

Science and Ethics: An Assessment of Some Genetic Therapies

Asira Enya Asira, PhD

Okeke, Jonathan Chimakonam, Ph.D

Department of Philosophy
University of Calabar, P. M. B. 1115
Cross River State, Nigeria.

Abstract

Genetic therapies and all forms of cross species manipulations of genes are being promoted by the industry's stake holders i.e. biotechnologists or genetic engineers. They argue that it holds great promise for the future of mankind in Medicare, agriculture and other forms of artificial modifications and enhancement. However, it is also believed that the application of this technology promises great dangers for life and human health. In this paper, we discussed some of these scientific techniques in the light of their ethical implications.

Keywords: genetics, ethics, therapy, science, health, xenotransplantation, Allotransplantation, Genetic Enhancement, Somatic and Germ Line Gene Therapies.

1. Introduction

Most gene-therapy cases in humans would involve transplanting human DNA from one individual to another (Allotransplantation). It is still debatable that research on and application of these techniques is going to use genes from an animal species to treat human genetic diseases. It is more likely that techniques involving the transplantation of genetic material from one animal species to another would be useful in agricultural or industrial applications; work of this kind has already been performed (involving human genes being moved into certain agricultural animals). But worries are beginning to rise alongside the demand for organ transplant and the acute shortage all over the world, calling in cross-species transplants (xenotransplantation). The most far-reaching experiments of this sort are designed to increase understanding of mechanisms of genetic control and gene regulation.

It is expected that continuous research in this area will improve scientists' ability to work with the genes of individuals within a species, and thus decrease the need to transfer genetic material between species in future therapeutic endeavors. The question has arisen, though, as to whether such work should be completely avoided or terminated because of an inherent danger or impropriety in "violating species boundaries." In this paper we consider some of the ethical concerns of different genetic therapies.

2. Allotransplantation.

This is also called homograft, a transplant of body organs between members of same species. It is contrasted with xenotransplantation which is cross-species organ transplantation. The main challenges remain organ shortages and the case of rejection resulting from incompatibility. Although there has been considerable progress in the understanding of immune responses, the diagnosis and management of rejection still remain one of the major problems after organ transplantation. After a kidney allotransplant many clinical symptoms and signs and laboratory investigations have been assessed for the early detection of rejection (Merrill, 1967; Hume, 1967; Russell, 1968). Unfortunately none is sufficiently reliable to be used alone and the clinician must rely on an assessment from as much information as he has available in order to decide on the need for antirejection therapy. According to Papadimitriou and others (99) this is particularly difficult should there be a period of acute oliguric renal failure after the operation since other causes of decreased kidney function may develop during this period, namely, ureteric obstruction or thrombosis in one of the renal vessels.

Also, Hume, Magee, Kauffman, Rittenbury, and Prout (1963) indicated that one of the earliest signs of rejection was the appearance of renal tubular epithelial cells and lymphocytes in the urine. Other investigators also suggested that the study of urinary sediment was a valuable guide to the fate of a transplanted kidney, especially when the urine was examined daily as a routine procedure (Calne, 1964; Mowbray, Cohen, Doak, Kenyon, Owen, Percival, Porter, and Peart, 1965; Taft and Flax, 1966; Spencer and Petersen, 1967). Nevertheless, Kline and Craighead (1967) recently reported that cells diagnostic of immunological rejection of the homograft were not observed in their patients. Besides the issue of rejection, Philosophers contest the morality of homograft as a therapeutic measure in medical practice. Individuals are created with different identities and the substance of these is internal, hence the reckless reshuffling of these vital organs simply amounts to switching of identities. Although this practice may save lives but of what value is a life with lost identity or fragmented personality? Ethicists therefore urge us to consider human dignity and the very fundamental principle of existence carefully before sanctioning a wide range application of this technology.

3. Xenotransplantation.

According to D. Cooper and others in a paper titled "Xenotransplantation" (1-6) the concept of blending parts derived from different species goes back centuries. Centaurs, mermaids and other creatures from classical mythology come vividly to mind. Homer, for instance, described the chimaera as consisting of a lion in front, a serpent behind and a goat in between. It was a fearful creature, swift of foot and strong, that spat flames at all who came within its range. In contrast, the lamassu was a benevolent beast that guarded the gates of cities and palaces. It had a human head and the body of a lion or a bull with wings that were believed to represent spiritual elevation.

