

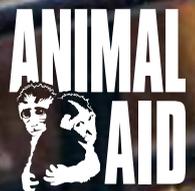
# The Case Against Animal Experiments

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Animal experiments are both unethical and unscientific. Animals in laboratories endure appalling suffering, such as being deliberately poisoned, brain-damaged and subjected to inescapable electric shocks. The pain and misery inflicted on the victims is enough, on its own, to make vivisection worthy of public condemnation. But animal experiments are also bad science, since the results they produce cannot be reliably translated to humans. They therefore offer little hope of advancing medical progress.

*The Case Against Animal Experiments* outlines the suffering of animals used in research, before providing a clear, non-technical description of the scientific problems with vivisection.

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[www.animalaid.org.uk](http://www.animalaid.org.uk)

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## How animals are used

Each year around four million animals are experimented on inside British laboratories. Dogs, cats, horses, monkeys, rats, rabbits and other animals are used, as well as hundreds of thousands of genetically modified mice. The most common types of experiment either attempt to test how safe a substance is (toxicity testing) or attempt to investigate human diseases and how they could be treated (disease research).

Toxicity tests typically involve animals being force-fed substances through a tube into their stomach, or having them rubbed onto a patch of shaved skin. Some tests involve animals actually being poisoned to death. In disease research, animals are physically injured or genetically modified in order to mimic some of the symptoms of the illness being investigated. This can involve, for instance, breaking animals' bones, removing vital organs and subjecting them to near-drowning experiences.

Toxicity tests on animals are often contracted out to private laboratories. But a great deal of disease research takes place at universities and is frequently funded by the taxpayer. Many major medical research charities are also involved in funding animal experiments, such as the British Heart Foundation and Cancer Research UK.

This briefing explains why we believe that neither animal research, nor the organisations that fund it, are deserving of public support.

## The Suffering of animals in laboratories

### Cruel experiments

The suffering inflicted on animals in laboratories is truly disturbing. Experiments recently uncovered by Animal Aid (and supported by UK medical research charities) have involved:

- Monkeys being brain-damaged with a toxic chemical and given the street drug ecstasy.<sup>1</sup>
- Pregnant sheep and their unborn lambs being surgically mutilated, partially suffocated and then killed.<sup>2</sup>
- Rats and mice being poisoned with an industrial chemical for around six months to induce cancer.<sup>3</sup>
- Genetically modified mice being bred to suffer limb paralysis, anxiety and motor dysfunction, then suspended by their tails to assess abnormal behaviour.<sup>4</sup>

Proponents of vivisection would no doubt claim that these are extreme examples, hand-picked to support our case. But the European directive that governs animal experiments, in Britain and other member states, makes it clear that distressing suffering is an accepted part of the experimental programme. The legislation divides experiments into three categories of 'severity' and provides examples for each.<sup>5</sup>

Experiments that fall into the benign-sounding 'mild' category include force-feeding animals substances and restraining them in 'metabolic cages', where they are deprived of social contact. Examples of 'moderate' experiments include removing part of the animal's skull to expose their brain, and giving them a dose of irradiation. Research that falls

into the 'severe' category includes subjecting animals to inescapable electric shocks, and deliberately injuring them to produce multiple organ failure. These are not isolated, cherry-picked experiments, but research that EU legislators considered commonplace enough to include as examples.

Animals used in experiments are often deprived of anaesthesia. In 2013 (the latest data available), 71 per cent of all animal 'procedures' were conducted without any form of anaesthetic.<sup>6</sup> Animals are even used in repulsive pain research experiments where inflicting suffering on the victims is the aim rather than a by-product. Some of the most commonly used pain tests include the 'tail flick', 'hot plate', 'paw withdrawal' and 'writhing' tests, the cruelty of which needs little explanation.<sup>7</sup>





### A failing inspection regime

The pro-vivisection lobby frequently claims that animal experiments are tightly regulated. But, in reality, just a handful of inspectors are expected to police around four million animal 'procedures' that take place in the UK every year. In 2013 (the latest data available), the equivalent of just 15.7 full-time inspectors were responsible for approximately:

- 16,100 individuals licensed to conduct experiments on animals.
- 174 animal laboratories.
- 2,670 experimental projects involving animals.

This means that each full-time member of staff was allocated around 1,000 licences for individuals, 11 animal laboratories and 170 experimental projects.<sup>8</sup>

Such severe under-staffing makes it impossible for the law on animal experiments to be effectively enforced. The Home Office department that regulates vivisection releases an annual report that includes details of law-breaking incidents in UK animal laboratories. These consistently reveal a catalogue of disturbing cases, and the 2013 report (the latest available) is no exception. Reported incidents include:

- Animals chewing off their feet or toes.
- Animals being starved and deprived of water.
- A lab worker decapitating animals without authorisation.
- A ventilation system failure leading to the deaths of more than 1,000 animals.<sup>9</sup>

But these public reports only include incidents that were either self-reported to the Home Office or discovered by inspectors.

