ISTITUTO SUPERIORE DI SANITÀ

rapporti istisan

Biomedical Experimentation and Laboratory Animals: Hot Behavioural Issues

Edited by E. Alleva and G. Laviola

ISSN-0391-1675
ISTISAN 90/29

ISTITUTO SUPERIORE DI SANITA'

Biomedical Experimentation and Laboratory Animals: Hot Behavioural Issues

Selected issues from the
Workshop on Laboratory Animals: Hot Behavioural Issues

in the framework of the 1990 Summer Meeting of
the Society of Veterinary Ethology
Montecatini Terme (Pistoia), May 17, 1990

Edited by E. Alleva and G. Laviola

Laboratorio di Fisiopatologia di Organo e di Sistema

Roma

Istituto Superiore di Sanità, Rome (Italy)
Biomedical Experimentation and Laboratory Animals: Hot Behavioural Issues.
E. Alleva, G. Laviola (Eds)
Dec 90, 38 p. Rapporti ISTISAN (ISTISAN Reports) 90/29 (In English)

Different aspects (ethical, methodological, regulatory, etc.) of animal experimentation are dealt with. These issues were also discussed at the Workshop on Laboratory Animals: Hot Behavioural Issues, Society for Veterinary Ethology, held in Montecatini Terme (Pistoia, Italy), on May 17th, 1990. These reports will also help the reader to make deeper some basic points related to the ethical, scientific and legislative aspects of the use of living animals in biomedical experimentation. The reference lists are arranged to provide an appropriate starting point to make the reader familiar with new aspects and hot issues.

Key words: *In vivo* Experimentation, Laboratory animals, Scientific ethics.

Istituto Superiore di Sanità, Roma
Gli animali da laboratorio nella sperimentazione biomedica: aspetti comportamentali e di gestione.
E. Alleva, G. Laviola (Ed)
Dic 90, 38 p. Rapporti ISTISAN 90/29 (In Inglese)

Sono raccolti contributi di alcuni ricercatori interessati ai temi della sperimentazione animale e discorsi selezionati del Workshop on Laboratory Animals: Hot Behavioural issues, Society for Veterinary Ethology, svoltosi a Montecatini Terme (Pistoia) il 17 Maggio 1990. Questi interventi aiuteranno il lettore ad approfondire alcuni punti essenziali relativi alla problematica etica, scientifica e legislativa legata all'uso e al mantenimento di animali vivi per la sperimentazione biomedica. La bibliografia citata dai singoli autori costitutisce inoltre un punto di partenza per approfondire la conoscenza di aspetti più specifici.

Parole chiave: Animali da laboratorio, Etica scientifica, Sperimentazione *in vivo*.

INDEX

TOWARDS BETTER CONDITIONS FOR CAPTIVE NONHUMAN PRIMATES: ROUTINES, REQUIREMENTS, AND RESEARCH

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Introduction

In this paper we aim to put across the following two major points: First, some simple alternatives to traditional research and maintenance routines with nonhuman primates can significantly improve conditions for the animals (and thereby improve quality of the data obtained in research). Second, attempts to enhance the psychological well-being of primates should be guided by knowledge of individual species' natural behavioural propensities and needs. This goal cannot be achieved satisfactorily by indicating a global set of rules and regulations. The adequacy of the environment for captive primates can only be properly evaluated on the basis of empirical studies of how the animals react - of different indicators of well-being.

Following an introduction to the use and maintenance of primates in captivity and to some useful procedural innovations, we will describe two enrichment strategies, and conclude with a discussion of the importance of within-and between-subject comparative studies in deciding upon which strategies to implement.

A preliminary premise: Primates are not pets!

The vast majority of nonhuman primates in captivity are to be found in zoos and laboratories. However, a significant number are kept by private individuals as pets, and on this point we would like to make an important premise: Primates are not suitable as pets. The reasons for this are many. From the owner's point of view, what starts out as a small and cute baby monkey can grow up into a competitive and temperamental, potentially destructive, dirty and dangerous adult. Unlike dogs and cats, primates have not been selectively bred for behavioural traits which humans find desirable. Monkeys are highly agile and readily exploit vertical space, which along with their well-developed manipulatory propensities, increases the potential for destructive acts and accidents involving household objects (e.g., contents of drawers or cupboards, jars, cookers). "Training" a monkey to be a human pet is far more demanding job than training a dog, and much less likely to succeed. Other disadvantages from the owner's point of view include the facts that primates are messy and often feed in a wasteful manner, and that many species have a characteristic, strong odour.

From the animal's point of view, a "pet" monkey will probably have been taken from an already diminishing population in the wild, is likely to develop abnormal behaviours, and will most likely end up being incompatible with conspecifics and unable to reproduce. There are too many cases of troublesome pet monkeys being offered to laboratories or zoos and for which the future looks bleak because of the impossibility of integrating them into estabilished groups and getting them to reproduce successfully. Abnormal behaviours, such as self-directed aggression and repetitive stereotyped movements are aesthetically unappealing and almost certainly indicate compromised well-being. Finally, there are real chances of (sometimes very serious) disease transmission from pet monkeys (Johnson-Delaney, 1990). In this context we would like to see veterinarians and primatologists working closer together in a common effort to dissuade individuals who want to have a monkey at home as a pet.

Primates in research

Nonhuman primates provide the best models for research in a number of biomedical domains (Council on Scientific Affairs, 1989; King et al, 1988) and for reconstructing patterns of hominid behaviours (see chapters in Kinzey, 1987). They are also the best subjects for certain types of psychological research. However, many of the 200 or so species are threatened with extinction (e.g., Mittermeier and Cheney, 1987), primarily due to the disappearance of the fragile habitats (tropical zones) in which most of them live. Human encroachments takes diverse forms: agricultural development, cattle ranching, industrial logging, and hunting and trapping all contribute towards the demise of natural populations. It is only relatively recently that scientists have started to make serious coordinated efforts towards achieving the double aim of assuring the survival of remaining populations and satisfying research requirements (e.g., Benirschke, 1986).

The diversity of primates

Primates are extremely diverse in size, form, and behaviour (Richard, 1985). They range in size and weight from the tiny mouse lemur (average adult male weight 60 g) to the huge silverback gorilla (over 150 kg). Some are nocturnal (many prosimians), most are diurnal. Some spend most of their time alone (orangutans), other live in tightly knit family groups (e.g., titi monkeys, marmosets, gibbons), and others in large groups of more than a hundred individuals (macaques, baboons). Their dietary regimens may consist almost entirely of insects or small vertebrates (e.g., tarsiers) or mainly leaves (e.g., some colobines), or they may be comprised of a wide range of animal and vegetal resources, including fruits, seeds, leaves, roots, flowers, and exudates (e.g., over 200 types of plants and animal prey species for chimpanzees, Nishida and Uehara, 1983). Preferred methods of locomotion vary across species, and include vertical leaping and clinging (e.g., sifakas, tarsiers), brachiation (gibbons), knuckle-walking (chimpanzees, gorillas) and plantigrade quadrupedalism (most species of monkeys). In fact, enormous species differences exist for most primate parameters, including cognitive abilities, and this variability must be taken into account when considering environmental factors influencing the well-being of captive primates.

Captivity: conventions and conflict.

