

**Can xenotransplantation solve the organ donor shortfall?  
Explain the science and explore the issues.**

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Xenotransplantation, although at present only in its experimental stages, is being considered as a foreseeable alternative to allotransplantation. Hundreds of thousands of people are dying worldwide each year because they aren't able to receive an organ transplant because of organ shortages. There are schemes aimed at increasing the number of registered donors. However the results will never successfully meet the acute organ shortages. With further research, xenotransplantation could become a viable therapeutic procedure. Although the future of xenotransplantation could contain great benefits, it raises many serious health issues and important ethical questions.

In the early stages of xenotransplantation, a fundamental question was which animal to use. Animals and humans, no matter how similar, have important physiological differences. The more distinct these differences, the more difficult it is to successfully transplant an organ from an animal to a human. Initially primates were favoured as organ donors because of their similarity to humans. But that very similarity means it is widely considered unethical to use them as donors. There are strict regulations about using primates for research in New Zealand. The use of primates also raises other issues: they pose a greater threat of passing on infectious diseases and their needs are much harder to meet those of other animals in captivity. Pigs, which have similar sized organs to humans, are now the organ donor of choice. They have been domesticated for centuries and produce large litters, both important qualities in terms of rearing pigs in captivity and more efficient organ production.

Immunological responses to foreign xenografts are the biggest hurdle researchers must overcome before xenotransplantation will be viewed as a viable solution to the organ shortage. Organ rejection can occur in allotransplantation. However it is usually prevented by immunosuppressant drugs. In xenotransplants, the immunosuppressant drugs used in allotransplantation cannot overcome certain aspects of xenograft rejection because there are several different processes by which our immune system fights off invading organisms. Present immunosuppressant drugs are not effective in preventing the types of transplant rejection which occur in xenotransplants but not allotransplants.

The challenge of xenotransplantation is to find a way to deceive the human immune system into accepting an animal organ. Following an animal human organ transplant, hyperacute rejection occurs. The body reacts in the same way as when it is faced with an infection, recognizing the organ as 'foreign' and attacking it, eventually causing the organ's blood to coagulate, resulting in the organ being starved of oxygen and dying. The most feasible strategy to overcome hyperacute rejection is the development of transgenic pigs. All cells have proteins on their surfaces, called regulators, which prevent the activation of 'complement'. Complement is an aggressive component of the immune system which is responsible for attacking foreign organisms but can also attack the body's own cells, hence the need for regulators. Transgenic organs would contain human 'regulator' proteins, preventing the organ being recognized as foreign and consequently attacked by the complement.

Although xenotransplantation technology is being developed rapidly, there are still many ethical and health-related issues concerning the practice. One key issue is animal welfare.

Many people believe that the benefits of xenotransplantation outweigh the suffering of the animals. However many people believe it is unethical to kill an animal to perpetuate a human life. One of the main anti-xenotransplantation arguments is that the potential benefit to humans is overstated and the suffering of animals understated. Another difficult implication raised by xenotransplantation regarding animal rights is that of transgenic modification.

Does inserting human genes into an animal make it part 'human' and could it cause negative side effects in animals? The issues of animal welfare raised by xenotransplantation all point to the question of whose lives we put in higher regard – those of our own race or those of other species which are unable to defend themselves. Is inflicting suffering on an animal justified by the fact that it could decrease the suffering of a person with an incurable illness?

Xenozoonoses are debatably the largest implication of xenotransplantation at present. They are the reason why small-scale xenotransplantation applications, such as using pig islet cells in diabetics, have been turned down in New Zealand. Xenotransplantation has the potential to cause the transfer of viruses and harmful bacteria from animal to human. Many researchers argue that this risk could be overcome by screening animals and breeding them in captivity in sanitized conditions. However the major drawback is the limited knowledge we have of diseases animals carry, such as xenotropic organisms. These are pathogens that live harmlessly in one species but become pathogenic once transferred to another.

Endogenous Retroviruses (ERVs) are of concern. ERVs are viruses embedded in genetic material which do not cause obvious signs of disease. However they can be activated at any time. If a xenograft contained an ERV it could become activated in the recipient, infect them, and potentially spread to other people. This is concerning because the worst case scenario could result in an epidemic of a disease that doctors know nothing about. Most pigs

have a retrovirus called Porcine Endogenous Retrovirus (PERV). It has been proven that this virus can spread from animals to humans. Although most researchers believe that the risk of virus transfer is low, it cannot be entirely ruled out.

Xenotransplantation is still in its infant stages. At present, the risks concerning the transfer of viruses are not quantifiable. In regard to animal rights, the potential xenotransplantation has to alleviate suffering outweighs animal sacrifice. Furthermore, the existence of implications concerning xenotransplantation does not mean that we should rule the procedures out. All surgical operations contain degrees of risk, some higher than others, but the potential benefits of these medical treatments, including xenotransplantation, outweigh the risks. With further research, xenotransplantation could not only eliminate organ waiting lists, but offer hope for combating incurable diseases such as Parkinson's, Huntington's and type 1 diabetes. Although it will be years before it becomes common practice, it is apparent that xenotransplantation will be the answer to solving the organ donor shortfall.