Undercover investigations by animal protection groups suggest that these are merely the tip of the iceberg. In 2012, the BUAV (now Cruelty Free International) conducted an investigation at Imperial College London, and found that cruelty and incompetence were rife. Incidents revealed by the investigation included:

- A rat who had been given insufficient anaesthesia lifting his head while his organs were being removed.
- A researcher causing young rats to squeal in pain by removing ear tissue with scissors.
- A rat struggling in a guillotine as a member of staff attempted to decapitate him.<sup>10</sup>

## Secrecy and misinformation

Animal experiments are conducted in the utmost secrecy. The law that governs vivisection in the UK has for decades contained a notorious 'secrecy clause' (Section 24), which is used to prevent even the most basic information about animal experiments from being released. The law allows for anyone who discloses information about animal experiments that could possibly be considered confidential to be sentenced to up to two years in prison.<sup>11</sup> Only now, after years of intensive lobbying, are there plans to weaken the secrecy clause. But bringing information about animal experiments into the public domain will still be a challenging task, with obstacles presented at every turn.

Compounding the legislative secrecy is a campaign of misinformation by the pro-vivisection lobby. Many animal laboratories, for example, are only too willing to provide tours for sympathetic journalists, but such visits are invariably highly restrictive in what the reporter is permitted to see, for instance bypassing any animals who are visibly sick or suffering. Just one example was the 2014 BBC news report from Oxford University's notorious primate laboratory. A monkey was shown performing a task that involved being given a food 'reward' for touching a picture, but the report failed to mention that primates are often deprived of food or water in order to condition them to perform such tasks.<sup>12</sup>

'Compounding the legislative secrecy is a campaign of misinformation by the pro-vivisection lobby.'

## The GM mouse myth

Proponents of vivisection often try to airbrush the statistics by arguing that figures are boosted by counting the actual breeding of GM mice. The regulators and proponents of vivisection are keen to convince the public that this is a harmless process that causes little suffering to the animals involved. In fact, a large number of GM animals are additionally subjected to appalling experiments. These have included being locked in plexiglass chambers and forced to inhale tobacco smoke, or having acid injected into their stomachs. But the breeding itself also involves significant suffering. The creation of GM mice generally involves several painful and invasive procedures, including castration, major surgery and ear or tail mutilation.

Creating just one 'founder' mouse with the required genetic alteration can entail the deaths of hundreds of others. These unwanted mice are often killed by being gassed or having their necks broken. Building and maintaining colonies of GM mice involves drastic manipulation of the animals' behaviour and reproductive cycles, such as subjecting females to overcrowding in order to synchronise their reproductive cycles.<sup>13</sup>



# The Scientific Case Against Animal Experiments

## Summary

Public debates about the scientific validity of animal research usually involve protagonists battling back and forth examples of 'successes' (e.g. the development of the cancer drug Herceptin and diabetic insulin) and 'failures' (e.g. TGN1412 and Vioxx, both of which caused immense harm to people that was not predicted by the animal trials).

Sometimes animals and humans happen to react similarly to a drug or other treatment, but to be of value a research method must produce *reliably predictive* results.

Key reasons why animal 'models' are not *reliably predictive* are:

- Major differences exist between species relating to anatomy, organ structure and function, metabolism, chemical absorption, genetics and lifespan.
- A homogenous group of animals living in controlled experimental settings cannot predict the response of varied human patients living in natural conditions.
- Artificially created diseases in animals in laboratories do not reflect naturally occurring human illness.
- Common adverse reactions to drugs cannot be detected in animal tests. These include nausea, mental disturbance, dizziness, fatigue, depression, confusion and double vision.

The scientific case against animal use is now being voiced in the mainstream scientific media. A recent example is the *British Medical Journal (BMJ)* article by Pound and Bracken. They noted that systematic reviews are exposing the fundamental weaknesses of the animal model, and went on to criticise pro-animal research lobby group Understanding Animal Research for relying too heavily on expert opinion, 'one of the weakest forms of evidence'. The authors also argued for more human-centred clinical research.

Research on genetically modified mice – which is undertaken on the false assumption that genes function similarly across different species – also fails the reliability test. Examples of GM mouse research 'successes' that failed in clinical trials include drugs for cancer, Alzheimer's disease, chronic heart failure, breast cancer, emphysema and asthma.

The fruitless attachment to particular animal models of human diseases can persist for years, cost billions of dollars and result in dozens of worthless drugs. This has occurred in relation to stroke, cancer and inflammatory disease, as well as the search for an effective HIV vaccine.

Animal research is misleading in another way: a drug that damages animals in early tests – and is therefore abandoned – could potentially be safe and effective in people. Valuable drugs that were nearly lost because of toxicity in animals include the breast cancer drug tamoxifen and the leukaemia drug Gleevec.

Translational problems beset both toxicity studies and disease research – a reality recognised by leading US regulatory and research agencies such as the National Institutes of Health and the Environmental Protection Agency.

There are numerous non-animal, human-relevant research methods now available, and it is a rapidly growing field. Lifestyle changes can also produce dramatic health benefits.

In an era of evidence-based medicine and of powerful analytical tools such as systematic reviews and bioinformatics, the fatal weaknesses of the 'animal model' will inevitably become more widely known. For those involved in research into the causes of and remedies for human disease, the rational choice is to embrace modern, productive non-animal methods.

