Transplantation: Therapy or Experimentation.
When Does a Medical Procedure become an Accepted Therapy and a Legal Right?

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I. INTRODUCTION

A. What can be Achieved in Transplantation?

The awarding of the Nobel Prize to Dr. Joseph Murray and Dr. Donnall Thomas shows that transplantation has finally come of age. Dr. Murray performed the first successful kidney transplant in 1954. Dr. Thomas, in an article published in 1957, described a transient marrow graft and proved that bone marrow could be safely injected intravenously.

Several hundred thousand transplants have been performed worldwide over the last four decades. Increasingly, the treatment of choice for irreversible end-stage organ failure is transplantation. Except with kidney failure (when dialysis may be offered), transplantation is often the only therapy for end-stage organ failure.

The discovery in the early 1980s of Cyclosporine, a new immunosuppressive drug, marked a transition in transplantation. Results leapt from approximately 50% one-year graft survival in kidneys to 80-85%; from 45% to 80% for heart transplants; and from 35% to 75-80% for liver transplants. Although less than ideal, the long-term survival of the transplanted organ has been stable. After the first year, the annual risk of recurrent organ failure is 2-3%. Although survival of high-risk patients is less satisfactory, these figures apply to most transplant patients. Cyclosporine has manageable side effects including some cosmetic changes (increased growth of hair) and an increased likelihood of hypertension and kidney dysfunction. But, Cyclosporine has now been used for over ten years and provides better results than other drugs in the past. New drugs in early clinical studies may provide improved long-term benefits.

Tissues that can be transplanted include cornea, bone, skin, heart valves, and bone marrow. These transplants are routinely done throughout the Western world. Dr. Thomas, who pioneered bone marrow transplantation, transformed that procedure into the treatment of choice for newly diagnosed leukemia. Transplantation of pancreatic islets, which secrete insulin, is predicted for treatment of insulin-dependent diabetes. Some centres, including our own, have begun this procedure experimentally. Ultimately, this minor surgical procedure, with Cyclosporine to maintain the graft, may become the treatment of choice for insulin-dependent diabetic patients.

Diseases of the brain have been treated with fetal brain tissue in patients. Experimentation with fetal brain cells for Parkinson's disease was approved recently in Halifax. Reports of others' limited success, and the preceding animal experiments, suggest that this may be a feasible therapy. There have also been reports of genetically transformed cells to treat inborn errors of development or metabolism and, potentially, certain forms of cancer. In these experiments, cells are taken from individuals, then genetically transformed to produce an enzyme that was deficient and made the patient's immune or metabolic systems inoperative. The first human experimentation using genetically transformed cells in the treatment of cancer has now been approved and the outcome will be watched with interest.

Organs that have been transplanted include kidneys, heart, lungs, liver, pancreas, small bowel, and testes. Kidneys are by far the most common organ transplant procedure and is the treatment of choice for patients with kidney failure. Currently, dialysis treats about 1500 potential recipients who are on Canadian waiting lists. Heart, lung and liver transplants are the only treatment for failure of these organs since the alternative is death. Approximately 10-20% of patients waiting for a heart or liver die prior to receiving an organ. Transplant grafts not only have a 75-80% survival rate but, with liver and heart transplants, 70-80% of patients return to work or school. Death while waiting occurs more frequently for lung and heart/lung patients since the availability of lung donors is scarce. Some centres transplant the pancreas although the usefulness of pancreatic transplantation, with respect to the quality of life, is debatable. Transplantation of pancreatic islets, if successful, may provide a better quality of life. Two years ago, our transplant service performed the first successful small bowel transplant. Small bowel transplantation offers the only alternative to intravenous feeding, which provides an extremely poor quality of life. In China, testicles have been transplanted in a few patients with successful return of sexual function and impregnation. The application of this procedure has limited scope.