Cooper et al goes further to stress that xenotransplantation (the transplantation of organs, tissues or cells between different species, e.g. pig-to-human) dates back more than three centuries, when in 1682 a Russian physician reportedly repaired the skull of a wounded nobleman using a piece of bone from a dog. According to them (Cooper and others), Blood transfusions from various animals, particularly sheep, were used in humans as early as the seventeenth century, although they must undoubtedly have been associated with major complications and even death. It was not until early in the twentieth century, however, that scientists made attempts to transplant body parts across the species barrier. In 1905, according to Cooper et al, a French surgeon inserted slices of rabbit kidney into a child who had renal failure and, in the years that followed, doctors attempted to transplant organs from the pig, goat, lamb and nonhuman primate into patients. Not surprisingly, all of the grafts failed rapidly, as this was at a time when the immunological basis of the rejection process was not understood. Scientific interest in the transplantation of animal and human tissues waned.

Further, Cooper et al states that the first scientific efforts were made in the 1960s by Keith Reemtsma and Tom Starzl who respectively transplanted chimpanzee or baboon kidneys into patients in terminal renal failure when human organs were not available. Starzl went on to transplant occasional chimpanzee or baboon livers in critically ill patients. James Hardy and Leonard Bailey carried out single chimpanzee and baboon heart transplants in patients in 1964 and 1984, respectively. All of these attempts Cooper et al declare, were ultimately unsuccessful, although one patient with a chimpanzee kidney and one with a baboon liver survived for months rather than days or weeks, as in the majority of cases.

3.1 Argument for Xenotransplantation. The transplant of organs, using human donor organs, as a form of surgical therapy according to Cooper et al (1) began in the middle of the twentieth century, when Joseph Murray and his colleagues performed the first truly successful renal transplant between identical twins in Boston. From the success recorded in this, other attempts were taken to other areas and with other organs such as kidneys between more distantly related and unrelated donors through the use of what is called immunosuppressive drugs such as azathioprine and glucocorticoids and, more recently, ciclosporin and tacrolimus.

Up until the contemporary times, it is estimated that close to 500 000 patients worldwide have received life-sustaining renal transplants (Cooper and Others, 1). One great fall out of this development is that surgical expertise have continued to grow affecting different previously unexplored areas like the heart, lung, liver, pancreas and intestine transplantation.

For Cooper and others (1) Organ transplantation is one of the success stories of the second half of the twentieth century. Indeed, it is its very success, resulting in the referral of ever-increasing numbers of patients that has generated a crisis in donor organ supply. Even before the emergence of the new field of cell transplantation, there was a serious shortage of human donor organs and tissues. Considering the fact that, in the USA alone, more than \$US400 billion are spent each year to care for patients who suffer tissue loss or end-stage organ failure, it is clear that the pressure to transplant animal tissues into humans will grow and intensify (Cooper and Others, 1). In addition to patients with heart, liver, kidney and lung disease, over 8 million patients in the USA suffer from neurodegenerative disorders, such as Alzheimer and Parkinson diseases, over 17 million patients suffer from diabetes and millions more from immunodeficiency disorders, haemophilia and other diseases caused by the loss of specific vital differentiated functional cells.

Our improved understanding of the immune system and the immune rejection process has resulted in developing therapies that hopefully will overcome the vigorous immune responses associated with the transplantation of xenogeneic tissues. It appears likely that, during the next few years, human clinical trials utilizing animal cells and organs to treat some of these diseases will become a reality.

Indeed, the US Food and Drug Administration (FDA) has previously approved clinical trials in patients using baboon cells for the acquired immune deficiency syndrome (AIDS), pig cells for diabetes, Parkinson disease and epilepsy, cow cells for intractable pain and pig livers as a temporary support until a human organ becomes available.

At present, Cooper et al continues, tens of thousands of patients are waiting for donor organs to become available. All too frequently, patients with life-threatening illnesses succumb while awaiting organ transplantation. In the USA, for instance, almost 90 000 patients await an organ of one type or another and yet in 2004 well under 30 000 donor organs became available. The issue facing the medical profession and society as a whole is how to resolve this dilemma.

