

An Overview of the Biological, Social, And Ethical Implications of Current and Potential Organ Replacement Therapies

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ABSTRACT

The objective of this research paper is to provide the reader with a general overview of the biological processes associated with the various current and potential organ replacement therapies (allotransplantation, xenotransplantation, mechanical circulatory support, anti-rejection drugs) and the related procedure of embryonic stem cell research. The social and ethical implications of these procedures are considered in turn, followed by an in-depth and timely analysis of current and future research using embryonic stem cells. The issues of organ scarcity, zoonosis, chimera production, and moral disagreement as to the beginning of life are addressed. The author's opinion as to a potential solution to the current stem cell research debate is also offered.

INTRODUCTION

The problem of organ scarcity for the approximately 62,000 Americans currently awaiting an organ transplant is a tremendous one. While it is true that over 21,000 people received transplants in 1998 (3), there exists a profoundly more startling statistic. Every 16 minutes in the United States, a potential transplant patient enters his/her name on the national waiting list, and because of this overabundance of demand and dire lack of supply, approximately 4000 Americans die each year while waiting for an organ donation (3).

Through a variety of new technologies, this dim outlook for an organ transplant patient's future of procuring an organ has begun to brighten. While there are a few distinct and decidedly separate technologies playing their hand in this game, it is most likely through a combination of them all that the greatest good will be obtained. The technologies and research presented in this paper all began as unique projects and yet have managed to converge with the common unifier's being the prospect of being able to help the thousands of people annually who are denied a life-saving organ transplant.

Allotransplantation (person-to-person grafts), xenotransplantation (animal-to-human grafts), mechanical circulatory support, and *in vitro* tissue and organ engineering are either current or potential therapies for persons with failing organs. Many of these technologies have futures that lie squarely in the hands of the outcome of current research on embryonic stem cells. Most of these procedures would be directly improved, and all would at least be indirectly improved, from the ability to utilize stem cell lines for research and therapy (6).

Stem cell research has generated a large amount of attention from the medical community, academia, the media, and society as a whole within the past few years. Former President

Bill Clinton created a special National Bioethics Advisory Commission to consider many of the ethical and social implications of instituting stem cell research as a legal procedure (6). Current President George W. Bush has taken a more conservative stance and is expected to ask the Senate to ban all human cloning experiments (2). The bulk of the controversy surrounding stem cell research is due to the source of the cells. The most promising stem cells are called ESCs, or embryonic stem cells, and are taken from human embryos. While studies of another form of stem cells (those taken from adults) have been somewhat successful, most experts agree that the brightest future for therapeutic medical technologies lies with ESCs. These ESCs, and the harvesting of human embryos for research, have prompted one of the largest public debates over ethical concerns that the world has ever seen. Because of new and more precise technologies, the medical community has found itself being drawn deeper and deeper into murky ethical waters. What is the definition of the beginning of life? When does an embryo begin to be deserving of moral status and thus the reprieve from experimental research? These questions, and many more, are what scientists, physicians, ethicists, and society are confronted with today.

Since the cloning of Dolly was published in 1997 (6), much science fiction has begun to become reality. By transferring a nucleus from one cell into the enucleated oocyte from a donor, Ian Wilmut and colleagues were able to bring to life a clone in every sense of the word. However, much of the U.S. responded to this new technology with terror, imagining a person able to “grow” an entire army of cloned machines. This perception has led to distrust of the scientific community. It has also led many religious and social leaders to call for an outright ban on cloning, including ESC research, a form of “therapeutic cloning” (2).

Each transplant procedure that will be discussed here is accompanied by its own biological, social, and ethical implications, and these are what will now be considered. From allotransplantation to the furthest horizons to which ESC research can deliver us, it is vital that the public has a firm knowledge of how these procedures are carried out, what medical implications this will have on the human species, and the ethical concerns brought about by each one. Although the various procedures are extremely complicated scientifically, it is my hope that I can begin to shed some light on, and thereby offer a small part in the way of an explanation of, the ethical concerns.

Allotransplantation

Allotransplantation is by far the most commonly performed organ transplant procedure available today (3). However, while allotransplantation currently represents the majority of transplant operations performed, it is antiquated and riddled with problems that currently have no easy solution. It is the hope of medical professionals that in the near future, allotransplantation will be completely replaced by other viable procedures that do not rely upon a human as the next available organ source.

