Education and Training: A Basis for the Introduction of the Three Rs Alternatives into Animal Research

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Summary — Education is a highly effective way of promoting the introduction of alternatives into the everyday practice of biomedical research and testing. In some countries, specific requirements for the education of persons involved in animal experimentation have been made compulsory by law. In The Netherlands, young scientists must take a course on laboratory animal science as part of, or in addition to, their biomedical graduate programme. This course provides information on the proper design of animal experiments, but also covers alternatives, animal welfare issues and ethical aspects of animal experimentation. The Three Rs of Russell & Burch are the guiding principles of the course, during which participants are challenged to seek methods or techniques that can replace, reduce or refine the use of animals. Since 1985, more than 2500 people in The Netherlands have taken the course, and evaluations have indicated that a large majority of the participants appreciated this education as a contribution to both the quality of experiments and the welfare of the animals, and considered the course to be indispensable for those who are responsible for the design and performance of animal experiments.

Key words: education, animal experimentation, alternatives.

Introduction

Until recently, no formal requirements existed on the education and training of people responsible for the design of animal experiments. For a long time, it has been common practice for the proper use of animals for experimental purposes to be learned practically, from those who were supposed to be experienced in the field. In this respect, the use of animals was not thought to differ from the use of scientific equipment. The experimental animal was seen as an object rather than a subject. Thus, there was no motivation to educate the young scientist in the moral implications or welfare aspects of animal experimentation. The fact that in most scientific journals the animals used in experiments are documented under the heading *Materials and Methods*, could be taken as an indication that, in science, this view of animals is still prevailing.

This situation is gradually changing. It is now generally recognised that animals have an intrinsic value and attitudes toward animals are no longer based solely on their utility. Recognition of an intrinsic value implies that animals cannot be killed, or subjected to pain or distress, unless there are reasons strong enough to overrule this principle. Whether or not animals can be used in a given experiment needs to be discussed by an ethics committee. Experiments which are considered to be acceptable must be performed as carefully as possible, by researchers who are fully competent. These people must not only be qualified in the biomedical discipline of the experiment, but must also be educated in the relevant aspects of laboratory animal science. This education should contribute both to the quality of experimental results and to the humane use and care of the animals.

In EU *Directive 86/609/EEC* on the pro-

tection of animals used for scientific purposes (1), three sections deal with competence. Article 7.1 states that experiments should be performed solely by competent authorised people, or under the direct responsibility of such a person. Article 14 indicates that people who carry out experiments or take part in them, and those who take care of animals used for experiments, should have appropriate education and training. According to Article 19.2b, a veterinarian or other competent person should be charged with advisory duties in relation to the well-being of the animals. The implementation of these provisions at the national level in EU Member States has not yet been fully accomplished, although several countries have already issued regulations on competence.

The US *Animal Welfare Act* and the National Institutes of Health also mandate specific training of personnel involved in the use and care of laboratory animals. Courses on laboratory animal science are offered for people working in this field at several universities and other institutes in the USA (2, 3).

As reflected by *Directive 86/609/EEC*, at least three categories of people involved in animal experimentation can be distinguished: investigators; animal technicians; and laboratory animal specialists. The education and training of these three categories of individuals are equally important, but, according to the Federation of European Laboratory Animal Science Associations (FELASA), the education and training of the investigator in laboratory animal science should now have priority (4). Although the investigator plays a key role in the design of animal experiments, at present there are only a few countries where courses on laboratory animal science are organised for this group of people.

In The Netherlands, legal requirements on competence for the scientist who is responsible for the design of an experiment were issued in 1985. Such people must have graduated in one of the biomedical sciences (for example, biology, medicine, pharmacy, veterinary medicine) and must, in addition, have taken a course on laboratory animal science. According to the law, this course must concentrate on the humane and careful use of animals and must include information on alternatives and the ethical aspects of animal experimentation. Based on these legal provisions, a programme for a three-week course has been developed by the Department of Laboratory Animal Science at Utrecht University. Initially, this course was held at only one location, i.e. Utrecht, but now five universities are running the course several times a year. All of the courses are centrally coordinated by the Head of the Laboratory Animal Science Department at Utrecht University.

