SCIENCE WITHOUT SUFFERING

A REPORT BY THE DR HADWEN TRUST FOR HUMANE RESEARCH
The Dr Hadwen Trust is the UK’s leading medical research charity that funds and promotes exclusively non-animal techniques to replace animal experiments. Our vital work benefits humans, with the development of more relevant and reliable science, whilst also benefiting laboratory animals. We believe that excellence in medical research can and should be pursued without animal experiments.

Our portfolio of high-quality, peer-reviewed and innovative research combines strict ethical principles with scientific excellence, and has involved projects in a range of fields including epilepsy, cancer, meningitis, asthma, diabetes, drug testing, arthritis, Alzheimer’s disease, lung injury, whooping cough, vaccine testing, dentistry, heart disease, tropical illness, fetal development and pregnancy, brain tumours and AIDS. The Dr Hadwen Trust is internationally recognised as a leading authority on replacing animal experiments and actively promotes the concept and practice of non-animal research through publications, workshops, debates and the media.
In Britain, nearly 3 million animal experiments are conducted every year using 2.8 million individual animals. Species such as cats, dogs, rabbits, hamsters, mice, monkeys and sheep may be force-fed poisons or injected with harmful substances, infected with lethal viruses, subjected to brain damage, heart attacks, stroke or cancer; and are ultimately killed.

The government and the animal research industry often reassure a concerned public that in Britain animal experiments are tightly controlled and that animal suffering is kept to an absolute minimum. This is misleading – the truth is that current legislation still permits animals in laboratories to endure high levels of physical as well as psychological suffering. Indeed, an animal procedure in this country only requires a licence if the Home Office itself assesses that it is likely to cause "pain, suffering, distress or lasting harm". In some experiments, the level of suffering endured is very high indeed. We believe that if the public was aware of just how much suffering animals in laboratories are allowed to experience, they would be extremely alarmed.

As well as causing pain and suffering, animal experiments are scientifically unsatisfactory because differences between humans and animals can give rise to misleading results.

This review contains six recent examples of British animal experiments typical of those involving high levels of animal suffering – the reality of life for these animals will contrast markedly with the all too often sanitized and palatable version of ‘animal use’ that the research industry would have us believe is the norm. These examples include deliberately brain damaging non-human primates, inducing heart failure in mice and subjecting guinea pigs to lethal infectious disease.

For each example, a compelling case can be made against the scientific justification of animal use. Additionally, more relevant non-animal research approaches could be available. The Dr Hadwen Trust believes that animal experiments have significant limitations which are of particular concern given the degree of confidence that is generally placed in them, invariably without proof of validity. Species differences in anatomy, metabolism, physiology or pharmacology inevitably will arise, underlain by further species-specific genetic variations. Even subtle molecular differences can have a significant effect on the validity of results for extrapolation from animals to humans.

In addition, the Dr Hadwen Trust believes that if the government applied the relevant UK legislation correctly, experiments such as these that involve significant suffering and dubious scientific validity, should never have been licensed at all. Section 5(4) of the Animals (Scientific Procedures) Act 1986 contains what is commonly referred to as the ‘cost/benefit test’. This means that before a licence is granted to perform an animal experiment, consideration should be given as to whether the likely perceived benefit of conducting the research is outweighed by the animal suffering it would cause.

Whilst the Dr Hadwen Trust does not support this utilitarian approach to the ethics of animal experimentation, for as long as it is in place and trumpeted by the government and the animal research industry alike as offering so-called ‘protection’ to animals, we believe it should be applied fairly and rigorously so as to have some meaning. One of the major weaknesses of this system is that, because the species assumed to potentially benefit from experiments is the same species making the judgements (ie: people), the current threshold for potential benefit is unreasonably low, such that animal suffering is perceived to be outweighed by benefit in the majority of cases.