Unfortunately, there is often disagreement between what primatologists propose as ways of promoting psychological well-being in captive primates and the guidelines or standards set by veterinarians. For instance, there is now widespread agreement that allowing primates to forage for small food items on a floor-covering such as woodchips is an effective enrichment technique (e.g., Canadian Council on Animal Care, 1984;

Whitney and Wickings, 1988), but this practice is not easily reconcilied with estabilished guidelines which prohibit placing food on the floor where it may come into contact with faeces and urine (e.g., U.S. Department of Health and Human services, 1985). Another example concerns installing wooden perches or branches in cages. This has proven to be beneficial to the animals, permitting the expression of a number of otherwise suppressed behaviours (e.g., gnawing, manipulation and shaking: Reinhardt et al, 1987). Hollow wooden cylinders have been filled with gum and stacked to form a "tree" to elicit and reinforce the natural behaviour of "gouging" in marmosets (McGrew et al, 1986). Experience with branches is a necessary component of rehabilitation training of captive-born golden lion tamarins if these rare primates are to be successfully re-introduced to the wild (Kleiman et al, 1986). However, regulations existing in the USA explicitly prohibit the use of cage furnishing such as wooden structures which cannot be fully sanitized. Clearly, there is a need for greater coordination and cooperation between ethologists and veterinarians, so that such discrepancies between ideas for environmental enrichment strategies and conventional husbandry practices and concerns can be overcome.

Criteria for assessing well-being.

It is not easy to define psychological well-being. Many scientists have tried to do this, and a variety of criteria have been used. It is interesting to note that here, again, veterinarians and ethologists have tended to diverge in their preoccupations, as illustrated in Figure 1.

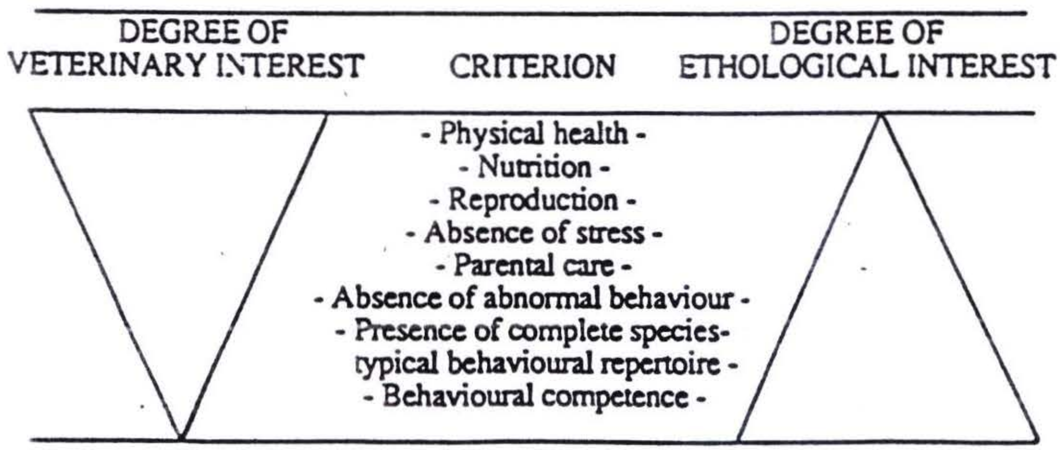

Figure 1

Some criteria used in assessments of the welfare of captive primates, showing traditional areas of concern for veterinarians and ethologists.

Traditionally, veterinarians have been primarily concerned with aspects such as physical health and nutrition, whereas ethologists have developed particular expertise in understanding behaviour patterns. Whereas ethologists have long considered adequate nutrition and physical health to be conditions sine qua non for an animal's well-being, vetrinarians do not always show equivalent concern with regard to behavioural indices such as competence or the presence of a species-typical repertoire.

Another way of looking at this problem is given in Table1. Here, five different environments, from the most impoverished to the most natural, are evaluated according to the two most "extreme" veterinary and ethological criteria shown in Figure 1 (Visalberghi and Anderson, in prep., discussion and development this approach in more detail). The contrasts between the most extreme environments and how they may be seen from the two different perspectives are clear. However, this does not mean that a concensus cannot be reached. One facet of the development of veterinary ethology is the increasing importance is being given to identifying specific "behavioural needs" of the animals and to the recognition of the interface between behaviour (normal and abnormal) and physiology. Progress requires incorporating fulfillment of these needs into housing and management systems while also satisfying the economic and professional requirements of keepers, researchers, vets, and so on.

Table 1

Five living conditions for nonhuman primates evaluated according to two "veterinary" and two "ethological" criteria of well-being. Maximum score: 5; minimum score: 1.

CONDITIONS

	Single cage	Pair housing	Indoor group	Outdoor group	Wild
"Veterinary" criteria					
-Physical health	5	4	3-4	3-4	2-3
-Nutrition	5	4	3-4	3-4	2-3
"Ethological" criteria					
-Behavioural competence	1	2	3	4	5
-Breadth of repertoire	1	2	3	4	5

Humans are excellent empathizers, and are probably very good at perceiving the psychological needs of our closest nonhuman relatives. Empathy with primates is certainly more evident than with more distantly related species (Dawkins, 1990). However, managements mistakes are often made, and they may be expensive. Research which takes into account natural behavioural variability related to species, age, and even sex of individuals is important for improving primate husbandry techniques (see McGrew, 1981), and investigations aimed specifically at comparing the effectiveness of enrichment techniques across species have already begun, as illustrated later in this article.

A problematic area: Space, and well-being.

One example of domain in which humans' interpretation of a nonhuman primate'need' may sometimes be erroneous concerns the amount of space available to the animals. It has long been believed, and there is some supporting evidence, that undesiderable behaviours (e.g., aggression, stereotypies) increase in frequency or intensity in spatialliy restricted conditions. However, the widespread idea that overcrowding in humans and other animals must result in increased aggression has been criticized (Barnett, 1988). Recently, de Waal (1989) reviewed the literature on rates of aggression in primate groups living in widely different conditions, and concluded that behavioural coping mechanisms characteristic of each species help to stabilize aggression rates under varying spatial conditions. There is no simple relation between space and aggression. A good illustration of how cage layout rather than available space can be influential is presented by Erwin (1979). Contrary to expectations, aggression increased when a group of pigtail macaques had access to two interconnecting rooms. In this case, the control role of the alpha male was made moire difficult by the visual separation of subgroups in the two rooms. Recent studies (Bayne and McCully, 1989; Line et al, 1989) have specifically examined the influence of cage size on several behavioural variables and on heart rate (Line et al, 1989) in rhesus monkeys, and have found no important effects of housing the animals in cages up to 40% larger than their usual ones.

In conclusion, although it has been stated that 'it is hard to imagine a case where simply increasing usable cage space would not constitute an enrichment procedure' (Chamove and Anderson, 1989, p. 184), hormonal and behavioural benefits of a simple increase in cage size are not always demonstrable. What does appear certain from this area of research is that the "quality" or "complexity" of available cage space, rather than the mere volume available, is probably of more importance in promoting well-being.

Examples of trauma-reducing experimental techniques.

A number of methods have recently been developed that allow the collection of biological information while reducing the need for repeated capture or forced physical restraint of the subjects (and repeated involuntary removal from familiar surroundings and forced restraint are both stressful for monkeys: Adams et al, 1988; Goosen et al, 1984; Willott and McDaniel, 1974, but there are important species differences in vulnerability: Clarke et al, 1988). Implantable biotelemetry systems have been used to obtain several biological measures including heart-rate, body temperature and EEG (Reite and Short, 1981). Although this technique still requires invasive surgery, it eliminates the need for subsequent restraint of the animals because of electrical leads. Technological advances now permit data such as heart rate to be measured using surface telemetry in free-ranging animals, the electrodes being attached to the skin and kept in place by a lightweight, resistant vest worn by the animal (Rasmussen and Suomi, 1989).

