



Animals containing human material

Report synopsis

The Academy of Medical Sciences

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Introduction

Animals containing human tissues, cells or genetic information in their bodies play an important role in medical research, and have done for many years. We call them animals containing human material (ACHM). Researchers use ACHM as better research models and to test new drugs and therapies.

As they develop these approaches, there is a need to ensure that a robust system of regulation exists for research using ACHM, which protects animal welfare, maintains the highest standards of safety and ethics, and keeps public views on the acceptability of research at the forefront. Experiments involving ACHM are covered in the UK by general animal research regulations, but there are no special provisions for this particular kind of research.

The Academy of Medical Sciences set up a working group, chaired by Professor Martin Bobrow CBE FRS FMedSci, to consider the scientific, social, ethical, safety and regulatory aspects of research involving ACHM. Our group aimed to make recommendations to ensure that in the future, valuable and justifiable research involving ACHM can continue within an effective regulatory system that is capable of responding to developments in scientific knowledge and societal attitudes.

It was felt important to seek non-specialist, as well as expert, views on such a potentially controversial topic. The Academy commissioned a public dialogue on research involving ACHM to collect such views. Its findings, already released as a separate report, proved a valuable source of input to the working group in its own deliberations.

This summary offers an account for non-specialists of the main findings of the Academy's full report, 'Animals containing human material'.

“ I have friends with MS and epilepsy. They are still alive thanks to the drugs they are taking. I am glad to still have them around me. I love animals to bits, but we have to move forward in medicine, saving the lives of our families.”

– Participant of public dialogue on ACHM

Why create an animal containing human material?

The use of animals in medical research has received much public attention and remains unacceptable to some people. Our study specifically looked at research involving ACHM, rather than the wider use of animals in research. And we did so in view of the current UK context, in which animal research is:

- Legally allowed only when it is carried out for good reason, where there are no appropriate alternatives, and it is under strict regulation.
- Accepted by the majority of the UK population as a valuable, and in some cases irreplaceable, source of insights into the workings of the human body and the benefits of intervening to tackle disease.

That said, animals are not humans; researchers must be cautious when assuming that findings from the one are good predictors of what will happen in the other. One way to minimise these differences, and so diminish the likelihood that animal findings will prove misleading, is to create embryonic or adult animals which incorporate human tissues within their bodies and are therefore, in certain defined respects, more like us. This, broadly speaking, is the value to biomedical research of ACHM.

More specifically there are three overlapping reasons for creating ACHM:

- To understand human bodily functions and human disease where cell- or computer-based alternatives alone will not suffice, and it is morally or practically impossible to do the necessary studies in living people.
- To determine the role of a specific piece of human DNA, our genetic material, by seeing what effect it has in a living animal.
- To test and develop methods of diagnosis, drugs and other treatments for human disease.

The animals most often used for these studies are mice, but a wide range of animals may be used for particular purposes.

How do you create animals containing human material?

In several different ways. You can alter an animal genetically by adding to it the human genes that you wish to study or by changing its genes so that they are the same as those in man. Alternatively you can create chimeras: animals formed either by mixing human and embryonic cells, or by implanting human material into an animal. Special types of cells called stem cells are often used to make chimeras. Box 1 outlines some examples of the many uses already being made of ACHM.

Box 1 Examples of the use that science already makes of ACHM

Where a human disease is known or suspected to be caused by a specific gene or some variant of it, the role of that gene can be studied by incorporating it into an animal. Studies on conditions as varied as migraine, anxiety disorders, osteoporosis, diabetes, heart disease and cancer have used this approach. Genetically altered animals can also be used to make human-type proteins and other substances for treating people whose bodies cannot make enough (or any) of the materials themselves. For example, a protein involved in the human blood clotting process but made by genetically altered goats was licensed for use during surgery on patients with a blood clotting disorder.

Mouse chimeras have been used to study liver diseases including hepatitis B and C, and to test antiviral drugs. To make the chimeras, human liver cells are introduced into mice that are unable to prevent the colonisation of the cells, producing a mouse in which up to 95% of its liver consists of human cells. Similarly, by introducing human stem cells into a type of rat predisposed to suffer from stroke it becomes possible to study the human brain's potential for repairing the damage caused by stroke, and to assess possible methods of enhancing this potential.