The Dr Hadwen Trust would like to see the replacement of all animal experiments; however, at the very least we would like to see a swift end to experiments causing animals significantly high levels of suffering. We believe that the government has a moral and scientific responsibility to hasten the cessation of animal use in science, for the benefit of animal welfare and human health as well as the economic and time-saving advantages that non-animal techniques bring with them. For this reason we also call on the government to commit to a targeted time-table for the complete replacement of all animal experiments with non-animal research methods. In other words, a strategy to achieve science without suffering, for the benefit of people and animals alike.

\[^{a}\text{in which the interests of certain individuals — animals — are sacrificed to try and achieve the greatest good for the greatest number, almost invariably humans.}\]
In this experiment, researchers studied the combined effects of two fungicide treatments on experimental infection in guinea pigs. A total of 96 guinea pigs were injected in the abdomen with a chemical to weaken their immune systems, making them more susceptible to infection. Some animals died from this pre-treatment alone. Surviving animals were then injected with lethal doses of a fungus (Aspergillus). Previous tests had shown that guinea pigs died just 3 or 4 days after infection with this fungus.

After the lethal doses, some of the animals were administered two fungicides; one orally by having a tube inserted down their throat twice daily, and the other by painful daily injections into their abdomen. Other groups of animals received only one fungicide and control animals received none.

Inevitably all of the control animals were dead within a few days. Researchers only monitored the guinea pigs twice a day, so many may have suffered for between 9 and 15 hours (e.g. overnight) before researchers even became aware of their suffering. When eventually discovered, those showing severe distress were killed. After 21 days any surviving guinea pigs were also killed. The animals’ kidneys were removed and examined. The researchers concluded that treatment with fungicide prolonged survival.

The dose of fungus used in these experiments was enough to kill a guinea pig within 4 days. Fungal infections kill by destroying the affected organs. This can cause blindness if the eye sockets are infected and can destroy the liver, kidneys and other major organs. Another research paper in which very similar procedures were conducted on guinea pigs in the USA, reports that the animals developed extensive infection throughout the liver, kidney, lung and brain.

In particular, the control group of some 20 guinea pigs, who received no fungicide treatments, are likely to have suffered substantially. They were all dead within 5 days. Their organs were attacked by the fungal infection until it either killed them after days of suffering, or they were finally put out of their misery by scientists.

In addition, the interactions of Aspergillus fungus with human airway and lung cells can be studied in culture in the laboratory and the effects of anti-fungal therapies can also be investigated in the test tube.

Although test tube methods are widely used to study infectious fungi, differences between results from test tube and animal experiments have led to some confusion as to whether combining anti-fungal treatments is actually beneficial or detrimental for patients. We believe that using animals – a different species – is one of the causes of such confusion. In the future, computer models based on test tube and clinical data might also help to predict more accurately responses in patients.

Species differences mean that results from one species may not apply to another. Even within the same species, results can vary. For example, different strains of mice show different patterns of susceptibility and resistance to infection with Aspergillus fumigatus, and other fungal pathogens. Results from animal experiments can confuse rather than clarify the clinical situation.

Another major weakness of this experiment is the use of an incorrect route of infection. Aspergillosis is a lung infection that arises from inhalation of fungal spores. The guinea pigs used in this experiment were injected with the fungus directly into a vein, which leads to infection of the kidneys.

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**Scientific weakness and non-animal replacements**

Using guinea pigs in these experiments has contributed very little of real value or relevance to the human situation. Non-animal research routes could and should have been used and we believe the extreme degree of suffering experienced by the animals should have precluded the government from licensing them.

Aspergillus is a fungus that infects the lungs, particularly in patients with weakened immune systems such as those with AIDS, transplant recipients or cancer patients. Shockingly, the anti-fungal treatments studied in this experiment are already in clinical use, and so combined treatments might have been studied in groups of volunteer patients. Patients for whom conventional therapy with a single fungicide had failed to work may have been particularly willing to consent to participate in such initial trials.

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**Fatal fungal infections in guinea pigs**

*University of Aberdeen*

- 96 animals
- Abdominal chemical injections whilst conscious
- Lethal fungal injections
- Fungicides forced down throat
- Slow and painful death

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**Appalling animal suffering in UK labs**
Pain research in animals may involve purposely inflicting pain on animals and then administering painkillers and watching the animals’ behaviour to see whether they are effective. The control groups of animals used in these studies receive no painkillers and are forced to endure unabated pain, often until they die.