Many hormonal measurements can now be made on the basis of urinary or faecal samples (e.g., Hodges et al, 1986; Risler et al, 1987), reducing the need for stressful capture and bleeding of animals, and increasing the potential for valid behavioural endocrinological studies in free-ranging animals. In the laboratory, vervet monkeys have been trained to provide urine samples using positive reinforcement (Kelley and Bramblett, 1981); there is no a priori reason why this method should not be applicable to other species. Where regular blood samples need to be taken, with patience and considerate training animals can learn to cooperate and voluntarily present the appropriate body part (Vertein and Reinhardt, 1989). Procedures are also being developed that permit hormonal treatments of primates while reducing the frequency of captures and injections (Bercovitch et al, 1987). Halloren et al (1989) have recentlydescribed a non-traumatic procedure for marking neonate cotton-top tamarins for identification purposes; this is achieved by the technician entering the cage and calmly feeding family members until their confidence is gained. Successive approximations to the final marking act (gently swabbing the infant's head with dye) are carried out during the feedings. All of these examples show that many traditional techniques can be replaced or refined so as to reduce stress (and risk) to both animals and humans.

Deep litter as an enrichment technique

In the previous section we described some methods designed to reduce stress during experimental manipulations. In this and the following sections, we are more concerned with the 'everyday" psychological weell-being of captive primates. In an attempt to increase activity and reduce aggression in laboratory-housed stumptail macaques, Chamove and Anderson (1979) provided the monkeys with a floor-covering of woodchips onto which small food itms (e.g., maize, wheat, sunflower seeds) were sometimes scattered. The effects of this simple change to the animals' environment were dramatic: aggression was reduced considerably and feeding rates were equalized as the animals foraged through the litter. Abnormal behaviours such as self-directed aggression were also reduced when the monkeys could engage in the simulated foraging activity, which continued even when free food items were available (Anderson and Chamove, 1984). Other species of primates since tested have shown similar reductions in aggression and/or increased activity and use of available space with a floor-covering present (Chamove et al, 1982; McKenzie et al, 1986; Tripp, 1985; Westergaard and Fragaszy, 1985).

Conventional wisdom dictates that captive primates should be preventd from coming into contact with urine and faeces, in order to avoid disease transmission. It is usually recommended that, where litter is used with primates, soiled material should be removed daily (e.g., U.S. Department of Health and Human Services, 1985). Chamove et al (1982) assessed the potential for disease transmission arising from the continuous use of litter with a group of 25 stumptail macaques. Samples of the litter were collected from the floor of the pen over an 8-week period. Microbiological analysis of the samples indicated decreasing coliform bacteria counts across weeks. Further, a similar patter of reduced survival of Salmonella typhimurium injected into litter samples was obtained. Thus, as in poultry breeding, deep litter actively contributes towards microbial decomposition of excreta.

Objects as an enrichment technique.

Providing objects or manipulanda is a more common method of enrichment for captive primates, partly because it is more easily applied with singly housed animals in mesh-bottomed cages. Objects presented range, in increasing order of cost, from simple wooden sticks or PVC pipes (Reinhardt, 1989), hard nylon balls or sturdy toys (e.g., Renquist and Judge, 1985; Ross and Everitt, 1988) to mechanical food-puzzles and electro-mechanical feeding and stimulation devices (e.g., Bloomstrandt et al, 1986; Markowitz and Spinelli, 1986). For reasons of space we will restrict discussion to the use of simple and cheap objects. Installing a wooden stick or branch into individual rhesus monkeys' cages allowed the animals to increase their repertoire with behaviours such as gnawing and perching, while self-directed activities were reduced (Reinhardt et al, 1987; 1989). Installation can be done in such a way as to meet veterinary concerns over hygiene (Reinhardt, 1987). Although giving onjects is a popular enrichment practice, apart from the above-mentioned studies, there are as yet few rigorous assessments of the long-term effectiveness of simple inanimate objects as enrichment materials. In fact, some authors have indicated habituation to them after only a few days (Line et al, 1989, nylobn balls) or virtually no response to certain objects (Bryant et al, 1988, ball, hanging rope).

The comparative approach.

There is increasing interest in comparing different potential enrichment methods in the same subjects (e.g., Bryant ety al, 1988; McKenzie et al, 1986; O'Neill, 1989; Reinhardt, 1989). It is also valuable to assess the effects of a given environmental modification in different species (e.g., Chamove et al, 1982; Evans et al, 1989). Both approaches can contribute importantly by distinguishing between effective and ineffective strategies, detecting potential additive or interactive effects of manipulations, and by identifying potentially undesiderable effects. Combette and Anderson (in prep.) recently compared the behavioural effects of the two enrichment techniques described above (deep litter, objects) in two species with quite different psycho-social and ecological profiles: brown capuchins (Cebus apella) and black lemurs (Lemur macaco). Capuchins show more or less continuous high levels of activity when awake and are well-known for impressive tool-using performances and object-manipulation in captivity (Visalberghi, 1990). In contrast, the lemurs show long periods of relative inactivity and quiet social contact during the day, and are much less manipulative. Table 2 shows the effects of four different environmental conditions on four behaviours in a captive group of each species. The presence of diverse objects (pieces of PVC, Lego, tobacco tin, etc.) and the presence of a woodchip floor-covering (with or without food added) both reduced locomotion in the capuchins, whereas only the woodchips + food condition affected locomotion in the lemurs, increasing it almost two-fold.

Table 2

Effects of four environmental conditions on selected behaviours in group-living Cbus apella and Lemur macaco. Values represent percentages of 30-sec intervals.

		CONDITION			
BEHAVIOUR		BASELINE	OBJECTS	WOODCHIPS	WOODCHIPS + FOOD
Locomotion	Cebus	61.5	45.8	53.3	49.1
	Lemur	23.4	26.9	26.0	43.4
Object manip.	Cebus	3.5	29.5	4.4	2.3
	Lemur	0.4	10.1	0.3	0.3
Foraging	Cebus	2.8	0.7	3.7	32.0
	Lemur	0	0	0.5	1.5
Social contact	Cebus	11.2	12.5	10.1	9.9
	Lemur	62.0	56.6	53.6	32.3

Object-manipulation, always much more prevalent in the capuvhins than the lemurs (accounting for almost 30% of the 30-sec observational intervals in the capuchins when novel objects were offered), was reduced in the capuchins by the presence of woodchips. Further contrasts between the two species emerged regarding foraging activities. Foraging for food items in the woodchips was more common in the capuchins that the lemurs; the latter frequently sniffed while on the woodchips, but they rarely took food-items. A final difference in the two species' reactions to the environmental modifications concerned nonaggressive social contact: this class of behaviour occurred in around 10% pof 30-second intervals in the capuchins in all conditions, i.e., it was not affected by the presence of objects or woodchips. In the lemurs, however, although social contact was always more common than in the capuchins, the woodchips + food condition led to a marked reduction this behaviour.

Conclusions

The data presented above serve to illustrate one of our main arguments, namely that so-called enrichment strategies may have quite different effects on different animals. Consideration of species-typical behaviour combined with empirical studies are necessary for identifying optimal cost-effective strategies (see also Novak and Suomi, 1988). Using this approach, specific behaviours may be targeted for treatment (enhancement or reduction). For example, as described above, the expected increase in locomotor activity resulting from provision of a deep litter is not a foregone conclusion in capuchin monkeys. Instead, a relatively sedentary but otherwise highly active object manipulation may take precedence. A desirable activity for some Cebus apella - tool-aided nut-cracking - can be further enhanced by treating walnuts with a non-toxic paste to make them more resistent to hammering (Visalberghi and Vitale, 1990). Stereotyped rocking, which usually develops in isolation-reared infant macaques, was specifically eliminated by providing an artificial mother that moved around the cage on an irregular schedule (Mason and Berkson, 1975). The mobile surrogate-reared monkeys also showed better adjustment than stationary surrogate-reared ones in later life. Another example of the selective reduction of an undesiderable behaviour, this time in a zoo setting, is reported by Gould and Bres (1986), who showed that an unaesthetic behaviour in gorillas - regurgitation and reingestion - can be reduced by providing the apes with browse.

