Xenotransplantation

http://www.cec-kek.org/English/cq0228e.htm

CONFERENCE DES EGLISES EUROPEENNES
CONFERENCE OF EUROPEAN CHURCHES
KONFERENZ EUROPAEISCHER KIRCHEN

XENOTRANSPLANTATION

This report seeks to evaluate the ethical and social issues raised by xenotransplantation in the perspectives of a Christian understanding. European churches seek to reflect areas of general consensus and also points where we differ.

The report was produced by the working group on Bioethics and Biotechnology of the Church and Society Commission of the Conference of European Churches (CEC). The Conference is the regional ecumenical organisation for the whole of Europe comprising 127 churches of all traditions (Protestant, Orthodox, Anglican, Old Catholic) except for the Roman Catholic Church.

In June 2002, the Executive Committee of the Church and Society Commission of the Conference of European Churches commended this document to the member churches of CEC for study, reflection and, where appropriate, action.

Its working group on Bioethics and biotechnology consists of specialists in areas such as medicine, genetics, bio-chemistry, theology, ethics and law.

Abstract

Xenotransplantation (xt), the transplantation of cells, tissue or an organ from an animal (pig) into a human being is in an early stage of development. Although this technology might eventually contribute to alleviate the structural shortage of tissues and organs in the field of transplantation, which can be seen as the dominant ethical motive behind it, it is also (morally) problematic in various

respects. This Report is an attempt to deal with some fundamental and other moral problems in the context of xt from a Christian perspective. Issues like biblical law, ‘playing God’ in (bio-) technology, (un-) naturalness and human identity, but also feasibility and efficacy, risks, use of animals, and alternative technologies are dealt with. The Working Group does not pretend to solve these problems, but rather to be of some help for the process of reflection inside and outside the member churches of CEC. The conclusion is that, although xenotransplantation is morally problematic and should be put into perspective, there is no reason to see it as fundamentally wrong. The Group pleads for a policy of great prudence in developing this technology. Therefore it supports the Draft Recommendation of the Steering Committee on Bioethics of the Council of Europe. (http://www.legal.coe.int/bioethics)

Introduction

The relative success in treating certain serious diseases by human organ transplantation (allotransplantation) has led to an increase in demand for replacement organs which greatly exceeds the likely supply. One proposed solution is to use the organs or cells of a suitable animal adapted by genetic modification. This is called xenotransplantation (xt) or xenografting. It poses considerable scientific and medical challenges and also controversial ethical questions, which we examine in this paper.

The focus of discussion is on transplanting live cells (e.g. insulin producing pancreatic islet cells), or whole organs such as hearts and kidneys from pigs into humans. The word ‘live’ is added, because not-living animal material, for instance pig heart valves, is already used in human health care. Xt technology is in an early stage of development and, particularly in the case of organ transplantation, it is far from being proven, In the mid-1990’s expectations ran high and the scientists involved in research made optimistic claims of providing treatments in a few years, which are now in considerable doubt. It has proved much more

difficult technically and has required considerably more research. Meanwhile it has attracted much attention in society as well. On the one hand patients are encouraged at the possible contribution to the removal of organ shortage, but on the other there is much concern over the risks and ethical problems.

The aim to an increase of life expectancy and quality of life of very ill people, may be seen as a dominant ethical motive behind xt. Life and health are fundamental human values. Xt would also make us less dependant on human organs, which are in most cases obtained in very sad circumstances such as road accidents. It would enable a less hectic preparation procedure than is often the case for patients undergoing allotransplantation (who must be operated on within hours after an organ has become available). It might discourage the illegal trade in organs. Other benefits include an increase of knowledge in immunology and an economic impulse for bioindustry, including pharmaceutical industry.

However, in order to ‘prepare’ the animals (pigs) as good organ donors they have to be raised in pathogen free circumstances and they have to be genetically modified, mainly to avoid (hyperacute) rejection of the grafts. Furthermore, what is special about xt is that animals are used in a new way - not for food, clothing, transport, haulage, or as pet animals, but as tissue and organ donors. This combination of genetic modification of animals and a new way of using them does not only yield many scientific and technological problems but also many ethical, philosophical and religious questions, and, last but not least, much public concern. It is, therefore, a social and political problem as well. It has been the subject of major studies in several member states of the EU and regulatory bodies have been set up. The Council of Europe set up a working party on xt, under the joint responsibility of the Steering Committee on Bioethics (CDBI) and the European Health Committee (CDSP). Xt is thus on the social and political agenda, and churches and other groups in civil society, like patient support groups and the animal protection movement, are intensely involved in the discussions.

