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**A European thought about
Animal experimentation**

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Introduction

During the EU Socrates/Erasmus Programme, IP Project “Bioethique en sciences de la vie et de l’environnement”, students from different European countries approached different topics. The aim of our subject is to make a reflection about animal experimentation. We carried out research about historical and ethical aspects, relations between humans and nature, the biological approach of animal suffering, legislation regarding animal experimentation, the three R’s and alternative methods in order to obtain enough tools for discussion.

Historical and Ethical aspects

The Ancient Greek civilization created a paradigm of man’s superiority over the animal world. In Plato’s (427-347BC) hierarchy of values, animals are situated far below man.

Aristotle (384-322BC) considered that animals were equal to objects because they don’t speak. In Ancient Rome, animals were treated as objects there only for human pleasure. Publius Vergilius (70-19BC) was the first to say that animals couldn’t be treated as objects when they were suffering.

In Christianity, Saint Augustine (350-430) and Saint Thomas Aquinas (1225-1274) agreed with Saint Francis of Assisi (1181-1226) and Saint Anthony of Padua (1195-1231) when they said different beings should not be treated equally because we have different origins and animals should always serve humans.

A few centuries later, Immanuel Kant excluded animals from ethical considerations because of their incapacity of rational thought. Baruch de Spinoza (1632-1677) was the first to admit that animals were able to suffer as opposed to Descartes (1569-1650).

Voltaire (François-Marie-Arouet) and Jean-Jacques Rousseau protest against the differences between men and animals and were opposed to vivisection.

According to Charles R. Darwin (1809-1882):

“There are no better or worse forms of life, they all deserves respect”.

Jeremy Bentham (1748-1832) was the founder of the ethical doctrine of utilitarianism (Bentham 1958) and he introduced the concept of pleasure and pain: Can animals suffer? Do we have the right to feel superior to animals?

Peter Singer is an Australian philosopher (1990) who rejects speciesism (a theory where the human species is considered superior to other species) and defends a particular concept of equality between humans and animals. Singer formulated a new code of ethics based on five “commandments”, which replace those of traditional ethics (Singer, 1980). Instead of:

- “Treat all human life as having the same value”, the first new commandment is “Accept that the value of human life can be changed”,

- “Never intentionally kill an innocent human being”, he suggests “ Accept responsibility for the consequences of your own decisions”,
- Never take your own life and try to prevent the suicide of others” he suggests “Respect the wish to live or die of another person”,
- “Be fruitful and multiply” he suggests “Bring only wanted children into the world”,
- “Always treat a human life as more valuable than an animal life” he says “Do not discriminate on the basis of the species criterion”.

“Science sans conscience n’est que ruine de l’âme” (*Pantagruel*, chapitre VIII), Rabelais

C’est justement la bioéthique qui permet, et de plus en plus oblige, le scientifique à avoir une conscience. La bioéthique est la recherche de normes morales applicables à la recherche biologique et tout ce qui concerne les manipulations techniques du vivant. On ne remet pas ici en question le comportement moral lui-même mais comment sa prise en compte dans la manipulation du vivant peut être compatible avec un gain financier ou le prestige personnel. La bioéthique couvre des domaines variés, dont l’expérimentation animale sur laquelle nous nous interrogeons ici.

L’éthique appliqué à l’expérimentation animale est une préoccupation ancienne.

An European thought about animal experimentation

The relationship between humans and animals has always been influenced by mythology and religion: in Greek mythology, for instance, most of the divine creatures are half-animal and half-man. In one of the Greek myths, the gods gave different characteristics to all animals (fur, claws, wings...) and had nothing left for humans. It seems that ancient civilisations were conscious that even though they had gained certain characteristics like reason and the capacity to think in the future, they had lost physical capacities like speed and strength.

Humans have a delicate tool such as the ability to develop thoughts and to be convinced in them based on the sensibility of their soul. We could say one of the main traits of mankind is the knowledge that we lead a finite life. This ability has created in humanity several ways to understand life and the relationship with nature. On one hand, since human beings follow the evolutionary laws, their instinct tells them to do all they can to preserve their species, to insure reproduction and welfare, regardless of sustainable management. On the other hand we have the capacity to project our actions in the future, thus making us able to foresee that we must protect and preserve what we need.

Based on the evolutionary theory, Rachels wants to underline the consideration of human dignity: he says “the theory of evolution undermines the idea of a special humanity” which implies that human individuals should be treated differently because they belong to the human species. This idea is enhanced by the religious concept that man has been created in the image of God. Against this religious vision the theory of evolution affirms that humans are not radically different in kind from the non-human animals.

On the other hand what Petrinovich says has to be taken into account: “people very clearly tend to have intuition of stronger moral obligation to relatives than to strangers and to human than to non-human animals”. This theory, like Rachels’, follows the natural evolutionary behaviour of an individual part of a species: the survival law.