Based on the experience of the past ten years, we will discuss the content and training format of the Dutch course, to illustrate that education and training in laboratory animal science can provide an effective tool for promoting the introduction of alternatives into animal experimentation.

Course Content

From the beginning of the course, heavy emphasis is placed on the fact that the scientist is the central person in the design and performance of animal experiments, and that he/she has specific responsibilities with respect to the welfare of the animals used. It is made clear that the use of animals can be accepted only under a set of strict conditions. Among these are that the experiment must be approved by an ethics committee, and must be conducted by persons who are fully competent. An outline of the course is given here.

Introduction

Brief overview on the use of animals in the course of history; numbers and purposes of present animal use. The animal protection movement and laboratory animal science associations. Factors that influence increase/decrease in animal use. Legislation on the protection of animals used for scientific purposes.

Biology and husbandry of laboratory animals

Comparative aspects of anatomy and physiology of commonly used animals; reproduction and breeding of these species. Housing conditions in relation to the behavioural needs of the various animal species; possibilities for enrichment of the cage environment; tips for avoiding stress and improving the predictability of environmental factors for the animal. Nutrition and feeding conditions; nutrient requirements; advantages and disadvantages of *ad libitum* feeding. Genetically defined animals; genotype–environment interactions; choice of animals for genetic

uniformity or genetic heterogeneity; genetic characterisation and quality control.

Gnotobiology and diseases

Microbiological standardisation; germ-free and specified pathogen-free animals; housing conditions of gnotobionts. Health monitoring and prevention of diseases; quarantine. Diseases of laboratory animals; zoonoses; interactions of diseases and experimental results. Safety aspects of working with infectious animals.

Design of animal experiments

Evaluation of the necessity of an animal experiment; preparing the protocol; literature search; choice of the animal model; defining the genetic background of the animals and the environmental conditions, including the experimental circumstances; standardisation of these conditions in order to increase the reproducibility of experimental results and to reduce variation, thus reducing the number of animals needed per experiment. Design of the experiment with information on the advantages and limitations of stratification/blocking. Interference of housing (group versus solitary) or procedures with experimental results. Statistics; power analysis in order to calculate the number of animals required in test groups and control groups. Organisation and management of animal experiments.

Experimental techniques

Demonstration and hands-on experience of some of the basic experimental techniques; principles of (micro)surgery. Recognition of pain and distress; methods of anaesthesia; anaesthetics and analgesics; choice of anaesthesia and anaesthetics in relation to the animal species and the nature of the experiment; interaction of anaesthetics with experimental results; complications of anaesthesia; postoperative care and management of animals. Euthanasia; pharmacochemical and mechanical-physical methods. Possibilities for refinement.

Alternatives

Concept of alternatives; replacement, reduction and refinement of animal use; survey of alternatives that are available in research, education and testing; need for validation of alternatives; organisations for the study of alternatives and validation; possibilities and limitations of alternatives; future of alternative methods.

Ethical aspects

Attitudes toward animals; human–animal relationships; intrinsic value; different approaches in ethical reasoning; discussion of the admissibility of animal experiments; moral problems in the ethical dialogue; pitfalls in reasoning.

The Three Rs as Guiding Principles

It is now generally accepted that the term "alternatives" is best defined by the Three Rs concept of Russell & Burch (5). Education of the young scientist is probably the most effective way of introducing this concept into the everyday practice of biomedical research. When designing the course, the Three Rs were used as the guiding principles. Throughout the course, it is emphasised that, in animal experimentation, no step should be taken without considering whether all or part of the problem can be solved without the use of animals and, if not, whether there is a possibility of applying an alternative method or technique leading to a reduction in the required number of animals or to a decrease in the degree of suffering of the animals to be used.

