Younji Lee

AP English Language

Gingrich 1

15 May 2012

The Plausibility of Xenotransplantation

The desire to live is a potent force, commandeering patients to venture into unconventional methods of medical treatment. Each year, thousands of people die because their dysfunctional organs cannot carry on life's essential bio-chemical processes. Their deaths constitute an ever-growing issue impossible to eradicate due to the dearth of sufficient organ donors. Although a new person is added to the organ list every ten minutes, the supply of organs is severely limited ("The Need is Real: Data"). For these individuals who lack a properly functioning heart, kidney, or brain, their futures are bleak; death is surely imminent. For these bereft individuals, the prospect of death puts a number of considerations into perspective, activating a prehistoric, human trait – an inherent fight for survival. At this point of desperation, some consider xenotransplantation, receiving organs, tissues, or cells, from another animal speciesa viable treatment option. Though initially, they may grimace at the idea of having something so alien entering their pristine body systems, the possibility of death compels the individual to view the foreign invader as instead, a necessary life-saver.

However, the ethics and feasibility of xenotransplantation is a topic of fervent discussion. The human immune system utilizes systematic biochemical mechanisms to detect foreign invaders, as evidenced through the results of faulty blood transfusions across people with different blood types. If the possibility of tissue rejection occurs across the same human species, understandably, there are serious medical issues to consider when tissue, cell, or organ transplantations occur across *different* species. However, given the severity of organ shortages in the United States, I myself view xenotransplantation as an integral field for the future. I cannot fathom the pain and anxiety that people on the organ waiting list must suffer every day of their lives. Eventually, their daily prayers, fervent wishes, and most of all, their pure hope for the prospect of an organ donor are bitterly shattered asunder when they perish from their body system's failures. Given the injustices of their situations, I look past the risks of xenotransplantation and instead view the abundance of animal tissues as a gold mine. Personally, I aspire to be a surgeon because, simply, I want to mend individuals. People deserve to live despite the lack of a human organ donor. In the future, I hope that xenotransplantation, after extensive modifications to ensure little risk to the human recipient, will truncate the organ donor waiting list. I envision a future in which xenotransplantation will always present itself as a plausible option for patients.

Though xenotransplantation may initially appear to be a novel idea, and simply that - an idea, certain surgeons have attempted the process in the past decades. The first documented cases of xenotransplantation occurred as early as the seventeenth century, when surgeons performed blood transfusions on humans using animal blood (Dooldenyia and Warrens 1). During the twentieth century, researchers boldly attempted solid organ transplantations, using primate tissues. Failures were more frequent than success, as their patients' immune systems triggered responses that led to infection, ultimately leading to death. However, surgeons were sometimes victorious in their efforts. Dr. Reemtsma, a surgeon at Tulane University transplanted chimpanzee kidneys into thirteen human recipients, and one patient was able to survive nine months with that kidney on primitive immunosuppression drugs ("A History" 1). Initially, the multitude of similarities, both genetic and physiological, between the different primate species makes non-human primates the most ideal candidate for xenotranplantation. Unfortunately, the world does not possess an endless supply of primate organs; many primate species are endangered, and their breeding the animals for human organs would be impractical, given their slow reproductive process (Dooldenyia and Warrens 1). As a result, another unlikely animal appears as another organ-donor contender – the pig. Pigs are more efficiently and quickly bred, and due to their considerable phylogenetic distance from the human species, there is less risk of cross-species transmissions of viruses (Dooldenyia and Warrens 2). Indeed, given their efficacy in conjunction with shortage of human organs, pigs present themselves as viable options for medical patients in need of transplants.

