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Xenotransplantation Procedure and its Potential Effect on Man

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ABSTRACT

Xenotransplantation is not yet a clinical procedure, such that one can just work into a clinic and demand for it to be carried on him/her. However, considering the energy and enthusiasm with which researches on xenotransplantation are carried out, it is reasonable to think that in the near future, it will become a clinical success. There are already series of debate as to the potential benefits of xenotransplantation – would it introduce a world plague to humans or would it provide a better life for them. This is a heated debate. This paper joins in this debate and avers that xenotransplantation should be halted, for it is better to halt actions when one is in doubt. Since the safety of xenotransplantation is in doubt, research on it need to be suspended, until we are certain that it is risk free.

KEY WORDS: Xenotransplantation, Xenoosis, Potential Effect, Recipient

INTRODUCTION

Xenotransplantation is not yet a clinical success but would possibly be in the near future considering the research effort that is currently invested in it. This research warns of the potential dangers that xenotransplantation carries and advises that an urgent action should be taken to halt the ongoing research on it.

Xenotransplantation is capable of obliterating the line that separates humans from animals. It would deepen the already intractable personal identity problem; make the recipient a sort of prisoner who needs to be monitored all his life to ensure that a new disease does not spring up. Xenotransplantation would put the recipient as well as the whole community of human beings at perpetual risk and fear of a world plague. These problems far outweigh the potential benefits that would accrue from xenotransplantation.

In the light of these problems that xenotransplantation is capable of putting forth; the researchers believe that an indefinite moratorium should be placed on the research on xenotransplantation. This is because, it is far better to prevent a fire than to struggle to quench it. It is better to prevent a disease that would come from xenotransplantation than struggle to cure it.

Meaning and History of Xenotransplantation Procedure

Xenotransplantation is a procedure in which a human patient receives an organ (like kidney or liver) or living cells (such as brain cells) that come from a healthy animal instead of from a human donor. It also refers to transplant between any two different species of animals. However, in this work it is looked at from the perspective of animal to human transplant.

Alexis Carrel is generally known as the founding father of experimental organ transplantation, because of his ground breaking work with vascular technique. Carrel and colleague Guthrie contributed tremendously to the science of transplantation. They performed autogenous vein grafts, performed leg replantation in dogs, and developed the famous patch-graft technique for

widening narrowed vessels. They also performed heterotopic experimental transplantation; for instance, parts of a smaller dog were transplanted into the neck of a larger dog (Samdanihttp://emedicine.medscape.com/article/432418-o.).

Due to the remarkable success of Carrel and his colleague Guthrie, other scientists made several frantic attempts in transplantation. These results gave confidence to scientists, that xenograft survival and function was possible. Many attempts were therefore made thereafter to cure ailments through the use of animal organs and tissues. For instance, in 1906 Jaboulay transplanted kidneys from goats, sheep and monkeys into humans. In 1910 Unger tansplanted a nonhuman kidney into a man dying of renal failure. In 1932, Neuhof transplanted a lamb kidney into a patient with mercury poisoning (samdanihttp://emedicine.medscape.com/article/432418-o.) In 1984, a baboon heart was transplanted into a newborn infant, named Baby Fae, who suffered from hypoplastic left heart syndrome (Bailey 3322). Also Starlz et al reported how a baboon liver was transplanted to a human patient suffering from hepatitis failure (65). According to Rood and Cooper, Porcine islet cells have in several occasions been transplanted into patients to aid in the cure of Type 1 diabetes in children and young adult (1270). Also porcine skin has been grafted into burn patients and pig neuronal cells have been transplanted into patients with Parkinson's disease and Huntington's disease (Fink et al 274).