In particular, refinement is an area where education and training can contribute to improvement. The course on laboratory animal science has been made compulsory in The Netherlands, mainly to prevent animals from unnecessary suffering due to the ignorance of the responsible investigator. The humane treatment of animals before, during and after the experiment not only requires an understanding of the animals' nature and optimum environmental conditions, but also knowledge of experimental techniques, including anaesthesia and analgesia. One of the objectives of the course is to provide relevant information on these topics. In their book (5), Russell & Burch showed that the humane treatment of animals is often a prerequisite for a successful animal experiment. This implies that investment in refining experiments does not conflict with the aim of carrying out good quality research but, on the contrary, will usually improve the work.

Training Formats and Teaching Materials

The course in The Netherlands is offered as a full three-week block programme. The advantage of such an approach is that the participants have to set aside their research or other obligations during this period, which improves concentration and also gives time for reflection. The maximum number of participants is 20.

During the course, lectures and hands-on workshops alternate with demonstrations, videos and discussions. The multidisciplinary nature of the course requires the participation of lecturers from several disciplines. Specialists are invited to participate in each course as lecturers. The staff are encouraged to prepare problem-based learning programmes and to organise workshops for the discussion of these topics. The hands-on workshops deal with proper handling and restraining techniques for the common laboratory animal species and some simple procedures and techniques. Also during the course, small groups of three or four students are given the task of preparing a protocol for an animal experiment (for example, a protocol for an experiment to test the potential therapeutic effect of a new drug for the treatment of prolactinomas). Such a protocol should include all the different factors that must be taken into consideration when designing an animal experiment, such as the choice of animal species/strain, the origin of the animals, the number needed in test and control groups, the housing conditions of the animals (solitary or group housing), the environmental conditions, whether or not induction of prolactinomas is needed, and the methods of anaesthesia or euthanasia (if required). Included in the task is an examination of whether or not replacement alternatives are available and what possibilities exist for minimising suffering. If no replacement alternatives are available, students must decide whether an experiment is acceptable from an ethical point of view. In other words, they have to step aside and act as members of an ethics committee and give a judgement on the admissibility of their own experiment. A presentation of the protocol, with a group discussion, completes the task.

Students are also asked to give a critical analysis of selected papers on animal experiments that have been published in a scientific journal. They are asked to look for strong and weak points in the design of the experiments described. These tasks contribute to the integration of the material covered in the various parts of the course, and help to develop a critical attitude toward the value of animal experiments.

During the course, students have full access to PREX, the on-line information system of the Department of Laboratory Animal Science at Utrecht University. PREX is accessible via the Internet or by direct modem-connection, and contains several databases which have been developed to assist in the proper design of animal experiments. Besides specialised databases in the field of laboratory animal science (for example, catalogues of inbred strains, transgenic animals, biological values, audiovisuals, alternatives and book contents), PREX covers large biomedical databases, for example, Medline and Vet CD. The theoretical part of the course is covered by a multi-author textbook (6). In addition, many videos, slide and tape programmes, and interactive computer-based learning programs are available to support lectures and workshops. Several of these programs have been used to replace living animals. A written examination is part of the course. Participants who pass the examination obtain a certificate.

Conclusion

The course has been attended by more than 2500 participants since 1985. They were all either students in the final stage of a biomedical graduate programme or had recently graduated in one of the biomedical sciences. Ideally, the course should be taken before a person becomes actively involved in any animal experiments.

After the course, participants are asked to complete (anonymously) an evaluation form. The majority of the participants seem to be very satisfied with the objectives of the course, which is seen as an important contribution to the quality of animal experiments, and to a more careful use of test animals. More than 95% of participants indicated that they would recommend the course for all scientists who intended to enter a research area where animal experiments would be performed. Varying opinions on the duration of the course have been expressed. Students generally favoured a three-week course, whereas most of the junior scientists, in particular those who were preparing a thesis,

or who had other responsibilities for a research project, tended to favour a shorter course taking not more than two weeks. Nearly all the participants seemed to agree that the course as such was indispensable for those responsible for designing or performing animal experiments. Thus, we can conclude that this type of education satisfies a need, while stimulating a positive attitude in researchers toward the Three Rs.

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