In short, a wide range of genetically altered and chimeric ACHM are now in use. This work is well established, has made significant contributions in many fields, and is likely to be even more widely used in the future.

Particular areas that the study considered

Research involving ACHM has a long history. The majority of examples of studies involving ACHM do not pose issues over and above those associated with the general use of animals in research and proceed without major ethical or regulatory difficulties. But ACHM techniques are progressing quickly, making a wider range of experiments feasible. A key goal of our study was to identify emerging and future applications of ACHM research and to consider their implications. In line with concerns expressed during the public dialogue, our report identifies three topics meriting special attention.

The first of these is *research involving the brain*. One contributor to the public dialogue expressed his reservations like this: 'I don't have a problem with it [ACHM] until it gets to the brain...but bits to do with memories, that would be too far – it's a human thing to have a memory.'

One example of ACHM involving brain tissue is the introduction of human neural (nerve) stem cells into primate brains to support research on Parkinson's disease. The key question, which cannot at present be answered with any certainty, is whether populating an animal's brain with human cells could result in that animal developing some elements of human consciousness, or 'human-like' behaviour and awareness. The likelihood is that the kind of work currently being done could not cause this to happen. But, to be absolutely sure, more sophisticated experimental methods for detecting the emergence of any such capabilities will have to be devised. Our report recommends that where there is any uncertainty over possible changes to an animal's brain function following a procedure, the work should proceed cautiously and incrementally, and should be subject to additional oversight by a national body of experts. More later on such a body (see 'How should work with ACHM be regulated?' below).

The second area of special concern is *research involving the reproductive system*. Commenting on the use of animals carrying human reproductive cells one participant at the public dialogue was quite shocked: ‘...that is so far out there, just awful. Perhaps if there was no sperm left on earth, but otherwise no way.’

Animals containing human DNA and tissues are already used to explore the role of human genes in many aspects of reproduction from the development of eggs and sperm through to the process of birth. In experiments in this area, human reproductive tissues can be implanted in various places (such as under the skin) in the recipient animal rather than into its own reproductive system, so there is little possibility of fertilisation. But some work does result in the presence of functional human sperm and/or egg cells in animals – which raises the remote possibility that fertilisation between human and animal germ cells might inadvertently occur.

In practice, once again, this is unlikely. And even if it were to occur, it is very unlikely that the event would result in a viable embryo. That said, researchers who envisage even a remote possibility of this occurring should proceed with caution. Our report recommends that these sensitive experiments warrant careful scientific and ethical thought by the national body of experts before they are carried out.

The third area of concern is with *research involving human appearance or behavioural traits*. For example, the effects of radiation in sunlight that can lead to DNA damage and skin cancer can be examined using mice with human skin transplants. Techniques using animals to study human limb development are also emerging. Some participants in the public dialogue viewed physical appearance as key to the distinction between species and were disturbed by any blurring of these boundaries. Where experiments could significantly alter the appearance or behaviour of animals in characteristics that distinguish humans most from our close evolutionary relatives our report concludes that such work should again be considered by the national body of experts.

What about the animals?

All research involving animals is tightly regulated in the UK by the Animals (Scientific Procedures) Act 1986. This legislation is intended to ensure that animals used in research are not subject to unnecessary pain, suffering, distress or lasting harm. ACHM are covered by this Act, and work on them is therefore no less rigorously scrutinised.

The report considers whether the incorporation of human genetic or cellular material into an animal could of itself have the potential to cause some distinct or different suffering. We conclude that, in comparison to other licensed research involving animals, the research does not generally have such potential.

It is also unlikely that ACHM procedures will reduce the overall number of animal experiments performed, at least in the short term. But the report anticipates that the use of ACHM is likely to further efforts to improve welfare in the longer term by *replacing* animal use, *reducing* the number of animals needed or *refining* the procedures used to cause less suffering (principles known as the '3Rs'). For example, experiments on genetically altered mice may, in some cases, avoid the need to perform experiments on primates. This would be a welcome development.

Is it safe to use ACHM?

