Clive Hollands Memorial Lecture  
given by Dr Gill Langley  
Science Director of the Dr Hadwen Trust for Humane Research  

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Replacing Animal Experiments:  
Highlights and Headlines 1979 – 2009  

Introduction  
It’s great to have the opportunity to give the Clive Hollands Memorial Lecture here in Edinburgh.  

I first met Clive when he was the Director of Advocates for Animals, in 1979. We worked together for many years, so it seemed a good idea – in this review of the highlights and headlines of replacing animal experiments – to start with 1979 and look at the last 30 years of success stories, with a glimpse ahead one year into the future – to 2009.  

The Dr Hadwen Trust for Humane Research is Britain’s leading medical research charity funding exclusively non-animal research techniques to replace animal experiments, with the aims of benefiting people and animals. The Trust was established in 1970 on ethical anti-vivisection principles, so over the years we’ve contributed to and witnessed the fantastic achievements of the worldwide initiative to replace the use of animals in medical research and testing.  

Public concern about animal experiments has a very long history - centuries long! - and has intensified in recent years. Governments have struggled to find animal research policies that satisfy the concerned general public and the scientific community.
The basis of ethical concern about experiments on animals is their shared ability to feel pain and distress and experience harm. There’s no doubt at all that other animals, from monkeys to octopus, can experience “pain, distress, suffering and lasting harm”, as British law puts it. Since 1986, both our law and the European Union law require that animal experiments must be replaced by alternatives where these exist:

Animals are used in laboratories for many purposes, including to research and understand human medical conditions, to develop medicines to treat them, and in tests that aim to ensure that products including medicines, but also pesticides, household chemicals and food additives, are safe for us to use.

In all these experiments, the intention is that animals stand in for humans as surrogates, since it obviously wouldn’t be ethical for painful and distressing research and testing to be conducted on people.

But there are many problems with animal experiments.

Firstly, they undoubtedly cause considerable pain and suffering to many animals – the law permits “substantial suffering” to be inflicted if it’s considered necessary. Scientists researching fear, anxiety, stress and depression use mice and rats in place of humans, and discuss in the scientific journals which breed of mouse is the most emotional.

So we can’t kid ourselves that animals don’t suffer like us.

But there’s a second very important problem with animal experiments: it’s become clear over the last several years that they can’t be relied on to predict what will happen in humans.

It’s often claimed by scientists that medical progress has been dependent on animal experiments.

For example, the Royal Society says:
“We have all benefited immensely from scientific research involving animals. From antibiotics and insulin to blood transfusions and treatments for cancer or HIV, *virtually every medical achievement in the past century has depended directly or indirectly on research on animals*.”

The animal protection movement has always challenged those statements, but now scientists themselves are starting to question them. A 2008 article in the Journal of the Royal Society of Medicine addressed this precise claim and said of it:

“...it is far from clear that this statement has been, or even could be, formally validated. ...it is not possible to go beyond [these] anecdotal examples to the altogether more impressive statement now being promoted by various prestigious academic bodies and individuals.”

In the last year or two there have been a number of reviews of animal studies. The evidence suggests that their results have not reliably translated into expected human benefits. For example, a review published in 2007 in the British Medical Journal examined 221 experiments using over 7,100 animals in research into six different treatments for human illnesses. The researchers criticised the quality of the animal research and found that for three of the six treatments, the animal experiments completely failed to predict human outcomes.

According to the world’s largest medicines regulatory agency, the US Food and Drug Administration (FDA), currently, 92% of new medicines passing animal tests ultimately fail in humans, wasting time and money and putting the health of clinical trial volunteers at risk. The FDA is championing the rapid implementation of novel methods, many of them non-animal, to improve the drug development process.

Those are two good reasons why animal experiments should be replaced: because they cause an estimated 115 million animals to suffer every year in the world’s
laboratories, and because they can’t be relied on to tell us what doctors think they can.

Medical science desperately needs a solution – and the Dr Hadwen Trust and Advocates for Animals believe there is one. That is, to increase progress in replacing often outdated animal experiments with modern and advanced non-animal research techniques.

**What are replacement methods?**

What do I mean by replacement methods? They’re research or testing techniques that don’t use living non-human animals. Going from the smallest to the largest, they include:

- Molecular techniques, studying the basis of health and disease at the sub-microscopic level
- Cell-based experiments using donated human cells or tissues in the test tube
- Computer models and simulations that allow ‘virtual’ experiments
- Super-sensitive analytical techniques that can measure important substances in tiny amounts of donated blood or tissue
- Research using post-mortem tissues donated by patients after their death
- Safe volunteer studies of healthy people and patients, and
- Population-level research, to learn about the inheritability of illnesses.