## The Scientific Case Against Animal Experiments

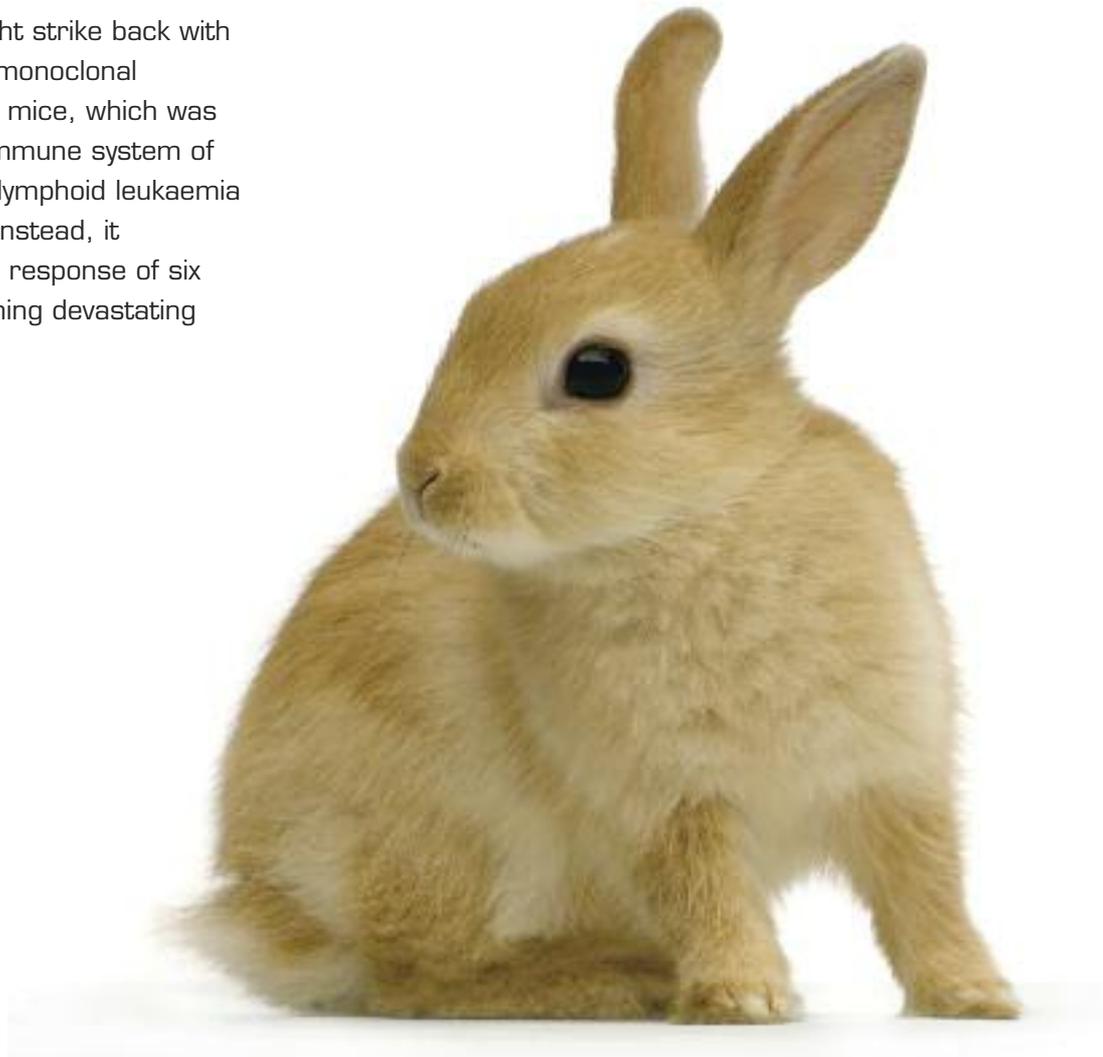
### 'Successes' and 'failures'

How useful are the results of animal experiments? How applicable is information drawn from animal research into, say, human cancer or neurological and cardiovascular disease? The traditional public debate on this question usually involves protagonists using, like missiles, examples of what they see as animal research 'successes' and 'failures'. Pro-use advocates will strike with, say, the breakthrough breast cancer drug, Herceptin, a mouse-generated monoclonal antibody.<sup>14</sup>

### The TGN1412 catastrophe

Animal-use opponents might strike back with TGN1412, a 'humanised' monoclonal antibody also derived from mice, which was designed to dampen the immune system of patients suffering chronic lymphoid leukaemia and rheumatoid arthritis. Instead, it supercharged the immune response of six human volunteers, unleashing devastating multiple organ failure.<sup>15</sup>

TGN1412 had been previously tested in rats, mice, rabbits and cynomolgus monkeys – the latter having undergone weeks of repeat dose toxicity studies at 500 times the dose later given to the human volunteers. No conspicuous side effects had been noted from these animal tests. However, the National Institute for Biological Standards and Control later demonstrated that the drug's catastrophic effects can be predicted through an *in vitro* test in which human endothelial and white blood (immune) cells are combined.<sup>16</sup>



## Dogs and insulin

The 'discovery of insulin in dogs' in the 1920s by Nobel Prize Winners Banting and Best is another missile that the pro-animal research lobby regularly directs at its opponents. 'Before the discovery of insulin', says Understanding Animal Research,<sup>17</sup> 'there was no effective treatment for the disease and people with diabetes usually died tragically young.' In fact, the link between diabetes and pancreatic dysfunction was established long before the 20th century.<sup>18</sup>

