

Replacing primates in medical research

Summary of an expert report by: Dr Hadwen Trust / FRAME / St Andrew Animal Fund

The full report provides a detailed analysis of the extent to which primate experiments have already been replaced by advanced non-animal alternatives, and describes how scientific progress in non-animal research methods have the scope to replace primates in medical research.

The report includes five case studies in different fields of research – malaria, cognition, stroke, AIDS and hepatitis C – where the use of primates has provided very disappointing contributions to medical advances.

Increasingly, technological and scientific developments are generating advanced alternative techniques to the use of primates, with the advantage of providing data directly applicable to humans. Primates are often subjected to invasive and painful procedures and are restricted to a lifetime of laboratory incarceration; thus it is increasingly unethical to pursue such inadequate ‘models’ of human illnesses.



Malaria

Malaria, a parasitic infection that kills 1-2 million people per year, has been the focus of intense research for decades. Several malaria vaccines originally developed and tested in primates have failed to generate immunity in humans. One of the factors hampering progress is that the species of parasite used in primate studies may not naturally infect those hosts. This may lead to contradictory results, when data acquired through an artificial setting is transferred to natural infections. A realistic alternative to the primate models has recently been developed

involving *in vitro* human liver cell cultures, where the liver stage of the infection can be studied. Using such cultures, it will soon be possible to identify vaccine candidates and screen anti-malarial drugs. Human studies are essential for understanding why malaria parasites differ in their infectivity and to elucidate how individual differences in immune response contribute to the infection outcome.

Cognition

Research into human psychological processes, for example, memory, depression, learning and perception, regularly uses monkeys. Many experiments involve placing electrodes in, or removing parts of, the brain, or injecting toxins and tracers, in order to study areas that are active during certain tasks. Invasive and recurrent procedures are likely to inflict a high degree of stress on these intelligent animals. Furthermore, differences between the human and primate brains complicate or invalidate the findings from experiments using monkeys. Modern alternatives approach the problem in novel ways, commonly using safe human volunteer studies. Advances in non-invasive imaging have provided a range of cutting edge techniques, including the creation of temporary ‘virtual’ lesions in the human brain. With these more relevant techniques available, the use of primates is scientifically outdated as well as being ethically inappropriate.

Stroke

Stroke is a leading cause of death and disability and therefore research into the causes and potential treatments is critical. For over 170 years, experiments with various species of animals have been carried out, frequently involving invasive and painful procedures and yet failing to yield effective new drugs for people. Strokes artificially induced in laboratory primates are very different from sudden strokes in people. Furthermore, known risk factors, such as smoking, hypertension and diabetes, only affect humans and are important contributors to the disease. Collectively, population studies, brain imaging, post-mortem brain analysis and

in vitro multi-cell cultures, may provide more useful data than primate-based stroke research.

AIDS vaccines

For the past 25 years, scientists have been trying to develop a vaccine for HIV, the virus responsible for causing AIDS. While many simple prevention programmes have been successful in reducing infections, the same is not true for vaccine development. Primates, specifically rhesus macaque monkeys, are the favoured 'model' used to study human HIV infection and develop vaccines. More than 37 HIV vaccine candidates have undergone clinical trials involving 17,500 volunteers and they have all failed. A combined approach, relying on population studies, human blood and cells in the test tube, employing molecular biology and computer modelling, has the potential to overcome the hurdles imposed by using a different species. By making the most of available methods, basic information regarding HIV infection can be directly applied to humans and will eventually result in better ways to combat the infection.

Hepatitis C

Hepatitis C, a viral infection for which there is no definitive cure or vaccine, is another human disease for which primates are used experimentally. Research was originally carried out with chimpanzees particularly to study the replication of the virus, but this caused ethical concerns and chimpanzees do not develop the same symptoms as humans. Mathematical modelling has benefited hepatitis C patients by allowing an understanding of the *in vivo* dynamics of the virus, and drug treatment to be improved accordingly. Great progress with human cell cultures enabling studies of the behaviour of the virus now allows much hepatitis C

research, including drug screening, to proceed without the use of primates. Further development of early markers of vaccine and drug efficacy will enable safer clinical trials in volunteers, by-passing many primate tests.

Report recommendations

It is clear that there is a high level of public concern about the use of primates in research, and if policy makers are to pay genuine heed to this, non-animal replacement techniques urgently need to be properly funded and taken seriously as centrally important research methods, not just as adjuncts to primate research. Private and public funders of research and scientists themselves can help to bring about strategic change in the planning and conduct of medical research, so that primate experiments are replaced.

The current review of legislation governing animal experiments in the EU, Directive 86/609/EEC, provides a unique opportunity to implement a targeted and time-tabled strategy for replacement of primates in European research. This will help to avoid large-scale animal suffering, to enhance medical progress and to accelerate the development of novel, enabling technologies with wide applicability throughout the scientific world. It would also provide a lead to other national authorities to implement similar policies and drive forward change on behalf of patients and primates throughout the world.

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The full report is available as a pdf from:
www.focusonalternatives.org.uk

Printed copies of the full report can be ordered from: science@drhadwentrust.org



Focus on Alternatives brings together leading British non-governmental organisations which fund the development, or promote the acceptance, of methods that replace laboratory animals in research, education and testing. Focus on Alternatives' strategy is to work by educating, lobbying, facilitating access to information and by organising workshops on specific topics of concern.

Focus on Alternatives contributors to this report are the Dr Hadwen Trust for Humane Research, Fund for the Replacement of Animals in Medical Experiments and St Andrew Animal Fund.