These attempts were highly unsuccessful, because of the problem of immune system rejection of the xenograft. The immune system fights against foreign elements in the body which include bacteria, fungi, viruses and other bodies that are perceived to be foreign to the body, including xenograft. Thus, when organs of animals are transplanted into humans, the human immune system detect these organs as foreign and thereby fight seriously against them, leading to the destruction of these transplanted organs. This is what is called immune system rejection. This has been the problem that for several years militated against the success and growth of xenotransplantation. The problem of immune rejection led to a decline in interest in xenotransplantation. This interest was rekindled after Michon and Hamburger successfully performed transplantation on twins without using immunosuppression. Michon and Hamburger successfully performed a living related donor kidney transplantation in Paris in 1952, between monozygotic twins and they survived (Michonet al1420).

The advent of immunosuppressive drugs for the prevention of immune rejection also contributed to the renewed interest in xenotransplantation. Thus since 1990, there have been various transplantation of animal organs into dying patients (Erlickhttp://www.nelsonerlick.com/htm/xenofactsheet.html). In 1995, according to Erlick, a patient in the United States got a bone marrow from a baboon. Although, the immune system of the patient rejected the baboon bone marrow, the patient continued to live a normal life. There have also been significant successes in areas of cellular xenotransplantation. For instance, ten patient received cells from pancreas of pigs and none of the patients got sick from the transplanted pig cells. Other cases that involved hooking up a patient up to a pig liver, functioning as a substitute liver, for a short time until a suitable donor organ is sought for have also been recorded.

Types of Xenotransplantation

Xenotransplantation procedure is categorized into; solid organ xenotransplantation, cell and tissue xenotransplantation, extracorporeal perfusion and human/animal hybrid. Solid organ xenotransplantation: this is a procedure whereby an animal organ like kidney or liver is transplanted into human as a replacement of the original organ.

Cell and tissue xenotransplantation: it is the transplantation of tissues and cells from source animals to human beings as replacement of the original tissues in humans.

Extracorporeal perfusion: This is a procedure whereby the blood of the patient is made to circulate outside of the human body through animal organs, such as a liver or a kidney, or through a bio-artificial organ produced by culturing animal cells on an artificial matrix.

Human/Animal Hybrid: this is a procedure where human cells are grown in a culture with non-human animal cells that are transplanted back into human patients.

Source Animals for Xenotransplantation

Chimpanzees were generally considered to be the best source animals for organ transplants compared to other primates because of their close affinity with humans, but due to their endangered status, attention were shifted to baboons. Baboons being the next most preferred source animals though existing in abundance, fared badly in captivity, have a long gestation period and are capable of few offspring. According to FDA (Food and Drug Administration) committee known as BRMAC (Biologic Response Modifiers Advisory Committee), nonhuman primate donors pose the greatest threat of transmitting latent, intracellular, or unidentified organisms, including retroviruses. The committee therefore, recommended that nonhuman primates should not be used as sources of xenotransplantation (US Food and Drug Administration. http://www.fda.gov/cber/rules/frigene011801.htm). This recommendation led the search for other suitable animal donors of organs. Most of the scientists are of the agreement that pigs have the potential to be the right candidate for organ donation. This is because pigs are in abundance, quick to mature, breed well in captivity, have large litters, and have vital organs that are roughly the same in size to that of humans. Their use is also argued to be less resentful to the society because they are already an accepted source for societal meat. Pigs are also believed to be less likely to introduce new diseases to human because of their distance to humans in the evolutionary chain. Other reasons why pigs are preferred include:

- Pigs because of their ability to fare well in captivity, can be raised in a highly controlled way, thus, their organs are less likely to transmit infectious diseases to humans.
- Pigs could be genetically engineered to contain human genes. This would make the animal organs or cells to be readily accepted by the patient immune system.
- In spite of these advantages, pigs xenografts is believed to be capable of experiencing severe immunologic barriers than the nonhuman primates because of their distance from man in the evolutionary chain.