## Tragedy of Vioxx

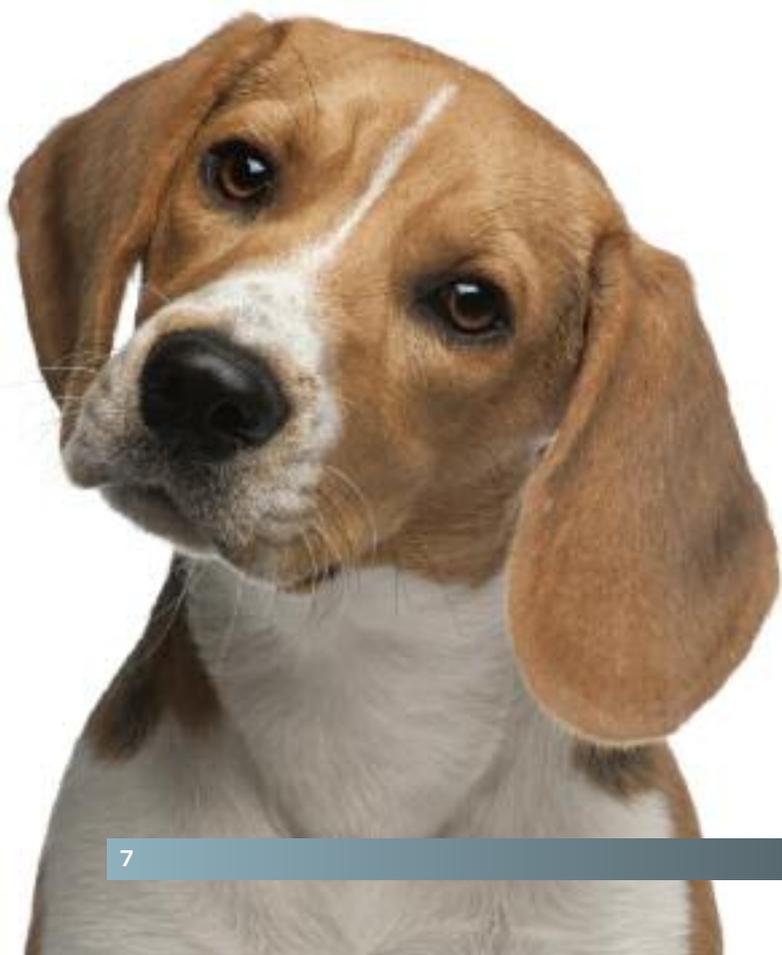
In response to the diabetes claims, anti-vivisectionists might cite the case of Vioxx, a non-steroidal anti-inflammatory drug linked to thousands of strokes and heart attacks, even though it went through comprehensive pre-clinical trials and was shown to be protective of the hearts of several animal species on which it was tested.<sup>19</sup>