The cost of transplantation remains considerable. A kidney transplant costs approximately $36,000 (the alternate therapy of dialysis costs $40,000 per year) with cost savings in the order of $800,000 over the subsequent years. The costs of heart, lung, or liver transplants range from $90,000 to $130,000 and cannot be proven necessarily as a cost saving since the patient's immediate death probably would be cheaper. Yet, these costs compare favorably with the cost of treating patients with widespread cancers, trauma victims or AIDS patients. The outcome is clearly better than these comparative diseases and their therapies.

B. Sources of Donor Tissues and Organs

The most common source of a donor tissue or organ is the cadaver. Corneas can be retrieved within 24 hours of cardiovascular death. As well, the large potential supply of bone and skin tissues does not have the same time constraints as other organs. There are an estimated 2,000-3,000 potential donors in Canadian hospitals each year. However, only about 600 of these potential donors become actual donors. The number of actual organs fails to meet the requirement for all organs, particularly kidneys. If there were a greater supply of donors, the number of potential recipients on waiting lists for liver, heart, and lung transplants also would increase. It is a recognized fact that the scarcity of organs inhibits the identification and referral of patients for transplantation.

All cadaveric donors must be declared brain-dead. The definition of "brain death" follows criteria established by the Canadian Congress of Neurological Sciences. Brain death must be determined clinically by an experienced physician who is not related to the transplantation process. This separation between those declaring brain death and those involved in the transplant procedures is problematic. The transplantation process starts with approaching the relatives about organ donation. The patient is referred for transplantation in consultation with the physicians or surgeons associated with the retrieval. These steps frequently involve the neurologists who cared for the brain-injured patient. This necessary overlap occurs frequently and yet appears, on the surface, to contravene the *Human Tissue Gift Act.*[1]

We have had patients declared brain-dead in a community hospital and referred to our hospital as donors. By our hospital policy, these patients must be referred to the neurological service and brain death must be confirmed. There are instances of patients, referred as brain-dead, who had reversible conditions that were detected and, in one incidence, full recovery occurred. In other instances, the full criteria for brain death were not present and patients had to be observed for longer time periods until full criteria were met. It is often difficult for community hospitals to find physicians to declare brain death and yet absent themselves from any interaction with the transplant team. Further changes need to be implemented to meet the practical need while not offending the spirit of the *Human Tissue Gift Act.*

The use of anencephalic babies (children born without the development of their forebrain but with an intact brain stem) as organ donors remains a highly controversial area. Some proponents suggest that these babies should be declared "not live" at birth because they have no potential for the development of cerebral activity. Therefore, organs could be retrieved immediately at birth. Others have resisted this suggestion to change the criteria for brain death for this special category. Instead, we are exploring the possibility of resuscitation after cardiovascular death and observing the patient until full brain death criteria are met. Then we may proceed as with any cadaveric donor. To change the brain death criteria for anencephalic infants could seriously affect cadaveric organ donation. The public may perceive this change as expediency by the transplant community and an offense to traditional medical practice. It can be argued that many babies would benefit from this source of organ donors and that the parents of anencephalic babies may benefit from a useful outcome from this terrible malformation. However, any change should occur only after a carefully done pilot study shows that it is feasible, not harmful to the parents, and acceptable to society. The possibility of meeting the criteria for brain death after resuscitation must be fully explored before the alternative of a special category of death is even considered.

The use of fetuses as tissue donors is an area fraught with many problems. I have termed the aborted fetus a "biological goldmine underlying an ethical minefield". The potential use of early, differentiated fetal tissues is theoretically enormous. Issues, such as the necessary technology, the impact on the technical aspects of the abortion process, and the question of consent, demand that principles of ethical practice be enunciated. For this, we look to the Royal Commission on New Reproductive Technologies of Canada for guidance. But, if a fetus, obtained in an ethical and legal manner, is provided to a transplant service as a cadaveric donor, there is little difference in using these tissues or using the organs retrieved from an individual who died of homicide. The question could be asked about the ethics of wasting those potentially beneficial resources.