In developed countries, the survival law has developed into something of a “comfort law”, we don’t only suffice to our immediate basic needs but want to live a longer, healthier and happier life. Animal experimentation is one of the tools mankind has to make our life more comfortable. But is this welfare really needed by humans? In other words, is it natural to desire more and more and to try to keep life as long as possible? Humanity has constantly been dealing with desires and trying to find ways to fulfil them. The desire to obtain more and more comes from the development of consumerism, technologies and the need to concretise those desires in any possible way. This vision we can call the Western way. It contrasts with the holist world view of the Eastern world, based on spiritualism and the contact with Nature. For instance, for an occidental person the acceptance of death is very hard because his society is based on practical elements and animal experimentation can be an important tool to save human life. But on the holistic world view death can be more easily accepted because the person who is going to die, like all life-forms, doesn’t need to be saved because it belongs to the life cycle in which nothing is going to disappear completely but everything, somehow, comes back to Nature.

In this way animal experimentation is something which seems absolutely necessary for some cultures, but can’t be applied to such cultures which have based their way of life on spiritualism.

One of the first questions that comes to mind is: how can we be sure that experiments carried out on animals provide conclusive results on the effects they are going to have on humans?

The predictivity factor

In 1956 the *Code of Medicine Ethics* adopted and signed in Norimberga with the presence of 71 countries the prohibition of using drugs in humans without previous testing on animals.

There is a 99% DNA homology between monkey and human genomes. This is because of genetical redundancy and the different three-dimensional structure of proteins. Animal experimentation in drug production is used to obtain information about their effects and specifically their effect on the active site of receptors “*in vivo*”. The small difference between interspecies genomes could concern the active site of receptors and so influence the action of a drug. In this case the animal experimentation seems to be unnecessary for the final use on humans because the experiments cannot be considered 100 % predictive. On the other hand the great similitude between the DNA of certain species should allow us to justify the experimentation on a given model species to insure the safety of the tested substance for humans.

The use of animal experimentation seems to be more efficient in the pharmacokinetic field than the “*in vitro*” analysis. That’s because to analyze the specific behaviour of the drug you need to know the enzymatic interactions in the whole

organism. But the progress in the development of alternative methods such as the cells cultures could mean that we do not need to test on animals in the future. The enzymes and receptors are codified by DNA, so it remains the same issue: the genetical redundancy and the three-dimensional structure of the enzymes can't be fully predictive like it was mentioned before. The genomic diversity occurs, in inter and intra-specific levels and also on the individual level (idiosyncrosis). For instance: in cats the glucorinil-transferasysis is absent. This enzyme plays a relevant role in the biotransformation of drugs. The drug tested on cats will not be predictive for humans because on them the drug will have different effects deriving from different biotransformation processes. Ivermectina, an anti-elmintic drug, is an example of the genomic intra-specific diversity concerning animal experimentation. It is toxic for Collies but not for the others common dog races.

What about public opinion?

In a study made in Denmark (Varner 1998, 2001, 2002) about public opinion on animal biotechnology by Jesper Lassen and Peter Sandoe, some of the arguments in favor used by the public were:

- the utility of the experiments related to the environment and animal welfare,
- health issues (or the preductivity issue)
- certain misconduct towards animals when it is carried out in poor countries.

On the other hand, the concerns towards this issue presented were:

- the risk, to the environment and health;
- the utility: is it really necessary and are the right strategies used,
- the integrity,
- the welfare.

Public concern isn't just related to the lack of information but mainly to a preoccupation and interest to be well informed. People considered that using utility as an argument must be more than a commercial success.

“If scientists want to keep using animal biotechnology in their investigations with the support of the public they have to enlarge their concepts of risk and utility in ethic and factual terms.”

These lead us to another problem that is information. Many organizations/associations take advantage of the internet and other easy ways of spreading opinions by using shocking and extreme stories and images. This isn't in any way a good source of information and knowledge.

Most people presume that animals “suffer”, with no biological consideration on animal suffering and discomfort.

Before having a proper debate about animal experimentation, we must first ask ourselves how we define animal suffering and discomfort. There are many physiological assessments of pain and stress that animals are susceptible to enduring in animal experimentation.

The biology

Emotional answers and their effects on the organism operation

Animal sensitivity, and its conscious representation constituted by emotions, is at the center of the debate on the animal experimentation. An emotion is defined as an emotional state depending on the representation that someone has of his environment. It is characterized by a subjective component (feeling), a somato-motor one (behavior) and a neuroendocrinous one (Dantzer 1984). The subjective component is not appreciable directly in animals since they cannot communicate verbally. However, the emotional state of an animal can be appreciated through the two other components: behavioral and neuroendocrinous modifications. Besides those present similarities between negative emotions, whether it be fear (emotional state induced by the perception of a threatening stimulus, Boissy 1998) or suffering related to physical pain (sensory or emotional experiments associated with a real or potential tissue damage, according to the definition of the International Society for the Study of Pain). These reactions were more particularly studied in mammals, birds and the generic term of stress is used to describe the more or less specific response of the organism concerning a threatening situation (Dantzer and Mormède 1979).