Benefits of Xenotransplantation

Xenotransplantation is believed to be capable of serving as a complete substitute for human organs, thus easing the current shortage available for transplantation. It could also serve as a bridge or temporary organ until a permanent human organ could be found. Other benefits of xenotransplantation include:

- Xenografting is helpful in the treatment of diseases. People with serious kidney, liver or heart disease, diabetes or Parkinson's disease which have defied all known treatment could be treated through xenotransplantation. People needing bone marrow transplants could also benefit from xenotransplantation. cellularxenotransplants for instance could treat people suffering from diabetes, Parkinson's disease or other diseases. People with liver failure could also be treated with an extra-corporeal (outside the body) xenotransplant using a healthy pig liver. In this process, the patient's blood circulation is made to pass through a pig liver that is kept outside the patient's body.

- Xenografts give the surgeon enough time to eliminate potential pathogens. In allografting (human to human transplantation) organ which are usually transplanted from a brain dead patient are given little or no time for examination to ascertain the health state of the organ, due to the urgency involved. The transplant organ therefore could come from a suboptimal donor with advanced age and chronic medical condition or from a carrier of undetected infectious agents or malignant cells. In contrast, in xenotransplantation, a donor pig is raised under controlled conditions and specifically intended for use as an organ donor. In this case, the donor pig can be extensively analyzed to eliminate all pathogens.
- In xenotransplantation animal donors are genetically modified to be resistant to many human pathogens specific to human tissues, such as HIV, hepatitis, and human cytomegalovirus. This is hardly possible in allotransplantation.
- Xenotransplantation eliminates 'black market' in human donor organs. Due to the scarcity of human donor organs and the large number of patients on the waiting list for organ transplantation, it is believed that human organs could be procured illegally. Some patients whose lives would have naturally been saved would be allowed to die by the doctors in order that their organs would be used for transplantation. Xenotransplantation it could be argued would help stem this abuse.
- Xenografting could save hundreds of thousands of livers. This is because, patients who otherwise would not have been eligible for transplantation because of shortage of human organ, would receive organs and tissues through xenotransplantation.
- Xenotransplantation eliminates poor quality of life situation for patients. It improves the living condition of patients, making them enjoy what they would otherwise not enjoy without xenotransplantation procedure.

Risks of Xenotransplantation

In spite of the numerous advantages that could accrue to humans if xenografting becomes a clinical success, there are a lot of risks that are associated with xenotransplantation. these risks include:

- The risks of introduction of xenoosis: xenoosis is the infection of human by agents like bacteria, viruses, fungi. The possibility of transmission of infectious agents raise questions regarding the safety of using xenotransplantation in individuals, but it could also potentially place the general public at risk. Like humans, animals may also be infected with microorganism which could be specie specific (that is, it is not transmittable to other species). For instance, the transmissible virus of pigs causes diarrhoea in pigs but does not cause any sickness in people. However, other kind of micro-organisms is not specie specific, which means some of them can infect animals and also cause disease in humans. An example of this is influenza. The flu first infected birds and pigs and though, it does not make these animal sick, when it passed to humans, it makes them sick. The word xenozoonosis therefore, refers to zoonotic diseases that may pass to human through xenotransplant (Vanderpool 1311). Most mammals are known to have a kind of virus embedded in their DNA known as "endogenous retroviruses." These viruses are passed from one generation to the next without causing havoc in the host species. All pigs are believed to carry such viruses called PERVs (Pig or Porcine Endogenous Retroviruses). These are normally inactive and thus do not cause disease to the pigs. The concern among scientists is that PERV may become active and infect the human cells.
- The xenograft may not work well especially if it is replacing an essential organ of human. Since the environment in which animal organs function are quite different from the one the human organ function in, it is feared that these organs may not function well in humans. For instance, the temperature which pig organs function in is 39 degree Celsius which is different from the 37 degree Celsius of humans. Also the life span of a pig is

roughly 15 years, which brings the fear as to whether or not pigs transplants in man would live more than 15 years.

