

Replacement of animal experiments is the ultimate aim

Carol Newman

Animal experiments are the weakest link in the chain of scientific research and discovery. Replacing them would provide substantial benefits for both animals and humans, and must be a priority.

Globally, scientific research uses millions of animals in experiments every year. Humans have always exploited other animals, for food, clothing and other purposes, but having always done something is not a reason to continue to do it. After all, humans have a long history of exploiting both other humans and animals in ways we no longer find acceptable, such as slavery, child labour or bear-baiting.

Today, a growing recognition of the intrinsic value of animal life, coupled with a rejection of the idea that animals exist merely for our own ends, has led people to question the ethics of animal experiments.

Human uniqueness

Our acceptance of human exploitation of other animals is based on the assumption that human beings are special and superior to other life forms. Yet when we try to explicitly define our uniqueness the dividing

ABSTRACT

Ethical concerns about inflicting animal suffering and the scientific limitations of data from animal experiments have fuelled the search for more humane and advanced methods of conducting medical research. There have been notable successes in replacing animal experiments with alternative approaches, such as *in vitro* techniques, computer models and increasingly sophisticated tools for safely investigating humans. The value of alternative approaches has begun to be acknowledged and the potential for future developments in this field remains enormous.

lines become blurred: the more we learn about the abilities of other animals, the less unique we appear. Captive apes have been taught to use sign language; wild chimps and crows design and use tools; dolphins, whales and even fish have culture, passing behavioural traditions on between generations. Why should we value some of our abilities above those of other animals, such as the ability to fly or breathe underwater?

There clearly are differences between humans and other animals, but the only relevant characteristic when making a moral decision on conducting experiments on sentient creatures is the ability to experience pain and suffering.

Pain and suffering

That animals are sentient is recognised by animal welfare legislation across Europe. The main thrust of the ethical argument against animal experiments is that animals, at least vertebrates (possessing a central nervous system and brain), can experience pain and suffering. This is detectable in laboratory animals in terms of their behaviour, levels of stress hormones or brain function (Figures 1 and 2).

Beyond pain, there is also persuasive evidence that animals, in particular mammals and birds, have thoughts, intentions and memories. This means they can be harmed by confinement, frustration, fear, isolation and loss of life – experiences unavoidable for animals confined in laboratories and used in experiments.



Figure 1 We know that animals can suffer in ways similar to ourselves. (Photo, BUAV.)



Figure 2 The fact that many animals used in experiments are rodents does not diminish the suffering involved.

The fact that animals do experience pain and suffering in many ways similar to humans, is the very reason why they are subjected to experiments to

investigate pain, anxiety and depression, and to test painkilling drugs. UK legislation requires animal suffering in experiments to be kept to a minimum, but does not prohibit it. Indeed the very definition of an animal experiment in the Animals (Scientific Procedures) Act 1986 is a scientific procedure conducted on an animal '*that is likely to cause pain, suffering, distress or lasting harm*'. Animals certainly *do* suffer in experiments, sometimes substantially. Examples of severe procedures liable to cause substantial suffering to the animals involved include: acute lethal toxicity tests in which a proportion of animals are poisoned to death by the test substance; potency testing of *botulinum* toxin in which mice may suffer paralysis and death from suffocation; brain-damaging monkeys to induce tremors, rigidity, compulsive behaviour, and other symptoms as a model of Parkinson's disease.

For the greater good?

The justification used for inflicting suffering on animals in scientific experiments is that it will benefit humans. However, taken to its logical conclusion, this could also justify the use of a few vulnerable non-consenting humans in experiments for the potential benefit of the rest of humankind. Indeed, such human experiments have taken place in the not too distant past on subjects who were black, Jewish, orphans, prisoners or soldiers.

Under UK law, animal experiments should only be permissible if the benefit to humans is likely to outweigh the cost to the animals involved. The reality is that these assessments are relative and subjective. It is difficult to accurately quantify the degree of suffering experienced by an animal, or assess the potential benefit to humans of an experiment the outcome of which is unknown. The cost paid by most animals in experiments is ultimately their lives, whilst the benefits to humans may be some basic biological knowledge, a new medicine, or a new household cleaner or food additive.

It is disingenuous to claim that every medical breakthrough is the result of animal experiments. Animals are routinely used as a standard research methodology; it therefore follows that most advances will have *involved* animals at some stage but not that they were *dependent* upon them. Only advances that manage to clear the hurdle of animal testing reach us, but what of those that falter at animal tests? There is no way to identify how many useful avenues of

research or potential new therapies have been abandoned due to negative findings in animals.

Predictive value of animal experiments

There are serious scientific limitations to data from animal experiments, so that extreme caution is needed when attempting to extrapolate results from animals to humans.

This is partly due to differences between species that occur in anatomy, metabolism, and physiology, from organs right down to the cellular and molecular level. Even when specific differences are known and can be taken into account, there will always be unpredictable differences, for example in responses to a new drug (Figure 3).