It is hoped that a new consciousness regarding organ donation would make more human organs to be available, even if it still remains insufficient. Cooper and others (2) state that the deficiency in the supply of donor tissues is increasing dramatically each year, and will become even more critical if pancreatic islet transplantation develops as an effective therapy for diabetes. Diabetes alone they estimate, afflicts an estimated 140 million people worldwide, whereas only a few thousand pancreatic glands become available annually. As multiple glands may be required to isolate a sufficient number of islets to treat a single diabetic patient, it is clearly imperative that techniques be developed to transplant islets from animal sources to diabetic patients on a routine basis.

From the foregoing, it is understandable why the pig according to Cooper et al (2) has been singled out as the most suitable potential donor of organs and tissues for humans. This is because they are easy to breed and raise, they mature quickly, and have organs that are comparable in size and physiology to humans. They are also said to be free from certain designated pathogens have been raised for many years under carefully controlled conditions. Also, ethical concerns favour the donor organs from pigs than from a non-human primate. To the ethical issues involved in xenotransplantation we now turn.

3.1.1 Ethical Issues. The ethical and social policy issues relating to xenotransplantation can be categorized into two sections according to Carter (2) (1) issues that relate to research involving human beings and; (2) issues that relate to animal welfare. Crossing the species barrier is a deep-seated taboo in human culture held by some members of our society. Those who hold this view believe that the integrity of human beings may be compromised if xenotransplants become common practice. Loss of identity by the human recipient is another concern expressed by opponents of xenotransplantation. The possibility that recipients will experience psychological problems as a result of animal-to-human transplants is another ethical issue that needs further debate. Some commentators have expressed a concern about an absence of a relationship between the giver and the receiver in xenotransplantation. The importance of a giver-receiver relationship has been widely held by professionals working in human organ donation settings. It is yet unknown how the absence of this relationship might affect recipients of xenotransplants.

Lifelong monitoring of xenotrans plant recipients and their close contacts is required when participants undergo xenotransplant procedures. This requirement is considered mandatory primarily because of the potential risk of zoonotic infections spreading to the wider community. The preservation of related individuals' privacy and personal autonomy is an issue that has attracted debate in the literature. Ethical issues with human subject research in xenotrans plantation trials include the voluntary consent of individuals, respect for the individual's autonomy, issues surrounding risk communication and issues relating to equity. The research conducted must also carry a direct therapeutic benefit to the patient. Instrumental use of animals has been put forward as a major ethical concern. According to Carter (1) the current Draft Guidelines require researchers to respect the welfare of source animals and procedures must minimise the impact on animals. The legislation proposed by NHMRC establishes researchers' obligations for keeping animals bred for xenotransplantation research in a natural and comfortable environment.

4. Gene Therapy

Gene therapy involves the use of genes for medicinal purposes. It also involves the transfer of a therapeutic or working gene copy into specific cells of an individual in order to repair a faulty gene copy. Thus it may be used to replace a faulty gene, or to introduce a new gene whose function is to cure or to favourably modify the clinical course of a condition. The scope of this new approach to the treatment of a condition is broad, with potential in the treatment of many genetic conditions, some forms of cancer and certain viral infections such as AIDS. Gene therapy remains an experimental discipline however and much research remains to be done before this approach to the treatment of certain conditions will realise its full potential. The majority of clinical gene therapy trials are being conducted in the United States and Europe, with only a modest number initiated in other countries, including Australia. The majority of these trials focus on treating acquired conditions such as cancer. The only gene therapy that has been approved for routine treatment so far is for a form of cancer which was approved in China in early 2004.

A form of immune deficiency called adenosine deaminase (ADA) deficiency was the first condition to be treated with a gene therapy approach in humans in the early 1990s. It is also the first condition for which therapeutic gene transfer into stem cells has been attempted in the clinical arena (Candotti, 2001). *A case study of gene therapy for a genetic condition* Another form of immune deficiency is due to a mutation in a gene located on the X chromosome and is called Severe Combined Immune Deficiency (SCID). This 'X-linked condition' only affects boys. The use of gene therapy in 2000 in the treatment of this condition by a French research group led by M. Cavazzana-Calvo was hailed as the first example of a genetic condition being successfully treated by gene therapy and is a milestone in medical history.