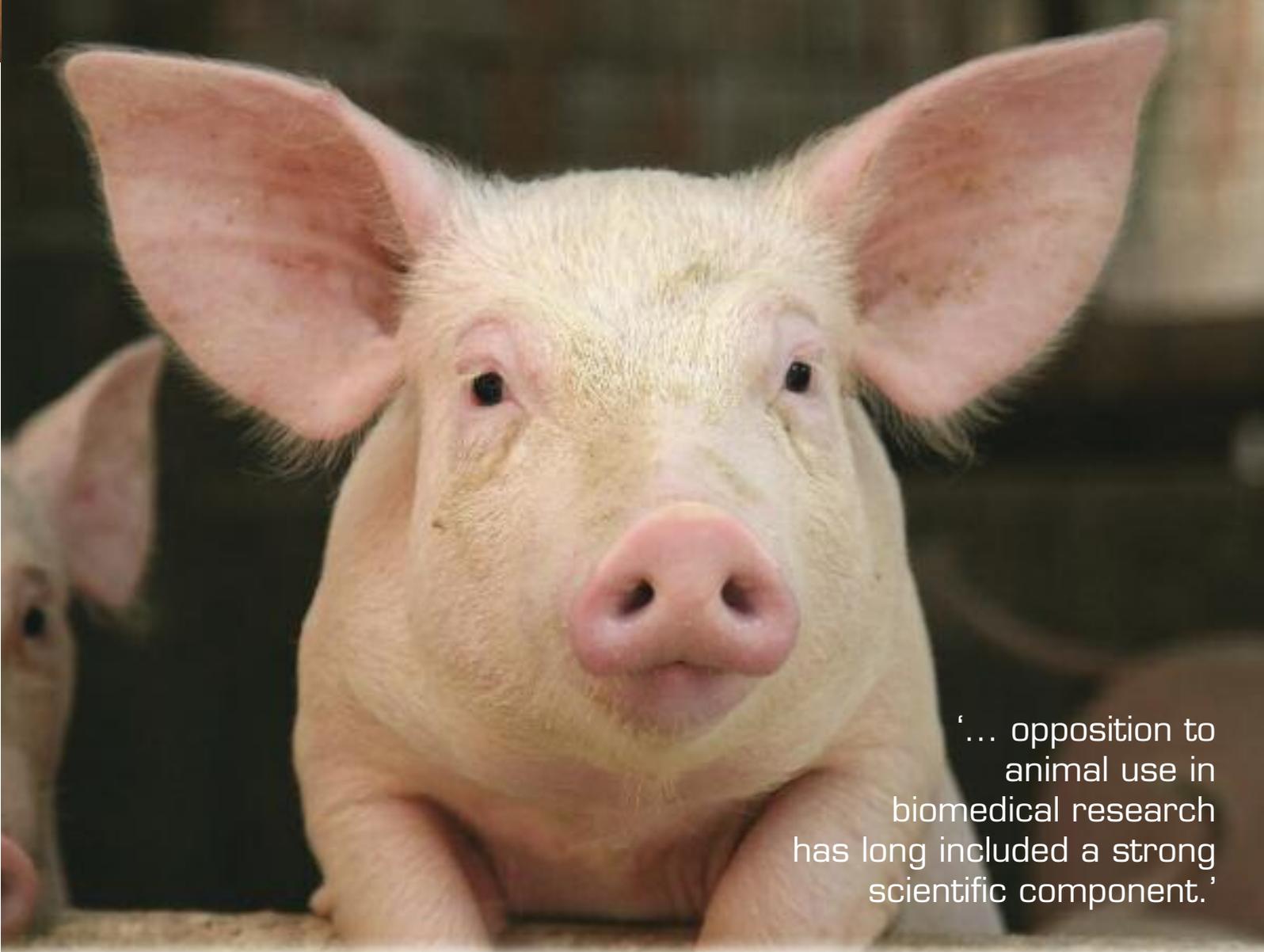
## Four key problems

Batting back and forth examples of the 'successes' and 'failures' of animal use clearly won't resolve the question. It is the case that animals and humans sometimes happen to react similarly to a drug or other therapeutic intervention. But any biomedical research methodology – if it is to avoid unnecessary patient harm, missed opportunities and squandered resources – needs to be *reliably predictive* of human outcomes. The use of animal models for disease research and drug development and testing is simply not *reliably predictive* because of four fundamental factors:

- There are key differences between species, as expressed in anatomy, organ structure and function, metabolism, chemical absorption, genetics, mechanisms of DNA repair, behaviour and lifespan.
- A homogenous group of animals living in controlled experimental settings cannot predict the response of varied human patients living in natural conditions.
- Artificially created diseases in animals in laboratories do not reflect naturally occurring human illness.
- Some of the most common adverse reactions to drugs are not outwardly visible and therefore cannot be detected in animal tests. These include: nausea, mental disturbance, dizziness, fatigue, depression, confusion and double vision.

'Artificially created diseases in animals in laboratories do not reflect naturally occurring human illness.'





'... opposition to animal use in biomedical research has long included a strong scientific component.'

### 'Case against' enters scientific mainstream

For many years, opposition to animal use in biomedical research has included a strong scientific component. The fresh development is that it is now increasingly common for that opposition also to be articulated in the mainstream scientific literature. A recent example is an influential Pound and Bracken article published in the *British Medical Journal* in May 2014.<sup>20</sup> A key theme was the 'lamentably low' number of systematic reviews (SRs) to which animal studies are subjected, even though the number of SRs conducted was now said to be doubling every three years. With more published SRs has come increased evidence of the poor quality of much pre-clinical animal research. In

particular, there is a lack of best practice to prevent bias. Also evident is a high degree of selective analysis and reporting, and a tendency to publish only positive results.

### Species differences

Even where research is conducted 'faultlessly', Pound and Bracken report, 'animal models might still have limited success in predicting human responses to drugs and disease because of inherent inter-species differences in molecular and metabolic pathways'. Failures of the predictive value of animal studies were identified by the authors in the fields of stroke medicine, amyotrophic lateral sclerosis and inflammation.

### Lobby group criticised

Understanding Animal Research, an organisation financed mostly by those conducting or funding animal research, came in for severe criticism in the Pound and Bracken paper because of the way four of its highlighted reports 'rely solely on expert opinion, one of the weakest forms of evidence according to widely agreed standards'. Pound and Bracken favour more use of systematic reviews, whereby all credible available evidence on a given research area is aggregated and distilled.

### Clinical versus basic research

What this is 'beginning to suggest', say Pound and Bracken, 'is that it is clinical rather than basic research that has the most effect on patient care'.

The Pound team's analysis made uncomfortable reading for biomedical researchers wedded to the conventional view of animal models and their utility – all the more so because the team's findings were essentially echoed by the *BMJ*'s Editor in Chief in a comment article in the same issue: 'Funds might be better directed towards clinical rather than basic

research,' she observed 'where there is a clearer return on investment in terms of effects on patient care.'<sup>21</sup>

### The limits of research using GM animals

The burgeoning use of genetically modified animals (usually mice) is aimed at defeating a key problem identified by Pound and Bracken, that of species differences. But such an approach is often predicated on the notion that genes operate largely independently of each other,<sup>20</sup> which of course they don't. Equally, the GM approach presumes that, locked within genes, is much of the answer to human disease and frailty. The evidence doesn't support that view. A human being's genes, about 20,000 in all, represent just one to two per cent of his or her DNA. The rest of the non-gene coding stretches of DNA, some of which in earlier years was dismissed as 'junk', turns out to be critically important in controlling how genes actually function – turning them off and on in complex and subtle ways.<sup>22</sup>

'Funds might be better directed towards clinical rather than basic research, where there is a clearer return on investment in terms of effects on patient care.'