From a behavioral point of view, a stressed animal will be able to react by escaping or trying to. This type of reaction is very often observed in gregarious animals showing strong reactions when separated from the group: increase in motor activity, vocalizations, attempts to leave the isolation room (pigs: Dantzer and Mormède 1981, bovines: Boissy and Neindre 1997). In other species - like birds - and in young animals, immobilization is often observed (Epsmark and Langvatn 1979, Faure and Mills 1995). These reactions are also largely observed when animals that are not used to it are handled by man. From a neuroendocrinous point of view, several systems are implicated in the stress reaction. The reactions most usually described are the activation of the autonomous nervous system, in particular the sympathetic nervous system, and the activation of the hypothalamo-hypophyso-corticosurrenalean axis, also called the corticotrop axis. The activation of the sympathetic system involves a catecholamine release which has powerful effects on physiology and metabolism: it increases the respiratory as well as the cardiac frequency and its contractile strength, it acts on the vascular walls which support the blood redistribution from skin and internal organs towards muscles and the brain, it increases hepatic glycogenolysis and lipolysis. The activation of the corticotrop axis leads to a glucocorticoid releasing which, while increasing the neoglucogenesis and supporting the action of catecholamines on the vessels, will increase the effects of these chemicals. The description of the effect of catecholamines and glucocorticoids leaves no doubt about the need, in order to avoid any artifact, to limit stress as much as possible during experiments if their aim is to study the general physiology or metabolism. However, the energy metabolism is classically studied in individuals isolated in respiratory rooms during several days. In order to avoid an overconsumption of energy due to stress, the animals must be previously accustomed to the procedure and never be isolated visually from their kind (Mr. Vermorel, comm. perso.). Other neuroendocrinous systems can be implicated in stress reactions like, for example, prolactin and beta-endorphins (in connection with

the corticotrop axis) which are released in acute stress situations (Guillemin *et al.* 1977, Mormède *et al.* 1984, Parrott and Thornton 1989). The activation of the central opioidergic systems seems to be the cause of sensitivity reduction to the pain induced by stress (Fanselow 1984, Gamaro *et al.* 1998, Rushen *et al.* 1999). For this reason the effectiveness of analgesics can only be evaluated correctly in absence of stress.

When a threatening or unpleasant situation lasts, the behavioral and neuroendocrinous answers tend to be reduced, as the animal is getting used to it. However, some of the changes in organism operations can remain, showing adaptation difficulties. Modifications of the reactivity are described when action possibilities are limited by a situation (hypo-reactivity in fastened sows, Broom 1987) and when animals are not stimulated (hyper-reactivity in calves in an isolation room, Veissier *et al.* 1997). The activities of the neuroendocrinous systems can also be modified. When repeatedly stimulated, the pituitary gland becomes less sensitive to the corticoliberin action, the corticosuprarenal one more sensitive to the corticotropin action and the corticoids negative retrocontrol less effective. These modifications can be evaluated with pharmacodynamic tests consisting in injecting dexamethasone, corticotropin or corticoliberin (Friend *et al.* 1979, Janssens *et al.* 1995). Chronic stress can also have an effect on the animals' growth and their sensitivity to pathogenic agents. Once again, interferences with experimental results should not be neglected.

Acute pain can be expressed under the same forms as acute stress. For example, branding with red iron produces reactions such as vocalizations and attempts to escape (Lay *et al.* 1992, Watts and Stookey 1999). Pain can also be expressed in a more specific way (for review: Chapman *et al.* 1985). Antalgic postures can be observed (for examples: removal of a painful member support, arched back due to rachis pain), and slowness or moving difficulty (standing difficulties are often due to articular, bone or visceral pain). Neuroendocrinous activations due to stress can also exist. Thus, acute pain is often accompanied by an autonomous nervous system activation resulting most of the time in tachycardia. However, from a physiological point of view, acute pain is distinguished from stress by the efferent nerves' activity (more frequent discharges of the nociception receptors) and the potentials evoked which it creates in the cerebral cortex (Chapman *et al.* 1985, Dotson 1997). As for chronic pain, it is characterized by a hyperalgesy which can be detected by sensitivity tests in which detection threshold or tolerance to a mechanical electric or thermal stimulus is measured (heating laser beam for example) (Ley *et al.* 1989, Svensson *et al.* 1991). In conclusion, pain - and more particularly chronic pain - can be compared to an extreme state of stress. For this reason, it must be avoided in order to obtain scientific results free of artifacts.

Animal suffering evaluation

Pain and stress mechanisms having been quickly reviewed, it remains to know how to detect stress or pain in animals subjected to experimentation. The following paragraph presents simple means to evaluate this suffering.