Fundamentally wrong?

So xt seems to be (morally) problematic in various respects. But perhaps there is more. In this Report we shall argue that, although xt is (morally) problematic indeed, it is not fundamentally wrong from a Christian point of view. Therefore, we want to elaborate firstly some fundamental issues in the context of xt and then deal with (other) moral questions. We shall conclude by making some remarks on public policy. Of course we do not pretend to be able to solve all fundamental and moral questions in this area, but we hope that the results of our deliberations may contribute to the process of reflection inside and outside the Member Churches of CEC. We gratefully make use of two other reports on the issue of xg, namely *The Ethics of Xenografting*, a document issued by the Society, Religion and Technology Project (SRT Project) of the Church of Scotland (Edinburgh 1995). In *Xenotransplantation. Eine Hilfe zur ethischen Urteilsbildung*, edited by the Kirchenamt der Evangelischen Kirche in Germany and the Secratariat der Deutschen Bischofskonferenz (Bonn 1998), one can find a helpful overview of the pros and cons of xt, which is partly based on a xt technology assessment project of the Swiss Science Council. We also want to draw attention to the Basic Social Concept of the Russian Orthodox Church, where the issue is discussed.

Biblical law

Xt involves the transfer of a live pig organ to a human, the addition of human genes to a pig and also the elimination of genes from the pig. Inside and outside the churches there is a feeling among many people that these are *fundamentally* problematic or even wrong, because they seem to be at odds with biblical laws and presuppose manipulation of the created and the natural order, which is often labelled as ‘playing God’. To address this we examine the relevant biblical texts.

That xt is problematic in a fundamental respect might be based on some biblical texts, like *Leviticus* 19,19 and *Deuteronomy* 22,9f, where the intermingling of

animal kinds, seeds or yarns is forbidden. In particular the former text, which has its origin in the so-called Priest tradition in the Old Testament, could be interpreted as the application of a theology of creation which can be found in *Genesis* 1. God created animals and plants 'after their kinds', in other words He created the kinds, and human beings are not allowed to go into the opposite direction.

The problem, however, is not only that already in Old Testament times mules, a crossbreeding of a horse and a donkey, were found everywhere, but also that many of the Biblical laws, in particular ceremonial and sanitary laws, were not taken over by Christian tradition, mainly because they are seen to be fulfilled in Christ. It is not clear whether for instance *Leviticus* 19,19 belongs to this category or whether it reflects a moral teaching that is still relevant today. (It might refer to Israel's distinctiveness in relation to the surrounding nations –including a ban on luxurious clothing-- rather than being a general statement about God's creation). Moreover, the exchange of genetic material is not unknown in nature. So these texts may have lost their original relevance. One could add here that for many Christians there is not this sharp contradiction between faith (Creation) and science (biology). Christian faith is not a rival scientific hypothesis or theory, but a meaningful way of looking upon this world. And it appears very well possible to integrate an evolutionary way of thinking into a Christian belief in Creation (and the other way around). This is at least the opinion of our working group. However, more exegesis and hermeneutics are required to find an answer to the question as to how to use these old Biblical law texts in Christian ethics (if at all).

Created order and unnaturalness

We support and welcome the prudent approach expressed in the Draft Recommendation of the Committee of Ministers. Xenotransplantation might include very sensitive issues related to the human identity of a person as a personality and as a representative of a generational family. Human identity

would be especially challenged if xenotransplantation were to go as far as to include e.g. brain cells or reproductive cells.