In conclusion, attempts to improve the psychological well-being of captive nonhuman primates require, first, consideration of the animals' natural lifestyle, then discussion, cooperation and compromise among researchers, husbandry personnel, and veterinarians. But attempts must be made. We hope that the present article shows that the goals of the various interested parties need not be incompatible.

Acknowledgements

This is an expanded version of a paper presented to the Society for Veterinary Ethology, Montecatini Terme (Italy), May 1990. We thank Dr. E. Alleva for organizing the "Hot Behavioural Issues'workshop".

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ETHICAL AND BEHAVIOURAL ISSUES IN RODENT EXPERIMENTATION

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The use of animals in biomedical research raises a series of important ethical issues. Studies in laboratory settings necessarily involves keeping animals in cages. Manipulative procedures, anesthesia and even surgery may be necessary to achieve specific research goals, but any potential gain in knowledge should be always weighed against the adverse consequences for the animals used as subjects (Bateson 1986).

Several scientific associations and editorial boards of scientific journals have now formed Ethical and Animal Care Committees. These Committees have produced guidelines (ASAB 1986; Flemming 1987; Sechzer 1983; Tannenbaum 1986; Wall 1982) about the use of captive animals in research, in order to give information to all investigators interested in avoiding brutal procedures and designing non-stressful experiments. The committee also monitors all articles submitted for publication, rejecting papers which appear to violate the spirit of the guidelines. This form of control is important because publication in a leading journal is currently the only way a scientist can establish a reputation and/or obtain funds for research work. Moreover, it represents a self-regulation of experimental work based on both ethical and methodological grounds.

When application of painful stimulation appears unavoidable -- e.g., when assessing pain threshold or the efficacy of a new analgesic compound -- it should be minimized as far as possible under the requirements of the experimental design (Wall 1982; Flemming 1987; Sechzer 1983). Furthermore, as a rule the animal should have the possibility to stop or to avoid the painful event (e.g., hot-plate and tail-flick tests), while an accurate verification of the scientific value is necessary in the case of experiments which use painful events of fixed duration (CER, learned helplessness and related paradigms). Other empirical examples from behavioural research come from studies of predator/prey interactions or fighting among conspecifics (Huntingford 1984; Alleva & Aloe 1989). Investigators should firstly consider that field studies of naturally occurring aggressive encounters should be used wherever possible. Where staged encounters are unavoidable, the use of model predators should be considered. Both kinds of experiments call for special care in ensuring that a maximum of information is gained and a minimum of suffering caused. The investigators should also make sure that (a) the behavioural state of the animal has been monitored accurately, (b) the experiment has been made as short as possible, (c) the number of subjects is kept to a minimum. This can be achieved through the use of (i) statistical tests enabling several factors to be assessed simultaneously, (ii) strictly controlled experimental conditions, which reduce external variability, and (iii) genetically homogeneous animal samples (e.g., inbred strains). The latter decrease variance, and hence the number of subjects required for given statistical power (Still 1982). However, generalization from studies using a few inbred strains must be cautious.

Evidence is now growing that the experiments themselves are heavily affected by the way laboratory animals are kept (i.e., social housing conditions such as isolation or overcrowding). Investigators often neglect the physiological or behavioural attributes of their subjects at the beginning of an experiment. In fact, when animals are under stress, they are mostly in the middle of a coping event. Changes in hormonal levels and in immunological reactivity produced in response to a stressful condition, might well alter the results of an experiment, particularly in toxicological and microbiological tests (Alleva & Aloe 1989; De Simone et al 1990).

In conclusion, animal welfare and the usefulness of animals to science are both better served by close attention to their biological needs. Even if it is find it hard to establish an ultimate definition of animal suffering, ethological observations can tell us a great deal about how to improve the physical and social conditions in which animals are kept.

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CARE AND WELFARE OF LABORATORY ANIMALS

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The welfare of laboratory animals is increasily emphasized during international meetings as well as in the legislative guidelines for animal care.

The definiton of the laboratory animal is that of an animal destined to be the object of experimental activity with the aim of scientific research that frequently requires specific operations as drastic and traumatic as they are necessary and irreplaceable.

Therefore the term "welfare" in this case represents a complex task , which any professional researcher who is both scientifically and ethically aware should gladly undertake as an obligation. At the basis of laboratory animal care and welfare are simple but essential measures for good housing. The organization of a rationally planned animal care facility and the choice of simple but functional equipment represent the first of long series of musts. The wide diffusion of scientific knowledge now available in the animal care field, the growing availability of new materials and advanced technology and the establishment of precise national and international directives have brought remarkable improvements to what can be defined as the structural organization of an animal house.

The growing interest in laboratory animals has meant that more care is now being taken in the design and choice of animal models, nowadays rigorously standardized regarding microbiological profile and economic returns. The growing use of well-defined animal models such as Specific Pathogen Free models, or SPF as they are more commonly known, is a good example of this breakthrough.

At the same time increased sensitivity to the problem by animal care operators has created new commercial possibilities in a field where many companies have invested a major part of their economic resources. Consequently, a series of products is now on the market, ranging from dust-free sterilized bedding to disposable paper absorbent sheets, balanced diets for the various stages of growth in different animal species to specific detergents and disinfectants to combat bacterial and viral contamination.

Of all these measures, particularly important are the efforts made by many institutions to train their staff in terms of motivation and efficiency. With this goal in mind, the organizing of professional training courses draws new impulses from the growing diffusion of audiovisual means as well as from the notable involvement of most scientific institutions in the field, spurred on as they are by the ever more specific directives issued for the purpose; they therefore invest in training courses and regular seminars to keep their staff up to date. Above all, from my personal point of view, there is yet another aspect which is represented by the urgent necessity for every institution involved in experimental activities to define and apply within their own research facilities pre-and post-surgery care programs which must be specifically aimed at the experimental protocols in force.

The use of efficient anesthestic products is today an essential practice in every research institution. The directive in force in each country, however, sets out strict, clear-cut rules in this respect to be observed at all times.

On the other hand, more general instructions are supplied for the post-surgical recovery period, or more broadly speaking, for the phase following experimentation. The Directive EEC 609/86 provides for example "to adopt intensive standards to correct opportunely defects or sufferances eventually observed" without examining the matter from a more detailed point of view.

This is not brought about by the legislator's superficiality but by the difficulty in defining, for each single experimental situation, a precise scheme for specific intervention.

Each individual research institution has therefore to provide an accurate analysis of the experimental protocols in use in its laboratories and, consequently, its requirements for the type of pharmacological intervention.

This subject has been the object of international scientific associations operating in the laboratory animal science field great attention that has brought them to the definition of a classification of the experimental activity on the basis of the grade of intensity and of stress induced in laboratory animals.

The Canadian Council on Animal Care (1989), for example defines the following as the 5 classes of intervention:

a- Experiments on most invertebrated or on live isolates

b- Experiments which cause little or no disconfort or stress

c- Experiments which cause minor stress or pain of short duration

d- Experiments which cause moderate to severe distress or disconfort

e- Procedures which cause severe pain near, at, or above the pain tolerance threshold of unanesthetized conscious animals

The use of antibiotic, antiinflammatory and analgesic drugs during the post-surgery phase is sometimes strongly contested by the research scientist who worries about the possible interaction of these drugs with the experimental protocol in act or more specifically, with pharmacological treatment which is being tested by the experiment itself.

In this sense the availability of always more information regarding the incompatibility of different drugs, some of which already mentioned, represents a certainly acceptable guarantee, even in consideration of the fact that while the pharmacological treatment for post-surgical recovery has to applied exclusively during the period immediately after surgery, on the contrary the study of the long-term effects induced by the "experimental" administration of a new drug forsees a treatment generally extended in time

The attached tables report as an example same indications about the dosages, possible adverse effects and uncompatibilities of same of the more commonly used antibiotic and anesthetic drugs.

