7.3.4 Maternal-Fetal Research

Maternal-fetal research, i.e., research intended to benefit pregnant women and/or their fetuses, must balance the health and safety of the woman who participates and the well-being of the fetus with the desire to develop new and innovative therapies. One challenge in such research is that pregnant women may face external pressure or expectations to enroll from partners, family members, or others that may compromise their ability to make a fully voluntary decision about whether to participate.

Physicians engaged in maternal-fetal research should demonstrate the same care and concern for the pregnant woman and fetus that they would in providing clinical care.

In addition to adhering to general guidelines for the ethical conduct of research and applicable law, physicians who are involved in maternal-fetal research should:

(a) Base studies on scientifically sound clinical research with animals and nongravid human participants that has been carried out prior to conducting maternal-fetal research whenever possible.

(b) Enroll a pregnant woman in maternal-fetal research only when there is no simpler, safer intervention available to promote the well-being of the woman or fetus.

(c) Obtain the informed, voluntary consent of the pregnant woman.

(d) Minimize risks to the fetus to the greatest extent possible, especially when the intervention under study is intended primarily to benefit the pregnant woman.

AMA Principles of Medical Ethics: I,III,V

Opinion 7.3.4 Maternal-Fetal Research extracts content from previous guidance and associated background report(s):

CEJA Report 3-A-16 Modernized *Code of Medical Ethics*

CEJA-CSA Report A-89 Medical applications of fetal tissue transplantation

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AMA Principles of Medical Ethics: I,III,V

Joint Report of the Council on Ethical and Judicial Affairs
and the Council on Scientific Affairs, A-89
Medical Applications of Fetal Tissue Transplantation

INTRODUCTION

The prospect of therapeutically effective fetal tissue transplants for disorders such as diabetes and Parkinson's disease has raised new questions in the ethical discussion on fetal research. These questions are distinct from those addressed in the 1970s that focused on invasive procedures performed by some researchers on living, viable fetuses. They are also separate from the questions that were raised by the development of new techniques for prenatal diagnosis such as fetoscopy and chorionic villus sampling. Although the use of transplanted tissue from a fetus after spontaneous or induced abortion would appear to be analogous to the use of cadaver tissue and organs, the moral issue for many is the possibility that the decision to have an abortion will become coupled with the decision to donate fetal tissue for the transplantation procedure itself.

The utilization of human fetal tissue for transplantation is, for the most part, based upon a large body of research data derived from experimental animal models. At this time, the number of such transplants performed has been relatively small but the various applications are promising avenues of clinical investigation for certain disorders. The purpose of this report is to (1) review the data on fetal tissue transplantation in animals and in specific clinical disorders and (2) to review the legal and ethical issues involved in fetal tissue transplantation.

FETAL TISSUE TRANSPLANTATION

Human fetal tissue research has led to the development of a number of important research and medical advances. Embryonic human tissues have been the source of scientifically valuable cell lines in culture that have been important research models for studying cell-to-cell interactions and gene expression. Historically, the research and development of polio vaccine was accomplished with the use of human fetal kidney cells. Currently, human fetal cells are being used to study the mechanism of viral infections and to diagnose viral infections and inherited diseases.

Fetal cells have four basic properties that make them clinically useful for grafting or transplantation applications: their intrinsic plasticity, their ability to grow and proliferate, their ability to produce growth factors, and their reduced antigenicity compared to adult tissue (although this property does not always apply).

The plasticity of transplanted fetal tissue has been demonstrated in numerous animal studies. Embryonic wing tissue from a chicken retains the functional capacity to differentiate into a leg when transplanted into the appropriate limb bud region of the developing chick. In experiments in which the recipient is a fully differentiated adult, intracerebral implants of fetal neurons can establish extensive synaptic connection and become partially integrated into the circuitry of adjacent neural tissue. The ability of fetal cells to grow and proliferate in vivo following transplantation increases the success rate of functional engraftment. An important example of this property is the recent experiment in which human lymphatic tissue was transplanted into immunodeficient mice.[1] This was accomplished using a strain of mice with

severe combined immunodeficiency (SCID) as the recipient and human fetal liver (containing both T- and B-cell lymphoid progenitor cells), fetal thymus, and fetal lymph node cells as the donor tissue. Following transplantation, the human fetal tissues established themselves in the SCID mouse and developed further to produce a functioning human immune system. The SCID-hu mouse with its human immune system may become a valuable model in studying acquired immunodeficiency syndrome (AIDS).