Another reason for considering xt as fundamentally problematic is that it is seen as a manipulation of the created order, and therefore as unnatural. The phenomenon of (hyper-) acute rejection might indeed be seen as symptomatic. Since Xt would, therefore, not be feasible without the genetic modification of the source animals, it is a ‘high tech’ operation, and thus highly artificial. The question is, however, does that matter? In ‘creating’ transgenic animals, we make novel uses, on a micro-level, of processes that are present in nature, in order to make these animals more useful for us. In this respect it does not differ very much from selective breeding of animals and crops. However, there is a qualitative difference between genetic modification and selective breeding, for instance by crossing the borders of species that would not be possible by breeding, and a quantitative difference in effectiveness. In both cases we try to modify nature for human interest. Xt may be taken as unnatural but the same is true of allotransplantation, and both are done because "nature" fails! For the same reason we wear glasses and hearing aids, have artificial hips and knees. In short, that something is unnatural does not mean that it is necessarily morally wrong.

It is however not the place here to open a sophisticated discussion on natural law. Suffice to say that the expression ‘nature knows best’ is in many respects a debatable point of view. We have the impression that there is perhaps some ideology emerging, of a form of holism which implicitly evaluates nature as intrinsically good, or at least much better than any human intervention could be. According to this trend, nature is seen as having a sort of taboo status, something, which is nearly divine. And human intervention becomes almost per definition an infringement of the ‘holiness’ of nature. Such a view is very problematic from a Christian point of view. That nature is divine, is strongly rejected in the Old Testament. The world is God’s creation; it is not God.

Moreover, this world is spoiled by sin and evil. This means, as already said, that nature is not intrinsically good and that the intrinsic moral order in nature is not simple and immediately obvious.

'Playing God'

Biomedical technology means that not only do have we begun to understand the genetic blueprint of living organisms but also that we are more and more in a position to apply this knowledge in 'manipulating' life in an unprecedented manner. In this context the term 'playing God' is often used as a rather vague expression of uneasiness and concern about this 'new biology' and biotechnology. As Christians we find it an interesting phenomenon that this expression often emerges in a secular context. In other documents (for instance on Genetically Modified Food, 2001) we have already elaborated on this expression and the concerns behind it. Here we summarise our analysis.

On a closer look, it may be seen as a cluster of at least four fundamental concerns. Firstly, the idea that biomedical technology crosses the boundaries of human finitude. One could call it the promethean aspect, or the 'original' sin of human pride and arrogance. In manipulating life, human beings misappropriate something that belongs to God (or Nature, or Evolution). Secondly, the term 'playing God' contains an awareness of the suggestion that science and technology pretend to be the 'saviour' of the world. One could call it the aspect of the 'Tower of Babel', an old Biblical image (in *Genesis* 11) for autonomous technology, which pretends to pave a way to heaven without God's help., or in more secular words to a society where the good life will become an inevitable reality. Thirdly, there is a fear for the possible runaway consequences of biomedical technology for society, the aspect of the sorcerer's apprentice. We do not know enough, we do not have enough wisdom, and therefore we run considerable risks, which is irresponsible. As to xt we shall come back to this aspect below. This aspect equates to the problem of 'risk society', discussed by

Ulrich Beck and others, and to the question of our human responsibility within it. Finally, ‘playing God’ expresses a feeling of alienation. It is the uneasiness of not being at home any more in, or of not being able to cope with a world where traditional borderlines and certainties are constantly fading away. Biomedical technology and information technology both create implications for human self-understanding. This is not only a challenge for theological anthropology but also of pastoral theology.

However, in the light of Christian faith there may be another interpretation of the term ‘playing God’ as well. It is the belief that humans are created ‘in the image of God’. This means that they are supposed to resemble God in their life and work, that they are called to ‘work and care for’ the garden of Eden (i.e. the earth) and that they are called to follow Jesus Christ in his creative, redemptive and loving relation to the world. It is the appeal ‘to make and to keep human life human’ (Paul Lehmann), which includes, in the context of biotechnology, to commit ourselves to biodiversity and sustainability. This interpretation of ‘playing God’ implies that there is nothing wrong in principle with using science and technology to cross boundaries. For some, this could even be seen as a part of human vocation. God does not reveal Himself as only being present in the past but on our way into the future as well. ‘Jesus Christ (is) the same, yesterday, and today, and forever (Hebrews 13,8). From this perspective, not crossing boundaries as such is not the real issue (except for moral boundaries of course), but *why* we are doing it, what we are *aiming* at, and at what *price.*

Both interpretations should be taken seriously. We could use Pascal’s terminology in saying that both interpretations show that the *grandeur* and *misère* of humankind are two sides of the same coin, and that the first interpretation is always menacing the second. In the case of biotechnology and of xt it means a plea for great prudence.