The availability of drugs with a longlasting effect reduce even more the intervention of the animal care staff and of the research scientists and allows the application of an effective recovery program post-surgical with a sole contemporarary and daily administration of more than one drug repeated during the 2-3 days following the experimental operation. Some of the antibiotic, antinflammatory and analgesic drugs used following the various dosages according to the animal species and to the their respective action will be presented.

In conclusion taking into consideration what has been discussed up to this point, I wish to emphasize the incongruity of the fact that while for mankind no doctor would dream of intervening surgically without having arranged and applied an accurate pharmacological post-surgery intervention program, whereas for laboratory animals often this type of intervention is left to the sensitivity and to the professionality of the research scientist interested and yet does not represent, as it should be right and desirable, a routinary protocol applied everytime one intervenes on the animal.

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TABLE 1 - INHALATION ANESTHETICS

GENERIC AND (TRADE) NAMES	ACTIONS AND INDICATIONS	PRECAUTIONS
Ether	Potent analgesic and mild respiratory stimulant in light stages of anesthe-; sia good muscular relaxation. Induction requires 15-20% concentration; maintenance requires 5-10% concentration.	Highly volatile and flammable; vapor is explosive. Irritating to respiratory membranes; slow induction accompanied by salivavation and laryngospasms
Methoxy-flurane (Metofane)	Excellent analgesia and muscular relaxation which persists into recovery period; irritation to respiratory membranes negligible.Comparatively safe anesthetic for laboratory species. Non-explosive at room temperatures. Induction requires 2-4% concentration; maintenance requires 0.5-1.5% concentration.	Eye reflexes poor indicators of anesthetic depth. Anesthetic absorbed by polyvinyl chloride plastics and rubber. Induction slow and may be accompanied by vomition in subhuman primates Premedication with atropine and preanesthetic recommended.
Halothane (Fluothane)	Moderate analgesia; used in conjunction with N_2O for increased analgesia and cardiovascular sparing effect. Rapid induction and recovery; anesthetic levels can be varied rapidly. Non-explosive and non-irritating to respiratory membranes. Induction requires 2-4% concentrations; maintenance requires 0.8.-1.2% concentrations.	Eye reflexes poor indicators of anesthetic depth. Lethal concentrations reached rapidly;precision vaporizer and careful moni-monitoring required. Produces some cardiovascular depression when used alone. High absorbed in rubber and corrosive to all metals except nickel and titanium
Nitrous Oxide	Good analgesia; normally used as a supplement to other anesthetics. Reduces circulatory depressant effects of halothane.	May be ineffective or produce erratic general anesthesia when used as sole anesthetic agent in healthy, vigorous patients. Rapid induction and emergence due to relative insolubility of N_2O in blood and body tissues.

TABLE 2

DISSOCIATIVE ANESTHETICS

GENERIC AND (TRADE) NAMES	ACTIONS AND INDICATIONS	PRECAUTIONS
Phencyclidine (Sernylan)	Corneal, pupillary, patellar and swallowing reflexes retained. Response ranges from sedation to catatonia to anesthesia with increasing dosages. Used as immobilizing agent for nonhuman primates.	Muscular tone increased at most dose levels: clonic convulsions at higher dosages in dogs, guinea pigs and monkeys. Produces hyperactivity in rats and mice. Hallucinatory disturbances, emergence reactions and prolonged recovery periods in individual animals. Premedication with atropine recommended to prevent excessive salivation. Use as sole surgical anestethic not recommended.
Ketamine (Ketalar, Ketaset, Vetalar)	More rapid induction and shorter recovery than phencyclidine; improved muscular relaxation. Pharygeal and corneal reflexes maintained. Combined with phenothiazine tranquilizers for smoother recovery and increased muscular relaxation.	Respiratory depression reported at higher doses but convulsions extremely rare in nonhuman primates. High concurrent doses of (1 ml/kg) reported to prolong anesthetic period.
Tiletamine	Pharyngeal and palpebral reflexes retained; good muscular relaxation. Normally administered in combination with a tranquilizer.	Drug is still in experimental stages; documentation of side-effects and possible controindications is incomplete.

TABLE 3

DISSOCIATIVE ANESTHETICS
Dosages in mg/kg

GENERIC AND (TRADE) NAMES	ROUTE OF ADMINISTRATION	DOG	CAT	NONHUMAN PRIMATES	RABBIT	GUINEA PIG	RAT	MOUSE	HAMSTER
Phencyclidine (Sernylan)	I.M.	N.R.*	0.5-2	0.25-5	5	1-3	N.R.*	N.R. *	2-4
Ketamine (Ketalar,)	I.M.		11-33	10-40	15-55	22-44	22-44	22-44	
Ketaset, Vetalar)	I.V.	4.4-8.8 **							
Tiletamine	I.M.	5.5-12	6-16	2-6	N.R. *	N.R. *			
	I.P.						20-30		

* Not Recommended
** Premedication with acetylpromazine or diazepam recommended

TABLE 4

BARBITURATE ANESTHETICS

GENERIC AND (TRADE) NAMES	ACTIONS AND INDICATIONS	PRECAUTIONS
Pentobarbital sodium (Diabutal; Nembutal)	Intermediate in duration of anesthesia (1-3 hrs.). Administer 1/3 to 1/2 of calculated I.V. dosage rapidly to avoid excitatory stage then titrate carefully to desired surgical plane. Dilute to 1-3% solution for species weighing less than 10 kg.	Wide variation in dose response. Narrow margin of safety in rabbit, guinea pig, rat and mouse. Prolonged recovery characterized by excitatory stages in some species. Anesthestic period prolonged with concomitant administration of chloramphenicol.
Thiopental sodium (Pentothal)	Short duration of anesthesia (10-45min); slow administration not as likely to produce excitatory stage as pentobarital. Lower doses (10 mg/kg) suitable for induction and intubation in canine and non human primate.	Rapid administration may produce transient apnea. Perivascular injections prone to produce venospasms and local tissue necrosis.
Thiamylal sodium (Surital)	Short duration of anestesia (10-30 min); advocated for longer procedures in nonhuman primates using incremental supplementation.	Similar to thiopental but approximately 1.5 times as potent.
Methohexital sodium (Brevital)	Ultra-short duration of anesthesia (5-15 min.). Less residual depression than thiobarbiturates.	Transient apnea occasionally produced with rapid intravenous administration.