Another major limitation of animal research is the artificiality of 'animal models' used to study human diseases. These involve inducing symptoms of a human illness in an animal, as a model of the condition. For example, a classic animal model of stroke involves injecting tiny beads into the blood stream to form a 'clot'; high blood pressure is induced in animals by clamping an artery; and irritant chemicals are injected into joints and paws to cause inflammation that mimics arthritis. The relevance of these animal models to the human conditions is questionable, as they do not accurately replicate the human disease or the underlying causes of it.

It is often just assumed that animal models are valid and relevant, despite a lack of evidence for this. Surprisingly few objective reviews of the validity of animal experiments have been carried out. Two recent independent and authoritative reports on animal research by The Animal Procedures Committee (2003) and The Nuffield Council on Bioethics (2005) have

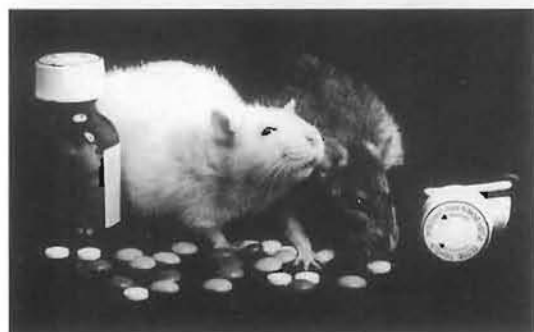


Figure 3 Species differences can be unpredictable. (Photo, BUAV.)

highlighted the outstanding need for a detailed critical evaluation of animal experiments on a case-by-case basis.

For some conditions where little progress has been made, in spite of decades of animal experiments, the conclusion must be that the animal models are failing to elucidate the human condition, and may even have obscured our understanding of it. For example, a recent in-depth review of multiple sclerosis (MS) research concluded that the acceptance of the animal model, known as EAE (Experimental Allergic Encephalitis) is based on faith rather than science. Therapies devised on findings in animals with EAE have consistently failed in humans with MS (Behan and Roep, 2002). Stroke has been modelled in animals for over 150 years, yet of some 49 promising neuro-protective drugs that have been trialled in patients, none has proved effective in treating human stroke (Gladstone and Hakim, 2002).

All new medicines undergo a barrage of animal testing, yet some 40 per cent of investigational drugs subsequently fail in clinical trials (Lappin and Garner 2003). The poor predictive power of animal testing results in a massive waste of animal lives, as well as time and money for the drug industry.

With animal experiments providing such unreliable and potentially confusing results, we need to find a better way – a more humane and scientific method of conducting medical research.

A better way – the rise of alternatives to animal experiments

In 1970 the Dr Hadwen Trust for Humane Research was established with the aim of developing superior research methods that could replace animal experiments. The Trust was named in honour of a prominent early anti-vivisectionist and general practitioner, Dr Walter Hadwen (1854–1932) (Figure 4).

Undeterred by nay-sayers who pronounced it impossible to replace animal experiments, the Dr Hadwen Trust funded many pioneering projects that have since borne fruit. These included the first-ever research into replacing the Draize eye test – in which chemicals are tested for irritancy by dripping them into the eyes of rabbits immobilised in stocks – which led to the development of a test-tube method now widely used in place of rabbits, and saving them from untold suffering (Figure 5). Other recent notable successes for the Trust have included developments in brain-scanning and imaging technology, enabling

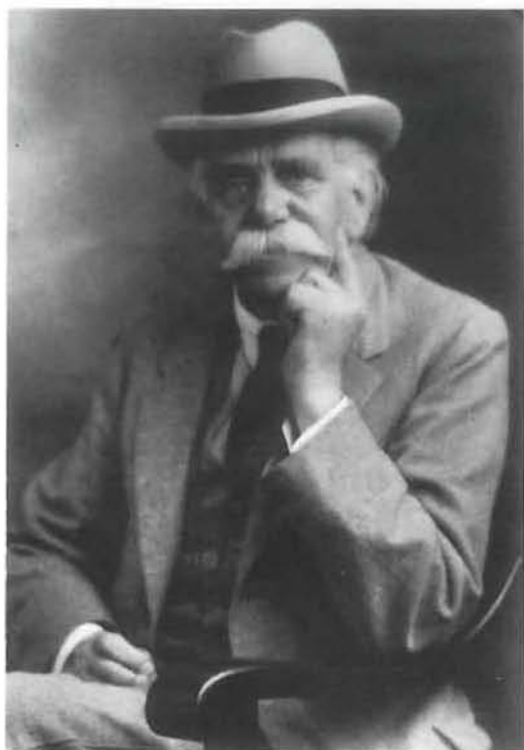


Figure 4 Dr Walter Hadwen, a pioneering anti-vivisectionist.

safe, non-invasive brain research directly in humans, in place of invasive experiments on animals (Harding, 1997) (Figure 6). Trust projects have harnessed powerful computing methodology to model complex biological systems and ask questions that would once have been investigated in living animals in areas as diverse as research into cancer, dentistry, epilepsy and safer pregnancies (Talbert and Johnson, 2000) (Figure 7). A recent project demonstrated how laser technology can identify infectious strains of bacteria, in place of animal tests (Shah, Keys, Schmid and Gharbia, 2002).