The Human - Animal relationship

Following the line of thought of the previous sections, xt and biotechnology should make us aware of another fundamental question, namely our place as humans within the created order, and more specifically the human-animal relationship. Because it is clear that the blueprint of life is shared by all organisms, a question may be raised. What is so special about human beings, compared to animals and plants? There is a tendency to challenge the idea that humans are the 'crown of creation'. Interest groups involved in animal rights and deep ecology attack anthropocentrism in favour of taking nature or the biosphere as the point of departure of their thinking. While not inclined to follow such a radical approach, the instrumentalization of animals in bioindustry and in biomedical research have concerned many in the churches for a long time. The relationship between humans and animals and the place of humans in nature is firmly on the agenda of theology and philosophy. It means that we are challenged to think, in the light of Christian faith, about the fundamentals of human selfunderstanding, about notions of hierarchy in creation, and about our (mis)use of animals. Our starting point is that being created 'in the image of God' means a vocation to be faithful 'housekeepers' or stewards in creation. This places us in a position of responsibility towards our fellow creatures and our environment.

In a strict sense, pigs bred for xt would not suffer especial pain, because they would anaesthetised before the organ removal procedure, but other issues are raised. The development of xt would require a huge amount of experiments on laboratory animals, as well as the breeding of source animals (pigs) in specific pathogen free (SPF) conditions. There is debate about whether in a SPF environment, it is nonetheless possible to come close to their natural habitat. Experiments on animals, however, are widely seen as morally problematic but which may be sometimes a necessary evil in the context of human medicine. Against this background the so-called 'three Rs' principle is well established as a rule in animal experimentation. If possible, *Reduce* the amount of animals, *Replace* animal experiments by alternatives, and *Refine* the experiments. Xt would of course considerably add to the number of animals being used.

Apart from these aspects, in the case of xt we meet a new way of using animals for human interests. It is not for food or for the development of science and technology, but for the production of organs, tissues and cells. That could be seen as a new step into the direction of the instrumentalization of animals. They are bred to be a 'kit of spare parts' for transplantation into humans. It could be argued that this represents one more proof of the reduction of the value of animals to their practical value to us.

This objection may be met by the answer that, if xt is successful, the use of animals for the aim of human health and well being could be seen as morally justifiable, in view of the fact that xt of organs would be performed for very ill people. Some have even argued on rather utilitarian grounds that the use of animals for xt is much more vital, and in this sense better, than the use of animals for food production. However, the moral justification of creating and sacrificing animal lives even for seriously ill humans is not unconditional. It would depend on the degree of medical success which would be achieved, and as we shall see there are some serious doubts. Therefore this new use of animals is an extra reason to look carefully at the relation between humans and animals, and in particular to the question as to the limits of the use of animals for human interests.

Human identity and Animal Organs

In the case of xt we are confronted again with an old problem in Western tradition, namely human identity and the role of the body. Xt technology seems to imply a reductionist understanding of the human body, insofar as the body is seen as functional or instrumental with regard to human identity. For instance, if the heart is just a pump to spread the blood throughout the body, if it does not function any more, it should be replaced. But is the body merely a collection of organs that can be replaced freely? In the Western (also Christian) tradition, for centuries the body was not seen as essential for human identity. Although the

resurrection of the body was part of the Christian confession, which meant that the body was integral to salvation, in practice the soul was taken to be the essence of the human being. In the 20th century this dualistic image of the human individual was severely criticised in philosophy and theology, and today it has been replaced by a more holistic image of the human being. Body and mind are both essential for human identity. In the case of xt one gets the impression that we are, at least in practice, back to dualism again.

