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About the Future of Laboratory Animal Science in Europe

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Introduction

During recent years biomedical research in Europe has been confronted with social and legal developments that have lasting repercussions on laboratory animal science (LAS). A variety of events have initiated considerable changes in concepts and practical work. They extend from controversial views on techniques in husbandry to questioning the terms of reference, professional responsibilities, and legitimacy to serve the purposes of biomedical research. It began with a public dispute on the necessity and justification of animal experiments. The future prospects for LAS in the Countries of Western Europe depend less on the advancement of professional knowledge and skills than on the public and political decisions resulting from the dispute. At this stage we need to recall the scientific, social and humanistic developments which have led to LAS in the present. The future of LAS cannot be simply derived from an extrapolation and continuation along the lines of its previous programmes and activities.

The professional concern about animals in research in Europe took roots first in Britain, from where offshoots spread to the United States and to the Continent. LAS developed slowly from surveying animal breeding and experimentation into an integrated multidisciplinary science. The development can be divided into four periods of varying length featuring different interests and achievements. Based on a review of these four periods I attempt to look into the future of LAS. The four periods are: (1) the hygienic welfare period; (2) the optimistic expansion period; (3) the critical stabilization period; and (4) the realistic self-assuring period.

1. The hygienic welfare period

The concern about care and health of laboratory animals arose among a small number of individuals in Britain who were worried about the welfare of animals when biomedical research was much promoted during World War II. Soon after the war in 1945 the Laboratory Animal Bureau was established near London with the initiative of the Medical Doctor William Lane-Petter who compiled information about the demand for animals and their breeding and use under laboratory conditions. This nucleus was later enlarged by the Medical Research Council to the Laboratory Animal Centre in Carshalton. With the weight of a long tradition the situation in Britain was almost ideal for the promotion and development of a science on and about laboratory animals. There was already the Cruelty to Animal Act of 1876, requesting licences and inspectors for research laboratories, and the respected Universities Federation for Animal Welfare, UFAW, founded in 1926. The stage for a LAS was set when the first edition of the UFAW Handbook on the Care and Management of Laboratory Animals was published in 1947, and the essential breakthrough came after the second edition was published in 1957. The book appeared at a time when biomedical research was much promoted and was expanding rapidly in Europe and in the USA. It opened the eyes for seeing the needs and furthered the intentions to look professionally after the physical health and welfare of animals used in research. Information on the anatomy and physiology of the most demanded animal

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species was systematically compiled. Studies were initiated in laboratories to investigate the diseases of animals, in particular the communicable infections, and their nutrition, handling, and housing to warrant their welfare. The period is characterized by attracting the interest and getting together all those individuals and scientific circles who were concerned with the welfare and use of animals in research. The ideas were soon disseminated within the whole of Europe. Lecturers were sponsored to spread the growing knowledge about laboratory animals throughout the countries, national and international symposia were held to inform persons engaged in animal experiments, and national societies were founded. It was soon realized within larger university research establishments and pharmaceutical laboratories that informed and specialized persons were needed to ensure the welfare of animals and the quality of experiments. This led to the concept of the animal curator as the person who has the skills and is given the responsibilities to hold all strings of the prospected LAS.

2. The optimistic expansion period

In the late fifties, and during the sixties, biomedical research rapidly expanded as the economic conditions recovered and improved after the war. The economic developments allowed large investments and technical innovations. An optimism and positive belief in the value of animals for the advancement of biomedical research was building up and spread from small clusters to reach every research laboratory. The number of experiments began to rise exponentially. Consequently the demand for more genetically defined and healthy animals went up as new fields of research were tried out and developed. While continuing with the classical short-term type of experiment on which physiology was built new methods of experimentation were developed, such as long-term follow up studies in toxicology for which disease-free animals were mandatory. The category of SPF animals was defined and apart from producing them in increasing quantities every idea was put to the test and effort was made to concentrate on the quality of every single animal. The production of animals was commercialized as soon as the conditions for breeding and health control were generally agreed on. Professional breeding institutions were founded in most countries.

