



Xenotransplantation: Issues and Challenges.

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Abstract

Xenotransplantation is any procedure that involves the transplantation, implantation or infusion into a human recipient of either live cells, tissues, or organs from a nonhuman animal source, or human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues or organs. It is often suggested as an alternative to human organ transplantation due to the most daunting barrier to organ transplantation, which is the shortage of suitable human organs. Proponents of xenotransplantation state that transplanting animal organs into individuals with end-stage organ diseases will restore hope in them and will do away with the ethical issues in human-to-human transplantation such as the debates on organ allocation policies, consent, organ sale, using organs of heart-beating donors, anencephalic infants, embryo transplantation, and stem cells from embryos and fetuses. However, it is found out that xenotransplantation from animals to humans raises legal, ethical and religious issues and challenges such as the transmission of infectious diseases, the intense debate on the brutality in the use of animal organs as well as the controversy on whether the use of pig organs is permissible or forbidden in Islam. Consequently, this paper recommends the exercise of extreme caution in transplanting animal tissue/organs in humans due to the spread of infectious diseases and because such practice still remains experimental and controversial.

Introduction

Shortage of suitable human organs | transplantation thereby depriving
remains the greatest barrier to organ | patients with end-stage diseases of a

better and qualitative life. It is against this backdrop that xenotransplantation is considered an alternative to bridge the gap between the demand and supply of human organs. Xenotransplantation is any process that comprises the transplantation, implantation or infusion into a human recipient of either live cells, tissues, or organs from a non human animal source or human body fluids, cells, tissues or organs that have had *ex vivo* contact with live nonhuman animal cells, tissues or organs.¹ Both the experimental use of pig pancreatic islet cells to treat diabetes² and the implantation of human cancer cells in mice for tumour study are both considered xenotransplantation.³ However, this paper is restricted to human-to-animal organ transfer. Regardless of the benefits that may result from the use of animal organs, it raises a lot of issues and challenges in the context of infectious diseases, confidentiality, non-maleficence, animal rights, consent and the classification of animals in Islam as lawful or forbidden. These issues and challenges are viewed from the perspectives of medicine, ethics and Islam.

Attempts at Xenotransplantation

At the turn of the 20th century, random experimental xenotransplantation were regularly performed but it was not until the 1960s that sophisticated studies of xenotransplantation started. There were several attempts at transplanting kidneys, livers, and hearts from baboons, pigs, lambs and chimpanzees into humans in the 1960s.⁴ For example, pig heart valves have been used in human heart surgery for 30 years,⁵ to replace defective human heart valves. Their advantage lies in arousing almost no immune response because they are made of cartilage, which are mostly accumulations of dead cells retaining none of the molecules that attract antibodies and they are specially treated.⁶ However, most of the attempts at transplanting animal organs proved disastrous owing to organ rejection, which may be acute, chronic or hyperacute. Notwithstanding the progresses made in the field of immunosuppressive healing, survival rate following xenotransplantation remains a few months at best.⁷

The most famous case of animal-to-human transplantation of a vital organ is that of Baby Fae. Leonard Bailey, a paediatric cardiac surgeon performed the first of such, by transplanting a baboon heart into an infant (Baby Fae) in 1984. Born three

¹FDA, Xenotransplantation. Retrieved December 14, 2019, from <https://www.fda.gov/vaccines-blood-biologics/xenotransplantation>.

²Zhu, H., Yu, L., Yi Lyu, and Wang, B. (2014). *Optimal Pig Donor Selection in Islet Xenotransplantation: Current Status and Future Perspectives*. *J Zhejiang Univ Sci B*, 15(8): 681-691. Retrieved January 15, 2019, from <https://www.ncbi.nlm.nih.gov>

³Eidinur, H.A., Manaf, S.M. and Mat, N.F. (2016). *Genetic Barriers in Transplantation Medicine*. *World J Transplant*, 6(3): 532-541. Retrieved December 20, 2018, from <https://www.ncbi.nlm.nih.gov>

⁴American Medical Association, Council on Scientific Affairs, (1985). *Xenografts: Review of the Literature and Current Status*. *JAMA* 254:3353-57; Deschamps, J-Y, Roux, F.A., Sai, P., and Gouin, E. (2005). History of Xenotransplantation. *Xenotransplantation*, 12:91-109.