- Seven out of ten infants treated to date have restored immune function. Two of the children treated by the gene therapy however developed leukaemia in 2002 and 2003, caused when the virus used to deliver the therapeutic gene activated a cancer-causing gene (an *oncogene*) (Genetics Fact Sheet, 47)
- The clinical trials were halted but have now been resumed only for patients with no other treatment options
- This experience illustrates the need for this therapy to be conducted as part of clinical trials.

4.1 How does gene therapy work?

The challenge of developing successful gene therapy for any specific condition is considerable. The condition in question must be well understood and the underlying faulty gene identified. A working copy of the gene involved must be available, the specific cells in the body requiring treatment must be identified and accessible and finally, a means of efficiently delivering working copies of the gene to these cells must be available. Of all these challenges, the one that is most difficult is the problem of 'gene delivery' ie. how to get the new or replacement genes into the desired tissues. Some of the 'vectors' for the role of delivering the working copy of the gene to the target cells include using:

a) Harmless viruses

One of the most promising methods currently being developed is the use of harmless viruses that can be used to carry genes into cells. Scientists now have the knowledge and skills to remove the virus' own genes and to replace them with working human genes. These altered viruses can then be used to smuggle genes into cells with great efficiency. When viruses are used in this way they are known as vectors.

Some of these vectors are capable of not only carrying the gene into the cell but also of inserting the gene into the genetic makeup of the cell. Once in the right location within the cell of an affected person, the transplanted gene is 'switched on'. The transplanted gene can then issue the instructions necessary for the cell to make the protein that was previously missing or altered.

b) Stem cells

Another technique with potential is the use of stem cells in delivering gene therapy. Stem cells are immature cells that can differentiate or develop into cells with different functions. In this technique, stem cells are manipulated in the laboratory in order to make them accept new genes that can then change their behaviour.

For example, a gene might be inserted into a stem cell that could make it better able to survive chemotherapy. This would be of assistance to those patients who could benefit from further chemotherapy following stem cell transplantation.

4.1.1 Ethical Issues

It is medically known that while the body has many billions of cells, only a very small proportion of these cells are involved in reproduction, the process by which our genes are handed on to future generations. In males these cells are located in the testes and in females, in the ovaries. These special reproductive cells are called 'germ cells'. All other cells in the body, irrespective of whether they are brain, lung, skin or bone cells, are known as 'somatic cells'. In gene therapy, only somatic cells are targeted for treatment. Therefore any changes to the genes of an individual by gene therapy will only impact on the cells of their body and cannot be passed on to their children. Changes to the somatic cells cannot be passed on to future generations (inherited). Somatic gene therapy treats the individual and has no impact on future generations. Imagine, for example, a little boy with haemophilia, a condition that is caused by a faulty gene that makes his liver unable to make blood clotting factor 8 (Genetics Fact Sheet 40).

- Gene therapy would involve putting a working copy of the gene which codes for factor 8 into his liver cells so that his liver could then produce adequate levels of factor 8
- While the little boy himself would be cured, the altered genes in his germ cells would remain unchanged and he could still pass the faulty gene on to future generations. Also, Concerns with gene therapy of the egg or sperm cells The possible genetic manipulation of the egg or sperm cells (germ cells) remains the subject of intense ethical and philosophical discussion. The strong consensus view at present is that the risks of germ line manipulation far exceed any potential benefit and should not be attempted.

However, no therapy, established or experimental, is without some associated risk and the potential benefits of new treatments must always be balanced against such risks. The experience with gene therapy for the immunodeficiency condition SCID as described above illustrates the need for this therapy to be conducted as part of clinical trials. Safety will appropriately remain an important consideration as the field of gene therapy evolves.