Allotransplantation offers the patient an actual human organ from another living or recently deceased human. However, the advantages of the procedure end at this point. One huge problem facing allotransplantation is the lack of availability of organs for transplantation (3). Because there are a finite number of organs available, a vast number of patients in dire need of organs continue to wait for a suitable donor. This is a problem that will be nearly impossible to solve, and will continue to plague the practice of allotransplantation into the distant future.

A second problem that has haunted physicians for decades are the moral questions of which patient gets the organ and at what stage of a patient’s disease are they to be considered

suitable for an organ transplant (3)? Currently there is a system in place that rates patients on a numerical scale. Status one is severely ill with a life expectancy of one week, status two describes patients who are less ill [and further divided into 2A (severe) and 2B (less severe)], and status three consists of patients who are not at a high risk of death in the near future (3). Many patients also must be left out of consideration because of a short life expectancy, lack of medical compliance history, or bad habits such as smoking and alcohol consumption (9). Currently, this rating system delivers the scarce organs to the status one patients first, followed by status 2A, 2B, and then status 3. However, much concern has been raised about the fairness of this current system, especially with regard to the aspects of race and geography in the determination of who gets an organ transplant (3). In the face of accusations that many Caucasians from larger, more affluent cities were getting the majority of the organ transplants, the U.S. Department of Health and Human Services (DHHS) laid out the ground rules to answer the question of what organs go where in their regulation called the "Organ Procurement and Transplantation Network: Final Rule" in April of 1998 (3). This document supported the current rating system, and although objections were raised against this regulation as well, subsequent studies found the ruling to be fair and just.

There is a third problem with allotransplantation. While it is true that the patient benefits from a human organ, a patient's body does not always recognize and accept the new organ. This is called rejection, and is the most common problem faced by recent recipients of organ transplants. Each person has proteins attached to the cells of their organs that are individual and unique to that specific organ. When a transplanted organ is placed into another body, that body's immune system's T cells immediately attack and destroy the potentially beneficial organ. The T cells are capable of achieving this feat through the use of two protein signals that alert it to the presence of a foreign body. Currently, the problem of rejection that many patients experience is alleviated through the use of an uncomfortable and unhealthy solution of immunosuppressive drug cocktails that not only boost the risk of cancer and infections but are ironically themselves toxic to the kidneys. However, a recent study on a new anti-rejection drug by transplant immunologist Allan Kirk and endocrinologist David Harlan and their colleagues suggests a unique and exciting solution to this most common of problems (11). Using monkeys, the group administered a new antibody that helped block one of the body's protein signals, specifically the protein CD154. All T cells that encounter a foreign molecule in the body, especially the molecules found on transplanted organs, immediately become activated and begin to produce the protein CD154. This CD154 then binds to an immune cell receptor called CD40. This process is primarily what unleashes the devastating immune system attack on the transplanted organ. The new antibody that Kirk and Harlan have synthesized specifically targets the protein CD154 and prevents its binding to the CD40 receptor. This effectively stops the immune system attack and, according to preliminary research results, seems to be working extremely well. A test group of nine monkeys received kidney transplants and then weekly injections of the drug for one month, subsequently followed by monthly doses for five more months. Treatment then ended and eight of the monkeys were still alive one year later. The one death was attributed to a routine laboratory procedure (blood draw) and a subsequent autopsy showed that the monkey's kidneys were functioning normally. However, although this new antibody is definitely exciting and could potentially solve the rejection problem, the procurement and distribution of organs has shown itself to be a hotbed of dispute and remains a severe deficiency of allotransplantation.

Xenotransplantation

Xenotransplantation has also given patients, physicians, and researchers alike a glimpse into the future of organ transplantation. This procedure is similar to allotransplantation but utilizes a different organ source. By primarily using livestock such as swine as the organ donors, xenotransplantation bypasses one of the large hurdles of allotransplantation, providing an ample supply of organs.

However, xenotransplantation is not without drawbacks of its own. One current disadvantage of xenotransplantation is the recognition by the host's body of the foreign organ and the subsequent attack and rejection of that organ. There are two main sources of hope for researchers in this field: the new antibody previously mentioned (11), and a method in which transgenic pigs are bred in order for them to express human proteins (12). Another problem is the ethical concern many people have about creating a human chimera (part human, part animal). This concern has been played up by fiction writers of the past, for example, with human creations of the werewolf (part human, part wolf) and Spiderman (part human, part spider). These creations exemplify what many falsely see as the next step for xenotransplantation. Just as the cloned army was a false impression of what the cloning procedure was truly about, so too are these complete chimeras. However, while not exactly on the same scale as Spiderman, the idea of a human chimera is not entirely implausible and has received its attention most notably in the area of ESC research. Former President Bill Clinton, while setting up the National Bioethics Advisory Commission, was quoted as saying, "The creation of an embryonic stem cell that is part human and part cow raises the most serious of ethical, medical, and legal concerns. I am deeply troubled by the news of experiments involving the mingling of human and nonhuman species" (6).