Some examples of recent pain research conducted on animals in the UK:
- Studying bone cancer pain in rats by injecting breast cancer cells into the animals’ limb bones. This causes fast-growing, painful tumours and extensive bone damage. These gruesome experiments lasted for over 20 days and resulted in the animals being extremely sensitive to pain caused by the slightest touch to their damaged limbs, and making them limp in pain⁵.
- Injecting the chemical MIA (monoiodoacetate) into rats’ knees, causing the breakdown of joint cartilage and destruction of the leg bone. These experiments are designed to mimic the symptoms of osteoarthritis and used 400 animals, some of whom were left to suffer these painful symptoms for 35 days, with no pain relief. Others were dosed with painkillers to study the nature of their pain experience, but one drug had no effect and these rats suffered a full 28 days with no relief from their pain.

After 14 days, researchers found serious ulceration of the cartilage and bone in the rats’ knees and after 21 days, the animals suffered deep bone damage. Additionally, the joint damage caused injury to nerves close to the spine, inflicting yet another kind of pain. Rats enduring painful joint and nerve damage were made to stand so that researchers could observe to what extent they were limping. Animals injected with MIA were very reluctant to put weight on their affected limbs, a sure sign that they were in pain⁶.

Scientific weakness
Self-evidently, these are experiments that involve the deliberate infliction of substantial pain and suffering in animals, many of whom are refused pain relief and whose experience during the procedures raises serious ethical questions. Human pain is a very complex and subjective experience that cannot be replicated by these simplistic animal experiments. Results from these animals cannot reliably be applied to humans, and there is as yet no effective treatment for chronic (long-term) pain, despite the large volume of published animal experiments in this area.

Non-animal replacement
It is perfectly possible, as well as ethically and scientifically desirable, to effectively study human pain and analgesia without recourse to animal experiments. Knowledge of human pain is essential in order to develop effective pain therapies. Major new insights into the human pain experience and effects of painkillers are being produced with non-invasive brain imaging techniques such as fMRI, PET and MEG. With these techniques, volunteers are studied to

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Appalling animal suffering in UK labs

Pain research in rodents
Novartis Institute for Medical Sciences, London⁵
AstraZeneca, Cheshire⁶
- Deliberately inflicting pain
- Some suffered unabated pain until death
- Painful tumours
- Limping in pain
- Knees injected with chemicals causing ulcers and bone lesions

different condition in another species is unlikely to yield results that are reliably applicable to humans.

In the search for new molecular targets for painkilling drugs, notable species differences have been found between rodents and humans in key receptors involved in pain processing. Different species handle drugs differently and painkilling drugs can have widely differing effects in different animals. A well-known example of this is morphine, which has a sedative effect on humans but excites cats. Morphine also varies widely in its toxicity in different animal species.

Many of the animal experiments for pain measure changes in animal behaviour as a supposed indicator of the effectiveness of painkilling drugs. Yet veterinary surgeons know well that animal pain is extremely difficult to recognise and interpret, especially in rodents, which are naturally prey animals and so tend to instinctively hide pain and discomfort to avoid becoming an easy target. Thus, animal behaviour testing is not a very accurate or sensitive method of assessing the efficacy of painkillers.

Not only are there significant species differences, but human studies are also revealing gender differences in pain processing, and painkillers appear to work differently in men and women.

Non-animal replacement
It is perfectly possible, as well as ethically and scientifically desirable, to effectively study human pain and analgesia without recourse to animal experiments. Knowledge of human pain is essential in order to develop effective pain therapies. Major new insights into the human pain experience and effects of painkillers are being produced with non-invasive brain imaging techniques such as fMRI, PET and MEG. With these techniques, volunteers are studied to
identify the areas of the brain involved in different types of pain processing, the parts of the brain affected by analgesics, and the duration of these effects. These non-invasive imaging techniques are also being extended to study the spinal cord in humans, which is also involved in pain processing. A technique called microdialysis, in which a tiny probe is inserted into the tissues of a living human, has also been used to monitor biochemical changes at the tissue level in a range of human pain conditions. These techniques can be used with patients living with pre-existing pain as well as healthy volunteers.

One of the major advantages of these safe and largely non-invasive methods, is that the species of relevance (humans) is studied and that volunteers are able to directly communicate their experience of pain and pain relief in a way that is impossible with animal experiments. With osteoarthritis research, increasing the supply of normal and osteoarthritic tissues from human donors would accelerate understanding of the human condition.