- The high level of immunosuppressive drugs needed to overcome immune rejection may be counterproductive. This may leave the patient susceptible to other infections. The immune system fights foreign agents that invade the body like bacteria, fungi and viruses. Thus, suppression of the immune system would leave room for easy invasion of the body by these micro-organisms.
- Xenotransplantation may lead to a world plague. There are fears that xenotransplantation is capable of introducing novel infection to humans, which would be transmitted from man to man and thereby leading to a new world plague similar to HIV.
- Xenotransplantation may lead to the creation of a monster that is half animal and half human. There are fears as to the character this chimera would possess.

Effects of Xenotransplantation onRecipient

Xenografting is aimed at benefitting the recipient but looking at it critically it would become doubtful, if the benefits are actually worth the trouble. The recipient of xenotransplantation is placed at a perpetual risk and fear of suddenly developing a new infection – an infection transferred from the animal parts. There is also the risk of contracting diseases from known pathogens that would have access to the body because of its malfunctioning immune system. Every xenotransplantation recipient is given immunosuppressive drugs to reduce the effect of the immune system on the xenografts. This reduced immune system would enable the xenografts to work in the recipient body without being rejected, but it would also give greater access to pathogens infecting the body. By reducing the strength of the immune system therefore, xenotransplantation patients are left susceptible and perpetually at risk of being attacked by known and unknown pathogens. Xenotransplantation could therefore, be likened to the proverbial devil that gives with the left hand and takes from you with the right hand. It cures one sickness and opens the body for attack from thousands of pathogens.

In addition to the risk and perpetual fear the recipient is made to live in, he is also made to lose his/her freedom, which is the essence of human life. One of the guidelines prescribed by the Nuttfield report, is lifelong monitoring of xenotransplantation recipient to ensure that no new infection manifest (21). Being confined to lifelong monitoring is more or less like being imprisoned.

According to Richard Norman, xenografting will destroy the way human life or psyche is structured. Human life has always depended solely on the particular characteristics and limitations of their bodies (3). But with xenografting there would be a shift; the dependence on animals' bodies would be incorporated on human psyches. Thus, the understanding of what constitutes human nature would be shifted. **Francis Fukuyama**writes:

the most significant threat posed by contemporary biotechnology is the possibility that it will alter human nature and thereby move us into a post human stage of history. This is important, because human nature, exists as a meaningful concept, and has provided a stable continuity to our experience as a species. It is in conjunction with religion, what defines our most basic values. Human nature shapes and constraints the possible kinds of political regimes, so a technology powerful enough to reshape what we are, will have possible malign consequences for liberal democracy and the nature of politics itself" (1).

Human nature provides the ground on which we can claim common rights for humans, but when this is destroyed, even democracy would face some challenges. The concept of human rights is one basic stand point of democracy, and this concept is based on human nature, it is

obvious that when the concept is changed as xenografting would do, then the concept of human right would also change and possibly democracy too would change.

Xenotransplantation erases the line between human and animals. It makes the difference between human and animals to become only imaginary and not real. How can humans be essentially different from animals, when animals' parts could sustain him in existence? How could we sustain the religious teachings that humans alone possess souls, when there is no essential difference between humans and animals? If the difference between humans and animals is only accidental, why should animals not be entitled to eternal life like their human counterpart? Ursula cautions on this thus:

So it may seem churlish to introduce a note of caution in a discussion about the role of biotech discoveries in our future directions as human beings—but it is an important part of the bioethical debate being played out across the world. Part of being human is the desire, even the urge, to become better—to strive for perfection. And who could begrudge such an urge? But equally, part of what makes us human is our differences, our very imperfections. It is important, therefore, that we think clearly about the path we are taking towards the solution of all our human imperfections. How do we continue to cherish our diversity and individual uniqueness even while we try to use our human talents to improve our lot? (http://www.eurekastreet.com.au/article.aspx?aeid=2101#.U0Kkbpix7IU).

