The society and the use of laboratory animals

Scientific and ethical views

by *P. Schambye*, professor of biochemistry, Odense University, DK-5230 Odense M, Denmark.

Abstract

In this presentation we shall deal with the ways in which society obtains insight in the use of animals in experimental work, whether research or control.

The individual elements in this are shown in Table 1. The arrows indicate the flow of material whether on paper, verbal or in other forms without indicating the strength.

The upkeep of the standards in animal work is depending upon the correct use of the information collected in the laboratory animal science and the flow of information to the widely distributed users of animals. Society must control this and support progress. The use of experimental animals should be restricted and any use deemed necessary must be carried out with the highest degree of care and respect for the animal's integrity and without pain.

The wish to get insight must never result in the hampering of progress. On the other hand present days society and present days science are so deeply involved in each other that we experience an ever growing wish from the society to get insight into the ethics and means of the sciences.

The users of animals in research have nothing to hide. On the other hand the judgement of the reason for the experiments and the ways they are carried out requires the understanding of all the relevant data and the intricate knowledge of the animal science. Therefore the control wanted by society must be left to a control committee of experts headed by a publicly appointed »lay« person, e.g. a judge, as in Denmark.

Main text

No one can deny that society has benefited from the experimental work in which animals have been used over centuries to further our insight and knowledge in biological and medical sciences. This knowledge has been prerequisite to the prevention of damage to all living matters whether chemical, physical or microbiological. The

Table 1. The relations between society and animal experimentation.

Research, control and development		Executive bodies		Society demands
Applications of animals in:				
Universities	approval ←	Animal Research Control Committee	← laws instruction ←	Political
Institutes	reports ↔			Humanitarian
Control agencies	advice courses ←	Lab-animal-experts	information ↔	Ethical
Industry	facilities	Biomedicine		Given by:
Private users	animals ←	Animal suppliers		Government Politicians Public organizations Privates

increasing knowledge has been of benefit to all, also the animals themselves. We cannot stop making progress in these areas. There are plenty of unsolved problems and their solution will also continue to require the application of experimental animals. This application is now based upon the laboratory animal science, the progress of which – especially in the last 20–30 years – has been based upon the veterinary profession and the enthusiastic, knowledgeable and experienced staff of the laboratory animal units associated with all main experimental institutions in biology and medicine. It has also been depending upon the suppliers of animals of exceptional high quality and known genetic constitution.

Everybody, whether professional or lay, must respect the necessity of using animals and the use must be of the highest defined standard. The users will be controlled by society and they will be required to use their utmost care to prevent all pain or suffering by applying the most sophisticated techniques (Table 1).

Any dealing with these matters includes also the application of laboratory animals which is not strictly based upon the collection of new basic knowledge. The outcome of the work improves the prosperity of every society and it is done in order to protect the members of society in the widest sense. The activities to which I am referring are the applied sciences and the development research work carried out by many official and private laboratories of high standard. To this group also belong the official control laboratories and bodies which according to society's own laws and regulatory prescriptions shall work in the interest of society. The ethics involved in these types of work can be rather difficult to analyse in detail. In order to get rid of this dilemma the bodies involved in one or more parts of the work have put up a system named »good laboratory practice«. This system gives rules for the performance and the collection and registration of laboratory data. It also ensures that the laboratory animal data are collected with the utmost care. In order to do so the users of the animals respect the animals' integrity in the widest possible sense. This means that the user must show the same respect to the animals as is required by the scientists engaged in biomedical research. To them the experimentation on human beings is the final goal. In this research the Helsinki declaration gives the governing principles. This declaration also states that special caution must be exercised in work which may affect the environment, and the welfare of animals used for research must be respected.

Thus the professional ethics have been drafted and at the same time the Helsinki declaration states that the laws of society define the civil responsibilities and the ethical responsibilities, which have to be respected. In a society like ours this means the law on animal welfare and the law on experimentation using animals. But in addition the basic principles of the declaration state that the research involving human subjects should be based upon adequately performed animal experimentation. The declaration thus clearly states the necessity of having performed animal experiments. The animal presents an organism upon which you can have observed any effects or process which you want to study afterwards in humans. Adequate also means that animals have been used to safeguard the human-beings and learn about the possible environmental effects.