**Replacement achievements**

Many animal experiments have already been replaced by non-animal alternatives. To some extent it’s been a natural process over the last 50 years, as scientists have realised that a new technology or method can provide better results than a long-standing animal test.
In the 35 years from 1971 to 1996, the number of animal experiments in Britain, and in many other countries, reduced by about a half: in our case from 5.5 million to 2.7 million annually. It’s widely agreed that the biggest contribution to that fall in numbers was due to the replacement of animals by test-tube and other non-animal methods.

In the time period I’m reviewing, from 1979 onwards, there’s been a series of success stories that collectively have saved many millions of animals from the laboratory and advanced medicine progress and improved the safety of all of us.

Firstly let’s look at how animals have been replaced in the testing of new medicines and chemicals. Progress in these areas has been really good. Numerous replacement techniques have been successfully validated and approved and have made real contributions to improving human health too.

**Testing chemicals and medicines**

**Late 1970s**

In the manufacture and quality control of vaccines and biological medicines, hundreds of thousands of animals worldwide have been spared by the introduction of cell-based methods.

An example is the potency testing of yellow fever vaccine – each batch of the vaccine has to be tested to ensure it’s a standard strength. The original test, introduced in the 1950s, involved injecting yellow fever virus into the brains of mice and counting how many died as a result. This lethal dose method was never very satisfactory.
In the late 1970s, a cell culture test was found to be more practical, sensitive and reliable. Since its introduction, an estimated 1,500 mice each year have been saved – a cumulative total of about 45,000 to date.

Into the 1980s
Techniques that measure the chemical or physical properties of substances have been introduced as quality control tests for biological medicines. These techniques rejoice in names such as colorimetric assays and high-performance liquid chromatography.

An example is digitalis, a heart medicine derived from foxgloves that used to be routinely tested for its strength on pigeons and guinea pigs, by a lethal method involving intravenous injections.

In the late 1980s, guinea pigs were replaced by a chemical colorimetric assay which directly measured the strength of digitalis by means of a colour-change method.

In 1990
For many years, every batch of insulin was tested on 600 mice in a test called the mouse convulsion method. First, the numbers of mice used were reduced, and then in 1990 they were entirely replaced with high-performance liquid chromatography. This is a more precise technique so that, as in all my examples, people’s health was better protected when animal experiments were replaced.

Fast forward to 2003
In Britain, 17,000 animals a year were once used as living bioreactors in painful procedures to produce monoclonal antibodies. These are medical proteins important in research, in diagnosis, and as treatments.
The production process involved injecting cancer cells into animals’ abdomens. The resulting large tumours were regularly tapped by needle to harvest the antibodies. Since 2003, all 17,000 animals a year have been replaced with cell cultures – a cumulative total of about 85,000 animals have been saved since then.

2004 was a good year.
Mice used to be used in tests to detect whether medicines or chemicals are likely to cause a skin reaction in people when they’re exposed to sunlight. In 2004, a cell-based test was approved internationally that entirely avoids tests on mice.

Also in 2004, test-tube methods were approved for testing whether chemicals can cause corrosive burns if they splash on your skin. The new tests use tiny human skin fragments or artificial skin membranes, and they’ve replaced severe skin burning tests on rabbits.

When predicting the safety of chemicals, pesticides and some medicines, it's important to know whether they can be absorbed through the skin and into the bloodstream.

This used to be tested on mice and rats, but now, isolated discs of donated human skin can be used instead – removing any worries about whether animal skin reacts in the same way as human skin.

In 2007 – nearly up to date now! – two tests were approved that use human skin surrogates as replacements for skin irritation experiments on rabbits.

Another replacement success last year related to injectable medicines. Injected medicines must be tested for bacterial toxins to exclude the possibility of bacterial contamination. The original test, introduced in the 1940s, measured a fever response by a rectal probe in rabbits restrained in stocks. Some animals suffered
fever, breathing problems, organ failure or fatal shock. The test was also insensitive, time-consuming and costly.

In 2007, new tests based on human blood cells in the test tube became available.

The new methods are more sensitive, more accurate, quicker and more cost-effective than the rabbit tests they’re replacing. The European Commission estimates that more than 200 laboratories are already implementing the new methods, which will replace some 200,000 rabbit tests a year in Europe alone.