Fetal cells have the additional ability to produce trophic substances that not only can increase their own ability to survive and grow but also can promote regeneration of nearby damaged tissue. Angiogenic factors from fetal tissue can promote blood vessel formation, and nerve growth factors released by fetal neuroblasts can assist in neural tissue regeneration.[2]

A theoretically important factor in successful fetal tissue engraftment is the ability of the transplanted cells to escape the immune surveillance of the host, but this is not true for all fetal tissues. In general, fetal neural cells have been shown to be less antigenic than adult differentiated tissue. Fetal neural tissue transplants, for example, have not elicited a significant immune response in recipient rodent and nonhuman primate models. However, animal studies comparing the immunogenicity of fetal pancreata with adult pancreatic islet cells show that fetal tissue can be as immunogenic, if not more, than adult tissue. Fetal liver cells also have been demonstrated to be antigenic. Successful transplantation of canine fetal liver from histocompatible antigen-mismatched donors required pre- and post-transplantation immunosuppressive therapy in recipient dogs.

Human fetal tissue transplants have been attempted in a number of human disorders including Parkinson's disease, diabetes, severe combined immunodeficiency disease, DiGeorge syndrome, aplastic anemia, leukemia, thalassemia, Fabry's disease, and Gaucher's disease. With the immunodeficient disorders, restoration of immune function and long-term patient survival have been achieved. The following sections review the major research areas for the clinical application of human fetal transplants.

Immunodeficieny Disorders

Human fetal liver has been used in attempts to reconstitute immune function in severe combined immunodeficiency disease (SCID), while fetal thymus transplants have been somewhat effective in DiGeorge syndrome. Fetal liver is an important site of hematopoiesis during fetal development and contains abundant hematopoietic progenitor cells. Immunologically, fetal liver differs from adult bone marrow in that the former contains relatively few immunocompetent T -lymphocytes. Since graft-versus-host disease (GvHD) is a major barrier to the transplantation of allogeneic hematopoietic cells,[3] and since immnocompetent T cells present in transplanted bone marrow are associated with GvHD, fetal liver has been considered a possible alternative source of hematopoietic tissue.[4-6] Animal experiments have shown that transplanted fetal liver cells are capable of restoring hematopoiesis and immunity in lethally irradiated rodents. Even when the fetal tissue donor and recipient are mismatched for histocompatibility antigens, the resulting GvHD was mild and delayed compared to that which occurred following bone marrow transplants. Experiments in dogs have demonstrated that nonhistocompatible antigen-mismatched fetal liver grafts can restore T- and B-cell function in irradiated dogs that also were receiving cyclosporine for immunosuppression.[8]

Clinically, fetal liver transplants have been attempted in patients with severe combined immunodeficiency disease (SCID).[7] This relatively heterogenous condition often leads to death from opportunistic infections

before the age of one. Bone marrow transplantation (BMT) has resulted in long-term survival in patients with SCID; the success rate is as high as 80% when the donor is HLA genotypically identical to the recipient. In the absence of an HLA-compatible donor, patients can be treated successfully with a haplo-identical BMT. Haplo-identical BMT requires the in vitro removal of T -lymphocytes capable of inducing or enhancing a GvHD.

Fetal liver transplantation represents a third approach to immune reconstitution in SCID, but it currently is of less clinical significance than haplo-identical BMT. Sustained engraftment of lymphoid progenitor cells from fetal liver has been achieved in a number of patients. Complete immunologic reconstitution, including normal T -cell functions, has been demonstrated despite HLA mismatch between donor and recipient cells.[7] Fetal liver grafts may be optimal when used in conjunction with fetal thymus tissue from the same donor, but this has not been established conclusively.[7] Clinical experience indicates that the optimal age of fetal liver is 8 to 13 weeks; the risk of GvHD is higher in livers older than 20 weeks. The relative efficacy of fetal liver compared to HLA haplo-identical T-cell depleted BMT has not been studied.