For practical purposes standardization of animals and the conditions of their environment was proposed. The standardization of animals in breeding and experiment soon became a paradigm largely under the influence of the demands required in bio-assaying and drug safety testing. It was put into practice with such enthusiasm that it soon passed over to normative rules. Those who did not adhere to it, wondered about the inevitable restrictions, or were hesitant to accept its universal applicability, were branded as being either uninformed or unconcerned with the improvement of research. The call of ICLA in 1971 for "defining the laboratory animal", to be seen as a scheme to work with flexible purpose-adjusted standards, remained without resonance. During the course of this period standardization was equated with welfare. Standardization was driven toward a particular refinement of purity and precision of the animal as measuring instrument. It culminated in announcing an "animal pro analysi" used by a breeder (*Spiegel* 1963) to feature a product of top quality. By the time this term was invented animal house technologies such as the double corridor barrier system, control of air quality and indoor climate had been worked out, proved efficient and were widely applied. Ample housing space was provided for experimentation with large groups of animals. Much attention was given to automate and economize husbandry methods for production and experimentation in animal houses. This was on demand and in support of the concurrent application of biostatistics in the design and assessment of animal experiments. Experiments were in-

creasingly planned on the advice given by biostaticians to reach results of high statistical significance. In order to provide models of a particular biological phenomenon, such as a specific function, deficiency or disease, purpose-bred and purpose-conditioned animals were introduced. Standardized animal models were described, defined, and compiled to provide a sort of "cookbook" from which readily an appropriate model could be chosen. While these biological, medical, technical and experimental developments were gradually put together under one umbrella, the field Laboratory Animal Science emerged. The name was accepted and LAS established as an interdisciplinary academic activity referring to all knowledge about the animal species selected for carrying out research with particular attention to their welfare. LAS established itself as a professional body to act as supplier, helper, guide, and advisor for everybody performing experiments on animals.

During this period of optimism and trust in the future of animal experimentation the development of LAS was not unlimited. In the drive for simplicity, it was an error to equate standardization with welfare. Out of enthusiasm other errors were made. The puristic and mechanistic excesses such as the effort to provide animals "pro analysi" and advertise animals as measuring instruments and adequate disease models did not remain unchallenged. Among outside observers such developments insinuated the idea that for the sake of research animals were brought down to be used like controlled machines for selected work or simply as a reagent for a chemical analysis. The notion spread that animals were either reduced to technical tools or at least manipulated relentlessly with every restriction permissible as long as they served a purpose. The purposes were questioned and it was realized that the purposes for which animal experiments were applied often exceeded their potentials. Opinions of antivivisectionism came forth again after a long interval of silence. Researchers were interpreted as having lost their empathy for animals as beings, with their own needs and demands for life.

Today, we can understand that some views of LAS were bound to be misinterpreted and could provoke alarm and protest among observers not directly involved in research or objecting to it. The end of this period of establishing LAS with its wide national and international acceptance and impressive expansion came when the quest for knowledge in some fields stagnated or declined and the interest was shifted back to the animals themselves after the unrestrained demands for their use in research had been satisfied.

3. The critical stabilization period

During the middle of the seventies LAS was increasingly confronted with forces of resistance against expansive animal experimentation. By this time the previously unbroken belief in the progress of science for a better and safer future of humans was questioned, after insufficiencies and failures of animal experiments were reported, particularly in drug research. The media picked up some particularly impressive examples such as the thalidomide disaster. Actually, what turned out to be a lack of special knowledge about the importance of pregnancy in drug testing was interpreted as irresponsible manipulation by scientists for gain of academic fame or as greed for profit. Such new information, however, called for expansion of animal experimentation in the field of teratology. In spite of new fields of research arising the demand for animals had begun to plateau due to a decline of research in other fields. The slowing down of the previously steeply positive growth rate allowed time for reflection on the paradigms which had hitherto directed the course to LAS.

Until now the aim of working for the welfare of animals used in laboratories was restricted to the limits set by the requirements and demands of the researcher. The requirements of the animals themselves were considered of secundary importance. It was realized that

the variability of the responses of animals in an experiment is an innate characteristic, even within a controlled genome, and may be reduced but cannot be eliminated by additional environmental standardization measures. It was accepted that the animal is a self-regulating living system for the purpose of maintaining its own kind. In that case rigid normative standardization of breeding and husbandry was not really necessary or justifiable as any restriction of the requirements of the animal could also be expected to lead to a distortion of the results. The different adaptability of specific strain related traits of a species should then not be pressed into a standardization strait jacket but should be utilized to enlarge the applicability or sensitivity of the animal model. In practice the paradigm of normative standardization was to be modified to purpose-orientated standardization. It was realized that a liberalization of methods in husbandry without violating the health of the animals was not only scientifically justified, but also desirable. In that case the size of experimental groups could be reduced without conflicting with biostatistical methods. Undoubtedly, these reflections were instigated or even compelled by force by animal protectionists and antivivisectionists of various degrees of objection against animal experimentation, or of aggression against science.