Another problem faced by xenotransplantation is the possibility of introducing new diseases and viruses from animals into the human population (zoonosis) that never would have occurred in the absence of this medical meddling. It is quite likely that HIV-1 began its infamous career as a zoonosis from chimpanzees and therefore it is possible that HIV was the result of human meddling, particularly through propagation of poliovirus vaccines in chimpanzee kidneys by researchers in Africa (12). If such a devastating disease can be delivered into the human population simply by using a vaccine that was grown in chimpanzee kidneys, many more potentially dangerous effects may result from the transplantation of entire animal organs into a human being. Other zoonoses have also occurred, including hepatitis and tuberculosis (12). Because of these types of incidents, the notion of introducing an unknown zoonosis into the human population through xenotransplantation should not be taken lightly.

Pigs are the most commonly used animals for the procurement of organs for xenotransplantation for practical, ethical, and safety reasons. Because of this choice, a particular retrovirus has risen to the attention of many professionals. Pigs are known to carry a virus called PERV (porcine endogenous retrovirus), which cannot be eliminated by any known method (12). Recent studies have been done that involved a small number of patients with fetal pig nerve cells introduced into their brains in an attempt to slow the symptoms of Parkinson's and Huntington's disease. These patients have shown no signs of PERV infection; however, some PERV genomes have given rise to human-tropic PERV strains in culture (12). The observation that cultured PERV genomes can give rise to human disease is unsettling to many people who are worried about the possibility of a zoonosis being transferred to humans.

What upsets people in the scientific community and society at large is the news of occurrences such as a Russian study that took place a few years ago. Without any regard for the

ethical implications or that of the safety of their patients, Russian scientists ran their patient's blood through the spleens of farm fresh pigs in an effort to obtain data relevant to the field of xenotransplantation and microchimerism (survival of transplanted donor cells in the recipient). The scientists then made the potentially disastrous mistake of promptly returning the patient's blood straight from the spleens of the farm pigs (12). While such an experiment stands on shaky ethical grounds at best, it did provide researchers with evidence that while microchimerism existed for long periods of time after the procedure (eight years), there was no evidence to show that the PERV virus had appeared in the human population. However, the scientific community needs to desist from performing such experiments without public debates so as not to cross any ethical lines that society may wish to draw. This caution is needed if scientists wish to have the critical trust and support of the public majority.

While describing the future implications of the new recombinant DNA technology in 1975, Joshua Lederberg alluded to the "uncertain peril and certain promise" resulting from such technology (12). The same can be said of xenotransplantation, with the peril being the possibility of unleashing a devastating disease into the human population, and the promise being the ability to save thousands of lives every year through the delivery of animal organs into human patients. It is thus up to scientists to make sure that while the future promise retains a solid footing, the danger begins to slowly fade. Such an endeavor will require lengthy ethical debates between scientists and scholars, but hopefully will result in relief from suffering for thousands of organ transplant patients in the world.

Mechanical Circulatory Support

Mechanical circulatory support is another growing field of biotechnology with the strong claim of being the heir to allotransplantation. Currently this procedure deals only with the heart, but it is hoped that in the future many other organ failure patients will be able to benefit as well. The most rapid advance in this field has come under the auspices of TAHs (total artificial hearts) (9). A TAH is an entirely synthetic device that completely replaces a patient's heart. With a TAH, a patient would entirely avoid the need to find a replacement heart, thus shirking the varied ethical and methodological problems such procedures as allotransplantation and xenotransplantation have. A few burdens are being placed upon these TAHs, however, primarily with the amount of times such a device must "beat" during its lifetime. For a TAH to properly sustain its function, and thus the life of its recipient, it must beat around 35 to 40 million times per year. Also, while the current 5-year survival plan for heart transplant patients is 70%, TAH technology researchers are aiming for 90%. Just as is expected of the human heart, a TAH must perform perfectly. Blood clots forming around the valves are a large problem while a mismatch between blood flows from the left and right ventricles can also create serious pulmonary difficulties. Most TAH models currently on the market are too large for even most male candidates, not to mention women and children. In addition, should infection occur, IV antibiotics may not even work because of the synthetic nature of the device.