*BMJ* Editor in Chief



## Inflammatory disease and wasted resources

In a number of areas of medical research, the attachment to a particular animal model paradigm is both puzzling and depressing, given that it has resulted in year after year of unproductive and costly research activity. In February 2013, a study published in *Proceedings of the National Academy of Sciences* (PNAS) reported that the mouse models used extensively to study human inflammatory disease (in sepsis, burns and trauma) have cost billions of dollars but have proven to be entirely fruitless.<sup>27</sup> According to the authors of the PNAS paper, there have been nearly '150 clinical trials testing candidate agents intended to block the inflammatory response in critically ill patients and every one of these trials failed'.

Their study found that mice and humans respond in markedly different ways to inflammatory conditions.<sup>28</sup> There were variations in the turning on and off of genes, and in the timing and duration of gene expression. It was these differences that, the authors believe, led to the high drug failure rates. In a follow-up letter to their article, the authors declared: 'A vibrant discussion of the merits and limitations of animal models is long overdue.'<sup>29</sup> And an editorial in *Nature Medicine*, addressing the team's findings, observed: 'Rather than over-relying on animal models to understand what happens in humans, isn't it time to embrace the human "model" to move forward?'<sup>30</sup> Dr Richard Hotchkiss, a sepsis researcher at Washington University, responded more straightforwardly to the inflammatory study: 'To understand sepsis, you have to go to the patients ... get their cells. Get their tissues whenever you can. Get cells from airways.'<sup>31</sup>



## Mice and men

That these regulatory mechanisms operate very differently in, for instance, mice, rats and human beings – despite these species having in common around 70 per cent of their genes – is evident not only from their vastly different appearances but also from fundamental physiological disparities. These include the ability of mice to eat scraps off the street that would make us violently ill; the fact that mice cannot vomit; and the fact that mice appear to have not one but two functioning thymus glands, as well as an ability – not shared by human beings – to manufacture vitamin C within their bodies.<sup>23,24,25</sup>

## GM research failure

Given the above, it should come as no surprise that a long list of drugs that were both safe and efficacious when trialed in GM mice went on to fail in clinical trials. Among them were new compounds for Alzheimer's disease, chronic heart failure, breast cancer, emphysema and asthma.<sup>26</sup>



### Mouse model of cancer

An equivalent message has been voiced in relation to cancer research by Azra Raza, Professor of Medicine and Director of the MDS Centre, Columbia University, New York: 'An obvious truth that is either being ignored or going unaddressed in cancer research is that mouse models do not mimic human disease well and are essentially worthless for drug development.'<sup>32</sup>

Overseeing a significant proportion of this unrewarding mouse research – much of it using genetically modified animals – was Elias Zerhouni, former Director of the National Institutes of Health (NIH), the world's largest funder of biomedical research. Today, Zerhouni is an unabashed convert.<sup>33</sup> 'We have moved away from studying human disease in humans,' he said in a 2013 address to his former NIH colleagues. 'We all drank the Kool-Aid on that one, me included. The problem is that it hasn't worked, and it's

time we stopped dancing around the problem. We need to refocus and adapt new methodologies for use in humans to understand disease biology in humans.'

### Stroke and HIV vaccines

As well as cancer and inflammatory disease, a great deal of wasted energy has been expended in the search for stroke drugs and HIV vaccines. Decades of stroke research have resulted in thousands of publications reporting more than 1,300 successful stroke interventions in animals, including more than 700 for acute ischaemic stroke, *none* of which has led to human benefit. And while around 100 HIV vaccines were tested with positive results in non-human primates, *none* provided protection or therapeutic benefit in humans.<sup>34</sup>

'We need to refocus and adapt new methodologies for use in humans to understand disease biology in humans.'

Elias Zerhouni, former Director of the National Institutes of Health (NIH)



## Missing out on valuable therapies

The inverse of the problem of drugs working in animals but not in people are drugs that fail in animal tests yet turn out to be effective in human patients. Among highly regarded therapies that were very nearly lost to human medicine because of toxicity in animals are the breast cancer drug tamoxifen (it causes liver tumours in rats) and the leukaemia drug Gleevec (it causes severe liver toxicity in dogs).<sup>35,36</sup>

So we can see that the translational problems that beset the use of animals for research into human diseases are equally evident in toxicity (i.e. safety) testing. According to the Director of the NIH National Center for Advancing Translational Sciences, Dr Christopher Austin: 'Traditional animal testing is expensive, time-consuming, uses a lot of animals and, from a scientific perspective, the results do not necessarily translate to humans.'<sup>37</sup>

## Toxicity in the 21st century

This recognition has prompted major US Federal agencies, such as the NIH itself, the Environmental Protection Agency and the National Research Council of the National Academies, to press for a 'paradigm shift in toxicity testing'. Spelt out in the 2007 publication *Toxicity Testing in the 21st Century: A Vision and a Strategy*, the basic goal is to reorient testing to the molecular level rather than observing responses at the level of whole organisms.<sup>38</sup> The focus, in particular, is now on human 'toxicity pathways', the sequences of molecular changes within the body's cells that follow exposure to a toxic chemical. As these molecular pathways are mapped for different groups of chemicals and different toxic effects, computer technology will help identify the key steps and the most appropriate human-based safety tests. Unlike current animal methods, which are based on crude poisoning regimes, the new tests will be relevant to our own species; they will help explain the underlying cause of toxicity; they will help predict human variability; and they will offer insights into differential effects on embryos, children and adults.

'Traditional animal testing is expensive, time-consuming, uses a lot of animals and, from a scientific perspective, the results do not necessarily translate to humans.'