5. Genetic Enhancement.

Genetic Enhancement Technologies (GET) have to do with all those technologies which biotechnologists employ to improve the character trait of humans whether through surgery, IVF, designer baby syndrome and indeed all forms of body and character modification involving the human gene. The debate between those who believe that mankind's DNA should not be altered and those who hold that there is nothing wrong in enhancing our nature if necessary has heralded the questions: Are we good enough? If not, can we improve ourselves? If yes, are we free to do this? And would it be moral? Must we restrict ourselves to traditional methods like study and training? Or should we also use science to enhance some of our mental and physical capacities more directly? According to Baylis and Robert citing Stableford (1984) in their paper "The Inevitability of Genetic Enhancement Technologies" for some people, the development and use of any technology to enhance human capacities and traits is laudable – likely to improve the human condition. For others, the development and use of all but a narrow set of environmental enhancements (such as education) is deeply problematic (Kass, 1985).

Between these extremes are those who are not so much concerned with the technical means of enhancement – that is, whether the alterations are sought by environmental, surgical, pharmacological or genetic means – but rather who are worried about the nature of the alterations sought – that is, whether the enhancement technology will be used (alone or in combination) to make physical, intellectual, psychological or moral alterations to the self (Walters and Palmer, 1997). In the classification of *physical enhancements* there might be a range of alterations aimed at improving size, increasing muscle mass, reducing sleep dependence, increasing endurance, decelerating ageing, altering skin colour or changing gender. *Intellectual enhancements* might include alterations aimed at improving memory and cognitive ability, promoting multi-dimensional thinking, and increasing imagination. *Psychological enhancements* might include efforts to improve sociability, reduce shyness, and instill confidence. And, *moral enhancements* could seek to control violent behaviour, encourage kindness and promote the capacity for sympathy. Some of these types of enhancements are considered worthy of pursuit, while others are thought to be of questionable value.

Incidentally, to some people the concern is not with the technical means of enhancement or with the human characteristics to be enhanced, but rather with the underlying motivation(s). (Baylis and Scott, 2). Commonly, enhancements may be sought for a variety of reasons: to be in fashion; to improve performance; to gain a competitive advantage; to secure and exercise power; to promote and protect health and well-being; to increase the life-span; to assuage or even overcome existential angst; or to meet the demands of justice (Parens, 1999). And, depending upon the underlying motivation, the resulting alterations may be conservative (i.e., used to normalize the self), liberal (i.e., used to liberate the self) or radical (i.e., used to fashion a self that effectively challenges others' conception of oneself). From the perspective of some theorists, not all of these reasons for seeking to enhance human capacities and traits are equally meritorious.

For some years now, human enhancement has grown into a major topic of debate in applied ethics. Interest has been stimulated by advances in the biomedical sciences, advances which to many suggest that it will become increasingly feasible to use medicine and technology to reshape, manipulate, and enhance many aspects of human biology even in healthy individuals. To the extent that such interventions are on the horizon (or already available) there is an obvious practical dimension to these debates. This practical dimension is underscored by an outcrop of think tanks and activist organizations devoted to the *biopolitics* of enhancement. Already one can detect a biopolitical fault line developing between proenhancement and anti-enhancement groupings: transhumanists on one side, who believe that a wide range of enhancements should be developed and that people should be free to use them to transform themselves in quite radical ways; and bioconservatives on the other, who believe that we should not substantially alter human biology or the human condition (Bonstrom 63)

Also, there are also miscellaneous groups who try to position themselves in-between these poles, as the golden mean. While the terms of this emerging political disagreement are still being negotiated, there might be a window of opportunity open for academic bioethicists to influence the shape and direction of this debate before it settles into a fixedly linear ideological tug-of-war. (Bonstrom and Savulescu 2). Beyond this practical relevance, the topic of enhancement also holds theoretical interest. Many of the ethical issues that arise in the examination of human enhancement prospects hook into concepts and problems of more general philosophical significance— concepts such as human nature, personal identity, moral status, well-being, and problems in normative ethics, political philosophy, philosophy of mind, and epistemology. In addition to these philosophical linkages, human enhancement also offers thought fodder for several other disciplines, including medicine, law, psychology, economics, and sociology.

The degree to which human enhancements constitute a distinctive cluster of phenomena for which it would be appropriate to have a (multidisciplinary) academic subfield is debatable, however. One common argumentative strategy, used predominantly to buttress pro-enhancement positions, is to highlight the continuities between new controversial enhancement methods and old accepted ways of enhancing human capacities. How is taking modafinil fundamentally different from imbibing a good cup of tea? How is either morally different from getting a full night's sleep? Are not shoes a kind of foot enhancement, clothes an enhancement of our skin?