For man, pain can be described verbally. Evaluation grids like Mc Gill Bread's were

developed to evaluate pain; other methods, such as the layout of a line or the pressure on an object are also used (for review: Chapman *et al.* 1985). These tools cannot be used with animals. However, by analyzing the relations between the appreciation they give and the observable parameters such as behavioral modifications it is possible to validate them as pain indicators. Moreover, the observation of the effects of analgesics also brings elements of validation for this pain indicator. Several observation grids have been created and adapted to laboratory animals (Morton and Griffiths 1985, Brugère *et al.* 1992, Lawrence Podolsky and Lukas 1999). These grids consist in observing postures or unusual behaviors and the modifications due to the activation of the sympathetic nervous system.

The criteria given by the authors mentioned above are explained in table 1. Many are not specific to pain or stress. Thus polypnea can be observed in dogs as soon as the weather is hot. Some elements can only be evaluated subjectively, like fear during a handling, which can be seen when an animal lets himself be handled but remains contracted. Finally, some variations are opposed to one another; like apathy and agitation. So during an observation the modifications of an animal's state can only be seen by comparing it with its normal state. It is thus necessary to know an animal well to detect a painful state.

It is clear that animals suffer, if not psychologically as much as humans, at least physically in the same way. For this and other reasons, principles have been developed to reduce this suffering as much as possible, and limit the use of animals in experiments.

The three R's

Research organizations are encouraged to apply the "Three R's" principle in the use of animals in experiments. These principles are:

Replace - whenever possible avoid the use of animals; replacement is defined as the substitution for conscious living higher animals by insentient material. There are a number of alternative methods that can be used to replace live animals in either all or part of an experiment. A number of organisations around the world are working towards the development and validation of alternative methods. (<http://www.animaethics.org.au/reader/arrp-3rs/arrp-replacement.htm>)

Reduce - reduction in the number of animals used in experiments; to achieve this, the Australian Code of Practice – for example - requires that:

- Studies are designed to be scientifically and statistically valid
- The minimum number of animals possible should be used
- Studies should not be repeated unnecessarily

(<http://www.animaethics.org.au/reader/arrp-3rs/arrp-replacement.htm>)

Refine - refining the ways that animals are used in experiments so that suffering is reduced; refinement is any decrease in the incidence or severity of "inhumane" procedures applied to those animals that still have to be used. (<http://www.animaethics.org.au/reader/arrp-3rs/arrp-replacement.htm>)

There are two key issues:

- To assess the impact of any procedure or condition on the well-being of the animal
- Strategies to eliminate or minimise that impact

(<http://www.animaletics.org.au/reader/arrp-3rs/arrp-replacement.htm>)

The European Centre for the Validation of Alternative Methods (ECVAM) was set up in 1992 by the European Commission, and contributes £6.3 million annually. EU regulations state that researchers must assess the pain that an animal may feel during an experiment, and justify its suffering by what research can achieve. (<http://www.bbc.co.uk/science/hottopics/animalexperiments/index.shtml#Keypoint>)

The three R's seem like very vague principles, and if they're all perfectly taken into account there are so many parameters that have to be dealt with that it doesn't even seem possible to do so. These rules appear like a sort of "de-culpabilisation" of the use of animals in experiments, they come across as a confession of guilt. They appear to have been created because of the public opinion's pressure, and many scientists think it hinders their research. The public opinion is aware of what happens in laboratories simply through mass media, which has given a very bad impression of what goes in labs. With time, research labs have tried to protect themselves from the incessant critics of the media, and today experiments are performed under conditions of security matched only at military institutions. We could say they protect their conscience with the three R's, but all the ideas presented in these principles are already followed by researchers. For example, when it comes to replacement, even if we consider things solely on a financial point of view, it is much cheaper to use alternative methods than to have animals in a laboratory. Likewise, the fewer animals are used, the cheaper and faster the experiments go.

Alternative methods

For an alternative method to be accepted, it has to be tested by the ECVAM. This validation is a long and expensive process (Super interessante abril,2007).

Since 1997, only 16 techniques have been approved: six were approved in 2006, they are pre-clinical models that use cell cultures for testing the toxicity of anti-tumoral medication or to identify contamination factors in drugs (Super interessante abril,2007).

These models could replace the use of dogs in experiments.

- The other five alternatives are based on *in vitro* tests with human cells to determine the contamination factors in drugs that are injected. These tests could avoid the use of the 200 thousands of rabbits per year, in Europe alone (Super interessante abril,2007).

Stem cells, genetically modified cells, synthetic membranes, computer models and new scanning technologies are others alternatives to science investigations (Super interessante abril,2007).

- Today, hundreds of cosmetics and household-product companies have turned their backs on animal testing and begun taking advantage of the many sophisticated

non-animal test methods available , which range from cell and tissue cultures to computerized “structure-activity relationship” models. For example, EPISKIN and EpiDerm, multi-layered skin models made up of cultures of human skin cells, have been scientifically validated and accepted around the world as total replacements for rabbit skin corrosion studies. Similarly, the cell-based “3T3 Neutral Red Uptake Phototoxicity Test” has become a widely accepted alternative to the use of guinea pigs and mice to assess sunlight-induced skin irritation (http://www.peta.org/mc/factsheet_display.asp?ID=91).