While the previous list of the problems associated with TAHs seems to be quite formidable, researchers are touting the existence of a new technology called a VAD (ventricular assist device) (9). Such a device is built upon research that shows that damaged cardiac muscle can repair itself if allowed to rest for a time. Most patients suffering from heart problems have one ventricle that is worse than the other. The VAD is designed to allow that ventricle to rest while it begins to repair itself. If a TAH fails, then the patient will quickly die, whereas if a VAD fails, then the patient's heart is still able to support the patient for some time. This

clears the way for a small margin of error that the TAH does not enjoy. Also, many models of VADs are engineered with textured outer surfaces that allow the blood cells to layer slightly on their surfaces. This is promising because the layering allows the future blood cells to flow by much more smoothly than in the absence of layering.

The only ethical argument against these procedures is the question of whether someone with a TAH or VAD is fully human. An interesting occurrence along those lines is the phenomenon the VAD creates wherein a patient may actually be resting comfortably with no pulse at all. This disturbs some people, as it takes away a human feature that is still used to determine life status. However, although the human vs. machine argument is a valid one, through the history of medicine it has been shown that relatively few patients (or society as a whole) have a problem with this ethical issue. For example, society has allowed the existence of life-support machines for many years now, and the VAD definitely does not pose the same ethical concerns that many have about this older technology.

Additional therapies, when combined with VAD and TAH technologies, promise even greater rewards. Adding muscle stem cells to the VAD technology would allow the damaged heart to repair itself more quickly. Drugs such as the beta-agonist Clenbuterol (9) would help achieve many of these same goals, also aiding in repair of the heart muscle. While mechanical circulatory support is still in its early stages, rapid advancement has been made in recent years. As a result, researchers have hope for this new technology as it manages to provide much relief for patients while sidestepping major ethical and safety concerns.

***In vitro* Tissue and Organ Generation**

A final technology that is currently being studied to help patients in need of organ transplants is the generation of tissues and organs in a laboratory setting. This research is quite possibly the most promising, but at the same time, it delves into an area rife with ethical quandaries. The ethical concerns with this technology are primarily in the field of ESC research, and will therefore be largely addressed in that section. To be able to “grow” tissues and complete organs in the proximal past was mere science fiction. Today, however, this technology is at the forefront of a worldwide effort to replace the procedure of allotransplantation.

At the simplest level, this technology allows the *in vitro* regeneration of tissues. Such a procedure has been performed before, and is becoming more and more medically feasible as research progresses. The technique is currently used for burn patients in need of new tissue, wherein the new tissue is grown in the lab and then grafted onto the patient (5). Previously, many patients were required to grow the extra skin needed for grafting directly on their bodies. This was an uncomfortable procedure, both physically and socially, and being able to simply grow the tissue on an artificial scaffold and then perform the graft alleviates this. This technique is currently an accepted medical procedure and scientists are now interested in complete *in vitro* organ generation. However, the move from generating mere tissues to generating complex three-dimensional organs has proven to be rather tricky mechanistically.

The only organ that researchers have currently been able to generate in a laboratory is the relatively simple urinary bladder. Recently, a Harvard research group led by surgeon Anthony Atala was able to generate urinary bladders for domestic dogs in the lab (5). These bladders were then transplanted into dogs and evidence indicated that the new bladders were working normally and holding their shape. In their nine-year quest to generate a bladder in the lab, Anthony Atala and his colleagues encountered, and hopefully solved, many of the same problems as scientists working on the generation of other organs.

Researchers previously had been trying to solve the problem of tissue thinness. The tissue capable of growing on the biodegradable polymer scaffolds used by the scientists was much too thin to ever be formed into an organ. This problem, which was caused by the inability of the interior cells to maintain proper oxygen intake during cell growth, was finally solved by the introduction of branched polymer scaffolds. Joseph Vacanti, a Harvard surgeon, was struck by inspiration while watching seaweed wave in the water, and soon thereafter, the solution to flat polymer sheets was born (5). Vacanti noticed how seaweed was branched to maximize the surface area available to soak up nutrients, and immediately realized that the same branching technique might work in tissue engineering. Such branched scaffolds are porous enough to permit and support living tissue growth as a direct result of the increased surface area available.

