Why do we still use animals in medical research?

Ted Griffiths

Understanding gene function is just one of the reasons why we still need some research using animals today

The British love of animals has long ensured that the care and welfare of animals has been a preoccupation for many. Any activity that may cause distress or suffering for animals is bound to attract column inches in the press. The use of animals in biomedical research in particular has always attracted media and public interest and opprobrium disproportionate to the numbers of animals used. We kill and consume some 800 million animals for food every year in the UK and destroy another 8 million as vermin compared to fewer than 2.8 million used in research and testing.

This preoccupation with animal welfare is reflected in our legislation and the UK was the first country to enact legislation to protect animals used in experiments. Under the 1876 Cruelty to Animals Act any person carrying out painful experiments on animals without the use of an anaesthetic was liable to punishment by fines or imprisonment.

Even 100 years ago public feelings were running high on the issue of animal experimentation. In 1903 the antivivisectionist, the Hon. Stephen Coleridge, accused the distinguished physiologist, Dr William Bayliss of University College London, of cruelty to a dog that had been operated on in front of an audience of students. Bayliss sued for libel and was awarded £2000, a considerable sum in 1903. A public fund-raising campaign to pay Coleridge’s costs raised double the required amount and antivivisectionists used the excess funds to raise a statue to the brown dog that was experimented on. The case led to riots on the streets of London and medical students destroyed the original statue, but a replacement bronze can still be found in Battersea Park.

The use of any animal for any purpose carries a moral responsibility to weigh carefully the benefit that may accrue, against the distress or suffering that the animal may experience. It is worth spending some time reflecting on some of the enormous benefits that biomedical research has already given us, both in increasing our longevity and improving the quality of our lives.

The benefits gained from biomedical research

Currently some 1.8 million people in the UK have been diagnosed with diabetes, an increase of 400 000 in eight years. About 330 000 inject themselves with human insulin produced by genetically modified bacteria. Others manage their condition by modifying their diets and lifestyles but many of these will also eventually become dependent on insulin. It is thought that in addition as many as 750 000 people suffer from undiagnosed diabetes. Without the pioneering work of Fred Banting and Charles Best in the early 1920s using dogs, first to confirm the involvement of the pancreas in the control of blood sugar levels and then to demonstrate the role of insulin in this process, many more, perhaps millions more, patients would have died of this dreadful and increasingly common disease. We

ABSTRACT

Animal research has undoubtedly helped bring about huge medical benefits, but it remains a matter of concern. From understanding diabetes to working out the role of genes, animal studies have a part to play. Not only are they important in delivering medical benefits, but also in understanding the basics from which applied advances emerge.
still cannot cure diabetes; we can only manage the
disease. Research using stem cells may provide a
longer-term solution to this problem but research to
establish this will also require animal studies.

Those of us in our late fifties will remember the
horror with which our parents would greet outbreaks
of poliomyelitis. Polio left youngsters condemned to
spend the rest of their lives in an iron lung after the
virus had ravaged their nervous system and left them
unable to breathe unassisted. Many more were left
crippled for life by this terrible disease, which was
called infantile paralysis because its primary victims
were young children.

The vaccines to protect children against this
disease were developed in the 1940s and 1950s using
monkeys as the most appropriate animal to develop
and test the vaccine. The poliomyelitis virus has the
ability to revert from the attenuated (weakened) form
used in the vaccine back into the virulent form, so
each batch of vaccine produced must still be safety-
tested before use. The only test currently available
that is acceptable to the regulatory authorities is to
inject a sample of the vaccine into the spinal fluid of
a primate. So even now, 50 years on from the first use
of the polio vaccine, monkeys are still playing a key
role in the protection of our children. However,
alternatives are on the horizon.

The use of primates in biomedical research and
testing is perhaps the most controversial area of
animal-based research and scientists are continually
striving to find alternative methods to carry out their
research and meet regulatory safety requirements.
They have developed a transgenic (genetically modified) mouse to replace primates in safety testing
of oral polio vaccines and this methodology is now
awaiting regulatory approval.

In the developed world at least, we now live free
from the threat of infectious diseases such as smallpox,
polio, measles and whooping cough, thanks to
effective and safe vaccines, the production of which
required extensive animal-based research and testing.
The surgical procedures, which we now view as
routine, such as open-heart surgery and organ
transplants, were all developed using animals, as were
the immunosuppressant drugs used to prevent
rejection of transplanted organs.

Animal research and testing played a key role in
the development and testing of anaesthetics,
anti-biotics and the myriad of drugs we have available
to control diseases such as asthma and high blood
pressure that afflict millions of people in the UK.

The knowledge gap

Why then, given the enormous gains in our biological
knowledge (it is thought to double every 18 months),
do we need to continue to use animals? The simple
answer is that there are still enormous gaps in our
knowledge and understanding of how complex
biological systems work, reproduce, interact and are
controlled. Indeed, many of the questions we thought
we were close to answering are proving to be increas-
ingly complex.

An indication of the extent of this knowledge gap
can be gleaned from the work on the human genome.
Originally there were thought to be some 100 000
genes in the human genome, although recent estimates
tend to reduce their number to around 30 000. What
the human genome project doesn’t tell us, and what
we really need to know, is: what is the function of
each of our 30 000-plus genes and which genes might
be implicated in causing disease?

Studies on mutations in, and functions of, genes
have so far only taken place on about 10 per cent of
known genes, about 3000 of the 30 000 genes we
know to exist. The complexity of the functioning of
these genes is now becoming more apparent.