Welfare of the animal was reconsidered in the light of the knowledge gained from the excessive use of animals under strictly confined conditions. Welfare can be defined as the care provided by humans for the safety and prosperity of animals. The notion was discussed of extending the welfare of animals in the hands of man to a well-being of animals leaving it to them to lead a life under human-set conditions. Quality was interpreted not only as a disease-free status and as being adapted to defined conditions within the standardization scheme, but also as not inflicting on the animal's needs and requirements. A postulation introduced almost 20 years earlier by *Russell & Burch* (1959) for reduction, replacement, and refinement of animals in research was brought up and moved to the centre of attention. This postulation is now widely known as the 3 R's. By the end of this period LAS had begun to shift emphasis from applying the skills and knowledge primarily to research with animals to considering the care for animals.

4. The realistic self-assuring period

During the eighties important social and political developments took place which significantly affected LAS. New animal protection laws were introduced, or old ones were revised, in the majority of the countries in Europe. The new laws imposed much restriction on free decision in research and increased the control over animal experimentation. The organization of experimentation with animals was shifted from being left to the authority and responsibility of the scientist towards more attention to a protection of animals. Applications for research had to be prepared in advance and submitted to Commissions for approval before experiments were permitted to be initiated. A barrier of governmental legislation and regional regulations under the pressure and untiring activities of animal protectionist groups was building up to control the researcher, the scope and extent of his research, and his choice of species. Researchers had to put up with opinions and decisions made by the reviewers and licence commissions.

The concept of the 3 R's was put into practice and converted into programmes. A reduction of the number of animal experiments was systematically encouraged. The stringent granting of licences and other measures for reduction imposed a negative growth rate of animal experiments. For LAS this was a relief which did not conflict with its aims. Annual national statistics were introduced and utilized to inform the public about the absolute and percentage reduction of the use of animals. Replacement was initiated to see to what extent research could be shifted from work with whole animals to work with isola-

ted cells or primitive systems such as bacteria as substitutes. In the wake of replacement the term "alternative methods" was invented and the search and promotion of such methods was to become a sort of shadow science which depends on the knowledge and ideas derived from whole animal research. The emphasis on the science of alternative methods had far reaching effects. LAS was confronted with the essential question of whether it should remain limited to the whole animal or include the research towards wider application of subsystems of the whole organism or isolated systems.

Refinement was the last criteria to be promoted. Refinement of husbandry and experimentation requires sound inside knowledge ranging from production of animals to their use in specified experiments. It is directly related to welfare. LAS has no problem with this concept as it has always been one of its main interests, through it was perhaps neglected and not classified as such for some times. Representatives of LAS were now in demand and got involved as experts for preparing new regulations for husbandry and care of animals. Even in these activities animal protectionists interferred and forced through their ideas.

The reduction of number of animals made more room available in animal facilities for use of larger cages and wider placing of animals. It also allowed the animal caretaker more time to pay closer attention to his animals. Concepts for refinement have stimulated modifications regarding the quality of animals to be maintained under more flexible and liberal schemes of husbandry. In addition LA scientists with an interest in research can now find more often open ears among researchers to assist them as advisors in the design of experiments and the choice of measures. Their expert knowledge of, and experience through continuous contact with, animals can be of value and is in demand by the researcher for advice on planning and improving the success of his experiment. Working along these lines LAS, picked up the role which was visualized at the very beginning, by acting for animal welfare as a go-between the animal protectionist and the animal experimentalist, in close liason with the latter.

By comparison, experimental strategies are revised and normative standardization is modified. After the hectic seventies the last decade of the second millenium is marked as being professionally relatively restful, with more time for the animal. However, the problems concerning the aims, needs and identification of LAS in the future have never been more prominent (*Uvarov* 1984).

The problem of the present

In the past LAS developed out of the intention to help the animal, and to help the researcher. This concept proved to be sound and formed the identity of LAS. The recent development has raised doubts about this identity. The role of LAS as a respected supplier of animals and companion of research, in close association with the promotion of science, is challenged by the antivivisection and research rejecting movements. There are essential problems both within LAS and in discussing LAS with related groups. The problems derive in the first place from the conflict with different concepts of ethics. LAS has principally followed the concept of an anthropocentric ethic, which accepts that the needs, interests and safety of man have a higher priority than those of other species. This is questioned and opposed by the concept of a biocentric ethic: man should not have priorities and privileges over other species.