⁵Nuffield Council on Bioethics. *Animal-to-Human Transplants: The Ethics of Xenotransplantation*. p.6

⁶Munson, R. (2002). *Raising the Dead: Organ Transplants, Ethics and Society* Oxford University Press, New York. p.206

⁷Anderson, M. Xenotransplantation: A Bioethical Evaluation. (2006). *Journal of Medical Ethics*, 32:4. Retrieved November 18, 2018, from <http://www.istor.org/stable/27719606>

weeks premature, Baby Fae was diagnosed with a congenital condition that results in the left side of the heart being physically under-developed in its entirety (hypoplastic left heart syndrome).⁸ Baby Fae survived the dangerous surgery and lived longer than previous human recipients of an animal heart, having died 20 days after due to organ rejection.⁹ However, the transplant birthed a series of controversies on the ethics of transplanting a baboon heart into an infant.

Although it is alleged that chimpanzees and baboons are the closest to humans in terms of genetics, they are however not used as sources of organs because of the risk they pose, as viruses hidden in them may mutate and cause a disease like acquired immunodeficiency syndrome.¹⁰ Instead pigs are regarded the most suitable source for transplantation because their gestation takes less than four months, they produce litters of as many as ten,¹¹ and the similarities in size and physiology between human and pig organs.¹² Pigs are also the preferred source for possible experimental xenotransplantation because genetic modification has facilitated the quest for the development of more immunologically ‘compatible’ animal organs, which resist hyperacute rejection (destruction of the graft within twenty four hours of transplantation).¹³ However, a range of immune complications, which ultimately lead to xenograft rejection happens between humans and pigs despite the preference of pigs over chimpanzees.

Rejection varies in relation to the use of pig organs and bone marrow/tissue cells. Pig organs have blood vessels running through them, the blockage of which causes tissue damage (a feature of hyperacute rejection) while pig bone marrow and tissue cells also provoke an immune response and are attacked by antibodies but immunosuppressive drugs are usually given to prevent their being rejected.¹⁴ However, genetic alteration of a pig’s complete set of deoxyribonucleic acid (DNA) is proposed as the solution to xenograft rejection.

Ethical Issues in Xenotransplantation

Xenotransplantation raises ethical issues from the perspectives of natural law, transfer of infections, animal rights, consent, full disclosure etc

Natural Law: The issue that is often discussed regarding xenotransplantation is the intermixing of biological material from one species to another. This is

8 Moore, S. (2011). A Discussion of Ethical Issues in the Case of Baby Fae. *JCCC Honors Journal*:2:(2), Article 2. Retrieved December 25, 2018, from <https://www.scholarspace.iccc.edu>

9 History. *Baby Fae Dies*. Retrieved December 24, 2018, from <https://www.history.com>

10 Munson, R. Op. Cit. p.209-210

11 Ibid, p.210

12 Kim, S.E., Kang, K.W., Seongso, S.G., Hwang, Sun. A. O, Shim, K.M., Jang, K., Choi, S.H., Lee, S. and Kang, S.S. (2018). Immunological Compatibility of Bone Tissues from Alpha-1,3-galactosyltransferase Knockout Pig for Xenotransplantation. *BioMed Research International Volume 2018*. Retrieved December 30, 2018, from <https://www.hindawi.com>

13 British Medical Bulletin. *Xenotransplantation – Current Status and Future Perspectives*. Retrieved December 27, 2018, from <https://www.academic.oup.com>

14 Munson, R. Op. Cit.. pp 205-206

considered a distortion of God's creation and plan for humanity. If same species transplantation such as human-to-human transplantation could face a lot of criticisms, more is expected in the discourse on animal-to-human transplantation especially in relation to the spread of infectious diseases. Downie argues that animal to human organ transplantation is unnatural but it does not indicate that such practice is essentially wrong as 'every medical intervention is in that sense unnatural.'¹⁵

Viral Infections: Even amongst human-to-human transplantation, there is the risk of exposure to infectious diseases. Infectious diseases are more pronounced in animal-to-human transplantation especially in the context of posing public health hazards. The foremost ethical issue to be addressed is balancing the interest of the sick with public health in view of unanticipated fatal outbreaks that may ravage societies.