Xenotransplantation may save life but could also render life dull by obliterating uniqueness. It obliterates the differences between human nature and animal nature. G.K. Chesterton observed that:

when once one begins to think of man as a shifting and alterable thing, it is always easy for the strong and crafty to twist him into new shapes for all kinds of unnatural purposes... It is a very well-grounded guess that whatever is done swiftly and systematically will mostly be done by a successful class and almost solely in their interests. It has therefore a vision of inhuman hybrids and half-human experiments much in the style of Mr. Wells's "Island of Dr. Moreau." ... Whatever wild image one employs it cannot keep pace with the panic of the human fancy, when once it supposes that the fixed type called man could be changed... That is the nightmare with which the mere notion of adaption threatens us. This is the nightmare that is not so very far from the reality. It will be said that not the wildest evolutionist really asks that we should become in any way unhuman... but this is exactly what not merely the wildest evolutionists urge, but some of the tamest evolutionists (180-181).

Stock in his book, *Redesigning Humans—choosing our children's genes* argues in the counter. According to him, these biomedical practices are inevitable (158) and thus, we should embrace them with optimism, and quotes a "letter to Mother Nature" from The Extropians:

truly we are grateful for what you have made us. No doubt you did the best you could. However, with all due respect, we must say that you have in many ways done a poor job with the human constitution... We have decided it is time to amend the human constitution... Over the coming decades we will pursue a series of changes to our own constitution... We will no longer tolerate the tyranny of aging and death... We will expand our perceptual range... improve our neural organization and capacity... reshape our motivational patterns and emotional responses... take charge over our genetic programming and achieve mastery over our biological and neurological processes (32).

Francis Fukuyama argues in opposition to Stock and The Extropians. Fukuyama argues that human genetic engineering is not inevitable and that we should take steps to prevent "what..... C.S. Lewis called the 'abolition of man'." (7). We solely agree with Fukuyama; there is no reason to suppose that genetic engineering is inevitable. To suppose so is to believe that we have been programmed by nature and therefore must follow this teleological course.

Another crises that xenografting would usher in which is a necessary follow up of the changing of human nature, is identity problem. The philosophical debate on personal identity had existed for many years but the advent of xenografting would take the debate to another level. Is the recipient of xenografting an animal or a human? Or is he an entirely new being? If he is a hybrid of human and animal, then he is possibly a new creation, with features of both humans and animals.

Xenotransplantation increases the crises that are already in the world. It would destroy beliefs both religious and ethical; it would cause confusion and distress to the recipient. The realization that he/she is partly animal and partly human would perpetually distress the recipient for the entire length of life. It is because of these considerations that we in this work advocates for the placement of a permanent moratorium on xenotransplantation procedures. It potential benefits are far outweighed by its potential risks.

Effects of Xenotransplantation on the Human Race

The single most serious ethical dilemma that proponents of xenotransplantation have over the years struggled to contend with, is the possibility of a transmission of a new and novel infection to humans. The Nuffield report explains that

It will be very difficult to identify organisms that do not cause any symptoms in the animal from which they come. Previous experience indicate that infectious organisms are normally identified only after the emergence of the disease they cause … put bluntly, it may be possible to identify any infectious organism transmitted by xenografting only if it causes disease in human beings, and after it has started to do so (6).

Since the infectious agents may not be identified in time before they start causing sickness, it therefore, means that before the discovery that infectious agents are actually also transferred, the infection would have caused unstoppable harm, for the agent would have spread to many people by the time the symptom is observed. The Nuffield report, because of this consideration concludes that the risk of a major epidemic is unquantifiable and therefore advocates for a precautionary principle, requiring "that action should be taken to avoid risks in advance of certainty about their nature … the burden of proof should lie with those developing the technology to demonstrate that it will not cause serious harm" (6). Its conclusion is "that the risks associated with possible transmission of infectious diseases as a consequence of xenotransplantation has not been adequately dealt with. It would not be ethical therefore, to begin clinical trials of xenotransplantation involving human beings" (6). The report gives the following guidelines to be followed before xenotransplantation can kick off:

- Enough information should be sourced as regards the risk of transmission.
- The source animals should be raised in conditions in which all known infectious organisms are monitored and controlled.
- Early recipients undergo regular monitoring and check-up.
- There should be a commitment to suspend, modify or if need be, discontinue xenotransplantation procedures at any sign that new infectious diseases are emerging.