Inflicting brain damage on monkeys
King’s College, London

- Toxic chemical injected into the brain
- Tremors, drooling, incontinence, compulsive behaviour
- Solitary confinement
- Disabling & abnormal movements
- Months of testing

More than 4,500 primate experiments were conducted in Britain in 2005, using over 3,000 individual animals. Britain remains Europe’s largest user of laboratory primates. At the Neurodegenerative Diseases Research Centre, King’s College, London, marmoset monkeys are regularly used in research into Parkinson’s disease (PD). The animals are injected with a toxic chemical, MPTP, which causes brain damage and is intended to replicate human PD. Monkeys injected with MPTP suffer substantially. They have tremors, rigidity, abnormal posture, loss of balance, drooling, incontinence, compulsive behaviour, constipation, and may be so severely brain damaged that they are incapable of feeding themselves.

In a recent typical experiment, eight marmoset monkeys aged 2-7 years were injected with MPTP daily for five days. Some of these marmosets were kept in solitary confinement, which is very distressing for any primate, and had to be hand fed for 8 to 10 weeks due to the severity of their brain damage. It is likely that they were also unable to clean or groom themselves normally, adding further to the animals’ distress.

The experiment aimed to investigate side-effects of drug treatments, and the effect of switching drugs used in the management of human PD. Long-term use of L-dopa, the current treatment, causes distressing repetitive, involuntary movements (dyskinesia), that are persistent in patients. After damage caused by MPTP, animals were dosed with either L-dopa or ropinirole for 30 days. Subsequently the animals were switched to a different drug treatment for a further 56 days. Approximately one month later all animals were again given a large dose of L-dopa, and their responses assessed.

Half-way through the drug treatment trial, marmosets being dosed with L-dopa developed moderate to severe dyskinesia. They suffered virtually continuous and disabling abnormal movements, including rapid random flicking of the limbs and writhing limb movements, causing them to form abnormal postures. These highly distressing symptoms lasted for three hours twice a day for 16 days.

These experiments lasted approximately 6 months in total and unusually, at the end these monkeys were not killed for post mortem analysis. The reason given for this was the relative scarcity of animals available at the time of the study. At the end of most experiments, sometimes after many months, the animals are killed and their brains examined. The fact that these animals were not killed suggests they were destined to be reused in another experiment.

Scientific weakness

Damaging the brain of a monkey with massive doses of a toxin is a crude, simplistic and highly artificial ‘model’ of human PD. The authors themselves point out that the MPTP-treated primates are not a complete model of PD, as it occurs in humans. Parkinson’s disease has never been fully or accurately re-created in animals, as they do not naturally suffer from this neurological disorder.
There are significant differences between human PD and the condition created in primates. For example, the cause of human PD is unknown; the symptoms develop gradually and worsen over time. By contrast, in the animal experiments healthy marmosets are deliberately subjected to rapid brain damage, from which a degree of recovery occurs when the toxin is withdrawn.

In addition, Lewy bodies, characteristic structures found in the brains of all PD patients, are rarely if ever found in the brains of monkeys.

The researchers concluded from the above animal experiment that late stage PD patients on L-dopa may benefit from switching to another drug – remarkably, a conclusion which has already been suggested by clinical experience with human patients. This being the case, why did researchers feel the need to investigate this useful clinical finding in an animal experiment they themselves acknowledge has the potential to be misleading?

Species differences and the artificiality of the animal 'model' make results from brain-damaged marmosets of dubious relevance to human PD patients. Focusing on animal experiments, rather than clinical studies, could actually delay medical progress rather than advance it.

### Non-animal replacement

In this particular instance, clinical studies of patients with PD had already provided relevant and important clues about the potential benefits of switching treatments in PD, meaning the animal experiments added little of value.

Non-invasive brain imaging techniques, such as MRI and PET, are currently being used to study brain activity in PD patients and have revealed disturbances in brain function. Clearly these methods will continue to play a key role in expanding our understanding of human brain diseases such as PD, and provide a means of assessing new therapies and improving current ones.

Post-mortem research using donated human tissue is also invaluable in following up the progression of a disease, and the effects of treatments and interventions. A few brain banks already exist in the UK, to which people can donate their brain after death, although the Dr Hadwen Trust would like to see far more pro-active and government-sponsored intervention to encourage the public to donate their organs to research via a properly regulated and nationally co-ordinated system. Studies of human tissues and cells are providing invaluable insights into the cellular mechanisms that bring about the death of brain cells in PD, and indications of possible treatments and interventions.

