Viewpoint

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Ethical Debate: Ethics of xeno-transplantation

Murali Krishna and Peter Lepping

Interest in cross-species transplantation has recently been rekindled[1]. This is due to many developments including the shortage of donor organs, advances in transplant medicine, investment in biotechnology research, and the non-availability of more ethically suitable alternatives to human organs. Increasing success rates in allotransplantations (organs from different member of the same species) has increased the demand on donor organs[1, 2]. Other types of transplantation include autotransplants (a person's own organs or tissues are used for transplantation) and isotransplants (organs from one person are transplanted into another genetically identical person, like an identical twin). These options are limited in terms of body parts used and numbers.

Good facts inform good ethics. It is therefore obligatory to look into the current research knowledge about xenotransplants (organs from one species to another, for example animal to human) in more detail. The advocates of xenotransplantation argue that it could provide organs "relatively quickly" and hence save more lives. If animal organs were easily available for transplantation most eligible recipients would receive the transplantation much earlier on in their illness. It is argued that this may decrease distress and suffering. Whilst xenotransplantation may theoretically increase the survival time, it is unclear, however, whether the negative impact on recipients' quality of life due to long-term immunosuppressant therapy and the risk of zoonotic infections would in fact worsen the overall long-term outcome[3]. Recent research suggests that xenotransplantation may be associated with the transmission of pig microorganisms including viruses, bacteria, fungi, and parasites. Because of the recipient's likely immunosuppressed state, infection and pathologic consequences may be more pronounced. Transmission of most microorganisms with the exception of the porcine endogenous retroviruses may be prevented by screening the donor pig and qualified pathogen-free breeding. However, porcine endogenous retroviruses represent a special risk as they are present in the genome of all pigs and infect human cells in vitro. Until now, no porcine endogenous retrovirus transmission was observed in experimental and clinical xenotransplantations as well as in numerous infection experiments[4]. Nevertheless, strategies need to be developed to prevent their transmission to humans. It is equally possible that many eligible recipients may be denied having a trial of xenotransplantation by doctors who believe that there is an unfavourable risk-benefit ratio. The limited long-term data on outcomes of xenotransplants thus renders ethical analysis difficult.

There is some evidence to suggest that the recipients of animal organ donation may develop a different self image with possible consequences for their identity[5,6]. This happens with human organs at times, but may be a more significant problem with animal organs, as the recipient knows that they have been given a non-human organ. Loss of identity jeopardises the core principle of autonomy, which underpins all medical treatment.

The risk of zoonosis to the recipient and to the wider society cannot be accurately estimated[7]. Hence there is a requirement for vigilant post-operative monitoring[5] with a possibility of engaging article5 and 8 of the European Convention of Human Rights (for England and Wales: Human Rights Act 1998)[†]. Article 12 may also be engaged as the recipients may be restricted from having physical relationships, carrying out their routine day to day activities and socialisation. This is because the prevention of possible risk to the wider public from zoonosis may require the recipient to be put under restrictions with regard to their engagement with others. This may include restrictions to go out, which can result into de facto temporary detentions at home. Hence consenting to xeno-transplantation would be "binding and contractual" over a long period of time. The subject may not have the right to withdraw. This is entering into a de facto contract with potential restrictions or even deprivation of human rights. This would restrict the ability to give informed consent even for a well informed patient, as it is difficult to be fully appreciative of future restrictions of one's liberty.

Autonomous decision making and thus informed consent may also be put at risk by other factors surrounding xenotransplantation. The decision to embark on xenotransplantation may be primarily driven by an instinctual wish to survive due to a lack of other viable alternatives. Patients in these circumstances may have little or no consideration to medium and long-term effects on themselves

and society. However, it is the consideration of such long-term consequences that make a truly autonomous decision, and differentiate it from a decision that is purely based on immediate instinct. Whilst the wish to survive is legitimate it is difficult to make decisions free of the pressure to survive when there is a lack of alternatives.