While xenotransplantation promises to increase the supply of organs considerably, most of the concern about the risks of infection from xenotransplantation focuses on viruses. This is because ... viral infections may have a long latent period during which the person has no symptoms of the disease ... If a new disease were to emerge as a result of xenotransplantation, it might be several years before the problem was identified. During this time the infection might be spreading throughout the population.¹⁶

Also, the threat of zoonosis, diseases that could be transferred from wild or domesticated animals to humans, combined with general aversion to the xenotransplantation, decreases the functionality of the technique.¹⁷ It follows therefore that tissue samples from the animals must be accurately screened for known pathogens as a preventive measure to curb the spread of diseases especially in the light of Hepatitis C (HPC) outbreak in 2000.¹⁸ Pigs, the favourites for transplantation also have a type of virus called porcine endogenous virus. This virus is incorporated in the genome of all pig strains and can infect human cells in vitro.¹⁹ Thus these viruses are considered obstacles to success in xenotransplantation.

Notwithstanding the preventive measures to curb the spread of diseases from animals to humans, there may still be flaws in testing. An animal incorrectly tested HPC negative, which led the pathogen to infect eight of forty transplantation recipients because he had not developed an antibody reaction enough for titre detection.²⁰ It is as a result of testing flaw such as this, that epidemiologists

¹⁵Carr, C. (2015). *Unlocking Medical Law and Ethics*. Hodder Education, p.305

¹⁶ Carr, C. Op. Cit. p.305

¹⁷ *Organ Donation Basic Issues*, <http://www.bc.edu> Retrieved on 27-05-2016 at 12:46pm

¹⁸ Xenotransplantation News. *Xenotransplantation* (2003) 10:539-4

¹⁹ Denner, J. (2003). Porcine Endogenous Retroviruses (PERVs) and Xenotransplantation: Screening for Transmission in Several Clinical Trials and in Experimental Models Using Non-Human. *Ann Transplant*, 8(3):39-48. Retrieved June 14, 2019, from <https://www.annalsoftransplantation.com>

²⁰ Anderson, M., Op. Cit. 206

recommend an international registry of xenotransplantation recipients with associated lifetime surveillance of the recipients, which may be stretched to the friends, sexual partners, and friends of the recipients.²¹ This will serve as a public health precaution to limit infectious spread of diseases. However, mandatory clinical monitoring and surveillance is ethically controversial as it violates the individual's right to privacy.

There is the risk of infectious diseases on third parties, who though did not consent to xenotransplantation but are put at risk as a result of contact with recipients of animal organs.

In the light of the above discussions, the basic ethical question that must be addressed is whether xenotransplantation should be made illegal in view of the serious public health hazard it poses. The reality about xenotransplantation is that infectious diseases are not specific to a beneficiary who must have consented to the risk of such transplantation; instead it may trigger an epidemic that may wipe out families and communities that did not consent to the risk taken by an individual. The Marburg virus outbreak of 1967 highlights this problem. In August 1967, laboratory workers in Marburg, Frankfurt and about four weeks later in Belgrade, developed severe and often fatal hemorrhagic fever as a result of the Marburg virus; all the patients with primary infection at the three locations had come in contact with the cell cultures, blood and organs from *Cercopithecus aethiops*, African green monkeys imported from Uganda.²²

Notwithstanding the fact that these monkeys were not used for xenotransplantation but for the reproduction of vaccine strains, the outbreak proves in handling animals, fatal diseases could be transferred from person to person and across countries especially in dealing with primates. Virologists contend that even though screening of primates may discover no active virus, they harbour at least thirty endogenous retroviruses in their DNA.²³