A notepad, similarly, can be viewed as a memory enhancement—it being far from obvious how the fact that a phone number is stored in our pocket instead of our brain is supposed to matter once we abstract from contingent factors such as cost and convenience. In one sense, *all* technology can be viewed as an enhancement of our native human capacities, enabling us to achieve certain effects that would otherwise require more effort or be altogether beyond our power. Pushing this thought further, one could argue that even mental algorithms such as we use to perform basic arithmetic in our heads, and learned skills such as literacy, are a kind of enhancement of our mental software. When we learn to calculate and read we are literally reprogramming the micro-structure of our nervous system, with physiological effects just as real as those resulting from the ingestion of a psychoactive drug, and often more durable and with more profound consequences for our lives. At the limit of this line of reasoning, *all* learning could be viewed as physiological enhancement, and *all* physical and organizational capital could be viewed as external enhancements. Stripped of all such “enhancements” it would be impossible for us to survive, and maybe we would not even be fully human in the few short days before we perished.

It should be admitted that at this point that if the concept of human enhancement is stretched to this extent, it becomes manifestly unfit for service as an organizing idea for a new and distinctive field of ethical inquiry. This need not trouble enhancement advocates who maintain that there is no morally significant difference between novel biomedical enhancements and all the other more familiar ways of enhancing. Those who object to human enhancement, however, must resist this inflationary interpretation of what enhancement is, drawing a line somewhere to distinguish the problematic new types of enhancements from the unobjectionable use of shoes, clothes, tea, sleep, PDAs, literacy, forklifts, and the bulk of contemporary medicine. Such a line need not be sharp. Many important and useful philosophical terms are vague. Nevertheless, two challenges must be met. First, some account needs to be given of what counts as an enhancement—an account that must be reasonably intelligible and non-arbitrary, capturing something that might plausibly be thought of as a kind. Second, given such an account, it needs to be shown that it tracks a morally relevant distinction. Unless these two challenges can be met, it would appear misguided to organize our ethical thinking in this area around the concept of enhancement. “Enhancement” might still be useful to flag a patch of territory consisting of a variety of loosely related practices, techniques, and prospects. But it would hardly make sense either to pledge allegiance to such a flag, or to devote oneself to opposing what it stands for. Instead, our ethical judgments would have to track different and finer distinctions that would reflect the concrete circumstances and consequences of particular enhancement practices: Precisely what capacity is being enhanced in what ways? Who has access? Who makes the decisions? Within what cultural and sociopolitical context? At what cost to competing priorities? With what externalities? Justifiable ethical verdicts may only be attainable following a specification of these and other similarly contextual variables. To accept this conclusion is to accept a kind of *normalization* of enhancement. That is, at a fundamental normative level, there is nothing special about human enhancement interventions: they should be evaluated, without prejudice and bias, on a case-by-case basis using the same messy criteria that we employ in other areas of practical ethics.

6. Somatic and Germ Line Gene Therapies

Gene therapy might be performed in either germ cells (sperm, egg cells, or the cells that give rise to them) or in *somatic* cells (cells that comprise all other body tissues). Alterations in somatic cells do not result in inheritance of the alteration, while modification of germ cells results in changes that could be passed on to subsequent generations if the recipient patient were to have children.

Genes are comprised of deoxyribonucleic acid (DNA). DNA, in turn, is composed of long chains of molecules called nucleotides. All the genetic information that is inherited by a cell is encoded by the sequence of nucleotides in its DNA. DNA ultimately controls formation of all of the substances that comprise and regulate the cell. Certain sequences of DNA contain information for specific proteins such as enzymes, hemoglobin (the oxygen-containing protein in red blood cells), or the variety of receptors on the cell’s surface. Stretches of DNA that contain the information for a specific product are called genes. The DNA of the gene would not be different for somatic versus germ line therapy, although there might be different sequences added adjacent to the gene depending on how the gene would be regulated in a particular experiment or treatment. The difference between somatic and germ line therapy is which type of cell is treated with DNA.