Although we do not agree that we are in a dualist situation, we think that more attention should be paid to the meaning of the body for human identity. People ask questions like 'What would it mean for a human being to live with a pig organ?' and 'Are some organs and tissues (e.g. the heart or brain cells) in this respect more 'special' than others (like kidneys or pancreas cells)?' These questions may be partly emotional but they are valid nonetheless. If there is no science based evidence, we can only reflect on psychological research in the field of allotransplantation, as far as it may throw light on the subject of xenotransplantation. People that received an organ by allotransplantation are known to experience, for a considerable amount of time, feelings of ambivalence and fear. This is probably partly so because of the circumstances in which the organs became available and partly because of the risky situation in which they still are living. It should of course be kept in mind that the transplantation of organs like heart or liver is a question of life or death. Either you receive the organ, or you die, or the quality of your life is very bad. What seems to be important in the psychological process of acceptation of a transplanted organ is the knowledge that it is donated. However that is also one of the differences between xt and allotransplantation, for the use of the word 'donation' in the context of xt would be odd. In short, we know next to nothing about the psychological consequences of xt.

(Other) moral issues

Beside these fundamental questions in the context of xt there are other moral issues as well. In the next section we shall pay attention to them.

Feasibility and Effectiveness

The justification for using animals for xt depends on whether this intervention and its attendant harms are in proportion to the *realistic* benefits to humans. Currently there are serious doubts whether xt, in particular xt of organs, will eventually be feasible. Research in this area has to cope with huge problems. They include in particular the problem of hyperacute rejection, by which animal organs are rejected by the human body within a very short time. Much effort is made to solve this problem by the genetic modification of the pigs that are to be used to obtain the organs. In order to be successful not one but several genes must be modified, and at least one pig gene responsible for one aspect of the rejection must be deleted. The first cloned "knockout" pigs were announced in January 2002, but it remains to be seen whether this deletion is stable, and would be viable in conjunction with four added human genes. But even if that could be done, there remains another problem, namely that of matching pig organs to human physiology. This must be solved as well, otherwise xt would not be effective. Moreover there are questions as to whether pig organs will fit in to human life span.

These are huge technical problems, but they are morally relevant as well. For if xt would eventually not be feasible or effective, it would mean *inter alia* that hundreds of thousands of laboratory animals would be sacrificed in vain and that huge amounts of money could have been spent in a much more fruitful way. These are all reasons why some interest groups (but also scientists) are against xt as such and ask for alternative ways to solve the problem of shortage of organs for transplantation. However, it is possible that xt, in spite of all the problems, will be successful in the end. Feasibility and effectiveness can only be shown *a posteriori.* This is an inherent aspect of science, namely that it is

developing by trial and error. Perhaps it could turn out to be partly feasible or to be a provisional solution, a good bridge to an other, more permanent one. There is a long and difficult way to go, which means that the donation of human tissues and organs will remain, probably for decades, if not always, necessary in transplantation medicine.

Risk factors

Another reason for concern is the risk aspect of xt. The risk of rejection of the transplants has already been mentioned in the former section. But there is a risk of transfer of germs and viruses, which may cause serious problems for the patient, who will also be treated with immunosuppressive drugs because of the risk of rejection. The most serious scenario will be that so-called retroviruses, which are unknown and 'hidden' in the genome of source animals and, therefore, difficult to detect, will be transferred to the patient's body and then become passed on to the wider human population. The probability is small, but it is there nevertheless, and risk assessment and safety conditions cannot reduce it to zero. One ambitious proposal is to genetically engineer the selected pigs to remove the retrovirus DNA from their genome, but this is far from sure. It means that we have to face, up to a certain degree, the risk of transfer of an unknown disease for which there exists no (effective) therapy, such as was/is the case with HIV/AIDS and BSE/Creutzfeldt Jakob Disease. Such a disease will have serious consequences for the individual patient, for the patient's family and friends, and for society as a whole. It may eventually become an international, even global, problem. What is meant to rescue an individual from immanent death may become highly dangerous for society, and thus for many people. At present more study is needed of the factors, but eventually it may be that we conclude that the potential medical benefit to the individual does not justify the risk to society. Looking at society, another societal risk factor may be mentioned here. What will be the effect of xt on people's willingness to donate organs for allotransplantation? In other words, xt could jeopardise such an important value

as human solidarity? Moreover, if xt will turn out to be successful, it will result in lowering the criteria to be eligible for transplantation, which means that more and more cells, tissues and organs (and thus still more animals) will be required. In short, these risks are morally relevant because they have consequences for important values like safety, physical and public health, psychological health and social solidarity ('health'). Until now, it is far from clear how we should deal with these risk factors.