But, opposition to the process is staunch. The risk of cross-species viral transmissions is a particularly crucial issue that has generated much hostility to the development of xenotransplantation. In certain cases, viruses latent in one species may evolve and prove to be lethal in another. The world has bitterly discovered this fact through first-hand experience. During the HIV/AIDS epidemic, researchers found that the same virus benign in the primate species viciously attacks the human immune system. In recent years, cross-species viruses continue to generate much public scare, reflecting on the mass global panic during the spread of the H1N1 viruses, avian influenza, and mad cow disease. The fear primarily stems from the incredibly foreign nature of the virus; these viruses have evolved from different animal species. How do researchers begin to consider stopping these alien viruses when they possess no rudimentary knowledge about them? The potential consequences of these pandemics instill great fear in the public. In fact, the FDA issued a temporary ban on the usage of non-human primates in 1999 due to the results of a controversial study (“A History” 3). This study, published in Nature, elucidates the risk of porcine endogenous retroviruses (PERV) present in pigs infecting human cell lines (Van Der Laan et al. 1). According to their studies, "pig pancreatic islets that produce PERV can infect human cells in in-vivo culture" (Van Der Laan et al. 2). Retroviruses in particular are distinguished from other types of viruses due to the fact that they function in a complete paradox with regards to their biological processes. They are able to generate a host's DNA copy from its RNA, whereas the conventional direction is creating RNA from a DNA template. Additionally, retroviruses integrate their own DNA into human chromosomes; therefore, they essentially become a part of the human genetic code, making them difficult to remove, a biological tattoo in the DNA. In a published interview with one of the researchers who conducted the study published in Nature, the interviewer asked the individual on his opinions on what potential illnesses the PERV virus could cause in humans. According to him, the possibilities are endless. Retroviruses can remain in the human host for years and years. Essentially, they can be silent assassins escaping detection by the host while simultaneously wreaking havoc to the body systems. They could potentially cause cancers, neuro-degenerative diseases, but there always exists a chance that they may be innocuous to the human host (Weiss 2). But, xenotransplantation specifically can provide blood-borne pig viruses a rare opportunity to easily cross over and infect the human species (Allan 3). Although humans have remained in close contact with pigs throughout history, these interactions are different from the blood-to-blood exchanges that xenotransplantation would introduce. Ultimately, the process would remove all natural barriers between humans and pigs, possibly serving as a ground of manifestation for blood-borne viruses. Though the FDA has since lifted its ban on xenotransplantation, there are a number of regulations set in place for clinical trials in order to prevent the possibility of cross-species viruses.

Lastly, surgeons need to overcome the hurdles of medical complications that arise from the body's immune system rejection of the transplants. The issue resides within xenoreactive natural antibodies (XNA) within the human body. XNA are programmed to recognize certain epitopes, a part of antigens that antibodies latch on to. Specifically, the gal epitope is the nemesis that impedes the success of xenotransplantation (Dooldenyia and Warrens 3). Humans lack the enzyme that creates the gal epitope, but non-primates possess this enzyme. Therefore, humans can immediately register the presence of the foreign gal epitope after a xenotransplantation. After this immediate recognition, the immune system unleashes a powerful immune response, one of which could result in necrosis, or premature cell death. These medical complications generally result in infection within the hosts and eventually lead to death. Finding methods of inhibiting this immune response would be invaluable for researchers. In the future, I hope that further development with xenotransplantation will render humans unable to distinguish between the transplanted, foreign tissue between their own.

That is not to say that researchers have not experienced successes with pig cellular transplants in recent years. There are a number of studies which suggest that transplanting pig neuronal cells within the brain could aid patients with Parkinson's disease, a disease which presently has no known cure (Rattue 1). Furthermore, in New Zealand, researchers are currently attempting to transplant pig pancreatic islets into diabetic non-human primates in the hopes of aiding them in the production of insulin (Rattue 1). Such a success would be a medical breakthrough of grand proportions, as there are no complete curative measures presently. Imagining the successes of xenotransplantation gives me optimism for patients who suffer from untreatable diseases. To determine whether or not xenotransplantation will ever fully integrate itself into clinical applications, I compared various case studies of people whom have undergone the process.