TABLE 5

BARBITURATE ANESTHETICS
Dosages in mg/kg

GENERIC AND (TRADE) NAMES	ROUTE OF ADMINISTRATION	DOG	CAT	NONHUMAN PRIMATES	RABBIT	GUINEA PIG	RAT	MOUSE	HAMSTER
Pentobarbital sodium	I.V.	30-40	30-40	20-33	15-46				
(Diabutal; Nembutal)	I.P.					20-37	30-40	40-70	60
Thiopental sodium (Pentothal)	I.V.	18-26	20	17-25	37-50				
Thiamylal sodium (Surital	I.V.	18-26	20	15-25					
Methohexital sodium	I.V.	12.5	12.5						
(Brevital)	I.M.			12-15					
	I.P					95			

TABLE 6

ANTIBIOTICS USED IN LABORATORY ANIMALS

Antibiotic	Possible indications	Adverse Effects	Incompatabilities
Ampicillin	Pneumococci, Streptococci, Escherichia coli, Proteus mirabilis	Rare anaphylaxis	Do not combine with any other drugs in intravenous solutions
Cephaloridine	Staphylococcus aureus (non-pencillinase producing), Streptococci, Klebsiella, Escherichia coli, Proteus mirabilis	Nephrotoxic; possible hepatotoxicity in cat	Tetracyclines, chloramphenicol
Cephalothin	Penicillin-resistant, Staphylococci, Escherichia coli, Proteus mirabilis, Synergistic with Kanamycin against Klebsiella pneumonia	Local thrombophlebitis	Lactated Ringers, Calcium gluconate, Calcium chloride
Chloramphenicol	Broad-spectrum; Penicillin resistant Staphylocci, Shighella, Salmonella	Occasional overgrowth of resistant organisms; myocardial depression	Diphenylhydantoin sodium, Hydrocortisone succinate, Oxytetracycline. Procaine hydrochloride, Tetracycline, Vit. B complex with C
Furazolidone	Escherichia coli, Proteus, Salmonella, Shighella, Aerobacter aerogenes	Hypersensitivity reactions, emesis	Amphetamines, Ephedrine; seda-, tives, narcotics and antithistamines should be used at reduced dosages
Gentamicin	Escherichia coli, Klebsiella aerobacter, Pseudomonas, Proteus, synergic effect against overwhelming sepsis when combined with cephaloridine or ampicillin	Nephrotoxicity; ototoxicity; neuromuscular blockade; relative bradycardia	Do not combine with any other drugs in intravenous solution
Griseofulvin	Microsporum spp. Trichophyton spp.	Chronic adm. produces hepatomas in mice, Embryotoxic and teratogenic in pregnant rats	Barbiturates, Dicoumarin

TABLE 7

ANTIBIOTICS USED IN LABORATORY ANIMALS

Antibiotic	Possible indications	Adverse Effects	Incompatabilities
Kanamycin	Escherichia coli, Proteus, Penicillin resistant Staphylococci	Ototoxicity; Nephrotoxicity; neuromuscular blockade; hypotension	Dextrose solutions of pH 3.5-6.5 Diphenylhydantoin sodium, Heparin sodium, Hydrocortisone succinate, Nitrofurantoin sodium, Pentobarbital sodium
Neomycin	Primarily enteric organisms; used in combination with other antibiotics for gut sterilization procedures	Nephrotoxicity; ototoxicity; decreased cardiac output; neuromuscular blockade	Oral Potassium, Penicillin V; Diuretics
Oxytetracycline	Broad spectrum but in vivo bacterial resistance common; activity against some Rickettsia, Mycoplasma (PPLO), and protozoa	Overgrowth of resistant organisms; decreased cardiac output; hypotension; neuromuscular blockade	Chloramphenicol succinate, diphenylhydantoin sodium, Heparin sodium, Hydrocortisone succinate, Penicillin G, Pentobarbital sodium, Sodium bicarbonate, sodium lactate, Lactated Ringers, Dextrose soln of pH 8.0 or higher.
Penicillin G	Pneumococci, Streptococci, some Staphylococci and some anerobes	Rare anaphylaxis	Chlorpromazine, Diphenylhydantoin sodium, Oxytetracycline, Tetracycline, Chlortetracycline
Streptomycin	Coliforms, Mycobacterium spp.; synergistic with isoniazid against Mycobacterium	Neuromuscular blockade; decreased cardiac output	Diphenylhydantoin sodium, Erythromycin glucoheptonate, Heparin sodium, Nitrofurantoin sodium, Norepinephrine bitartrate, Pentobarbital sodium, Sodium bicarbonate

TABLE 8

ANALGESICS, HYPNOTICS AND SEDATIVES

GENERIC AND (TRADE) NAMES	ACTIONS AND INDICATIONS	PRECAUTIONS
Chlorpromazine(Thorazine)	Blocks conditioned responses. Antiemetic and vagolytic. Reduces catatonia associated with dissociative anesthetics. Useful as sedative and preanesthetic.	Produces inconsistent effects in several species and may cause marked hypotension. Does not inhibit aggressive actions in nonhuman primates.
Acetylpromazine (Acepromazine)	Similar in action to chlorpromazine but more potent antiemetic, anticonvulsant and antispasmodic. Used extensively as sedative and preanesthetic.	Produces less hypotension than chlorpromazine. Block epinephrine induced responses to stress. Not recommended for restraint of nonhuman primates.
FENTANYL+DROPERIDOL combination (Innovar-Vet)	Narcotic (fentanyl) and tranquilizer (droperidol) produce neuroleptanalgesia Palpebral and auditory responses retained. Analgesia and sedation suitable for minor surgical procedues.	Marked respiratory depression noted in some species; especially nonhuman primates, but reversed by administration of narcotic antagonists. Bradycardia evident but inhibited by premedication with atropine. Self-mutilation reported in guinea pigs.
Morphine	Potent narcotic analgesic; produces profound sedation in dogs. Initial stimulation of salivation, vomitation and defecation followed by suppression of these reflexes.	Pronounced respiratory depression in most species; marked excitation in the cat and mouse at doses higher than 0.1 mg/kg.
Meperidine (Demerol)	Narcotic sedative and analgesic; less potent than morphine. Produces postoperative analgesia in dog and cat without vomition. Safe in cat at low doses.	Respiratory depressant effects similar to morphine.

TABLE 9

GENERIC AND (TRADE) NAMES	ACTIONS AND INDICATIONS	PRECAUTIONS
Xylazine (Rompun)	Nonnarcotic sedative and analgesic. Produces good muscular relaxation. Stimulates vomition in dog and cat.	Produces partial atrioventricular block and bradycardia. Higher doses reduce respiratory rate and may produce muscular tremors.
Atropine	Inhibits vagal stimulation of cardio-vascular and respiratory system; re-duces salivation.	Rapidly hydrolyzed by esterases in rabbits, rats and cats.
Nalorphine (Nalline)	Antagonizes depressant state produced by narcotic.	Controindicated in depressant states produced by tranquilizers, barbiturates and general anesthe-tics due to mild narcotic action of nalorphine.

TABLE 10

ANALGESICS, HYPNOTICS AND SEDATIVES

(Dosages in mg/kg)

GENERIC AND (TRADE) NAMES	ROUTE OF ADMINISTRATION	DOG	CAT	NONHUMAN PRIMATES	RABBIT	GUINEA PIG	RAT	MOUSE	HAMSTER
Chlorpromazine (Thorazine)	I.M. I.V.	2-5 I	2 I	N.R.*	25-100	25	25	25-60	
Acetylpromazine (Acepromazine)	I.M.	1.0	2.2		1-10				
	I.V.	0.5	1.1						
Innovar-Vet (0.4mg FENTANYL + 20mg DIROPERI-DOL/ml)	I.M.	1 ml/9kg	N.R *	1 ml/18-36kg	.15-.17 ml/kg	.08-.88 ml/kg	0.1-0.3 ml/kg	.002-.005 ml/kg	
Morphine	I.M. or S.C.	0.5-0.75	0.1						
Meperidine (Demerol)	I.M.	2.5-6.5	11	11		2	2	2	2
	As postoperative analgesic	5-10							
Xylazine (Rompun)	I.M.	1.1-2.2			8.8-9.9 followed in 10 minutes by 40-50 mg/kg ketamine				
Atropine	I.M., S.C. I.V.	0.04	0.06	0.04-0.1		0.5 ml of 0.5% soln			
Nalorphine (Nalline)	I.M., S.C., I.V.	Approximately 1 mg. nalorphine for each 10 mg. of morphine in all species; administer to effect							

* Not Recommended

BASIC RULES FOR QUALIFIED ANIMAL CARE: A GUARANTEE IN EXPERIMENTAL RESEARCH

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One demonstration of the critical role that animals play in medical and scientific advances is that 54 of 76 Nobel Prizes awarded in physiology or medicine since 1901 have been for discoveries made through the use of experimental animals. Research is necessary to find valuable therapies of many diseases, still incurable, which afflict the mankind and to reduce human and animal suffering. Biomedical advances depend on research with animals and not using them would be unethical, since it would deprive humans and animals of the benefits of research.