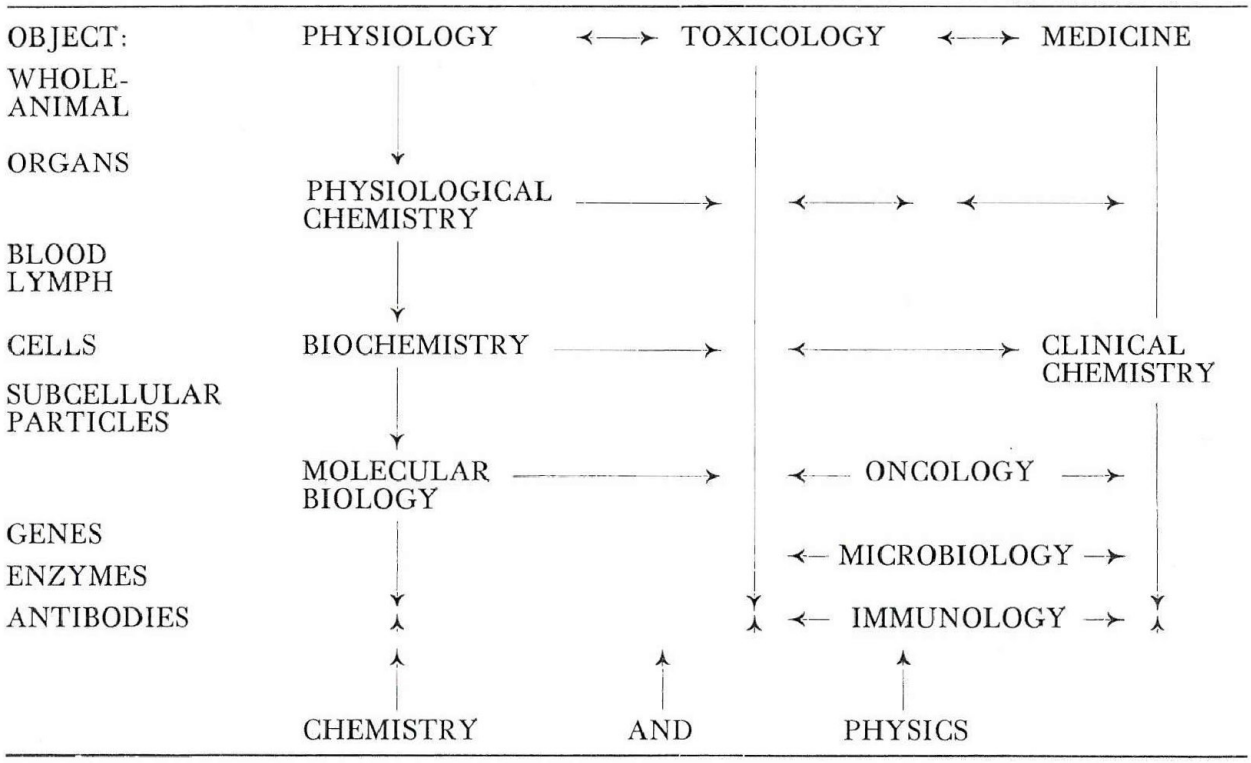
In that way the international society, professional or civil has again shown the double standard of morality based upon the old western religious principles – first God, then human beings and underneath so-to-speak the animals and the earth (soil and water). However, biologically trained scientists must also abide this attitude as we know that animals can provide us with much valuable and necessary information

because they represent the highly integrated systems of organs and tissues and cells which are also found in man. In addition man must try to master the world but certainly not misuse any of its elements, whether animals, plants, the globe or space. The ways in which we execute this role are determined by our ethical or moral codes. Society must control that the individuals engaged in this strive of safeguarding are submitting themselves to these codes.

To be provocative I am not so certain that »good laboratory practice« always means that the rules dictated by the laboratory animal ethics are followed. I am not stating that the use of animals is improper but rather that the type of work and numbers of tests involving animals are not always scientifically based. It tends to be a rather self-propagating or ensurance type of work. This to my mind is unethical. I shall therefore suggest suggest the establishment of a much closer collaboration between society's controlling agencies and the applied or developmental research institutions because that can prevent the surplus, and thus unethical use of animals. This will probably mean that instead of old, out-of-date regulations, the control work and its more appropriate progress will be based upon an up-to-date cell biology and not upon the search for toxicological after-effects and after-reasoning security measures (cf. Table 2).