Amanda Davis suffered from a stroke in her twenties, which paralyzed the entire left side of her body. Though doctors did not hold faith in the regain of her ability to walk, after a xenotransplantation of fetal-pig neurocells into her brain, a miracle occurred. Though doctors remain baffled, they conclude that these cells connected with her own neurons affected from the aftermath of the stroke; these connections rendered her capable of basic movement. Today, Davis can walk and run short distances, a feat incredible considering her initial circumstances with paralysis (Cowley 1). Since the effects of strokes are typically irreversible, the magnitude of her recovery is particularly incredible for the world of medicine. Similarly, another patient Jim Finn considered xenotransplantation as he suffered from a neurodegenerative disorder Parkinson's disease. Before the treatment, Finn lost control of basic motor movements, unable to walk or talk. The surgical process was unsophisticated to the extent where the procedure seemed even barbaric – after drilling a hole through Finn's skull, surgeons pumped fetal pig neurocells into his head (Abernathy 2). Miraculously, despite the crudeness of the surgery, Jim Finn slowly retained control of his movements. Researchers are stumped as they attempt to delve into the reasons why the fetal pig neurocells were able to repair the brain damage from Parkinson's disease. Evidently, an injection of pig neurocells into the head is a plausible option for those who suffer from disorders relating to the brain.

In 1992, Dr. Starzl performed six baboon kidney transplants into humans. Though the patients survived between 19 and 98 days, unsurprisingly, most of them eventually died of infections ("First Baboon to Human Liver Transplant" 3). In 1997, Robert Pennington, whose condition was rapidly failing due to his deteriorating liver, was desperate for a liver transplant.

At that time, because of Pennington's near proximity to death, the surgeon boldly ventured into areas out of their province and taking risks in hand, made the decision to perform a pig liver transplant. Incredibly, Pennington's immune system did not attack the liver. Though the pig liver was a temporary six hour fix until a replacement human liver was found, the truth remains that that liver performed basic kidney functions for those crucial six hours. (Brower 3)

Finally, Jeff Getty, after suffering from AIDs for many years, decided to risk a bone marrow transplant from a baboon in the hopes of vanquishing the disease. Ultimately, the researchers hoped that the baboon's inherent resistance to the virus would relinquish its hold onto the new, human host. His surgery was deemed unsuccessful; the baboon bone marrow cells did not remain in Getty, but his overall health did appear to improve in the aftermath of the surgery ("Jeff Getty" 1).

There is one trenchant similarity between all of these individuals: their willingness to gamble their lives, risking unconventional methods of treatment because of their drive to survive. Xenotransplantation was simply the only viable option to them, given the limitations of organs or lack of effective treatments. Most probably, these individuals would have eventually died from their medical conditions. Instead, they wanted to risk their lives, hoping for a medical breakthrough and knowing that they at least attempted to save themselves. Life is meaningless if one does not fight to keep it. Analyzing the case studies, with regards to neurodegenerative disorders, xenotransplantation offers a viable method of treatment. Though the process does not guarantee recovery of the patient, like most currently available treatments, it remains a plausible option. Furthermore, xenotransplantation appears to be a plausible, temporary treatment in cases where immediate organ transplant is necessary, acting as a stepping stone to the real human tissue. Even though the process still has risks, taking into consideration the lack of effective alternative treatments, xenotransplantation attracts a number of patients.

Ultimately, after conducting case study analysis, I realize that the main obstacle that impedes the success of xenotransplantation is the issue of rejection by the human host. At the crux of the problem are XNA antibodies; these miniscule molecules in the body immediately register the presence of the gal epitope from foreign tissues, a shark detecting the scent of blood in the ocean. To eradicate this issue, the animals can be genetically engineered to inhibit the enzyme that produces the gal epitope. Inhibiting gene expression can be done through DNA methylation, adding methyl, or methane alkyl, groups to DNA sequences to effectively "silence" the gene. Another potential process is through the advances of biotechnology – parts of the human genome can be integrated into pig genes to rid the enzyme production. However, genetic engineering also encounters much controversy in terms of its ethical issues. Ideally, it would facilitate the creation of a wealth of functioning organs for medical patients.