These methods seem to be the solution for stopping the use of animals in experiments but will they really replace all experimental tests? Mostly scientists don't trust the more recent alternative methods because although their results are faster and less painful it is very difficult to reproduce the same circumstances of one living creature. Likewise it is difficult to reproduce all information about the complex network interactions of one organism (Super interessante abril,2007).

Researchers, in order to limit their possible range of action and subjective decision-making, are submitted to a series of very strict laws (at least in developed countries).

Legislation

In 1986, the directive on the protection of vertebrate animals used for experimental and other scientific purposes was adopted by the EU Council of Ministers (directive 86/609/EEC). It applies to experiments likely to cause pain, suffering, distress or lasting injuries. All EU member states must transcribe this directive into national legislation, and “each member State shall designate the authority or authorities responsible for verifying that the provisions of this Directive are properly carried out.” (article 6)

The following objectives are laid out:

- to set out the legitimate objectives for which laboratory animals can be used,
- to guarantee the qualification of all research and laboratory staff (article 7 & 14),
- to limit the use of animals when alternatives are available (article 23); when there are no alternatives to animal use, animals with the lowest degree of neurophysiological sensitivity (or those which suffer the least) must be used provided that compatibility with the scientific objectives of the research is observed (article 8)
- to prevent unnecessary animal suffering
- to provide a system for inspecting animal houses and protocols,
- to set the basis for general care and accommodation
- to provide public accounting of the number of animals used (article 13)

In the United Kingdom and the Netherlands, the directive was transcribed into national legislation to also cover invertebrate animals. The directive stipulates that animals must be treated humanely before, during and after each experimental protocol.

Wild animals, on the other hand, should not be used unless other animals do not meet the requirements of the research.

All the experiments must be conducted under general or local anaesthetic, unless the anaesthetic is more traumatic than the experiment itself or is incompatible with the objectives of the experiment. If anaesthesia is not possible, then pain, distress or suffering must be limited and analgesics or other appropriate methods should be used (article 8). At the end of the experiment, a veterinarian or other qualified person must decide whether the animal should stay alive or be humanely put down. Animals should not be kept alive when they are likely to suffer from permanent pain or distress (article 9). In addition, no animal should be used more than once in protocols causing great pain or distress. This raises a number of issues, firstly: what is to be done with the animals when they for some reason cannot undergo experiments anymore but are still healthy enough to live? If the animal is to be kept alive, it “shall receive the care appropriate to its state of health, be placed under the supervision of a veterinarian or other competent person” (article 9). This is no doubt a hassle for the institutions where animal experimentation is carried out: they must pay for the veterinary care, and vets don’t keep animals until the end of their lives. So the animal must be homed, which is another tedious problem. According to the law and from research centre’s point of view it seems a lot easier to simply put the animals down when they cannot be used anymore. The authority may allow the animal concerned to be set free, provided that it is satisfied that the maximum possible care has been taken to safeguard the animal’s well-being, as long as its state of health allows this to be done and there is no danger for public health and the environment (article 11). In practice however this hardly ever happens. Secondly, the directive says that animals shouldn’t be used more than once in protocols causing great pain or distress (article 10). Isn’t this directive precisely supposed to prohibit causing great pain or distress to the animals?

The directive specifies an obligation to declare any use of animals in experiments as well as the users to the proper authorities beforehand. If the animal suffers great pain, the protocol itself must be declared and justified to the proper authorities. Authorisation will only be obtained when an essential contribution to humans or animals is expected. Does that make any more ethically justifiable?

In addition, national authorities must keep a record of the total number of animals used and compile statistics specifying the number of animals used according to the fields of application.

In each member state, only institutions approved by the proper authorities are authorised to breed and supply animals for research. Dogs, cats and non-human primates must be shipped with individual identification.

Institutions using animals for experiments must be approved by the authorities and have enough qualified staff. Only animals bred in animal houses or supplied by approved breeders may be used.

In the majority of cases, inspection — to check compliance with the regulations — is performed by experienced veterinarians or biologists under the supervision of the proper authority.

As regards ethical assessment, the directive does not stipulate the setting up of ethics committees. However, given the importance of the notion of well-being — or rather welfare — of experimentation animals to the general public, ethical reviews of experimental protocols on animals seem to be a major step towards experimentation on animals being accepted. In Belgium, Sweden and the Netherlands, ethical assessment is

regulated. In France, the United Kingdom and Finland, committees are responsible for conducting ethical assessments of protocols before any experiments and in Denmark, inspectors have the power to veto protocols on ethical grounds.