Dr Christopher Austin,  
NIH translational specialist



### Pointlessly 'sacrificed'

No safety testing system is perfect but the course charted by the US multi-agency project, that has come to be known as Tox 21, promises a way out of the current impasse. At present, millions of animals around the world continue to be 'sacrificed' every year in a massively expensive and time-consuming testing regime that produces dangerously untrustworthy human safety data. A 2012 study, for instance, showed

that animal tests missed 81 per cent of the serious side effects of 43 drugs that went on to harm patients.<sup>39</sup> Animals die needlessly and the public is insufficiently protected from exposure to harmful drugs, chemicals and environmental pollutants. That argues not for continuing with the current dysfunctional system but for everyone with a stake in better outcomes (and who hasn't got such a stake?) to speedily embrace the thinking and practices implicit in the Tox 21 vision.<sup>40</sup>



## Numerous non-animal research options

An equivalent transformation is urgently needed in the field of disease research. Here, as we have seen, there is also needless animal suffering and a waste of high level human resources. Experiments on mice or rhesus macaques, in whom disease has been artificially induced, teach us something about lab-damaged animals, not people. Once again, there is a compelling case for abandoning what has proven to be a dismal obsession with animal models and, instead, embracing the array of new and established animal-free research methods. They include: studies of human populations; *in vitro* research using human cell and tissue cultures; clinical studies; human autopsy examinations; computerised patient-drug databases and post-marketing surveillance; mathematical models and computer simulations; and non-invasive imaging techniques.<sup>41</sup>



## Lifestyle gains

Additionally, the promotion of beneficial lifestyle changes has the potential to deliver an immense amount of public good – more than all the above methods combined, some would argue. Healthier lifestyles could have prevented almost 600,000 cases of cancer in the UK between 2009 and 2014, Cancer Research UK has reported.<sup>42</sup> The potential for curbing dementia rates is equally dramatic, according to Professor A David Smith of the University of Oxford. ‘It’s time we stopped being obsessed with amyloid-related drugs and the search for genes’, he wrote in a letter to the *Guardian* newspaper, ‘and moved on to research and action on preventive strategies. Only one per cent of Alzheimer’s cases are directly caused by genes ... about half of all cases are likely to be due to modifiable risk factors.’<sup>43</sup> Smith is one of a group of 112 dementia researchers from 36 countries who have called for more spending on lifestyle research and the rapid application of known beneficial strategies such as the need for B vitamins, essential fats and keeping physically, mentally and socially active.

‘Once again, there is a compelling case for abandoning what has proven to be a dismal obsession with animal models and, instead, embrace the array of new and established animal-free research methods.’

Any biomedical research methodology – if it is to avoid unnecessary patient harm, missed opportunities and squandered resources – needs to be *reliably predictive* of human outcomes. The use of animal models for disease research and drug development and testing is simply not *reliably predictive*.



### Suggested further reading list

- 1) Smith R., 2014. 'Medical research – still a scandal', *BMJ*, 31 Jan 2014 (<http://blogs.bmj.com/bmj/2014/01/31/richard-smith-medical-research-still-a-scandal/>)
- 2) Seok, J. et al., 2013. 'Genomic responses in mouse models poorly mimic human inflammatory diseases', *PNAS* vol. 110 no. 9 (<http://www.pnas.org/content/110/9/3507.full.pdf+html>)
- 3) Pound, P. and Bracken M., 2014. 'Is animal research sufficiently evidence based to be a cornerstone of biomedical research?', *BMJ* 348:g3387 (<http://www.bmj.com/content/348/bmj.g3387>)
- 4) Leber, J., 2014. 'The Coming Human Body on a Chip that will change how we make drugs' (<http://www.fastcoexist.com/3033574/the-coming-human-body-on-a-chip-that-will-change-how-we-make-drugs>)
- 5) Gruber F. and Hartung T., 2004. 'Alternatives to animal experimentation in basic research', *ALTEX*. 21 Suppl 1:3-31. (<http://www.ncbi.nlm.nih.gov/pubmed/15586255>)
- 6) Oxford works with drugmakers to reverse 90% trial failure rate (<http://www.bloomberg.com/news/print/2013-05-03/billionaire-li-ka-shing-funds-medical-data-institute-at-oxford.html>)

## Frequently asked questions

### The law

#### Aren't animal experiments required by law?

It is usually a legal requirement that new drugs are tested on animals before they are given to humans for the first time in clinical trials. While the law provides some scope for 'scientifically accepted' non-animal drug testing methods to be used instead, it is clear that we urgently need a more progressive legal framework. But the vast majority of animal research is not legally required and is either curiosity-driven (designed simply to answer a question that the researchers are interested in) or concerned with attempting to mimic a human disease.

#### Isn't it illegal to experiment on animals when there are alternative methods available?

This is what the law on animal experiments states, but it is often disregarded. The Home Office inspectors who assess applications to perform animal experiments are hopelessly overworked (see page 3) and have little prospect of remaining up-to-date with all the latest non-animal methods in each specialist area. When researchers say that they have explored non-animal methods, Home Office inspectors simply have to take their word for it.