Alternatives

Last but not least, xt can be seen as morally problematic, if there are viable alternatives. The rule of the three Rs, mentioned above, means that, in view of experiments with animals, we should use an alternative if there is one. And instead of xt we could promote human organ donation – and the churches could be of great help here! --, in combination with a more efficient use of human organs and a better organisation of allotransplantation. However, although this may without doubt be of some help, it is nearly certain that it will not solve organ and tissue shortage. We could also invest much more money into the development of artificial organs, as well as in human stem cell research and tissue engineering. In particular the latter, although in a stage of early development as well, seem to be very promising. Stem cells are cells that can divide to produce either cells like themselves (selfrenewal) or cells of (a) specific type(s). They can be obtained from (1) very early human embryos, (2) human foetal tissue after abortion, (3) umbilical cord blood, (4) cloning techniques, and (5) adults . The idea is that, by tissue engineering, stem cells can be used to produce specific tissues for therapeutic aims. Thus cardiac muscle cells might be used to alleviate heart diseases, liver cells against hepatitis, neural cells against degenerative brain diseases, and so on.

But the use of human embryos and aborted foetuses are morally problematic too. In general, the alternatives for xt bring along their own ethical problems. The use

of adult stem cells is probably the least problematic, but they are more difficult to obtain than embryonic stem cells and may not have the same potential. We have discussed these issues in our recent discussion paper on stem cells. ("Therapeutic use of cloning and embryonic stem cells" – September 2000)

One could also ask whether these alternatives are really alternatives for xt. It is for instance far from proven that it is possible to grow organs by tissue engineering. In view of what eventually could be done, these alternatives probably only partly overlap each other, except of course allotransplantation. It is therefore reasonable to argue that xt *and* its possible alternatives should have a fair chance.

Provisional conclusion

There is much (scientific and theological) uncertainty in biotechnology in general and in xt in particular. Therefore there is no place for premature answers in this report, let alone for a simple 'Yes' or 'No'. What could be said, though, is that, although xt is clearly morally problematic, we would not condemn it as *fundamentally* wrong, or as evil in itself. The main motive behind xt, namely to find a solution for the increasing demand for replacement tissues and organs in the field of allotransplantation, is ethically sound. But the technology is still in its infancy and it is not clear whether, or in what respect, it will be feasible and effective. In this situation of uncertainty, a step by step policy might be a good practical translation of the ancient virtue of prudence. That is why we support the Draft Recommendation of the Steering Committee on Bioethics of the Council of Europe, in which we think that a policy of great prudence is manifest. We underline the importance of Article 31 on public debate, which reads that "Member States should take active steps to ensure that the fundamental questions raised by xenotransplantation are the subject of appropriate public discussion …". Moreover we plead for transparency regarding both the possibilities and the problems of this technology.

Prudence means something for an ethos of researchers. It is a plea for an attitude that includes the awareness of the social context of science and technology and the willingness and commitment to work in accordance with rules that reflect the basic values of our culture. In other words, ethics is not something outside science and technology but is an integral part of them both. Freedom of research and social responsibility should not be played off against each other. Researchers should be prepared and willing to be transparent in what they are doing but also to 'defend' their research in society and to reflect on the values on which their research is based.

Finally, the churches have an important role. It is beyond the scope of this report to discuss here at length the place and the task of the churches in our post-modern, highly industrialised, secular society. But we want to emphasise that the churches can play a vital role in facilitating the public debate. Our vocation of course includes equipping the community of believers for coping with the world they live in, but it also involves serving and engaging with wider society. The Gospel, we believe, is and will be forever the 'good tiding' for this world and it is vital 'to make and to keep human life human' (Paul Lehmann). But in order to be able to cope with the world, we must be well informed about what is going on in this world. That is why the churches need scientific information. As far as we can see the task of the churches includes to create networks and conditions in society, where the public, scientists, technicians, industrials and politicians can discuss in the open the questions of public concern, like xt. We sincerely hope that this report will contribute to this task.

Conférence des Eglises Européennes
Bureau de Strasbourg
8, rue du Fossé des Treize
F – 67000 Strasbourg
T : +33 3 88 15 27 60

F : +33 3 88 15 27 61
E-mail : csc@cec-kek.com