Kidney and bone marrow transplants use living-related donors. Recent attempts have used partial liver and lung donations from living donors. Tissues or organs transplanted between genetically similar or identical individuals have a higher success rate than cadaveric organs. The kidney donor experiences some risk, although small. Some deaths have been

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[1] R.S.O. 1990, c. H.20.

reported (approximately 1 in 1300-1600 nephrectomies). Family members are tested for HLA identity, and interest is focused on the member who is identical or most similar. The potential for emotional coercion is greater than when consent is sought from the relatives of cadaveric donors. Although most living-related donors express positive feelings about their donation, a few feel coerced and resent their "donation". If family members are reluctant or coerced, we may need to provide the potential donor with a medical reason for his or her refusal in order to maintain family relationships. Recent attempts to transplant partial liver and lung donations from parents to their children raised this issue of coercion and the ethics of a risky procedure for the parent.

In Canada, unrelated living donors, such as spouses and intimate friends, are known as "emotionally related" donors. We have recommended limiting living organ donation of non-renewable organs, such as kidneys, to individuals with close emotional relationships. In the past, spouses and friends were denied the opportunity to donate. The ethics of this approach are questionable since there is less likelihood of coercion in this situation than with related donations. Members of the general public have volunteered to donate kidneys. This "good Samaritan complex" exists in a significant proportion of the North American population and the propriety of retrieving kidneys from these individuals has not been explored to any great extent. Retrieval of kidneys from executed criminals no longer occurs, except in China. Two hospitals there retrieve kidneys for transplantation, without first consulting the relatives or donor.

In Canada, paid donors are illegal. In some countries, they are almost the only source of donors. In India, a very large trade for paid organ donors, frequently obtained through brokers, occurs. The International Transplantation Society is studying how this practice can be altered or become ethically acceptable. In North America, because of the shortage of organ donors, the idea of "rewarded giving" has been discussed. Possibly, donors would be reimbursed for the risk and their pain and suffering, or their estate would be financially rewarded. Since financial incentives may motivate people to place themselves at risk, this scenario appears to devalue human life. However, in the absence of cadaveric organ donation, people suffer and die from the lack of transplantable organs. Therefore, obtaining an organ is a benefit to that individual and society. If the "reward" were based on a recompense for risk, pain and suffering, it might not be interpreted as true payment for the organ but rather a reimbursement for a service rendered. Although one can base these arguments on a utilitarian logic, the fact is that 70-80% of cadaveric donors are wasted in North America. Our efforts should be directed towards resolving this waste. I would add, however, that desperate people do desperate things. If North American culture cannot resolve the inadequacy of cadaveric organ donation, "rewarded giving" or "buying" of organs will be rationalized and accepted to satisfy both recipient and donor populations.

Transplantation has used animal tissues for some time. The future possibility of using animal tissue for transplantation is enormous. Significant breakthroughs at a basic science level have occurred in the past two years and will likely result in successful animal-to-human transplants in this decade. Obviously, this will never be as ideal as human-to-human transplantation. Still, an identifiable source of animal organs to allow elective transplantation is attractive. The likely source of a donor tissue would be pigs because of their similarity to humans in weight and size. Primates have been used in heart transplantation on at least four occasions. Primates are not a feasible source from the standpoint of ethics, economics and their limited availability.

C. Consent Issues

Obtaining consent for organ donation has been an area for professional and public debate for some time. The *Human Tissue Gift Act* clearly allows the individual the right to give pre-mortem consent for post-mortem organ donation and the right of next-of-kin to consent. The *Act* protects medical practitioners since their actions are judged on what they believed was the last known wish of the donor.