The harvesting and inducing of growth of the outer smooth muscle layer cells from a dog's bladder in a petri dish proved not to be a problem for Atala's team (5). The process of getting the inner highly specialized epithelial cells (called urothelial cells) to grow was a large problem, however. When attempts were made to culture these urothelial cells, the cells would usually revert back to more primitive forms, thus functioning poorly and resulting in urine leakage. Eventually Atala's team was able to steer the cells into differentiation, and therefore were able to grow the all-important urothelial cells.

The next problem faced by the researchers was to determine what scaffolding to use. They finally decided upon a synthetic fiber called polyglycolide (approximately 10-20 micrometers in diameter). Scaffolds made from this fiber are also designed to slowly degrade over time, thereby allowing the polymer scaffold to be completely replaced by new tissue. Such polymers can also be engineered to slowly release growth factors during the decay process, allowing the new tissue to more readily generate. The scaffold was dipped in chloroform, shaped over a bladder-shaped mold, and then coated with a second polymer.

Next, the team seeded the inner surface of the scaffold with the urothelial cells. The outer surface was seeded with smooth muscle cells and the entire synthetic organ was then placed into a nutrient bath for seven days. After the nutrient bath, the organs were transplanted into six beagles where they managed to successfully retain their shape and function, and develop innervation.

Computer technology is also coming to the aid of researchers in the area of organ generation. Trying to figure out how best to form tissue into a complex 3-D organ is a mental struggle. By allowing a computer program to guide the tissue's growth in the lab, the procedure becomes much more simple. The computer is able to guide the tissue into the complex folds required to grow an organ. The hope is to eventually grow an entire organ outside of a human body with no direct human intervention.

The implications of this research are not as singular as they might first seem. While it is true that this procedure would provide vital relief to those suffering from a failing organ, another use has even wider applications. Being able to test new drugs on organs not connected to a human body would be a huge boon for the scientific and medical community. For example, hepatitis C is the leading cause of liver failure, and has infected over 170 million people throughout the world (5). Hampering the quest to find a vaccine for this disease is the fact that human hepatocytes quickly lose their liver-specific functions when cultured. This means that cultured human liver hepatocytes no longer are susceptible to viral infection and therefore cannot be studied. In addition, there are no small animal models for hepatitis C. Both of these problems are currently standing in the way of acquiring a vaccine for the lead-

ing cause of liver failure. The ability to use a lab-generated organ for research would allow researchers to concentrate solely on the vaccine itself, and not on the experimental conditions.

Embryonic Stem Cell (ESC) Research

In vitro tissue and organ generation may have great things in store for the medical community, but it is this same technology that brings about the most passionate ethical debates. This controversy stems from the fact that the only viable and truly revolutionary way to go about performing the *in vitro* generation of organs is through the use of ESCs. Many studies have been done, are being done, and will be done to determine the best possible treatments and therapies for patients with failing organs. The inclusion of ESCs in this research will be unavoidable, and thus the lasting decision will be one of whether or not federal funds should be used to support such ESC endeavors. With the knowledge of the inevitability of ESC and other types of therapeutic research, it is now time to delve into a discussion of whether or not federal funds should be used to support ESC research.

ESCs are pluripotent cells extracted from the human embryo. Pluripotency means that such ESCs are completely undifferentiated and can theoretically be induced to become any sort of cell in the human body. With ESCs, researchers would be able to perform procedures to induce the cells to differentiate into liver cells, kidney cells, heart cells, or any other type of cell that was desired. For example, if it were possible for ESCs to be isolated from every infant's umbilical cord and then safely stored throughout that person's life, virtually all medical problems related to tissue and organ failure would be obliterated. Through a relatively simple procedure the doctor would be able to grow another organ in the lab with the person's very own cells and then safely transplant that organ back into the patient without any fear of organ rejection.

While the massive amounts of attention the media has given ESC research may make it seem as if such technologies already exist, it must be noted that ESC technology is still in its infancy. It might seem remarkable that a technology with such an enormous potential to cure patients is not receiving a large portion of the government's support, and in fact it is bewildering to many people. However, to others there is no question why ESC research is not exploding along the exponential curve that it could be, and to these people the stagnation of ESC research is purely positive.

An intriguing aspect of the ESC debate is that there seems to be no clear-cut "sides" to the issue. However, it is simplistically possible to break the majority of people up into three main subgroups: 1) people who are completely opposed to ESC research at the most basic—fundamental of levels, 2) people who are intrigued by the possibilities of ESC research but do not believe all citizens should have to fund it and thus are opposed to governmental support of the research, and 3) people who are not only in favor of the research, but believe the government should be doing all it can in terms of physical, financial, and political means to further the study of ESCs and their potential medical benefits.