Animal Rights: Animal rights advocates consider the use of animal organs for the benefits of humans as an abuse and they oppose the use of animals for human advancement. Tom Regan, a professor of philosophy and an advocate of animal rights opines that animals cannot be seen exclusively as means for the support of other living beings because they are experiencing subjects which command respect.²⁴ Tied to this is the ethical issue of using animals as involuntary donors,²⁵ as their organs are removed without consent.²⁶ It is however inconceivable to seek the consent of animals, which are irrational beings. Thus, consent is only relevant

²¹ Ibid

²² Slenczka, W. and Klenk, H.D. (2007). Forty Years of Marburg Virus. *The Journal of Infectious Diseases*, 196(2):S131-S135. Retrieved June 14, 2019, from <https://www.academic.oup.com>

²³ Munson, R. Op. Cit. p.224

²⁴ Ibid, p.235

²⁵ Phillips, T. *The Xenotransplantation Ethics Debate: Using Animal Organs for Humans*. Retrieved June 16, 2019, from <https://www.thebalance.com>

²⁶ Veatch, R.M. and Ross, L.F. (2015). *Transplantation Ethics*. Second Edition. Georgetown University Press, United States of America. p.232

to prospective recipients and guardians of persons that cannot give their consent after being full informed about the surgery, the success rate and risks.

At the other divide are advocates for the utilisation of animal organs to save human lives provided the process is devoid of brutality. The Working Party of the Nuffield Council on Bioethics states that ‘It is difficult to see how, in a society in which breeding pigs for food and clothing is accepted, their use for life-saving medical procedures, such as xenotransplantation, could be unacceptable.’²⁷ It is pertinent to mention that the lives of humans are more sacred than the lives of animals and since they are slaughtered for food, it is surprising the condemnation on utilising them to save human lives and advocating instead the use of organs of the brain dead.

Non Therapeutic Interventions: In discussing xenotransplantation, a line needs to be drawn between therapeutic interventions and experimental procedures. In the notorious case of Baby Fae, it is asserted that the transplantation was nontherapeutic. Instead it was carried out “just to see what could be learned, with no hope of benefit for the baby.”²⁸

Veatch and Ross argue that if the assertion was correct, it would be a valid condemnation as it is commonly accepted that new procedures, particularly nontherapeutic, should only be carried out on consenting adults when feasible while such procedures are justified on non-consenting subjects only when the risks are very minor.²⁹

Full disclosure of every medical procedure is fundamental to giving consent or not; this is especially so regarding risky and experimental procedures such as xenotransplantation. Thus, it is important to weigh the advantages and disadvantages of such procedures before consent is given. Also, vulnerable persons are the most in need of protection from these procedures as against persons who can give their consent to procedures.

The Debate on Resource Allocation: Proponents of this view hold that significant resources that would better be spent elsewhere are expended in xenotransplantation as against more basic interventions in more simple treatments and preventive care. Thus, the question that follows is the ethics of expending millions of dollars on xenotransplantation when a high percentage of members of societies are without basic treatments and preventive care.

Islam and Xenotransplantation

In Islam, animals can be classified as falling under *Halal* (permissible), *Makruh* (detestable) or *Haram* (unlawful). Jurists are divided on the permissibility of using animal organs for transplantation especially where it involves the utilisation of

²⁷Samanta, J. and Samanta, A. (2015). *Medical Law*. Second Edition. Palgrave, United Kingdom, pp.344-345

²⁸ Capron, A.M.(1985). When Well-Meaning Science Goes Too Far. *Hastings Center Report*, 15(1):8-9; Annas, G. (1985). Baby Fae: The ‘Anything Goes’ School of Human Experimentation. *Hastings Center Report*, 15(1):15-17.

²⁹ Veatch and Ross. Op. Cit. p.236

animals that are unlawful or impure. Jurists are divided on the permissibility of using animal organs for transplantation especially when it involves the utilisation of animals that have been classified as *Haram*

The Islamic *Fiqh* Council has categorised animals into pure and impure. That organs from impure animals may be transplanted into humans as medical treatment provided the specialist doctors testify that the sick person is in such a need and there is no organ from pure animals.