The traditional pre-mortem consent is an organ donor card, frequently on the reverse side of a driver's licence. An individual indicates his or her wish to donate organs after death and can stipulate which organs are to be used. Although a signed donor card, under the *Human Tissue Gift Act*, provides full authority for organ removal, the family's consent is usually sought. There is no obligation for the physician to carry out the decedent's wish and the practice is to defer to the next-of-kin's decision. When a potential donor is identified, the next-of-kin is approached for consent, after they have been informed of brain death. Infrequently, the organ donor card is available and stimulates a request from a health care worker. However, frequently the family knows if a donor card had been signed and they are aware of the individual's wish.

Less than 30% of individuals sign donor cards in spite of the availability of public awareness programs. Surveys show that 80% of individuals would donate their relative's kidneys post-mortem if asked, 63% would donate their kidneys, but less than 30% sign the donor card. The role of the physician or health-care worker is paramount in this area. Sometimes fundamental disagreement about donation may occur between relatives. Then the usual course is to decline the donation. Simultaneously, the wish of the decedent may be determined by referring to the driver's licence, and may provide the incentive to proceed with donation.

In the United States, the law requires that health-care staff request organ and tissue donations from families of potential donors. In Canada, the role of the health-care provider in identifying and obtaining donors has not been well defined in practice. Participation by physicians, such as identifying potential donors and approaching the family for consent or obtaining the driver's licence, has not generally been specified in hospitals' medical bylaws. Instead, it was considered a charitable act for the physician or health-care worker to participate in this process. The societal view is rapidly changing.

In Manitoba, under "required consideration", the family is asked for organ donation if the patient is a suitable donor. But the procedures and outcome do not have to be recorded. The Canadian Medical Association has endorsed the idea of "recorded consideration". Under this policy, the medical records of the decedent must include a note indicating if he or she were considered a potential donor and if the family were approached for consent. If not, reasons are specified. The Ontario government, through amendment of regulations under its *Public Hospitals Act*[2] (June 1, 1990) has modified this approach. Hospitals must have a

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[2] *Public Hospitals Act*, R.S.O. 1990, c. P.40.

policy stating that families are to be informed of their right to donate. Implicitly, families have the opportunity to donate. However, most potential donors in this country do not become donors and their families are not approached. Failure to recognize a suitable donor, and the subsequent tragic loss of the organs for transplantation, is a "non event" in Canadian hospitals. I suspect that this situation will change as the direct relationship between lost donors and dead potential recipients becomes more apparent.

In about 15 countries, "presumed consent" exists. Without a written indication of unwillingness to donate, physicians may presume that the patient has consented. They can act on that presumption, with or without the consent of the relatives. A recent study in Belgium suggests that presumed consent substantially improved their organ donation and transplantation rates. With presumed consent, Belgium has a higher transplantation rate per million population than Canada. During a five-year period, this rate increased twice as much as the Canadian transplantation rate.

D. Distribution of Organs — Best Utilization versus Equal Access

In August 1989, Dr. C. Kjellstrand presented a paper at the Ottawa Congress on Ethics, Justice and Commerce in Transplantation. From American, Swedish and Canadian data, he consistently showed that female, nonwhite, poor or older patients had significantly less chance of receiving a kidney transplant. These differences could not be explained medically. Donated organs are increasingly recognized as a community resource. As well, the role that non-medical factors have played in selection of recipients has led to the determination of distribution formulae. Rather than the physician or surgeon deciding organ allocation, a computer-derived algorithm assigns the organ to a recipient based on factors such as blood group, tissue match, urgency, and time on the waiting list.

Of greater concern is patients' access to the waiting list. Transplantation of organs in the early years was limited to a few patients, usually young, self-sufficient, otherwise well, and with certainty of early death. Several of these categories have continued in spite of advances in transplantation. Until recently, age and some disabilities have precluded individuals from gaining access to transplant lists. At our centre, results for transplantation in older individuals (50-65 years) are similar to results in younger recipients. Age criteria are now being extended although there remains a bias toward younger patients. The likelihood of individuals dying from heart disease in their seventies is inversely proportional to the likelihood of those individuals getting on a transplant list. The propriety, and possibly the legality, of this practice is questionable.