The human and animal welfare depends on continuing medical and scientific progress; experimental animal welfare and the quality of scientific results depend largely on qualified animal care.

A good system of quality control applied to animal care makes sure researchers obtain the most useful answers to their questions in the shortest time, using the smallest possible number of animals. At the same time the risk of the results being complicated by extraneous influencing factors is kept to a minimum.

A qualified animal care system seems to provide an answer to ethical, legislative and scientific needs and can be proposed as a valid suporting strategy for animal experimentation in the debate between antivivisectionists and researchers. The arguments for and against animal use in biomedical research come under two obvious headings: "pros and cons". Both groups refuse vivisection, abuse and cruelty to animals; both groups agree on the need for severe regulations, on the need for research workers to take particular responsibility at all stages in caring for the well-being of laboratory animals. (Bridges et al 1988; Garattini and van Bekkum, 1990; Paton, 1984; Uvarov, 1985).

This agreement underlines the importance of qualified animal care as one tool in obtaining correct and worth-while scientific results and highlights the role of institutional ethical committees.

Ethical aspects of animal experimentation

The Encyclopedia Britannnica defines ethics as "the systematic study of the nature of value concepts like good, bad, ought, right, wrong etc. and of the general principles which justify applying such values to the studied subject" - in this case to animal experimentation.

Most scientists accept that animals need to be protected from the abuse, agree on searching for methods that do not require the use of animals and that reduce the number of animals, work willingly within the legislative limits regulating biomedical experiments causing pain.

Most experiments to-day do not involve pain, in particular in the behavioural studies. Degree of pain inflicted to animals during many experiments is greatly reduced through the establishement of rules for humane conduct of the tests.

A scheme for assessing levels of pain, distress and suffering in the commonly used laboratory species was proposed by Morton and Griffiths (1985). Useful contributions to the study of pain and animal behaviour have been reviewed by Dawkins (1980) and Wood-Gush et al. (1981).

Laboratory animal science in the past few years has mainly devoted itself to improving the use, quality and health status of animals, the environment in their housing facilities, the quality of nutrition and maintenance, and the technology of handling and experimental procedures. The laboratory animal sciences now comprise multifaceted and sophisticated disciplines whose aims are to refine methods of care to ensure the maximum welfare of experimental animals while at the same time obtaining results that serve as a reliable basis for predictions from animals to man (Dodds and Orlans, 1982; Ufaw, 1987). The best choice of animal models, the selection of procedures for minimizing suffering, knowledge of the social behaviour of animals and their threshold of pain, attempts to avoid stress, distress and anxiety, an awareness of the importance of human/animal relationships, and - in particular - the qualifications, expertise and training of scientific and technical staff are the main tools that will enable us to reach the goals proposed by Russel and Burch (1959): REPLACEMENT, REDUCTION, REFINEMENT.

Legislative aspects

National and international laws, codes and guidelines (Home office, 1986; CIOMS, 1985; EEC Directive, 1986; NIH, 1985, CCAC, 1980-84) are useful in setting up a framework within which the scientist can work. However, in the final analysis, animal welfare will depend on the scientists' conscience and integrity.

No legislative system currently in operation works perfectly in different countries. It is better to devise workable legislative systems which are feasible and are tailored to each country's particular needs and ways of working.

Voluntary systems of control, such as those adopted in Canada by the Canadian Council on Animal Care (CCAC) and in Sweden, are criticized as inadequate for enforcing strict controls. To be really effective, a control system must be designed to foster open discussion and cooperation between scientists, the controlling authority and the public as a whole. Any successful control system must then be tailored to each institution and to its specific research needs.

As scientists' sense of responsibility in this specific field has grown, Institutional Animal Care and Use Committees (ACUC) and Ethical Committees have been increasingly set up (Orlans et al, 1987). These institutional control systems, rather than the laws, work successfully because the whole staff is called into play to implement them on a day-to-day basis and guarantee the real control of animal experimentation.

The Scientist Center for Animal Welfare (May 1984-May 1985) in the United States made a survey to assess the opinions of members of the biomedical community on the composition of these committees and their functions. Most of respondents indicated their agreement that members with different occupations/backgrounds should serve on an Animal Care and Use Committee: veterinarians, researchers, authoritative non-scientists, laboratory animal technicians, non-istitutional representatives, "ethicists", graduate students. Other categories recommended for membership of ACUC were administrators, statisticians, animal welfare activists, lawyers, facility managers,humane society members, budget officers. In 1985 the Canadian Federation of Humane Societies isuued very detailed guidelines for Lay Members of Animal Care Committees (CFHS, 1985, CCAC, 1984).The essential functions of such institutional committees should include:

revision of research projects in order to assess the true utility of the proposed experiments and the resulting social benefits, to avoid repeating tests which give known results, to review protocols in order to assess the degree of pain in the procedures, the need for anesthesia, the number of animals to be used, to check the appropriate skill of the investigators, and to recommend possible alternative.

The conduct of the experiments is submitted to inspection by these committees in order to check the conditions of housing and experimental facilities, to survey transport, maintenance, handling and animal care, to plan how to reach compliance with laws and regulations, to improve the performance of animal care in relation to regulatory inspection, and to certify the annual report on activities.

These institutional committees are also responsible for veterinary control to guarantee the health status of animals, to prevent zoonoses, to keep records of sanitary schedules and maintain sanitary barriers; they are in a position to play a truly pivotal role in establishing and supervising teaching and training programs for investigators and other staff in day-by-day care

Specific rules of qualified animal care in research programmes focused on psychology

Some research programmes, such those focused on psychology, have certain particular features and involve such complexity of mechanisms that they require highly qualified control systems to advise scientists on proper animal care and on ethical and legislative principles. Specific guidelines for use of animals in psychology were published recently (CCAC, 1984, NYAS, 1988; BC, 1987; BPS, 1985).

Basic research in animal psychology has significantly improved our knowledge of complex processes like learning, memory, perception, motivation and emotion, and of behavioural adaptations of individuals and species to their environments. Results of these studies may have direct and indirect implications in human welfare for the understanding and control of depression, phobias, pain, anxiety, learning, disability, obesity, etc. (Blackman, 1974; 1987; Miller, 1985).

The behaviour of animals, when used as models for human studies, reflects a combination of the effects of various factors and may thus often present inexplicable variations. Why inexplicable? Because scientists still know too little about these factors. However we can do everything possible to minimize such variations by keeping the quality of the animals, their care and maintenance high before, during and after experiments.

The well-being of a laboratory animal can be defined as that steady state in which the animal is in physiological equilibrium and in which it is not experiencing any significant stress. Stress itself can be defined as one or more factors which upset the steady state of an animal, inducing compensatory mechanisms which, if inadequate to return the animal to "normalcy", may lead to pathological conditions. All environment and biological variables, including the experimenter, are examples of factors which can stress the animal, influence its response and may invalidate the results. Some physical, environmental or social factors may be considered as stressful: examples are too high or low temperature, excessive noise or silence, excessive air movements, insufficient ventilation, overcrowding, social incompatibility, social deprivation, isolation. The stress response is characterized by physiological, psychological, biochemical changes that interfere with scientific results.

The Canadian Psychological Association, in consultation with the Canadian Council on Animal Care, has set up specific guidelines (1984) to assist psychologists in making ethical decisions in behavioural research with animals. The ethical decision-maker is one who realizes that his choices are related to values, and weighs these values carefully.