In the future, biomedical engineers can attempt to construct pig cells, using realistic mechanisms that effectively aid the cells in evading detection by the immune system. Researchers have also tried to combat the issue in this manner. Recently, scientists in Europe "coated pig insulin-producing cell, or islets, in seaweed to protection them from the human immune system" ("Pig Sushi" 1). Specifically, the alginate in the seaweed prevents the human immune system from registering the presence of the islets, effectively camouflaging the pig cells. The process may appear to be simplistic noting how scientists have dubbed the cells 'pig sushi.' Furthermore, the likelihood of the alginate to corrode in the body in time is high, but the implications are enormous. Later, researchers will be able to discover more effective, advanced materials that conceal the pig cells. This method of cell disguise would yield fewer medical or ethical complications than genetic engineering.

Ultimately, there exists a future for xenotransplantation. However, the path towards the process becoming a practical option towards all medical patients is a labyrinth, full of twists and turns that impede its progression. The fear of cross-species viral contamination and religious beliefs on the sanctity of the human body are pervasive throughout the beliefs of the opposition. In response to their viewpoints, I must state, did doctors not take risks when making the decision to consider new types of medical therapy? Alas, it is the valiance and tenacity of doctors that have contributed to the most essential of medical discoveries, such as hormone therapy. In the end, the willingness of doctors to take chances is what saves millions of patients' lives. Having trepidation at the thought of crossing into unexplored areas will certainly impede the progression of mankind. By developing xenotransplantation to ensure that the human immune system does not recognize the foreign tissues, we will prevent the unjust deaths of patients on the organ donor waiting list. With xenotransplantation, no more will these innocent individuals perish.

Works Cited

Abernathy, Bob, dir. "Xenotransplantation." *Religion & Ethics*. PBS. New York. Television. Transcript.

Allan, Jonathan S. Interview. *PBS*. PBS. Web. <http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/interviews/weiss.html>.

Brower, Vicky. "Xenotransplantation's Big, Uncertain Future." *CRT News*. 27 Apr. 2007. Web. 14 May 2012. <http://www.crt-online.org/042700.html>.

Cowley, Geoffrey. "The New Animal Farm." *The Daily Beast*. Newsweek, 01 Apr. 2001. Web. 14 May 2012. <http://www.thedailybeast.com/newsweek/2001/04/01/the-new-animal-farm.html>.

Dooldeniya, M. D., and A. N. Warrens. "Xenotransplantation: Where Are We Today?"*Journal of the Royal Society of Medicine* 96.3 (2003): 111-17. Print.

"First Baboon to Human Liver Transplant." INEU. Web. 14 May 2012. <http://www.xenotransplant.ineu.org/xenotrans/news/19920629.htm>.

"A History of Xenotransplantation Experiments." *PBS*. PBS. Web. 14 May 2012. <http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/etc/cron.html>.

"Jeff Getty, 49, AIDS Activist Who Received Baboon Cells." *The New York Times*. The New York Times, 16 Oct. 2006. Web. 14 May 2012. <http://www.nytimes.com/2006/10/16/health/16getty.html?_r=3>.

"The Need Is Real: Data." *Organdonor.gov*. U.S. Department of Health and Human Service. Web. 10 May 2012. <http://organdonor.gov/index.html>.

"'Pig Sushi' Diabetes Trial Brings Xenotransplant Hope." *New Scientist* 205.2755 (2010): 7. Print.

Rattue, Petra. "Xenotransplantation From Genetically Engineered Pigs." *Medical News Today*. MediLexicon International, 21 Oct. 2011. Web. 14 May 2012. <http://www.medicalnewstoday.com/articles/236387.php>.

Weiss, Robin. Interview. *PBS*. PBS. Web. <http://www.pbs.org/wgbh/pages/frontline/shows/organfarm/interviews/weiss.html>.

Van Der Laan, et al. "Infection by Porcine Endogenous Retrovirus after Islet Xenotransplantation in SCID Mice." *Nature* 407 (2000): 90-94. *Nature.com*. Nature Publishing Group, 5 Apr. 2000. Web. 10 May 2012. <http://www.nature.com/nature/journal/v407/n6800/full/407090a0.html>.