The issue of self-induced or self-contributed disease has been a relative, if not absolute, barrier in many programs. The most obvious example is liver failure due to alcoholic cirrhosis. Death from liver failure of almost 50% of individuals is a result of alcohol abuse. These patients have largely been excluded from liver transplant programs. Results from our centre and others show that liver transplantation is as successful in patients with alcoholic cirrhosis as it is in patients with other causes. Therefore, the survival rates do not support this bias against transplanting alcoholics. Less than 20% of these patients revert to alcohol abuse post-transplant. Some programs have introduced tests of "rehabilitation", such as a minimum period of abstinence (usually six months), before transplantation.

Whether discrimination against individuals because of their age, disabilities, or self-induced disease is acceptable under the *Canadian Charter of Rights and Freedoms*[3] has not been tested. [The Supreme Court of Canada has held that hospitals as such are not bound by the *Charter*, but a governmentally endorsed program is, and hospitals are bound by provincial human rights codes that prohibit discrimination on grounds such as age, sex and disability.] The medical argument has been that the health care system is responsible for the best utilization of the organ, which is a scarce resource. From a medical standpoint, the best choice would be a young, otherwise healthy individual with evidence of social responsibility and compliance. Each of those factors could be translated into reduced life expectancy or level of rehabilitation. We continue to wrestle with our imprecise measures of "best utilization". Can these measures for groups of patients be used to decide a particular patient's acceptability for transplantation or allocation of an organ?

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[3] Part I of the *Constitution Act, 1982*, being Schedule B to the *Canada Act 1982* (U.K.), 1982, c. 11.

II. ETHICS AND JUSTICE IN TRANSPLANTATION

The following three examples are given to show the wide range of areas of concern in the ethics and justice of transplantation.

A. When is a Medical Procedure Accepted, Expected Therapy?

In *Re Minister of Social Services and P.*[4] the respondents were the parents of an infant suffering from an incurable liver disease. The prognosis was that the child would likely die within the next twelve months. The only possibility for survival was a transplant operation, which would offer a 70% to 75% chance of survival in the first year, assuming donor availability, and between a 60% to 65% chance of five-year survival. The child would experience a reduced quality of life after the transplant operation because of the continuing immunosuppressive drug therapy that would be required. After careful consideration, the parents refused to consent to the transplant operation. The Minister of Social Services, who disagreed with the parents' decision and who believed that surgery was appropriate, applied for a temporary committal of the child for a period of one year, pursuant to section 29(b) of the *Family Services Act*,[5] in order to authorize the surgery. The Minister argued that the parents were in breach of section 15 of that *Act* by refusing to provide proper medical or surgical treatment and that the child was in need of protection. At trial three doctors supported the parents' decision and one doctor the Minister's position.

The court held that the application should be dismissed. The Minister had not shown that his decision should be preferred to that of the parents. The judge concluded that the parents had made a thoughtful and carefully considered decision, which was totally within the bounds of current medical practice. A transplant operation of this nature is a difficult, complex, non-commonplace major surgical procedure. The decision whether to partake in this procedure is not truly a medical question. There is also an emotional, social and psychological component both for the child and the parents. The Minister had focused only on the medical component, while the parents had given a much more profound consideration to other components.

This case is an example of the attitude towards transplantation by the courts that in turn reflects the skeptical attitude of the public in general towards transplantation as a successful therapy. The results of transplantation far exceed the results from treatment of many other diseases. If this child had leukemia or bone cancer and the parents, for the same reasons, refused the only therapy with a chance at a cure, would the same judicial decision have been rendered? The responsibility of the courts to obtain data on survival, quality of life, and costs from reliable sources is essential. Opinions in a rapidly changing field are only as good as the current knowledge of the experts. Published, peer reviewed data should be used as a guide. Experts' opinions may reflect their philosophical attitudes towards death and life

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[4] *Saskatchewan (Minister of Social Services)* c. *P. (F.)*, (1990) 69 D.L.R. (4th) 134 (Sask. Prov. Ct.).