Medical research

My second group of successes is in the field of medical research – that is, research to understand human diseases, rather than product testing. Progress in replacing animals in medical research has been slower than in product safety testing, but there have certainly been some great highlights.

These three examples are from the fields of computer simulations, public health, and neurological research. Some of these are drawn from the Dr Hadwen Trust’s own success stories.

Computer simulations

A 1995 grant from the Dr Hadwen Trust supported the development of computer models of problems in human pregnancy. Based on human data, the simulations replaced experiments on sheep.

The computer simulations were first used to explain, for the first time ever, a blood flow abnormality that appears in pregnant women who are at risk of pre-eclampsia.

Then the simulations were used to help women pregnant with identical twins who develop a condition that can cause the death of one or both twins while in the womb.
The step forward was because the computer models enabled doctors to create a new clinical scoring system for the likely severity of the condition.

The computer models continue to be improved and to yield important medical insights including the effectiveness of new therapies.

Another example of computer simulations is research at Oxford University developing virtual models of the heart. The simulations have already been used to make surprising findings about the time limit for shocking a heart back to normal rhythm after a heart attack – something that might otherwise have involved experiments on dogs.

Public health
A Dr Hadwen Trust grant was awarded to the national Health Protection Agency a few years ago. The aim was to develop a technology called MALDI-TOF-MS to identify disease-causing bacteria, as a replacement for animal tests.

MALDI-TOF-MS is an example of a molecular level replacement method. It uses lasers to produce a unique molecular fingerprint of different microbes, so that the precise strain of bacteria causing diseases, such as dysentery, can be identified.

The technique is replacing laboratory animals such as guinea pigs. It’s simple, fast and cost-effective and is providing better methods for disease control. The Health Protection Agency uses fewer animals as a result.

Neurological research
Non-invasive studies of volunteers in brain research using novel imaging techniques have replaced many experiments on animals, notably primates.

For example, magnetoencephalography (MEG) identifies active regions of the brain by measuring tiny magnetic fields. MEG can be combined with other imaging
technologies to produce a clearer understanding of how the brain functions in epilepsy, stroke and other neurological conditions, in volunteers.

When the technology was so new that there were only two experimental MEG machines in the whole country, the Dr Hadwen Trust recognised its potential to replace animal experiments, and funded research to develop and validate it.

We’ve done likewise for other imaging and related methods, and we continue to fund novel developments in this area. These developments have had a real impact on medical understanding of serious neurological disorders such as vision, epilepsy and chronic pain.

Into 2009 and beyond

What does the future hold? I wish I had a crystal ball, but I’ve only really committed myself to looking ahead to 2009.

Already it’s widely accepted that non-animal methods are advanced techniques that can be quicker, more reliable, more versatile and sensitive, more cost-effective and more efficient than animal research.

For example, when the British government launched the National Centre for the Replacement, Reduction and Refinement of animals in research, it said that, “...alternative methods are often, in reality, ‘advanced’ methods broadening the scope and overcoming some of the limitations of existing animal models.”

The European Union Commissioner for Science and Research, in charge of all European level research, explained that “We are striving for a more humane science… which avoids and reduces the suffering of experimental science. Remarkably, this area is also at the forefront with regard to safeguarding the quality of science.”
The EU is already funding more than 14 major research projects aimed at replacing chemical and drug tests on animals, by developing non-animal techniques based on computers, cell cultures and molecular studies.

In the next year or two many of these projects will come to fruition, and they’re expected to have a big impact on replacing animal tests for chemicals, cosmetics ingredients and medicines.

In Europe, the pharmaceutical industry has just committed itself to revolutionising the way that new medicines are developed and tested, so that bottle necks can be eased and medicines brought more quickly and safely to the patients who need them.

The industry has acknowledged that many of the bottle necks are due to weaknesses in the animal tests, and they support moves towards more test tube and computer research methods. This is a big step forward that will certainly bring more progress in the next few years.

**Round-up**

But succeeding in replacing animal experiments isn’t just about new technology. There needs to be a culture change, in the scientific community as well as politically.

In a few years time, all animal tests for cosmetics will be banned by law throughout Europe. That’s a direct result of the strength of public concern, expressed by people making careful purchasing choices but also because they put sustained pressure on their MPs and MEPs. These are our representatives, in parliament, whose views and votes will influence government priorities – for example, to get governments to commit to a targeted strategy to replace animal experiments.
This is the potential win/win solution, for people and animals, that we can all support and help to make happen.