In planning the procedures in studies of animal behaviour, the investigators in psychology should also consider whether non-animal methods (e.g. human health volunteers, epidemiology, clinical historical data) could replace the use of animals in experiments which induce pain. When animals are needed, thought must be given: 1) what is the most appropriate model that answers the specific question; 2) what procedures could be used to reduce the number of animals; 3) where pain or distress is likely, to refining existing procedures so that the level of pain or distress to the animal is minimized.

Some suggestions for refinement of procedures must be considered in studies of animal behaviour in order to reduce discomfort, trauma, stress (OTA, 1986; NRC, 1985):

- considerable knowledge is needed so as to select the most appropriate species
- species-specific sensitivity to environmental conditions must be known (e.g. gravitational fields, hibernation patterns, atmospheric pressure, oxygen levels, etc.) and to the effects of any significant alterations.
- appetitive motivation is preferable to aversive stimulation
- when necessary, design the procedure for the least aversive combination of intensity, duration, frequency and type of stimulus
- whenever possible, allow the animal to control, alleviate, avoid or escape from aversive stimuli
- shorten or eliminate periods of food, water and sleep deprivation
- in long-term studies which involve body weight reduction, for most mammalian species, weight loss should not exceed 20-25% of the mean weight of control animals
- in long-term studies involving deprivation or excess of nutrients, consideration must be given to the metabolic and physical consequences
- expertise and proper procedures must be available in surgical and pharmacological manipulations
- all individuals involved in psychological research must be appropriately and fully trained, skilled and competent

Suitably qualified scientists and trained technical staff are the best guarantee of the comfort, health and well-being of animals in experimental procedures for behavioural studies.

In the United Kingdom, the 1986 Animals (Scientific Procedures) Act requires that psychologists who wish to carry out experiments on living animals must hold appropriate personal licenses issued by the Home Office, must submit an account of the objectives of the research, a summary of the procedures and an indication of their likely severity in order to obtain a project license.

In summary, ethical, legislative and scientific principles all have the same aim and stress the need for staff qualification: scientists must have the necessary skills and need to be highly and appropriately qualified, and all technical staff, students and research associates must be adequately prepared and trained.

Professional preparation for animal care in Italy

For several years now the Italian scientific community has been feeling the need for qualified researchers in laboratory animal sciences and for well-trained technical people working in biomedical research, as a guarantee of good animal care. The education and training of such staff is of particular concern because of the moral and ethical obligations to laboratory animals, because of the need to comply with national and international regulations, because the technology of laboratory animal science has become very sophisticated and finally because of the requirements imposed by the science to produce scientifically valid results.

Different approaches have been taken so far to reach these goals: many institutions have set up voluntary education systems, introducing intramural teaching and training schemes; others enable their scientists to attain this professional qualification through participation in specific academic courses in other countries.

Official educational programmes in Italy have been promoted only recently by public and private organizations in order to satisfy the increasing need for a more professional approach to the use of animals in research.

Courses at three levels are organized annually, by the Istituto Superiore di Sanità in Rome: these five-day-courses are presented with lectures and practical sessions and are open to participants from universities, health institutions and research centres. Special courses for graduate students in biomedical disciplines are being developed in some academic faculties, and a two-year course for high-school leavers has been proposed by the veterinary faculty in Milan and should start up in the next few years.

Against this background, a private organization was also formed in the light of several international comparisons. Its aim is to spread information on animal experimentation, to promote educational programmes at different levels, and to provide printed teaching material in the sciences of laboratory animals. The Italian Group for Laboratory Animal Sciences (G.I.S.A.L), part of the Society for Applied Pharmacological Sciences (SSFA), was set up in December 1986, and keeps regular contacts with sister organisations in other countries. It is currently developing educational programs for senior research staff, technicians, and young investigators; to promote the spread of information and of recent knowledge in the field of laboratory animal science. A scientific committee plans the group's activities.

G.I.S.A.L.'s activities to date are summarized here: a questionnaire to review the Italian situation in the field of animal care and educational programmes; three Mini-Simposia; one Study Day; the first two of a series of Italian Courses on Laboratory Animal Technology for senior technicians, and istitutional short courses for new experimenters. Publications include: Proceedings of the three Mini-Simposia (GISAL, 1987; 1988; 1990) and of the Study Day (GISAL, 1988); a bibliographic reference list (Scalvini and Guaitani, 1988) that will be updated every two years; a teaching manual (GISAL, 1989) outlining the basic principles of laboratory animal sciences (Guaitani et al, in press).

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RECENT ORIENTATIONS IN LEGISLATION ON THE USE OF ANIMALS IN BIOMEDICAL RESEARCH

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Although Italy was one of the first countries to promulgate animal welfare legislation (Law No. 924 of 1931), the laws in force today are antiquated and inadequate (Law No. 615 of 1941 and subsequent circolari explayning the system of control - the most recent of which was issued in 1987). From the Second World War until today, more than twenty bills have been debated by Parliament, as the law in force does not respond to current technical and scientific needs and the ethical and political pressures coming from society.

The comment of contemporary press regarding the use of laboratory animals is not always as balanced as one would like. The question is, where do individuals involved in animal research stand when it comes to ethics in the use of laboratory animals in research experiments? Some persons concerned with "animal rights" contend that the case for the moral rights of animals must be based on or be an extension of the case for human moral rights. If humans have a value system estabilishing the moral right not to be used as a mean to an end, then this argument can be extended to animals, including those routinely used in scientific research.

Today's society has changed its attitudes towards the exploitation of animals. While it was acceptable to display animals as caged specimens in zoos in the past; in most zoos today, animals are given an environment that attempts to satisfy normal behavioural and physiological requirements. Animal rights organizations range from those conceived exclusively for the protection of a single animal group (for example, primates), to those against all use of animals in research. Likewise, their objectives vary from total opposition to the use of animals in research to promotion of more rigorous standards for their use.

The legislation currently in force in Italy is aimed at providing information on the number and quality of animal experiments being carried out in the country. In actual fact, it gives a census of the type and number of animals used in biomedical research, rather than limiting that use. All scientific investigation must be registered, specifyng the type of experiment and the species, the number of animals, and the anaesthesia to be used. By law, only people with degrees in medicine, veterinary medicine, biology and natural sciences and students from the second year in those faculties can carry out biomedical experiments using laboratory animals. The following criticism can be directed at current legislation:

1) the scientist is not asked to prove the need for the experiment nor the expected profit to science,

2) it is up to the scientist to decide whether pain can be reduced or eliminated,

3) no specialization or certificate is required for the handling of laboratory animals, thus, no provisions are made for the training of animal laboratory technicians or assistants.

In November, 1986 the Council of the European Communities adopted a directive "on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes" (Directive EC 86/609). Member States were required to publish national laws implementing the directive by 24 November 1989. A new law is required to bring Italian legislation into conformity with the provisions of the directive. Although the most recent bills brought before Parliament cover all aspects of animal experimentation, they do not give adequate relief to the problem of training for animal handling, despite the fact that Article 7 of the directive states that experiments shall be performed by competent authorized persons and Article 14 requires that persons who carry out experiments, take part in them or take care of animals used for experiments shall have appropriate education and training. These two points - authorization and training for use of animals in experimentation - are central questions to be discussed. The Council directive concludes that the number of animals used for experimental or other scientific purposes shall be reduced to a minimum, that such animals shall be adequately cared for, that no pain, suffering, distress or lasting harm shall be inflicted unnecessarily, and that where unavoidable, these shall be kept to a minimum.

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Stampato dal Servizio per le attività editoriali
dell'Istituto Superiore di Sanità, Viale Regina Elena, 299 - 00161 ROMA

Reg. Stampa - Tribunale di Roma n. 131/88 del 1° marzo 1988

Roma, dicembre 1990 (n. 4)