We will now look at the particular case of France, and how this directive has been transcribed into national legislation;

In France, decree 87-848 of 19 October 1987 supplemented by three ministerial arrêtés from 19 April 1988 regulates the use of animals in animal experimentation. They stipulate that:

- 1) all experiments which cause any sort of suffering to vertebrates must be taken out if and only if there is no alternative method available and they are absolutely necessary; once this has been taken into account there are three conditions that must be respected:
 - a. only institutions approved by the proper authorities are authorised to breed and supply animals for animal experimentation
 - b. Those who have direct scientific responsibility for the experimentation must have been appropriately trained, and have an authorisation from the Ministry of Agriculture.
 - c. Institutions where animal experiments are being carried out must have been approved by the Ministry of Agriculture (by the Veterinary Services of the area) and in accordance with the 86/609/CEE directive. The institution must also keep a record of the total number of animals used.

These laws do not apply to certain experiments (the zoo technical and veterinary ones) carried out in the INRA (National Institute for Agronomic Research). This raises the problem of how we define zoo technical and veterinary experiments as opposed to other experiments. None of the laws provide any guidelines about this matter, thus subjecting it to the judgement of the people carrying out the experiments. Furthermore, it doesn't seem ethically correct that the legislation separate the different types of experiments seeing as the animals are susceptible to suffering the same amount of stress and pain.

In the countries where a protocol authorisation is necessary before starting an animal experiment, such as the USA, Canada, Australia and New Zealand (it's unfortunately far from being the case worldwide), ethical committees must evaluate the legitimacy of the experiments beforehand. These committees have to be constituted according to the law. In general:

- one third to half of the members do not work at the institution where the experimentation is carried out
- a quarter or less of them are researchers
- representatives of animal associations must be present

These committees must evaluate the justifiability of the experiments, study the protocols, try and suggest alternative methods and make sure the animals are treated according to the law when they are not being subjected to experiments.

Misconduct in the treatment of animals is prohibited and animal experimentations must only be carried out if absolutely necessary according to article 276 of the Rural Code. This article doesn't define what it considers as being "absolutely necessary". Is there ever a case where animal experimentation can be considered absolutely necessary? Because the law provides no system to evaluate the necessity of an experiment, it's up to the person or people carrying it out to use their better judgment (does the law automatically assume that human nature is good?) and decide themselves. In order to impose an ethical order of things, certain institutions have set up ethic committees to help the researchers come to a decision.

Having studied all the global aspects of animal's experimentation, we decided to get together in our study group and discuss certain matters that we find problematic or unclear.

Discussion

Do we have the right to consider animals like a part of a utilitarian community? How can we consider the weight of animal pain? Why do we justify insect killing for example and not cruelty to a dog used in animal experimentation? How and why can we decide the discrimination between animals? Why can we use some species and not others?

In our research we found numerous arguments for and against animal experimentation. We will now consider certain of them, and compare our different point of views. The following arguments were taken from a non scientific website supported by animal associations against animal experimentation, and represents what the public often thinks about the use of animals in these experiments.

Arguments against animal experimentation

By an animal welfare website:

- Animal experimentation can be misleading
- When locked up they suffer stress
- The stress that animals endure in labs can affect experiments
- Animals have as much right to live as human beings
- Deaths through research are absolutely unnecessary and are morally no different from murder
- Strict control have not prevented researchers from using animals in extreme experiments, although such instances are rare

- Animals are still used to test items like cleaning products, which benefit mankind less than medicine or surgery

True, animal experimentation can be misleading but a lot of tests have proven to be of great importance for the progress of science. Furthermore, until such time as alternative methods are perfectly reliable, they are the only solution we have. Of course animals are stressed, but for an experiment to be successful, the animal must be as close as possible to a normal physiological state, i.e. not stressed. It's common sense for a scientist to keep his animals as un-stressed as possible. This is not an ethical but a practical issue.

The question of the right or not to live seems somewhat hypocritical and beside the point. Most people, if they had to choose between their own life and an animal's, would decide to kill the animal. Furthermore, we believe that as human beings and scientists we have a duty to help improve the wellbeing of mankind. The question is really how far are we willing to go to protect our species?

Scientifically, many experiments have necessitated, at least in the past (i.e. by all estimates, at least one million monkeys died in the race to halt polio. By the early 1960s, when vaccine production was running smoothly, a previously dreaded disease that crippled or killed 20,000 people a year in the USA alone was afflicting a few people per year) the death of the animals, and in many cases a painful one. However we cannot consider scientists murderers. Murder implies taking personal pleasure out of killing someone or something. Researchers do it for a greater cause and whether this justifies it or not, it is the case. If anything, the term sacrifice seems more adapted than murder.

We are going to deal with the ethical aspect of legality. Public opinion is influenced by pictures and stories of researchers who have broken the law and carried out misconduct on animals, but we are not going to discuss this because it simply deals with cases where the law is broken.