I fully realize that some toxicological questions only can be answered and e.g. prolonged toxic events only can be observed by exposing the whole animal for a given period to a variety of doses and ways of administration. But many of the whole-animal expositions are started much too early, even if they are performed according to »good laboratory practice«. We

Table 2. Biology — Biomedicine — Medicine.
The Development in experimental methods and areas of interests and the interdisciplinary connections.



should not only advocate but require that a number of cell-biological questions are asked and answered before the whole-animal experiments start. These early questions can be answered by applying studies with isolated cells or cell-fractions, even organ-perfusion or anaesthetized animals which are never allowed to wake up again. A protocol of a great number of effects can be assembled, studied for supplementation and first then it may be of interest – or required professionally – to get results from a limited number of well planned, whole-animal experiments. This will mean that we shall establish a current exchange of information between the actual control agencies and the industry, and that cell-biologists get much more involved in the actual preliminary work or act as consultants to both parties.

Thus instead of wasting time, animals and money on the routine efforts of finding the so-called alternative methods, the profession as a whole should be encouraged or even forced to ask alternative questions. The answers to these can in a great many instances be simpler, quicker and more unexpensively obtained instead of using the complex system of the whole-animal.

Such an attitude and mode of operation is also, by the way, scientific and thus also ethical and has been the foundation of all scientific progress in the past (cf. the areas of research shown in Table 2).

Recently, many of the people who object to the use of experimental animals have inflicted that many scientists out of laziness and ignorance continue to use whole-animal studies. This statement which has no scientific background at all is also wrong. Simple questions – simple answers have always been associated with the most strict and correctly applied techniques. This has always been the way in which scientific progress has been made. Although many new thoughts have been started by unexpected answers or results, the experimental design was such that the data could be relied upon. The freedom should never be hampered by cross-examination of the approach by others with the sole aim of restricting the use of animals. The aim should only be clarification of matters.

Now we have dealt with what can be called the routine use of animal experimentation and the last part of my lecture shall deal with the experimental use within what is called pure and basic science.

Throughout the last century basic research activities have been protected against the control demands from the surrounding society. The freedom was used to elucidate problems or disclose the truth of any relation without the society's indications or demands of how it should be done. The selection of the scientific methods is free except for the use of infectious matters, radioactive material and experimental animals. The only demand from within the scientific society itself is that the results should be new, objective, unbiased and significant. This is inflicted by both formal and informal systems, where the main demand is publication of the results in highly respected, critical journals. Thus the quality of the approach is consistently controlled and many journals also require a very precise description of the animal experimental procedures. The standards are kept up by a control between colleagues.

The tremendous growth of the sciences and the personal or institutional ambitions involved has created a new situation. The possible conflicts have in the last decades caused the concern of the society and many have questioned if this internal control is sufficient. The interests of the scientists are not necessarily identical with those of the society. Ethical and political control agencies have been suggested.

Thus, society today questions the ethics of science as a whole and wants to get insight in the procedures applied in the performance of studies involving both genetic control and molecular engineering, egg transplan-

tation, human experimentation and in work with laboratory animals. The society realizes that not only the professional ethics but also the power or influence upon many society matters are involved.

In this country there is a further question. The administration of the general activities within university institutes is directed by a democratically elected group composed of both scientists and non-scientists. This means in reality that a number of experimental procedures especially with animals can be performed without any other responsibility involved than that of the experimenting scientist himself after he has been granted an unspecified or at least very general permission for a period of up to 5 years. The research work is very personal and may be performed without the intellectual influence or control from colleagues. This can result in a waste of resources in addition to the possible damage which can be afflicted to the animals used.

Thus there are many reasons for a change from the complete freedom of the science to the present days public interest in the control of ways and means.

Thus both the basic sciences and the developmental science and the toxicological control functions are presenting us with the same problem: How do we control the work without hampering it, maybe even improve it by promoting an additional kind of thinking.

Thus there is a need for a control function and to my mind it is presently insufficient in the way the Danish committee gains insight. Presently it only supervises the work performed by the grantees in a too general way and mostly after the work is over by the yearly submission of their experimental protocols. These protocols render only very general information concerning the type of experimental procedure and its aim.

This means that we shall require a further development of these arrangements in order to make a more intense control and obtain a more current insight in the actual work before and during its performance.

This is not the only necessary change which I shall propose. The increasing use of animal materials, isolated cells and organs, or even only the collection of immunological material means that many more people in widely distributed laboratories will be handling many hundreds of small animals over the years. Who shall guarantee that these scientists or their technical assistants are sufficiently trained? The use of anaesthetics, the correct and timely applied analgesics or other post-experimental handling and the required euthanasia is not common knowledge. The reason is that courses in research animal science are not formally included in the education of these scientists. Nor are they required for obtaining the permission to the use of animals. The required and scientifically supported increase in the application of cell biological methods also means that the materials from the animals are collected by scientists not necessarily experienced in the handling of research animals. The animals are in some instances even kept for years in locations which are very far from the high standard animal quarters e.g. found in the universities.