The controversy surrounding ESC research lies primarily in the source from which researchers must currently obtain the cells. The sources of viable ESCs are the extra eggs and embryos left over from couples receiving infertility treatments (4). Often when a couple decides to undergo treatment for infertility, the growth of many embryos will occur in hopes that an embryo will respond to treatment and thereby be induced to begin development. Since the primary goal is to achieve pregnancy, and only one embryo is required for this, many

extra embryos (and eggs) may be left over. It is current practice for scientists to receive their ESCs from these extra embryos and eggs, cells that would otherwise be destroyed with a drop of acid and the use of an incinerator (4). Hundreds of thousands of human embryos and eggs are destroyed every year after women going through infertility treatment either become pregnant or decide to terminate the treatment. In either case, the extra embryos and eggs are destroyed and rendered unable to continue their purpose of creating life. Currently, instead of undergoing the massive and senseless destruction of so many eggs, many of these eggs are then fertilized in a laboratory. This fertilization creates an embryo from which the vital ESCs can be obtained. Because of the pluripotent nature of ESCs, scientists are able to produce what are known as “stem cell lines”. These are cultures of ESCs that can be kept indefinitely as they continually grow and divide, supplying scientists with a ready supply of ESCs with which to conduct their research. Another source of ESCs for scientists is from aborted fetuses (4), a procedure that obviously does nothing to alleviate the ethical concerns related to the sources of ESCs for research.

The ultimate ethical question underlying the debates about ESC research seems to be “When does life begin?” The general public commonly has held a largely varied viewpoint as to when life in fact begins and religion tends to play a large role in how people answer this question. To many people, ESC research violates the most sacred of trusts, that trust which exists between an embryo and its mother. To people with this mindset, a “pre-embryo” (an embryo that is still capable of recombination and twinning) is in fact a potential fetus, a fetus is an unborn child, and unborn children deserve the right to life just as an adult does. To a person with this viewpoint, it is abhorrent to even consider the thought of fertilizing a human egg without the intention of ever implanting it in hopes of a resulting pregnancy. Consequently, for people with this viewpoint, it is even further morally repulsive to fertilize an egg without the intention of implantation and then perform experimental research upon the “unborn child” who has no voice to make known its displeasure about the ensuing actions. People of this mindset are fully convinced that conception is the beginning of “personhood” and thus the start of when a being becomes deserving of moral status and dignity (4).

Others, however, have defined the initiation of life differently. Some believe life may begin with what is commonly called the “primitive streak”, or the first trace of the embryo when implantation is beginning. At this moment the “pre-embryo” has still not obtained developmental individuality and is still in the blastocyst form. For still others, life does not begin until the child is delivered from the womb and begins to breathe air on its own. In between these two are a myriad number of different viewpoints as to when life begins, ranging from a few days after the “primitive streak” forms to a few months after conception to several months after birth (4). Because of their beliefs, these groups are typically more readily accepting of ESC research than people who believe that life begins at conception.

Interestingly enough, and not particularly surprising, most people’s beliefs as to when life begins can be ascertained from listening to their opinions about abortion. Those who believe in life at conception are generally those who are most passionately “pro-life” while those who find themselves siding more along the lines of life beginning at the “primitive streak” or later are usually moderately “pro-choice”, although their endorsement of abortion generally ends after early-term abortions. Finally, the proponents of life’s beginning at birth are usually passionately “pro-choice” and many are also supporters of late-term abortions.

A Potential Solution to the Controversy Surrounding ESC Research

Eventually, society as a whole is going to have to figure out some way to agree on a defining moment indicating when life begins. For many people, any definition other than life beginning at conception is intolerably against their faith. However, it is interesting to note that these same people are often not outraged at the thought of the thousands of eggs from infertility therapies being destroyed each year (4). It is true that many religions oppose infertility therapy, but none do so as actively as they do ESC research. In fact, the female body is equipped with more eggs than could ever be fertilized and brought to term, and nobody is calling for research on how to stop the female ovulation cycle. Because of these discrepancies, perhaps proponents of life's starting at conception may have to rethink the unflinching way that they are approaching this debate if there is ever to be any sort of agreement.