Lifestyle and genetic factors associated with the development of PD are also beginning to be revealed by population studies (epidemiology). For example, there is some evidence to suggest connections between an increased risk of PD and exposure to environmental toxins, such as pesticides, herbicides or metals. There are also indications that diet and smoking may play a role in susceptibility to PD. Further human-based investigation into confirming these links could help to prevent future cases of PD.

### The most recent Home Office Statistics reveal that over 5,500 toxicity tests using nearly 5,000 dogs were conducted in the UK in 2005. Substances tested include medicines, and chemicals used in agriculture and industry. Dogs are used in both short- and long-term toxicity tests, at the end of which the animals are usually killed for post-mortem analysis. Common tests on dogs include:

- **Repeat Dose Toxicity tests** to assess the toxic effects of repeated sub-lethal doses of a test chemical on the whole body. Groups of up to 32 dogs are (usually) force-fed for up to 90 days with a tube down the throat, and then killed.
- **Chronic (long-term) toxicity tests** look at the consequences of repeated doses, usually for one year, and may continue for as long as 2 years.
- **Toxicokinetic tests** examine the way a chemical or drug is handled by the animal’s body – how it is absorbed, digested, metabolised and excreted. The tests last up to 14 days, during which:
  - Thousands of dogs every year
  - Force fed toxic substances
  - Tubes forced down the throat
  - Up to two years of suffering
  - Vomiting, diarrhoea, organ damage & coma
which time animals are isolated in ‘metabolism cages’, may be repeatedly dosed by having a tube inserted down their throats and have multiple blood samples taken. Drug toxicity can lead to vomiting, diarrhoea, dehydration, lethargy, bleeding, excessive salivation, tremor or effects on heart or liver, and at worst coma, convulsions, and death. Painful biopsies may be done of the liver, kidney, fat and/or suspected target organs. Some animals may have another tube inserted through their abdomens for sampling bile from the bile duct. Eventually the dogs are killed and their organs removed.

Dogs are routinely used in regulatory toxicity testing in the UK. Tests are usually at contract testing laboratories like Inveresk Research and Huntingdon Life Sciences, on behalf of drug or chemical companies. The results of toxicity tests and the effects on the animals used in them are rarely published, as the information is considered commercially sensitive. The examples provided here have come from documentation leaked from Inveresk Research, Scotland.

At Inveresk (1998 - 1999) dogs force-fed a new psoriasis drug in repeat dose toxicity tests experienced vomiting, regurgitation, salivation, diarrhoea, loss of appetite, subdued behaviour, discharge from the eyes, lymph node swelling, hair loss and discoloration, swollen joints, vulval discharge, enlarged vulvae, bleeding gums, thinness and weight loss.

During these tests, appallingly, two dogs were accidentally dosed into their lungs, causing additional distress and salivation; one dog frothed red foam at the mouth. These dogs had to be killed.

Between 1999 and 2000 at Inveresk, 24 beagles were dosed for 28 days with a urinary incontinence drug. Dogs in the high dose group suffered large amounts of brown vomit, salivation and regurgitation of food, loss of appetite and weight loss, increased heart rate and decreased blood pressure.

A potential anti-depressant drug tested on dogs at Inveresk (1999-2000) caused stereotypic behaviour, agitation, reddened eyes with watery discharge, dilated pupils, irregular heart beat, excessive saliva and intolerance to light, reddened ears and gums and weight loss.

Routine tests like these continue to be conducted on dogs today despite the high degree of suffering they inflict and the inaccurate results they provide.

**Scientific weakness**
There are serious limitations to all animal toxicity data because of significant species differences, most notably in the way the liver and kidney handle and clear chemicals or drugs from the body. Animal toxicity data often varies between different animal species, strains and even genders, meaning the results from such studies can never be guaranteed to be relevant to humans and are often significantly different.

Animal tests do not reliably predict the effects of chemicals on humans, nor do they ensure the safety of new drugs. This is clearly seen by the large proportion (92%) of potential new medicines that pass animal tests but are found to be unsafe or ineffective in human trials.