True, strict control has not prevented abuse of animals because control and the law are flexible and adaptable. Many laws are vague enough for the scientists to be able to interpret them in a laxest way. Yet many researchers argue that regulations brought in to protect animals' welfare, far from making experiments more ethical for animals, have simply hindered the carrying out of experiments that must go to certain extremes to have the desired result (i.e. the first vaccine for polio necessitated to make animals suffer). Of course, some sort of legal system has to be set up to protect animals as much as is possible. But how can we expect lawyers, judges, politicians, animal associations and public opinion to pass or influence the creation of a law that concerns something they know little about? Couldn't some sort of deontological code set up by the scientists themselves (and maybe ethicists...) provide some sort of ethical conduct for all people carrying out experiments? It seems that the law simply reaches out to people's legal respect (or lack of it) of society, whereas a code really deals with their personal ethic, and is more adapted to the problem. This code could be universally supplemented by ethical committees also mainly constituted of researchers.

As concerns animal experimentation for means such as cleaning products and cosmetics, it seems to be completely beside the point because the law stipulates that all unnecessary experiments are illegal. How do we define necessary? That's up to the ethical committees, or a hypothetical deontological code we talked about above. It goes

without saying that ethical committees judge cleaning products and cosmetics not worth carrying out experiments with animals.

Arguments for animal experimentation

by Stuart Derbyshire

- Animal research has played a major part in the development of medicine, and will continue to do so
- There is no 'middle ground' between animal research and a broader concern with animal welfare
- Scientists who research with animals have made a moral choice - to put human life first

These three sentences are simply points from an article that we agree with because it also points out that if alternative methods are available, they will of course be used. Animals will only be used as long as no other reliable methods are available. There are hundreds of examples of vaccines that were found thanks to animal experimentation in the past. Today with all the regulations on animal welfare this would not be possible. Can we conceive that rabies and polio in everyday life still exist and kill people because animal experimentation does not promote animal welfare?

Isn't saying there should be a middle ground between animal research and animal welfare a hypocritical way of trying to put two incompatible things together? An animal in a laboratory, even if it has food, water, and is under no stress or pain is still not living in natural conditions. We cannot consider this as being welfare. The middle ground we have reached is an absolute absence of pain or stress. Animal welfare cannot be reduced to this.

By the same animal welfare website that gave arguments against animal experimentation:

- Animal testing has helped develop vaccines against diseases, antibiotics, HIV drugs, insulin, anesthetics and cancer treatments
- Operation on animals helped to develop organ transplant and open-heart surgery techniques
- Human life has greater intrinsic value than animal life
- Legislation protects all lab animals from cruelty or mistreatment

Saying that human life has greater intrinsic value than animal life is a subjective matter, it is as debatable as saying that all lives have the same value. There is no unique answer to this debate, points of view differ and we cannot base our arguments for or against the use of animals in experimentation on something that we know has no answer. There is no answer because it depends on the value we give to things, and value is subjective. It's important to point out that researchers don't refuse to give animals a value, but simply give them a different one.

We have already discussed the legislation about lab animals; it is strict but can always be manipulated. This is subject to the ethics of the person or people carrying the experiment out.

Conclusion

It is really hard to reach a consensus as to what should be done about animal experimentation, and to find an ethical justification. In a last case scenario, we would all put our lives before that of animals, that does not however mean that we do not give animals any value, or believe that their welfare should not be taken into account.

Ethically and scientifically, it is in everyone's interest that animals used for experimentation lead as normal lives as possible, and suffer as little as possible. We hope and are confident that alternative methods will one day come to replace the use of most/all animals in testing, and until that time the creation of a deontological code seems to be the safest and best solution. But this can give rise to other debates, such as the hypothetical creation of other such deontological codes for all the people who work or come into contact with animals (i.e. farmers, pet owners, people who work in zoos, circuses, aquatic parks, animal's transporters, etc.).

It is easier to justify the use of animals for experiments when we consider medical research, much less so (if at all) when it comes to cosmetics. This whole debate proves that we give a different value to things, and this is what makes it so difficult.

The sudden recent interest in animal welfare and a particular interest in it in animal experimentation is thankfully contributing to the disappearance of experiments on cosmetics, cleaning products, etc., but it is also hindering necessary experiments that could help science and medicine develop, and forcing researchers to be tempted to go underground and hide their researches even more, which could have disastrous effects on animal welfare.

This work has influenced our opinion in different ways:

Some people of our group with specialized background studies in animal biotechnology, veterinarian medicine and biology had already their own idea about animal experimentation based on the knowledge of the laws and ethical issues to discuss about this subject. The others, with plant biotechnology background or/even veterinarian medicine didn't have a precise idea because they weren't well informed and they didn't have the possibility to explore this topic. Consequently, this IP has been useful for all of us to understand the importance of ethical issues linked with animal experimentation.

In conclusion, we all agree with the animal experimentation for health care and medical research but only when there aren't available alternative methods.

This IP enrich our education, culture and personal development.