Similarly, those who support research up until such times as the third trimester and beyond may also have to back down to a more reasonable approach. Medical research has shown that during the third trimester the fetus begins to become alarmingly similar to a living human and thus the moral considerations given to such fetuses should perhaps therefore incrementally increase. Also, I believe an attempt at compromise must be sought, and nobody who believes that life begins at conception will ever concede to allow research to be done on an 8-month old fetus. The key component to successfully resolving the "definition of life" question lies in compromises and for this to occur, people of all viewpoints must be willing to make some adjustments to their agendas. The most promising of these compromises seems to be the "primitive streak", for no scientific research has yet indicated that an embryo at this stage has any characteristics of "personhood". This definition allows those with the life at conception viewpoint to make only a slight concession (in terms of molecular biology only, for proponents of life at conception can fundamentally accept no compromises whatsoever) while also allowing the proponents of ESC research around two weeks from the time of fertilization to obtain data. The key to this proposition is that people who hold the life at conception viewpoint must realize that ESC research will inevitably continue, and the only way for them to be able to voice their opinions on the matter is to allow a compromise to occur.

The question of whether or not ESC research should receive federal funding is an extremely important one for both political and ethical reasons. It is because of purely political reasons that ESC research currently receives such meager federal funding, and much of this political policy is based on a lack of separation between church and state. Religious groups have banded together in massive lobbying campaigns to convince similarly minded politicians to make policy with their faith instead of the best interest of their constituents. Such policy-making is detrimental to the well being of the nation, to the trust scientists must acquire from the public at large, and to the health of medical patients nationwide. This trend affects even the amount of research being done on the subject, as many researchers are unwilling to write grants for, and therefore apply their name to, anything so controversial as ESC research. An excellent example of the lack of separation between church and state is current President George W. Bush's choice of Elias Zerhouni to lead the National Institute of Health. Zerhouni has been on record as opposing any sort of ESC research on religious grounds, and is currently being considered for the top government position at an institute that has the final recommendation of whether or not certain research should receive federal funds. In the words of Paul Berg, a Nobel laureate at Stanford University, "...It's either because [Zerhouni] had to satisfy some requirement or that he is not open-minded to the scientific

issues. He's allowing ideology to prevail." President Bush has been quoted saying that Zerhouni "shares my view that human life is precious and should not be exploited or destroyed for the benefits of others" (8). Zerhouni has most recently gone on record stating that he will not stand in the way of ESC research, but this statement may merely have been to facilitate his nomination's smooth ride through congress. This politicking of religion in the field of scientific research must stop in order for the public to trust its scientists and physicians, and in this regard, federal funding of ESC research would be a gigantic step in the right direction for the United States government.

Federal funding would provide the much-needed financial base for ESC research to truly take off, but more importantly, such funding would require the ethical oversight of such research by ethical scholars and the society at large. If the government decides to ban ESC research, then the U.S. would be missing out entirely on an opportunity in which other countries with more liberal policies (such as the United Kingdom) would be able to actively engage. Without federal funding, ESC research will most definitely continue both at home and abroad, and three major problems present themselves when faced with the scenario of research that lacks federal funding in the U.S.

The first problem with this lack of funding is that the research will continue at a decidedly slower pace. Although the private sector will continue to finance ESC research, the slowing of ESC research will prevent healing for many people. For too many patients, ESC research is vital to their chances of survival, and without federal funding, such advancements needed to cure many of these patients will not be realized in time to prevent their deaths. It seems unnecessary and unethical to hamper research that holds such promise for the curing of so many diseases simply on the grounds of political policy.

The second problem that arises from the lack of government support for ESC research is the issue of patent rights on new technologies. With the private sector doing all of the research on ESCs, the door is left completely open for unethical business practices to threaten the health of many people. While ESC research holds the promise of treating millions, through copyright and patent laws a company with exclusive rights to a certain technology could withhold access to those without the proper finances. Federal funding would alleviate much of this problem, ensuring that the maximum number of patients could receive the benefits ESC research will bring about.

The third and final problem with the government's not providing federal funding for ESC research is the lack of ethical oversight that would inevitably occur. It is only through government involvement that those who oppose ESC research can be even slightly mollified. Those who oppose federal funding for the actual practice of ESC research thus find themselves in an ethical paradox. Faced with the fact that ESC research will most definitely continue, it is then left to decide if the private sector should be allowed to run rampant over the many ethical and legal lines that society would most likely draw, or whether the government should involve itself to maintain the ethical integrity of the upcoming ESC studies. One can only conclude that while it may be a lose-lose situation for opponents of SEC research, the choice of federal funding surely offers the more palatable of the two options.