[5] R.S.S. 1978, c. F-7.

and may not be an objective interpretation of the facts. Later in this report the judge referred to a statement by Hippocrates: "Life is short, the art is long, timing is exact, experience treacherous, judgement difficult". This is just as true today as it was in 400 B.C. However, since Hippocrates made his statement in 400 B.C., significant changes have occurred. Life is not as short. Medicine has advanced to where science forms a greater part of medical decisions than in his time, when art was used to obscure ignorance. The understanding of biological timing and intervention was faulty and superficial. Experience is still treacherous. Judgement remains difficult and rarely unanimous. Justice probably prevailed in this case, not because transplantation did not offer a reasonable future, but rather any therapy that involved continued medical monitoring was incompatible with this family's life and their philosophy.

B. When Does a Medical Procedure Become a Legal Right?

Suppose a patient with heart failure is in a hospital Intensive Care Unit (ICU). The patient is in blood group A, and listed as highest priority on the transplant waiting list. In the same ICU, a brain-injured patient (also blood group A) is being treated. This patient has signed the donor portion of his driver's licence. The brain-injured patient is declared brain-dead by two independent physicians, as specified in the *Human Tissue Gift Act.* The hospital has a policy that they will comply with Regulation 518/88[6] of the *Public Hospitals Act* which states:

> *4(1) Every board shall pass by-laws that,*
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> [...]
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> *g) provide for the establishment of procedures to encourage the donation of organs and tissues including,*
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> *(i) procedures to identify potential donors,*
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> *(ii) procedures to make potential donors and their families aware of the options of organ and tissue donations.*

Guidelines for complying with this policy were available at the hospital.

Instead, the brain-dead patient's body was sent to the morgue, his family was not given the opportunity to consent for organ donation. The potential recipient died in the next 48 hours because no donor became available. The families were together for periods of time in the waiting room of the ICU and became aware of each other's tragedy.

On reflection, both families felt aggrieved. The potential recipient's family believed their loved one had been denied a transplant. A potential donor, which they believed would

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[6] R.R.O. 1990, Reg. 965.

have been suitable, was not considered according to the intent of the hospital's guidelines. Evidence indicates that 80% of families will give permission if asked.

The potential donor's family believed that their wishes had been denied by hospital staff. They were not informed of their options in time to make the decision to donate. Because the decedent had signed a donor card, he had been denied his wish. The family had been denied the known comfort that donor families experience in the grieving process.

Both families joined in a lawsuit against the hospital. The medical facts confirmed that the brain-dead patient would have been a suitable donor for the heart patient and a successful transplant probably would have occurred. Lungs, liver, kidneys, pancreas, corneas, bone and skin likely would have been suitable for transplantation.

The issues in this hypothetical case are whether donor families have a legal right to be given the opportunity to donate and whether the decedent has a right to have a stated wish carried out. In this instance, the medical facts would have shown that this donor heart was suitable. The recipient would have been (under the algorithm for equitable organ distribution) the designated recipient of the heart. Barring a technical problem, the transplant would have been successful.

C. The Right of Access, Without Discrimination, to a Scarce Resource (the Donated Organ)

The rights of a potential recipient to an organ transplant are not defined. This issue includes the appropriateness of refusing patients because of age, disabilities, or self-induced (or contributed) disease. A current example is the refusal of patients for a liver transplant because of alcohol abuse. The medical rationale is that patients who have liver failure from other causes are more "worthy" or suitable (compliance issue) than alcoholics. However, these alcoholic patients have similar survival rates as non-alcoholic transplant recipients. The incidence of alcohol recidivism is less than 20%. Yet, the question remains unanswered: Does each individual have an equal right to be considered for a transplant irrespective of age, disease, or social considerations when we are dealing with such a scarce, rationed resource as the donated organ?