**Non-animal replacement**
There is a range of advanced non-animal approaches that could be used in a step-wise strategy to predict toxicity instead of animal tests. Initial information about molecular structure, cell culture toxicity tests and other test tube methods, combined with computer modelling, can be used to predict toxicity of a test substance. With further development, these approaches could provide more accurate predications of human toxicity than animal tests.
animals considerable pain, suffering and distress, particularly for those in the control groups who didn’t receive any antibacterial agents to prevent the infection spreading, and subsequently had to be killed.

In one experiment, twelve female sheep underwent surgery to have two pins inserted into their leg bones, and the wounds around the pins were contaminated with bacteria. Deep infection was found in the wounds of all the animals when they were inspected after 14 days, and the animals had probably been suffering substantial pain from these infections for at least a week.

The sheep then underwent further surgery to have a nail implanted into their leg bone (to act as an internal splint), but only half the sheep had their wounds cleaned and were given antibiotic treatment. Sheep were killed after 28 days for post mortem, but many had to be killed earlier due to the severity of their suffering.

Animals in the untreated ‘control’ group developed widespread infection, septic arthritis and abscess formation. All animals in this group had to be killed after 9-12 days, when overwhelming infections developed in the knee joint, the soft tissues and throughout the length of the tibia (lower leg bone).

Even in the treatment group, only 4 animals survived until the end of the experiment. Two had to be killed when they became unable to bear weight and were found to have suffered spiral fractures at the pin site. One suffered a fracture for several days and developed widespread infection. This animal must have suffered especially and it is a disgrace that any animal could be left for this length of time with an untreated fractured limb, particularly in what is supposed to be a closely monitored and controlled experimental procedure.

In another experiment, 12 female sheep were anaesthetised and their exposed lower leg bone was cut with a saw, and then infected with bacteria. A nail was implanted to stabilise the cut limb in all animals, but only six animals received anti-infection treatments. All animals were killed after 3 or 6 weeks.

Untreated animals suffered swelling, increasing inflammation and breakdown of the bone, and had to be killed after three weeks due to their intense suffering. In the treatment group two animals had to be withdrawn from the study (presumably killed) due to “excessive weight loss”. Despite treatment, animals developed infection at the site of the cut and along the length of the implant. Pus was present throughout the central bone cavity and an abscess formed at the site of the wound.

Animals were given analgesia, but being left for several weeks with an inflamed and infected wound in a weight-bearing leg must have caused these animals intense pain, distress and suffering.

**Scientific weakness**

Improving the treatment of infected wounds in humans is obviously a high priority for the Ministry of Defence, but inflicting such horrific wounds on sheep is not justifiable – it causes undeniably intense animal suffering but does not accurately recreate the human situation. Wounds heal at different rates in different species, and it is well known that species can respond quite differently to antibiotics, so the effects of testing treatments on sheep may not apply to patients with infected wounds. Infected wounds can easily lead to septic shock, a usually fatal condition for which animal experiments have proved woefully inadequate at identifying effective treatments.

**Non-animal replacement**

Cell culture models of infected wounds are already being used to study the effectiveness of antimicrobial treatments *in vitro*. More advanced non-animal methods are still urgently needed and clearly, experiments that inflict such a high degree of animal suffering should be made a priority for replacement. Direct clinical studies of patients are the gold standard of medical research and so, sadly, rapid advances in the treatment of wounds have come about during times of conflict, when doctors and surgeons are directly treating injured soldiers.

However, a current insufficiency in non-animal replacement techniques, where some but not all elements can be conducted *in vitro*, does not make these experiments on animals, which must have caused unimaginable pain and suffering, any more relevant or ethical.

The Defence Evaluation and Research Agency (DERA), part of the Ministry of Defence, has now separated into two organisations: QinetiQ and the Defence Science & Technology Laboratory (DSTL).
A total of 122 genetically modified and normal mice were subjected to surgery, when most had an artery near their heart tied off, in an attempt to mimic the effects of chronic heart failure. The mice must have suffered shortness of breath and intense chest pain after this procedure, highly distressing symptoms for mice. The Home Office accepts that inducing heart failure in animals has the potential to cause the highest degree of suffering permitted in Britain – i.e. substantial suffering. Around 60% of the male mice undergoing this surgery died within a week of this horrific procedure, from cardiac (heart) rupture or heart failure. Cardiac rupture causes recurrent or persistent chest pain and is lethal. The surviving mice were studied for up to 8 weeks following the operation, during which time they were put through another surgical procedure to invasively monitor their heart and circulation. Finally the animals were killed and their hearts removed.