There are then two other issues. First, should the government take an active role in the research, and thereby have a better ability to maintain ethical oversight, or should the private sector be allowed to maintain complete control over the research, and thereby maintain the control over the subsequent copyrights and patents? Second, what will be the general consensus on the issue of when life begins? Recent ethical advisory boards have sided with the primitive streak as the "definition" of when life begins, but will the public heed their advice

or try to agree upon a new definition? These are the two major questions that will need to be answered before ESC research can truly begin to revolutionize medicine, and the answers will drastically alter the way that the U.S. is involved in the process.

It should also be noted that a prevalent argument exists today against everything discussed in this paper. It exists as more of a philosophy as to what the purpose of the human species is, as opposed to an argument against the ethics of each specific procedure. Despite this, I will refer to it as an argument. Is it in fact moral to save all the patients currently dying from organ failure? Those who answer “no” to this question wonder, and rightfully so, whether our world is not already crowded enough, without also adding to it the people who were previously dying before a cure was found for their illness. It is interesting to note that via this argument, a liberal atheist and an ultra-conservative Christian could find themselves together supporting the same cause, the liberal because of environmental and global concerns, and the Christian because of theological ones. The concern for the earth’s finite ability to support a human population has existed for some time, quite popularly in Thomas Malthus’ Essay On The Principle Of Population (7). Today, many are reviving this argument after noting how the rapid advances in medical technology have drastically increased the average human life span and have therefore contributed to an exponential explosion in the human population. Regardless of such concerns, there is no doubt that medical research will continue to pursue cures for the diseases that plague our species. It is because of this inevitability that the ethics of the procedures previously mentioned in this paper are prevalent issues of today, and therefore must be treated as such.

CONCLUSION

Organ failure is a major cause of death in the United States and the world, and a multitude of scientists are racing to find the best cure. Many of these researchers are pinning all of their hopes on only one of the following options: allotransplantation, xenotransplantation, TAHs and VADs, anti-rejection drugs, or *in vitro* organ generation. While each of these separate technologies has their definite advantages and disadvantages, it is my opinion that the greatest good to be achieved for transplant patients will come from the confluence of all of these methods. The new anti-rejection drug therapy will work well in combination with the others, as will the continuation of ESC research. At the same time, a person who may not be suitable for an organ transplant may find himself or herself a perfect match for a TAH, VAD, or some other future sort of mechanical device. Because every person is unique, each person’s organ failure therapy will vary as well. It is a definite benefit for the medical community to be able to choose from a myriad number of ways in which to treat a patient. Having scientists pursuing such a diverse range of possibilities in the field of organ transplantation can only be seen as a step in a positive direction.

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REFERENCES

- Ferber, D. 1999. Lab-Grown Organs Begin to Take Shape. *Science* 284 (5413): 422-4 25.
- Fox, M. 2002. President Bush Leads Push to Outlaw Clone Research. Reuters.
<URL:http://www.reuters.com/news_article.jhtml?type=sciencenews&StoryID=793026&fromEmail=true. Accessed 10 April 2002.
- Gibbons, R.D., D. Metzler, N. Duan *et al.* 2000. Waiting for Organ Transplantation. *Science* 287 (5451): 237-238.
- Green, R.M., 2001. *The Human Embryo Research Debates: Bioethics in the Vortex of Controversy*. Oxford University Press, Oxford, New York, USA.
- Griffith, G.L. and G. Naughton. 2002. Tissue Engineering—Current Challenges and Expanding Opportunities. *Science* 295 (5557): 1009-1014.
- Lanza, R.P, J.B. Cibelli and M.D. West. 1999. Human therapeutic cloning. *Nature* 5 (9): 975-977.
- Malthus, T.R., 1963. *An Essay on the Principle of Population*. R.D. Irwin, Homewood, Illinois, USA.
- Mandavilli, A. 2002. So Who is Zerhouni? We'll See. Biomednet <URL:
<http://news.bmn.com/news/story?day=020401&story=1>>. Accessed 10 April 2002
- McCarthy, P.M. and W.A. Smith. 2002. Mechanical Circulatory Support—a Long and Winding Road. *Science* 295 (5557): 998-999.
- Montiminy, J., Neal, R. 2001. Stem Cell Research, The Law, Ethics And Common Sense. UniSci. <URL:<http://unisci.com/stories/20012/0601016.htm>. Accessed 10 April 2002.
- Vogel, G. 1999. New Drug Blocks Rejection in Monkeys. *Science* 284 (5420): 1594-1595.
- Weiss, R.A. Xenografts and Retroviruses. 1999. *Science* 285 (5431): 1221-1222.