For many types of animal experiment, it is over-simplistic to look at direct replacements. There is no non-animal means of tying off dogs' arteries to induce a heart attack, or poisoning mice with an industrial chemical to cause cancer, but these are crude and outdated approaches that have little relevance to human medicine. There are, however, numerous other ways in which researchers

can study heart disease and cancer, such as through the use of human cells and tissues, computer modelling, high-resolution scanning and, of course, by studying patients themselves.

### The science

#### Don't many animals share most of their genes with us?

This is correct, but these genes are regulated and expressed in completely different ways. Both humans and mice, for instance, share the gene for growing a tail, but it is only expressed in mice. It is also worth bearing in mind that genes represent only one-to-two per cent of our DNA. As indicated above, it is the way these genes are controlled through millions of 'switches' that accounts for the great variation between different species.

These days, mice are often genetically modified in an attempt to make them better 'models' of humans. But there is no way that knocking out or inserting a few genes can override the millions of years of evolution that separate mice and humans. We now know that identical twins can have different reactions to a substance, so there is no way that a mouse, even one with a few crude genetic alterations, can predict human responses with any accuracy.

#### Without animal experiments, wouldn't it be impossible to study the whole body?

Without using animals, it is indeed difficult to perform research on a whole, functioning body system. But using animals to research human diseases and reactions is to study the wrong body system, the results of which are



often misleading. It is like using a rabbit to study how a cat will react to a new vaccine for feline influenza.

Exciting developments in the field of non-animal research are increasing the possibility of studying the human body as a whole. Organs on a chip, for instance, are micro-devices lined with tiny human cells that mimic the functions and even motions of whole organs. By mid-2015 one company had already simulated the function of 15 organs including the liver, lungs and intestines. These mimic what goes on in the human body.<sup>44</sup>

### Isn't vivisection vital for veterinary research?

While it may appear scientifically valid to use members of one species to research treatments for that same species (e.g. dogs to test treatments for dogs), we believe it is unethical to deliberately make animals sick in

order to experiment on them. It is also the case that the stressful, unnatural laboratory conditions mean that data cannot always be reliably collected, even for animals of the same species. New veterinary treatments should first be extensively tested using non-animal methods such as cell cultures and computer modelling. When these have been exhausted, new treatments should be given to animals who are already sick in an effort to try and help them.

The pro-vivisection lobby often uses the case of veterinary research to argue that animals themselves benefit from vivisection. But in reality, veterinary research accounts for a tiny proportion of animal experiments (just four per cent in 2013) and many of these are not intended to help animals, but to improve the money-making potential of animals exploited by, for instance, the farming and horse racing industries.<sup>45</sup>

## The past

Don't we have animal experiments to thank for all the medical progress that has already been made?

Scientists have been experimenting on animals for centuries, and during this time some medical progress has undeniably been made. But these developments have occurred in spite of the misleading practice of experimenting on animals, not because of it. We do not know how many additional treatments we would now have, or how many people could have been saved from drugs that turned out to be harmful, if we had not relied on animal research.

There are, of course, times when, by chance, the species of animal being experimented on happens to react to a substance in the same way as humans. But this does not mean that vivisection is a reliable research method. In fact, studies have suggested that animal experiments are no more reliable than tossing a coin,<sup>46</sup> which is why nine out of ten drugs that pass animal tests go on to fail in human clinical trials.<sup>47</sup>

Vivisection may have seemed a scientifically credible – if highly unethical – approach when our understanding of biology and genetics was much less advanced. After all, most animals share a basic set of organs. But advances in the fields of biology, biochemistry and genetics make such an approach look hopelessly crude and simplistic. Humans and mice both have lungs, for example, and these look superficially similar. But mouse lungs lack respiratory bronchioles, which are the tiny airways where emphysema can develop in humans who smoke.<sup>48</sup> Before modern understanding of illness developed, doctors resorted to bloodletting and other similarly useless and harmful treatments. But when scientific knowledge improved, these

crude methods were abandoned. It is time that the same approach was applied to vivisection.

Couldn't animal testing have prevented the thalidomide tragedy?

The proponents of vivisection often argue that this tragedy could have been prevented if thalidomide had been tested on pregnant animals. But the historical facts suggest otherwise. When numerous babies were born with birth defects, researchers began testing thalidomide on pregnant animals. But the drug failed to produce similar birth defects in numerous animal species, including rats, mice, dogs, hamsters, cats and guinea pigs. Eventually, they found that the drug did cause birth defects in a breed of rabbit that was rarely used at the time (the New Zealand White), but only at doses 25-300 times higher than those given to humans. It is highly unlikely that the original researchers would have used the New Zealand White rabbit, and even less likely that they would have ignored the positive data from other species because of one negative result that occurred only at extremely high doses.<sup>49</sup>

## Taking action

If you don't support animal experiments, should you boycott pharmaceutical companies and not take drugs?

We certainly do not encourage people to boycott medical treatments and potentially put their health, or even lives, at risk. Unlike for cosmetics or household products, a patient wanting to use a conventional medical treatment cannot choose between one that has been tested on animals and one that hasn't, and efforts are better directed into campaigning against vivisection in other ways.



'At present, millions of animals around the world continue to be "sacrificed" every year in massively expensive and time-consuming animal experiments that produce dangerously untrustworthy results.'

To help end animal experiments, **please order a free action and information pack**. You can do so at [www.animalaid.org.uk/go/endanimalexperiments](http://www.animalaid.org.uk/go/endanimalexperiments) or by giving us a call on **01732 364546**.

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