This development should be changed. The drawing up of rules and the strict requirements to both users and keepers of these animals is the obligation of the government and its Control Committee. Society must support this and the necessary training of personnel and demand that all experimental animals are housed properly and under the optimal husbandry conditions. The argumentation against these proposals is often the increasing cost of the vitally important product or the unwanted restrictions to the liberty of enterprise. Such an attitude cannot be accepted.

Table 3. Conclusions

1. ANIMAL WELFARE
   The high standard husbandry, breeding, handling and care must prevail and be supported by society.
2. ANIMAL ETHICS
   Society must exercise a control with the aim that
   a) all experimental assaults on the integrity of any animal are based upon a sound, well-planned and scientific approach using up-to-date optimal techniques
   b) alternative questions have been asked which could have changed the procedures into a study of *simbler biological systems* before the experiments on whole-animals are justified

Conclusion

In all matters of using research animals the government's Control Committee should have a much more current insight which can easily be set up by requiring monthly reports and the use of modern data-handling. Cell-biologists must be called upon to assist the toxicologists and the public control agencies in the planning of provisional examinations of the many new chemicals appearing each year. Alternative questions based upon the most up-to-date cell biology should be asked, followed by other types of investigations not involving long-term uses of the whole-animal. The whole-animal should be reserved for the final approval of the fewer, very strictly selected products, and for the studies where the complex and integrated systems are necessary and even obligatory for obtaining new knowledge in the basic sciences and the medical profession. Thus the necessary progress will continue in the interest of the society, and its ethical or moral codes are respected (Table 3).

Presented at the Annual Meeting of SCANDLAS, Copenhagen April 25—26, 1985.

Dansk sammendrag

Samfundets holdninger til brugen af forsøgsdyr
Naturvidenskabelige og etiske vurderinger

Illustreret ved tre tabeller gennemgås de anvendelser, der gøres af forsøgsdyrene for at sikre, at samfundets interesser varetages inden for gældende love. Anvendelserne til beskyttelse af liv i alle dets former er underkastet Helsinki deklarationens standpunkter og retningslinjer, som også bekræfter en vis dobbeltmoral, som fastslår, at dyrene benyttes som garanter mod eventuelle skader på mennesker. Dette gælder især for lægevidenskaben, men forebyggelse af sygdom eller skader på alt liv har i de seneste decennier forrykket balancen over mod en toksikologisk orienteret garantiforskning eller kontrolforanstaltning. Derved får afprøvningen en rolle som grundlag for administrative beslutninger, og metoderne bliver rigide strukturer, der kun langsomt tilpasses eller erstattes af nye på basis af ny biologisk viden.

Der opfordres derfor til at inddrage mere moderne cellebiologisk ekspertise i en løbende tilrettelæggelse af kontrollen og de krævede metoder. Dette kan ske ved at stille andre spørgsmål end dem, der til besvarelse kræver anvendelse af forsøgsdyr i langtidsforsøg. Svarene på disse alternative spørgsmål kan så danne grundlag for de langt færre dyreforsøg, der af samfundet vil blive krævet som sikkerhed for de få produkter, stoffer eller fremgangsmåder, som når frem gennem den strenge cellebiologiske sortering. Vi ved i dag så meget om de cellulære mekanismer, at de kan indgå med vægt i en sikkerhedsafprøvning, selv om vi som biologer må fastholde, at det intakte dyr med sit samspil mellem højt specialiserede organsystemer er det eneste, der kan simulere, hvad der eventuelt sker i mennesker.

Derfor fastslås det også, at den biologiske og lægevidenskabelige forskning ikke kan undvære forsøgsdyrene i søgen efter ny viden. Denne søgen kan intet samfund undvære. Det understreges imidlertid, at samfundets og videnskabens interesser og kår er så dybt inte-

greret, at samfundet har en større og større interesse i at følge forskningens aktiviteter på en mere indgående måde end tidligere, hvor det i høj grad var den enkelte forskers egne etiske holdninger, der alene styrede. Denne øgede indsigt gives allerede på forsøgsdyrenes anvendelse, men den foreslås styrket gennem en registrering af de løbende aktiviteter. Derved vil justitsministerens Dyreforsøgsudvalg kunne befordre en af dyreforsøgslovens vigtige intentioner videre i en udvikling, som samfundet allerede gennem loven har ønsket. I dette arbejde ligger den virkeligt etiske problematik (tabel 3).