While most studies involving ACHM do not present additional safety issues compared to those associated with animal research in general, the report draws attention to the creation of ACHM that might present particular safety issues. Some ACHM experiments – for example, those in which animals are made susceptible to infectious agents normally confined to humans – need to be carried out in appropriately secure laboratory conditions. This is also the case with any animal experiments involving infectious organisms. Experiments that bring human and animal tissues close together might lead

to the activation of dormant human or animal viruses within an animal and allow them to recombine, swap their genetic material and possibly create new disease risks. Experiments of this kind should be subject to thorough risk assessment and appropriate control measures.

Is it ethical to create and use ACHM?

Many people do, quite understandably, feel an instinctive discomfort at the notion of engineering an animal to contain human material. The working group members who produced the report considered this matter closely. They concluded that humanising animals for the purposes of medical research does not create significant new ethical problems. They were not persuaded by the argument that humanising animals to benefit our own species introduces a new level of exploitation into the relationships between humans and animals. As with animal work in general, they took the view that, within carefully considered boundaries and robust regulation, the benefit to humans generally justifies the harm done to the animals involved, a view that was also echoed in the public dialogue findings.

“ I don’t necessarily like it, but if it delivers benefits then it’s worth it. ”

– Participant of public dialogue on ACHM

How should work with ACHM be regulated?

Evaluating work in this complex field of science requires specialist knowledge and sensitive judgements. The report recommends a national expert body is put in place to advise government on ACHM research and to draw up appropriate guidelines for researchers. To maintain trust and ensure

accountability this body needs to operate transparently and to engage with the public, as well as with the scientific community. Our report suggests that, rather than creating an entirely separate group of experts to oversee ACHM, the expert body that advises on animal research should take on the task (currently the Animal Procedures Committee), with expertise added as necessary to carry out this oversight. For practical purposes, such as regulation, the report recommends the creation of three categories to define ACHM experiments (see Box 2). The regulation in this area is complex, involving multiple government departments and bodies, all of which must work together to deliver a robust approach to regulating this research.

Box 2 Recommended categories of ACHM experiments

Category one. The great majority of ACHM experiments which do not pose issues beyond those that arise from the general use of animals in research. These studies should be subject to the same oversight and regulation as other animal research.

Category two. A limited number of ACHM studies that demand strong scientific justification. They should be subject, case by case, to additional specialist scrutiny from the proposed national expert body.

Category three. A narrow range of experiments that should not currently be licensed because they lack compelling scientific justification or raise very strong ethical concerns.

The boundaries of these categories should be kept under regular review by the expert body, and the results of their decisions made readily available to the public.

What happens in other countries?

As elsewhere in science, research using ACHM often involves the collaboration of scientists working in different countries. As in the UK, certain general regulations in those countries may cover aspects of work with ACHM. But no country has national laws designed specifically to govern ACHM research. There are also considerable differences between countries in the regulation of animal research in general. And while guidelines developed by international scientific groups can encourage common standards, these too are currently limited in relation to ACHM. All this creates uncertainty about what is acceptable – and also opens up the unappealing possibility of researchers seeking to locate their work in certain countries to avoid particular restrictions.

Consistency in standards of research practice and of ethics at an international level would be helpful and desirable. In the first instance this could be encouraged by initiatives designed to raise awareness of ACHM and the importance of consistency. Such initiatives could be led by regulators, policy-makers, national and international bioethics bodies, medical research councils and the research community itself. Given the attention paid to laboratory animal welfare in the UK, we are well placed to take the lead in encouraging such a development.

Does ACHM research have public support?

Participants in the public dialogue raised some specific concerns over this type of research, which are reflected in the Academy's report. However, the dialogue findings showed that there is a high degree of public acceptance of ACHM research, provided it is well regulated and justified by the potential benefits to our scientific knowledge or to our methods of treating medical conditions.

Further information on this study

Full copies of the report, 'Animals containing human material', can be downloaded from <http://www.acmedsci.ac.uk/publications>

Full copies of the report of the public dialogue, 'Exploring the boundaries', can be downloaded from <http://www.acmedsci.ac.uk/p209.html>

Full copies of the evaluation report of the public dialogue can be downloaded from <http://www.acmedsci.ac.uk/index.php?pid=240>

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Academy of Medical Sciences
41 Portland Place
London, W1B 1QH

Tel: +44 (0)20 3176 2150

Email: info@acmedsci.ac.uk
Web: www.acmedsci.ac.uk