The Makkah Academy permits this on the grounds of *Darurah* (necessity) provided the animal must have been slaughtered in accordance with Islamic rites. Thus, utilising the organs of animals that are *Haram* is not permissible. The India Academy agrees with the Makkah Academy.

The *Majlis al-'Ulama'* of Port Elizabeth has decided that it is forbidden to utilise a pig or its parts even for medical grounds because the *Shari'ah* considers a pig as *Najasad al-ghalizah* (grossly impure).³⁰ Al Qaradawi holds a contrary view that what has been prohibited in four verses of the *Qur'an* is consuming the flesh of pig. Thus transplanting its organ(s) is not eating it but benefitting from it. The Messenger of Allah (peace be upon him) permitted benefitting from the skin of carrion. In one authority from the *Qur'an*, both carrion and pig are prohibited thus if the law allows benefitting from the skin of carrion (by not eating), this legality is extended to benefitting from the skin or a part of pig (other than by eating).

It is narrated in the *Sahih* that the Messenger of Allah (peace be upon him) passed by a dead goat and asked about it. The people said, it is goat belonging to the freed slave of Maimuna (may Allah be pleased with her). He said, 'Why don't you take the skin, tan it and make use of it'. They said, 'It is a dead animal'. And he said, 'It is only prohibited for eating'.³¹

The Jurists hold different views on whether pigskin is purified by tanning and the ruling on making use of pigskin after tanning:³² Imam Abu Hanifah is of the opinion that tanning purifies all types of skin except the skin of pigs while Imam Ahmad and Imam Malik hold the view that tanning cannot purify skin of carrion. However, the Shafi' jurists are of the view that tanning purifies skins of all animals regardless of permissibility; thus, tanning purifies the skin of dogs and pigs. This view is held by Ibn Hazm, Dawud az-Zahiri, Sahnun among the Maliki jurists and Al-Shawkani.

Jurists that accept the permissibility of purity of pigskin after tanning have no doubt as to the permissibility of such skin for various purposes. However, some of the jurists that hold the view that tanning does not purify pigskin (such as the Hanbalis jurists) permit its use when it is dried but not when it is wet.

30 Ebrahim, A.M. (2001). Organ Transplantation, Euthanasia, Cloning and Animal Experimentation: An Islamic View. The Islamic Foundation, United Kingdom. p.24

31 SahihMuslim.com, Chapter: Purification of the Skins of the Dead Animals by Tanning Them. Retrieved June 4, 2019, from <https://www.sahihmuslim.com>

32 Islam Question & Answer. Is it Permissible to do an Operation on the Heart Valves using Pigskin? Retrieved March 17, 2019, from <https://www.islamqa.info>

Yusuf Al Qaradawi³³ is of the opinion that transplanting an organ from an animal which its impurity has been established such as the pig in a Muslim's body should not be resorted to unless on grounds of necessity. Necessity has its rules hence that which is permitted as a result of necessity should only be carried out within the scope of that necessity after trustworthy Muslim doctors have declared the benefit of such transplantation.

The best approach, which a Muslim should take regarding matters that are doubtful is abstinence, in line with the *Hadith* reported by Hassan Ibn Ali where the Messenger of Allah (peace be upon him) said: "Leave what makes you doubt for what does not make you doubt. Verily, truth brings peace of mind and falsehood sows doubt."³⁴ This is with a view to avoid transgressing the limits set by the Lawgiver.

Conclusion

Xenotransplantation is considered a treatment option for individuals with end-stage organ diseases due to the shortage of suitable human organs. However, it raises issues and challenges in the context of law, ethics, and Islam such as the risk of exposure to infectious diseases, organ rejection, consent, morality, animal abuse as well as treatment with animals that are classified *Haram* in Islam. Hence caution must be exercised especially in relation to the transfer of infectious diseases from animals to humans

³³Qaradawi, Y. *Fatawa Mu'asirah, Al Juz-uth thani*. Darul Qalam, Kuwait, p.538

³⁴Elias, A.A. Hadith on Doubt: Leave Your Doubts for Certainty in Truth. Retrieved May 28, 2019, from <https://abuaminaelias.com/dailyhadithonline/2012/08/18/leave-doubts-vageen/>