To answer these crucial questions, research
workers are making increasing use of genetically
modified (GM) animals, particularly mice. The
sequencing of the mouse genome has shown that
nearly all human genes have mouse equivalents.
Studying how genes work in mice is often the most
effective way of discovering their role in human health
and disease. Mice reproduce quickly, are small and
easy to handle, and their genes can be manipulated
very precisely at the molecular level. These attributes
have made the GM mouse an extremely valuable way
of studying human diseases.

Before this technology was available, scientists
studying a disease would try to find an animal with
an equivalent disease or try to mimic some aspects of
the disease in an animal by using drugs or surgery.
Now, with recent advances in gene technology, it is
possible to change genes in the mouse or introduce
human disease-causing genes and so provide a much
better way to study human conditions. Examples
include mice with a predisposition to various cancers
and mice that develop aspects of Alzheimer’s disease
and cystic fibrosis.

Media and hence public attention has focused on
the use of larger animals, with Dolly the sheep being
the best-known research animal celebrity. These larger
animals are rarely used to mimic human diseases but are becoming increasingly important in the production of medicines. Inserting copies of human genes for medically important proteins into sheep, goats and cattle has made it possible to produce medicines that are difficult or impossible to produce by other means. Here in the UK we have GM sheep that produce the protein alpha-1-antitrypsin, which will hopefully be used to treat lung disorders associated with emphysema and cystic fibrosis, and sheep that produce human blood-clotting factors for the treatment of haemophiliacs.

Justifying curiosity-driven research

Opinion polls and public dialogue tell us that where a clearly identifiable medical benefit can be seen as a goal then there is widespread public support for animal-based research and testing. But what about ‘blue sky’, curiosity-driven research that takes place mostly in our university and research council laboratories? How can we justify using animals in these research programmes? Many scientists and scientific philosophers would argue that the pursuit of knowledge for its own sake justifies the responsible and humane use of animals in research. Biomedical research history is littered with examples where curiosity-driven research, some of it using animals, has led to huge increases in our understanding of both the functioning and malfunctioning of biological systems and ultimately to benefits to patients.

The list of Nobel Prizes awarded for medicine and physiology is a rich source of examples where such fundamental research has resulted in significant advances (see www.nobelprize.org).

The late Sir John Vane shared the Nobel Prize for Medicine in 1982 for discovering that aspirin worked by inhibiting the generation of prostaglandins. This discovery provided the key to understanding the action of many other anti-inflammatories. Although Vane is most famed for his work on aspirin, his research was

![Figure 1](image-url) Numbers of animals used in biomedical research (HMSO, 2003).
of key importance in the development of medicines currently used in the treatment of hypertension. His work contributed hugely to some of the most frequently used medicines. Sir John Vane’s studies often used laboratory animals and because of this he became a target for animal-rights extremists and was subjected to firebomb and graffiti attacks at his home. Despite this he remained a staunch public advocate and defender of the responsible use of animals in scientific research.

The latest Nobel Prize to be awarded in physiology or medicine was to Richard Axel and Linda Buck for elucidating how we and other animals recognise and remember about 10 000 different odours. In their work on the olfactory system of the mouse they discovered a large family of 1000 genes, about 3 per cent of known genes, that coded for olfactory receptor sites. The principles that Axel and Buck discovered for the olfactory system appear to apply to other sensory systems, such as the detection of pheromones and the sensation of taste. The importance of this research alone would justify the use of the mice but this work may well have far-reaching implications for medical research. We can only speculate where this work will lead but any additional information we can gain about the workings of the nervous system may well lead to insights into normal and pathological conditions of the nervous system such as Alzheimer’s and Parkinson’s diseases.

Two-thirds of the Nobel Prizes for physiology or medicine awarded in the past 100 years have been for discoveries based on animal-based research. In a survey of living Nobel Laureates carried out by the patients’ advocacy group, Seriously Ill for Medical Research, all the Laureates who responded agreed with the statement ‘Animal experiments are still crucial to the investigation and development of many medical treatments’. (See SIMR website.)

The number of animals used annually now seems to have stabilised at around 2.8 million. The remarkable feature contained in the statistics is that, while the number of genetically normal animals used continues to decline, there has been a rapid increase in the number of genetically modified animals. These, together with animals with naturally occurring genetic defects, made up 37 per cent of all procedures (experiments) in 2003, indicating the importance of these animals, overwhelmingly mice, in biomedical research.

What types of animals are used?

About 85 per cent of the animals used in research are rodents, mostly mice and rats (Figure 2). With the continuing increase in the use of transgenic mice this percentage is likely to continue to rise. Just over 10 per cent of animal procedures are carried out using fish, reptiles, amphibians and birds, including many fertilised hen’s eggs. The animals most often associated with scientific research and which receive most public and media attention, monkeys, cats and dogs, together account for less than 0.5 per cent of the animals used. In 2003, 40 per cent of the scientific procedures involving animals took place in our universities while 36 per cent were conducted by commercial organisations such as pharmaceutical companies and contract research companies.

How many animals are used?

We can see from Figure 1 that the number of animals used in biomedical research and testing in the UK has halved in the last 30 years. Given the explosion in bioscience research that has taken place over that period this is a remarkable achievement and testimony to the success of the scientific community in implementing the 3Rs (replacement, refinement, reduction – see Robinson, 2005, this issue).

Figure 2 Types of animals used in research and testing (HMSO, 2003).
Scientists are continually striving to develop research methodologies to reduce, or better still, replace the use of animals. No one wants to use animals in research if it is not necessary. Alternative techniques are often more reproducible, more cost effective and ethically more acceptable than those using animals. However, for the foreseeable future we will continue to need to use animals in the research process. We still face many medical challenges and new diseases such as nvCJD, SARS and HIV are bound to arise in the complex and dynamic biological system that is the human body.

References

Website

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