate. The importance of all these components of the biosphere can be viewed either as equivalent or to be on a hierarchy of relativity that may change with time. Methods for measuring, and value frameworks for assessing the impacts of humans on all components of the biosphere are still developing. A comparative assessment of the consequences for animals of anthropogenic impacts within the broader range of consequences of human actions on all biological systems appears to be a desirable goal to strive towards.

Conclusions

Recognition that the livestock production industry uses animals in experiments as part of its commercial practices leads to dilemmas over the approaches that are currently used to assess the ethics of research involving animals. Experimentation to improve the management of the livestock industry is consistent with the principle of refinement, and experimentation to increase productivity per unit of livestock is consistent with the principle of reduction; however, experimentation to increase the quantum of livestock production, either locally or globally, appears to be in conflict with the principle of replacement. The exploration of approaches to assess the ethics of animal experimentation in agriculture highlights the tension between the views of consequentialism and deontology. It appears likely that a scientific enquiry, for an evidenced-based approach to assessing the impacts of animal use, will strengthen the hand of consequentialism. It will be interesting to see whether the development of scientific methods, to establish the determinants of the intrinsic value of moral subjects that influences the assessment of the rightness or wrongness of actions within the deontological viewpoint, can play a role in resolving these conflicts and help lead to an equitable framework for the assessment of the ethics of human impacts on animals.

Acknowledgements

Stimulating discussions with Andrew Fisher, Drewe Ferguson, Steve Atkinson and Caroline Lee are gratefully acknowledged. The recognition by a journal referee of the paradox of reduction in animal use though increased production potentially leading to increased demand is also gratefully acknowledged.

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