Somatic cell gene therapy is illustrated by following how physicians might attempt to correct the genetic defects that cause ADA or PNP enzyme deficiencies. ADA deficiency is caused by absence or inactivity of the enzyme adenosine deaminase. PNP deficiency is a different disorder with some clinical similarities, It is caused by absence or inactivity of the purine nucleoside phosphorylase enzyme. In ADA deficiency, the DNA in the adenosine deaminase gene is abnormal, and for PNP deficiency, there is a corresponding defective PNP gene. The genetic defect is due to an incorrect DNA sequence caused by a mutation. The mutation could be in the form of errant replacement of one nucleotide by another or loss (or addition) of one or more nucleotides somewhere in the sequence. The altered sequence encodes an abnormal enzyme that does not function, or causes insufficient production of the normal protein.

Because there is either not enough enzyme, or it is present in a dysfunctional form, the chemical reactions mediated by ADA or PNP do not take place normally in the cell. This leads to accumulation of some chemicals that would normally be destroyed by ADA or PNP, and a paucity of those chemicals the enzymes are responsible for making. In the case of both ADA and PNP deficiencies, it appears that toxic chemicals accumulate that inhibit the action of cells that are involved in body defenses.

The diseases are inherited as recessive genetic traits (the two diseases caused by the different enzyme deficiencies are slightly different, but not in a sense that is relevant here), and are usually fatal before age 2 if not treated (Kredich, 1983). Severe immune deficiencies can be treated by bone marrow transplant (Friedrich, 1984), but not all patients are eligible for transplant, and the procedure is quite risky and costly.

ADA or PNP deficiency might be treated instead by somatic cell gene therapy: removing an affected patient's bone marrow cells, inserting normal genes for the enzymes into them, and returning the treated cells to the patient where they could grow and perhaps produce enough of the needed enzyme to degrade the toxic chemicals, thus restoring immune function.

Although the details vary, most of the diseases that might be approached by gene therapy conform to this model: they are genetic defects that cause insufficient production of normal enzymes or production of dysfunctional ones. Gene therapy attempts to restore enzyme function by inserting DNA to produce normal protein.

Rather than treating only bone marrow or other somatic cells, germ cells or cells of an early embryo might be treated to correct a genetic defect. Such germ line treatment would affect all cells in the body, including both somatic cells and germ line cells. In the case of ADA or PNP deficiency, germ line therapy would likely be done by inserting the correct genes into an affected embryo within hours of fertilization. This might lead to presence of a normal ADA or PNP gene in all cells, and expression of the normal gene with production of a normal enzyme in the tissues where it would be needed to correct the immune deficiency. In somatic cell therapy, treatment affects only cells in the patients' organs and would not be passed on to children, while germ line correction would produce genetic changes that could be detected in all cells in the body and could be passed on to children. On the whole, as vast as the promises might be, we have one ethical caution against the practice of somatic cell manipulation and germ line gene therapy, let them remain at the level of clinical trial at least for a generation so we can assess their long term implications. Otherwise, we do not see any serious moral problem in using human genes as therapeutic measures to improve the health of humans.

7. Conclusion

There are different forms of genetic therapies and gene manipulations. It is the opinion of genetic engineers that this field of research holds great promise for mankind in the agribusiness, technology and on genetic modification or enhancement. However, this line of research also promises great dangers since it means crossing the species. A species is a community of organisms that is reproductively isolated from other such groups; that is, within a species there is interbreeding (exchange of genetic material) among individuals and their offspring, but none with individuals of other, different species. The problems with this widely used definition are several, and many of them are quite technical and esoteric. The most significant of these involve the existence and frequency of hybrids, or "crossbreeds" between species. If species are to be defined on the basis of reproductive isolation, a sort of "genetic quarantine)" then violations of this quarantine, hybrids, should be rare and unusual. This is emphatically not the case in nature. Hybrids are well known in higher organisms but in some cases signs which show that the practice is not healthy abound, (e.g., mules, resulting from a mating between a horse and a donkey which turns out to be sterile).

As most forms of genetic therapies are capable of crossing the species boundaries, if not now but in the foreseeable future, we took time to condemn where appropriate, extreme practices which are likely to trample on human dignity and on the very substance of life.