In spite of these guidelines Hughes believes that the risk of transmission cannot be reduced. According to him "source animals cannot be freed from all infectious organisms but only those that are known and can be reliably tested for … specified pathogens-free animals may still be infected with unidentified infectious organisms about which nothing is known (21). He also argued against the issue of monitoring, and strongly believed that it would not be effective. He writes:

The most difficult question is what procedures should be followed if it is found that a disease has indeed been transmitted from the animals used to provide organs or tissues to human xenograftrecipients ?in principle, steps should be taken to prevent transmission of the disease to other people. In practice, this is a very difficult issue. For a start, it is very unlikely that, at the outset, the mode of transmission of the disease will be understood. The appropriate response will depend on the mode of transmission and on how infectious the disease is. It would hardly be acceptable to isolate xenograft recipients suffering from an infectious disease, or to ask them to refrain from sexual intercourse or, in the case of a virus transmitted from parent to offspring, from having children (21-23).

Based on these therefore, Hughes holds the opinion that there should be an indefinite moratorium on xenotransplantation procedures. He argues that this is necessary, if we reflect on the difficulty, in spite of global attempt, in combating the dreaded AIDS, malaria and hepatitis. It would be risky to introduce a new disease into humans. The Department of Health report concurs with the Nuffield report as well as the argument of Hughes in asserting that the risk of transmission of infectious organism is too great to justify xenotransplantation.

On the other side of the debate, there are some who believe that the alarm given out as regards xenotransplantation introducing a new infectious disease is a false alarm. According to Janice Hopkins Tanne, the idea that xenotransplantation will create a plague is countered by the hundreds of thousands of transplant patients who have successfully returned to their families and friends. These recipients have not spread viruses, in spite of receiving immunosuppressive drugs. Also, human exposure to blood for years has not resulted to any major outbreak of disease, with the possible exception of AIDS. In Africa, he argues, hunters, farmers and butchers are exposed to blood of monkeys and other animals and yet no major outbreak of disease has been observed among them. According to him therefore, xenotransplantation is unlikely to introduce a new plague in the world, if this was to happen, then the various contacts with blood in the past would have given rise to an outbreak of diseases.

William Edward supports Tanne view. According to him, the risk of PERV becoming a public hazard is infinitesimal. This is because

PERV would not undergo a series of improbable transformation to make it both a pathogen and contagious. Many herds of pigs have been described in which PERV is not passed to human cell in coculture. Some stains of pigs have very little copies of PERV in their genome. The risk is further reduced by the extensive monitoring of patients and cohorts required and by the sensitivity of PERV to antiviral agents. The minimal potential risk of PERV is far outweighed by the potential medical value of xenotransplants and should not be a barrier to xenotransplantation" (http://emedicine.medscape.com/article/1014080-overview).

He also argues that although a large part of the world prepares and eat pigs, no known PERV related disease has been observed. He also claims that in a study of patients transplanted with viable pig tissue, no evidence of infection was observed. Though, a few subjects were found to have detectable PERV RNA but this was consistent with RNA from circulating blood cells. He

therefore, argues vehemently that the risk of PERV becoming a public health hazard need to be re-looked in the light of the current information. The risk of PERV producing a public health hazard is not greater than that of human based transplants.

CONCLUSION

The researchers would not want to judge which side of the debate is right for they lack the medical expertise to ascertain that. But they think that it is better to give the benefit of doubt to those who argue against xenotransplantation; because when in doubt, it is always better to halt action, especially in this case where an error in judgement could cause very dilapidating damage to the whole human race, both present and future.

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