It also brings up an even more important question: Can any person ***ever*** consent to a future restriction or deprivation of their liberty or other human rights? Even if there were an option to define acceptable future restrictions it would be likely that patients could still challenge the legality of any such agreements. They could quite reasonably argue that they have agreed to the restrictions under duress because of a lack of viable alternatives to their xeno-transplants.

Xenotransplantation touches questions of utilitarianism (greatest good for the greatest numbers) and public protection[2]. Utilitarianism takes into account the reasonable interests of society in good outcomes, fairness in the distribution of resources, and the prevention of harm to others. The Nuffield council on bio-ethics embraces a utilitarian approach. However, there are limits to the utilitarian argument for xenotransplants. Even if they were widely available, the treatment would be immensely expensive. Production of a pathogen free donor organ would involve rearing animals in strictly controlled environments, subjecting them to rigorous standards of examination and surveillance. The additional costs of developing a sustainable work force to provide transplantation and post-transplant surveillance of the patient and the community would be high. The insurance providers may not cover expenses of a xenotransplant. Public health care providers may decline to provide this treatment as it may not be recommended by expert groups as cost effective. Xenotransplantation may commence in the developing world where the regulations are lax and the poor can be more easily exploited[8]. Patients who would potentially benefit from xenotransplantation may not be able to afford it due to its cost with serious implications for fairness.

Xenotransplantation also raises other ethical questions in relation to the wider community. We have seen that consent of an individual to a xenotransplant has significant bearing on the protection of society[7]. Should the members of a community therefore be consulted if there were any xeno-transplantation experiments in their region? The risk is primarily due to the risk of zoonotic infections, the need for surveillance, and possible quarantine of contacts[7,9]. In addition, if health authorities were to fund expensive experimental interventions like xenotransplantation, other routine treatments of greater potential benefits to society may be jeopardised. Society may also have views about particular animals being used as donor animals[10]. For example religions like Islam and Judaism may feel that pigs are 'ritually unclean'. They may therefore not approve of certain animals to be used for donation, and more worryingly may fail to socially accept recipients with such 'unclean' transplants[11].

From a deontological perspective (this judges the morality of an action based on the action's adherence to a ruleor principle) some authors assert that animals have rights similar to those considered appropriate for humans[12,13]. The protection of animals has legal status in many countries. Consequentialists may view the suffering and death of an animal as acceptable for the betterment of a human patient, as they would judge the morality of an action primarily by its end result. They would argue that potential benefits and improvement in human welfare arising from xenotransplantation may justify the loss of animal life. However, this will never satisfy the animal rights lobby; especially as whilst minimising the risk of acquired infections, the animals have to forgo greater suffering in the form of isolation, monitoring and investigations. Furthermore, genetic modification can have both immediate and long-term negative effects on animals.

In summary, xenotransplantation has significant ethical consequences. On an individual level, there are the questions of pressure to consent that may negate autonomy and the validity of that consent as well as the difficulties that arise when patients are asked to consent to future restrictions of their human rights. On a societal level there are questions of cost and benefit analysis as well as risks from zoonotic infections. In addition, questions of animal rights need to be addressed before any programs are likely to go ahead.

†Appendix of articles of the Human Rights Act.

- Article 8 of the Human Rights Act 1998 (The right to respect for private and family life, home and correspondence)
- Article 5 (The right to liberty).
- Article 12 (The right to marry and found a family)

Competing Interests
None Declared
Author Details
MURALI KRISHNA MBBS MRPsych, Consultant Psychiatrist, CSI Holdsworth Memorial Hospital, Mysore, India; Associate Tutor, University of Edge Hill, St Helens Road Omskirk UK L39 4QP.
PROF PETER LEPPING, Consultant Psychiatrist, Associate Medical Director, Betsi Cadwaladr University Health Board, Wrexham; Visiting Professor in Psychiatry, Glyndŵr University, Wrexham, North Wales.
CORRESSPONDENCE: DR MURALI KRISHNA MBBS MRPsych, Consultant Psychiatrist, CSI Holdsworth Memorial Hospital, Mysore, India
Email: muralidoc@hotmail.com

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