Figure 5 Eye irritation testing on rabbits has now largely been replaced by *in vitro* methods.



Figure 6 A volunteer participates in research with the MEG brain-scanner at Aston University. (Photo, G. Barnes.)



Figure 7 A computer model of stresses in a human tooth used for orthodontic research. (Photo, J. Middleton.)

The drug industry has been quick to adopt some alternative approaches, using computers to design, model and predict likely actions of new chemical entities in the human body, replacing the old hit-or-miss early screening in animals (Figure 8). *In vitro* methods have also made a big impact on the numbers of animals used in producing and testing biological medicines and vaccines.

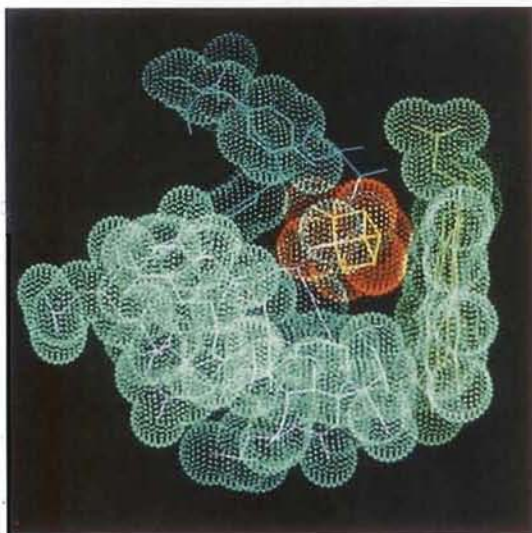


Figure 8 Computer modelling of the active site of cytochrome P450, a key liver enzyme, to predict drug and chemical metabolism. (Photo, D. Lewis.)

The figures speak for themselves. In areas of animal experimentation where alternatives have been developed and implemented, the use of animals has fallen, in some cases dramatically. A good example of this is the production of monoclonal antibodies (MAbs), which are extensively used in medical and scientific research, in diagnostic tests, and as new therapies. These were produced in large numbers by a process that involved inducing painful abdominal tumours in mice and rats; some 46 000 animals were used for this purpose in 1990 in the UK, and thousands more worldwide. Methods of culturing MAbs in laboratory flasks were developed, and, with the stimulus of some lobbying by animal protection groups, culture methods have now effectively replaced this use of animals (Figure 9). By 2003 no animals were used in this way in the UK (Home Office, 2004). A few immunised animals continue to be killed to provide cells to initiate new MAb-producing cultures; however, research is underway to eliminate even this



Figure 9 The 'Harvest Mouse' for culturing monoclonal antibodies in a laboratory flask, instead of in living animals. (Photo, TCS.)

use of animals. Several research groups are now working on ways to produce synthetic antibodies, entirely free of animal involvement and equally effective. At one time, replacing animal-sourced MAbs may have seemed like wishful thinking – but not now.

Animal experiments have roughly halved since 1971, a fall which has been generally attributed to the use of alternative methods (Figure 10). In recent years this downward trend has faltered due to the emergence of genetic engineering techniques, which are now being exploited to the full in laboratory animals, often in experiments driven more by scientific curiosity than medical relevance. However, other areas of animal use continue to fall, as more advanced research methods become available.

The way ahead

Replacement of animal experiments is no longer viewed as a 'crank' or fringe scientific endeavour in the way it was 35 years ago when the Dr Hadwen Trust was born. Alternatives have entered mainstream scientific thinking and their use in preference to animal experiments is enshrined in UK and European law.



Figure 10 *In vitro* methods have had a major impact on the numbers of animals used in research and testing. (Photo, ARS.)

Official recognition of the importance of alternatives to animals has at last been reflected in recent years by the initiation of awards for this purpose by several national funding bodies, and the establish-

ment in 2004 of a UK Government-backed National Centre for the Replacement, Reduction and Refinement of Animal Experiments. The Centre's mission statement recognises replacement of animal experiments as its ultimate aim (see Robinson, 2005).

Proponents of animal experiments claim that animals form a small but vital link between laboratory research and the patient, which cannot be replaced. When this link is both ethically and scientifically weak then every effort should be made to replace it with something better.

Are animal experiments really the best we can do? We don't think so. Science is synonymous with progress. Scientists help to bring about change and make advances possible. Claiming we will never replace animal experiments is equivalent to claiming we will never understand our universe, or we will never cure disease – it is to resist, rather than participate in, scientific discovery and progress. Why limit ourselves by such a short-sighted philosophy?

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Further information

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