Antivivisectionists insist on the postulate of "reverence for life" proposed by the cultural philosopher Albert Schweitzer: "Good is the maintenance and promotion of life, bad is the destruction and inhibition of life". In Switzerland, the Academy of Science has uprated this very personal view of Albert Schweitzer to a value of universal applicability and regulations for researchers are based on it. It was not realized that the authority of this postulate is questionable, contradictory and can

never be consequently implemented (*Gross* 1974). In the meantime the constructions of ethical demands have gone to even more extreme postulates. The views about a "dignity of an animal" and recently about an "unimpeachability of the dignity of an animal" are now under debate. Confronted with these ethical concepts, LA scientists are torn between two camps: in the one camp are the realists who have decided to stand up for the acquisition of biological information and who continue to work with whole animals considering both their welfare and their proper use in research. In the other camp are the conformers who go with the fashion, avoiders who do not want to get into trouble with animal moralists, and the opportunists, who feel it to be safer to go with the protectionists against the researcher than vice versa. In the middle between these camps is a large number of undecided doubters. During the recent past the balance has tended towards the side of the biocentric moralists. At LAS symposia and congresses the attention given to animal protection and alternative methods often outweights that given to animal experimentation.

Scenario for the future

At present, LAS is in a desperate position between an agitated ethically arguing, powerful lobby of fanatical animal protectionists and a shrinking number of well-intended, discouraged scientists, depending on whole animals for their research. LAS has never been really free and independent as a producer, provider and user of animals. There is no doubt that LAS has made an enormous number of contributions to the health of laboratory animals, widening the scope and the improvement of experimentation. This will continue. The future and viability of LAS in Europe is determined by the decisions and the impetus generated from the preferences for emotions, reason or mind over the issue of animals in research: one is the emotional decisions dictated by antivivisectionists and by some views of the public on animal protection and on the acceptance of research in the interest of humans; the other is the rational and humanistic decisions made by the LA scientists themselves. We will have to ask ourselves whether we are prepared to be pulled apart and dispersed to a half-hearted engagement in research or have the courage to stay as allies of the researchers for the best of their animals, which they entrust on us. The latter decision can be facilitated for LAS if the public can be convinced that some needs of the human society can be coped with solely by means of research using animals. Instead of giving in to the Zeitgeist, LAS has to defend its case and responsibilities.

Independent of this, for its own reputation and self-respect, LAS has to make clear and publicise the terms of reference for which it stands. Standing for the welfare and care of animals for research they are:

- to provide defined, healthy animals
- to provide expertise in breeding and husbandry
- to provide basic knowledge about the genetics, anatomy and physiology of the animals, give advice, and assist in experimentation.

LAS is an applied science. Its existence and activities are justified and required as long as animals will be used for research in life science. It is of great importance that the Federation of the European Societies for LAS, FELASA, which has recently been accepted at the Council of Europe, will voice and represent our case effectively within the countries of the European Union and their neighbours.

Summary and conclusion

During its short history of 50 years beginning after the Second Great War in the middle of this century it took more than 20 years until the concern about the welfare of laboratory animals had been worked out into a science for laboratory animals. After a short period of confirmation in the later seventies the new science was questioned under the rising opposition to the use of animals as a method for

biomedical research by animal protectionists, antivivisectionists and moralists. During the eighties the unexpected dogmatic opposition caused much confusion and uncertainty that called for a reflection on the significance and scope of LAS. The science began to question its own identity. Some scientists diverted from their former tasks and engaged themselves in animal replacement methods or turned to animal protection. These conflicts within LAS culminated during the late eighties and have not yet ceased. The future of LAS is determined by the controversial views of supporters and of opponents of biomedical research. LAS can fulfil its area of responsibilities satisfactorily only as long as it maintains its involvement and interests in biomedical research. A splitting of responsibilities with diversion to animal protection will be the same as moving into two opposite directions. Sincere support and sympathy with animal protection and antivivisection will make LAS obsolete and, in fact, unnecessary. The future depends on the demands of the society for health and welfare of the individual, public opinion, and legislation.

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