This experiment aimed to look at the effect of deleting a gene on heart failure in mice; deterioration in heart function was found to be worse in knockout mice (i.e. mice with a gene deleted). Inducing heart failure causes substantial suffering to experimental animals and the knockout mice are likely to have suffered from both the heightened effects of induced heart failure, and the known side-effects of this genetic modification (difficulty digesting food and weight loss).

**scientific weakness**

There are fundamental species differences between mice and humans, including size, lifespan, circulatory physiology and genetics. For example, mice have a metabolic rate seven times higher than humans, and a heart rate that is ten times faster. Mice are highly resistant to atherosclerosis, the narrowing and ultimately blocking of the arteries that leads to cardiovascular disease in humans.

Female and male mice reacted very differently in this study, with almost twice as many females surviving a week after the surgery than males. This sex-based difference indicates that test results are highly variable even before any species differences are accounted for. Laboratory mice are highly inbred to produce different strains (or breeds), which although similar within each strain, may react differently to other strains under the same conditions. Often the choice of mouse breed is made on the basis of convenience, without knowing which strain – if any – may most resemble humans. These and many more species differences make extrapolation of results from mice to humans fraught with difficulties and potentially misleading.

Heart failure in humans is usually the result of gradual narrowing and eventual blocking of arteries to the heart. The condition develops over many years, primarily in older people, and although there may be some genetic effects it is strongly influenced by lifestyle factors such as diet and exercise. Heart failure in these mice was artificially induced by surgical intervention and therefore fails to replicate the human condition or its underlying causes. Results from these animal experiments are of dubious and unknowable relevance to patients.

Genetically modified mice are no more reliable ‘models’ of the human condition than genetically normal animals. Even alteration of the same gene in different species can produce widely differing effects. For example, PLN-null mice used in cardiovascular research experience improved heart function, but an equivalent naturally occurring deletion of the human PLN (PLN-null) found in two families causes fatal heart failure in humans.

**Non-animal replacement**

The ‘gold standard’ of medical research is the study of humans. There are safe non-invasive methods of monitoring the heart and blood flow in healthy volunteers and in patients, which can be used to provide relevant information about human heart failure.

Biopsy and post-mortem tissue from patients with heart disease can also be used to study genetic and molecular changes that underlie heart problems, and identify targets for new drugs. In addition, complex computer models of the human heart are being used to shed light on irregular heart beat and heart failure.

Population studies have already identified the major risk factors for heart disease. New methods of DNA analysis of families and populations are now revealing the human genetic factors that influence heart conditions.
Conclusion

Contrary to the reassuring impression often presented by the UK government and animal researchers, animal experiments in Britain today can still involve very high levels of suffering indeed.

The examples outlined in this report are testament to that fact and demonstrate how starkly the reality of animal experiments often contrasts with the sanitized ‘PR’ spin presented by those who seek to defend and perpetuate them. They also demonstrate how meaningless the so-called cost/benefit test can be for so many animals used in research, who endure substantial suffering despite the scientific weaknesses of the procedures and the existence of more relevant and ethical non-animal approaches.

The Dr Hadwen Trust believes that dispensing with animal experiments which cause substantial animal suffering would represent a necessary first step in a carefully targeted time-table for the total replacement of all animal experiments. By utilizing the full range of sophisticated, cutting-edge, non-animal approaches and massively increasing the R&D budget in this area, a government commitment to such a strategy is entirely feasible. It would also result in tangible benefits for human health, animal welfare and the quality of medical research now and into the future.

Take action

1. Join the Dr Hadwen Trust's call for a government time-table for total replacement

2. You can help the Dr Hadwen Trust replace animal experiments with cutting-edge non-animal research techniques, by supporting our work.
   To become a member or to make a donation, contact us at:
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   84a Tilehouse Street
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   www.drhadwentrust.org

2. Animals (Scientific Procedures) Act 1986, page 2 paragraph 2(1), published HMSO.

3. The relevant passage reads "In determining whether and on what terms to grant a project licence the Secretary of State shall weigh the likely adverse effects on the animal concerned against the benefit likely to accrue as a result of the programme to be specified in the licence".