References

- Barlow-Stewart, Kristine. (2007) "Gene Therapy". *Genetics Fact Sheet, The Australasian Genetics Resource Book* : 27, 40, 47 www.genetics.edu.au (8th Ed)
- Baylis, F. and Scott, J. (2004) "The Inevitability of Genetic Enhancement Technologies." *Bioethics Volume 18 Number 1*. 1-26
- Bostrom Nick and Julian Savulescu. (2008) *Human Enhancement Ethics: The State of the Debate*. London: Oxford University Press.
- Candotti, F. (2001) "Gene therapy for immunodeficiency. *Current Allergy and Asthma Reports*". 1.5:407-415.
- Cavazzana-Calvo M et al. (2000) "Gene therapy of human severe combined immunodeficiency (SCID-X1) disease". *Science*. 288(5466): 669-672
- Calne, R. Y. (1964) "Renal transplantation in man: a review". *Brit. J. Surg.*, 51. 282-293.
- Carter, Lucy. (2002) "Office of Public Policy and Ethics Institute for Molecular Bioscience" The University of Queensland Australia <http://www.uq.edu.au/oppe>
- Cooper, David, (2007) Mohamed, Ezzelarab, and Hidetaka Hara. "Xenotransplantation". *ENCYCLOPEDIA OF LIFE SCIENCES*, John Wiley & Sons, Ltd. www.els.net¹
- Friedrich, W., Vetter, U., Heymer, B., et al., (1984) "Immunoreconstitution in Severe Combined Immunodeficiency After Transplantation of HLA Haploidentical, T-Cell-Depleted Bone Marrow, *Lancet* 1:761-764.
- Hume, D. M., Magee, J. H., Kauffman, H. M., Rittenbury, M. S., and Prout, G. R. Jr. (1963) "Renal homotransplantations in man in modified recipients". *Ann. Surg.*, 158. 608-644.
- Hume, D. M. (1967) "Renal homo-transplantation in man". *Ann. Rev. Med.*, 18. 229-268.
- Kass, L. (1985) *Toward a More Natural Science: Biology and Human Affairs*. New York. Free Press.
- Kredich, N. M., and Hershfield, M. S., (1983) "Immunodeficiency Diseases Caused by Adenosine Demaninase Deficiency and Purine Nucleoside Phosphorylase Deficiency," *The Metabolic Basis of Inherited Disease*, 5th ed., J. B. Stanbury, et al. (Ed.) New York: McGraw-Hill.
- Merrill, J. P. (1967) "Human tissue transplantation". *Adv. Immunol.*, 7. 275-327.
- Mowbray, J. F., Cohen, S. L., Doak, P. B., Kenyon, J. R., Owen, K., Percival, A., Porter, K. A., and Peart, W. S. (1965) "Human cadaveric renal transplantation; report of twenty cases". *Brit. med. J.*, 2. 1387-1394.
- Papadimitriou, M. d. Chisholm, A. Kulatilake, and R. Shackman. (1999) "Clinical Evaluation of the urinary Sediment after renal allotransplantation." *J. clin. Path.*, 23, (1970), 99-103
- Parens, E. ed. *Enhancing Human Traits: Ethical and Social Implications*. Washington: Georgetown University Press,
- Russell, P. S. "Kidney transplantation". (1968) *Amer. J. Med.*, 44, Stableford, B. *Future Man*. New York: Crown, 776-785.
- Spencer, E. S., and Petersen, V. P. (1967) "The urinary sediment after renal transplantation. Quantitative changes as an index of the activity of the renal allograft reaction". *Acta. med. scand.*, 182, 73-82.
- Taft, P. D., and Flax, M. H. (1966) "Urinary cytology in renal transplantation: association of renal tubular cells and graft rejection". *Transplantation*, 4. 194-204.
- Walters, L. & J.G. Palmer. (1997) *The Ethics of Human Gene Therapy*. New York: Oxford University Press.

Acknowledgment: We wish to appreciate the authors whose works we used extensively in this assessment especially Cooper D, Mohamed E, and Hidetaka Hara (2007) as well as Baylis, F. and Scott, J. (2004).