Bibliography

-Books

Bioethics in life and environmental sciences, Brumar 2007

-Magazine:

“Vamos continuar a torturer animais?” – Super Interessante Nr. 108, Abril 2007 – Portugal

1) *Animals and ethics – An outline of the main ethical approaches to animals*

Halina Kowalska-Pyłka, Wojciech Cybulski

Faculty of Veterinary Medicine, University of Agriculture, Lublin, Poland

2) *Animal models for experimentation*

Jean-Claude Desfontis

UPSP 5304 Animal Physiopathology and Functional Pharmacology

Department of Biology and Pharmacology

National Veterinary School of Nantes

3) *Animals and Pain. Charles-Henri Malbert*

4) *The regulation of animal research and the emergence of animal ethics: a conceptual history. Bernard E. Rolling. Theoretical Medicine and Bioethics.*

5) *Animal experimentation: Pro and Con arguments using the theory of evolution. Anders Nordgren. Medicine, Health Care and Philosophy.*

6) *EU directive 93/35/CEE (cosmetics)*

7) *EU directive 86/609/CEE (experimentation)*

8) *Decreto Legislativo 24 aprile 1997, n. 126. Gazzetta Ufficiale n. 112 del 16 maggio 1997(cosmetis)*

9) *Legge 12 Ottobre 1993 n. 413. Norme sull'obiezione di coscienza alla sperimentazione animale. Gazzetta ufficiale n. ???*

10) *Decreto legislativo 27 Gennaio 1992 n. 116. Gazzetta ufficiale n. ??? (sperimentazione)*

11) *STOICA-DIACONOVICI C. –ANDI- Prima maimuta modificata genetic. Adevarul 2001, 13 ianuarie, p.11.*

12) *Mihai Decun, Etologia, bunastarea si protectia animalelor. Editura Mirton. Timisoara, 2004.*

13) CIUDIN ELENA – Etica organizarii experientelor pe animale. Revista Romana de Medicina Veterinara, 1997, vol.7 num.4 pag 390-395.

- Sites:

- <http://www.medscape.com/medline/abstract/3469887>
- <http://www.theatlantic.com/doc/192609/dewey-animals>
- <http://www.chicagostudentsciencefair.org/student/stu-rules-anim.htm>
- <http://www.bbc.co.uk/science/hottopics/animalexperiments/index.shtml#Keypoints>
- http://ec.europa.eu/research/biosociety/news_events/news_welfare_survey_en.htm
- http://www.peta.org/mc/factsheet_display.asp?ID=91
- http://caat.jhsph.edu/publications/animal_alternatives/chapter5.htm
- <http://www.spiked-online.com/Articles/000000005547.htm>
- <http://philosophy.tamu.edu-gary/.az>
- http://articles.animalconcerns.org/ar-voices/archive/nozick_constraints.html
- <http://www.animaethics.org.au/reader/arrp-3rs/arrp-replacement.htm>
- http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3469887&dopt=Abstract
- <http://www.scu.edu/ethics/publications/ie/v1n3/cures.html>
- http://altweb.jhsph.edu/publications/journals/atla/34_2/Editorial%2034-2.pdf
- <http://www.morst.govt.nz/wayfinder/regulations/welfare.asp>
- <http://www.spiked-online.com/Articles/000000005547.htm>
- <http://www.inra.fr/internet/Produits/PA/an1999/num995/veissier/iv995.htm>

Annex

Anex

Table 1: pain and stress indicators for laboratory animals (Morton and Griffiths 1985, Brugère & al 1992, Lawrence Podolsky & Lukas 1999)

Activity modifications:

- decreasing of general activity (particularly in nutritional, grooming and motor activities)
- abnormal sleep cycles
- painful activities like licking or mutilation
- exceptions: ingestion of or new born (rodents, rabbit), animal persistently lying in a ball (rodents), head turned towards the back of the cage (rabbit), tail between the legs (dog), members and head folded back (cat), head forwards with arms around the body (monkey)

Vocalizations:

- from acute screams (rabbit, guinea-pig, rodent) to complaining (dog, cat), barking (dog), whistling and panting (cat), and howling (monkey)

Reaction modifications:

- agitation (rabbit: thumping with feet) or on the contrary apathy
- aggressivity or on the contrary tenderness (cat and dog: submission postures)
- anxiety (fear of handling, escape)

Other aspect modifications:

- weight loss
- exceptions: folded ears (cat), grimacing (monkey), abdominal torsion (mouse), penis protrusion and frequent miction (dog)

Motor modifications :

- member removal, jumping, contractions, increase in muscular tonus

Vegetatives modifications :

-circulatory: tachycardia, arterial pressure increase, darkened extremities of members and claws, eyes sunk into the head and pale (rodents), congestion with possible ictericia or cyanosis of the mucosae and non pigmented skin

-respiratory: fast and superficial respiration with growling during expiration, panting (dog)

-eyes and nose secretions (rabbit), anus (cat), glassy eyes (dog), sweating, salivation (dog)

-pilo-erection

-dilatation of the pupil, appearance of the third eyelid (cat)

-skin temperature variations