Fetal thymus transplants have been successfully used in the treatment of DiGeorge syndrome, a rare congenital cellular immunodeficiency associated with the absence of the thymus and parathyroid glands. Clinical manifestations of the disease are immune deficiency with increased susceptibility to infections as well as hypoparathyroidism, hypocalcemia, and congenital heart defects.[10,11]

Hematologic Disorders

More than 100 patients with aplastic anemia have undergone treatment with fetal liver transplants. However, because these patients still have functioning immune systems that react against HLA mismatched fetal liver tissues, the transplant cannot be successful in most instances; engraftment has been low (3%) as documented by cytogenetic analysis. Without pretrasplant immunosuppression studies, fetal liver transplants for aplastic anemia cannot be evaluated.[11]

Fetal liver transplants have been attempted in 39 patients with acute myelogenous leukemia (AML). In treating AML, it is postulated that human fetal liver transplants could result in a successful engraftment with reconstitution of hematopoietic function and/ or a fetal cell factor-expedited recovery of the patient's own hematologic system. However, transplantation failure is common in most patients treated. Antigenic barriers appear to be too great for successful engraftment without prior immunosuppression with drugs and radiation.[11] At this time, human fetal liver transplantation for AML has not been conducted under the appropriate immunosuppressive conditions that would permit evaluation of engraftment success. Part of the problem in determining the efficacy of fetal liver cells in accelerating hematopoietic tissue recovery is the dependency of this procedure on the initial effectiveness of chemotherapy against AML. Because of the variable response to chemotherapy, further evaluation of any additional improvement resulting from the fetal liver infusion will require controlled clinical trials.

Diabetes

The potential to cure experimentally induced diabetes mellitus in animals through the syngenic transplantation of fetal pancreata has been documented.[12] That human fetal pancreas transplants could

cure patients has been proposed as a result of these preclinical studies. However, .the application of fetal cell transplants to diabetes is complicated by the lack of an adequate quantity of viable fetal tissue, storage of such tissue, and engraftment success in immunosuppressed recipients.

Transplantation of cultured fetal pancreas cells has been tried in more than 100 insulin-dependent patients.[13] So far there have been no successful grafts as judged by complete long-term withdrawal from insulin therapy, but there has been one report of survival of transplanted fetal pancreas tissue for 13 weeks.[13] Reduced insulin requirements and increased C peptide production also have been reported, but the effects have been transient.[14] Although the current attempts have been relatively unsuccessful, human fetal pancreas does exhibit the necessary plasticity and proliferative properties outlined earlier. Human fetal cells transplanted into nude mice undergo selective differentiation into mature pancreatic tissue containing vascularized endocrine tissue, ducts, and fibrous tissue. Islet cells in these transplants also grow, leading to maturation of the insulin response to glucose and to reversal of the hyperglycemia in the streptozocin-induced diabetic nude mouse.[13]

With these encouraging results in animal studies, together with advances in the cryopreservation of the fetal pancreas tissue,[15] research on fetal cell transplantation for diabetes shows promise. An important challenge for this area of research is to understand the inability of the transplant to correct diabetes completely in patients. Engraftment problems may be due to residual immature lymphocytes that are strongly immunogenic. Purification of fetal pancreatic cells to separate out these lymphocytes is one potential approach.[16]

Other Metabolic and Genetic Disorders

Fetal liver transplants have been tried in a small number of patients with thalassemia, Fabry's disease, and Gaucher's disease. Treatment by this approach is preliminary but some beneficial clinical results have been reported.[17] Fetal tissue transplantation experiments for these and other inherited disorders have been suggested as precursors for eventual gene therapy.

Parkinson's Disease

Fetal nerve-cell grafts have been carried out successfully in animal models of neurodegenerative disease. The technique of neural grafting was initially used in neurobiology to study nerve cell development and regeneration, primarily in invertebrate models. The consistent transplant-induced improvements in motor, sensory, cognitive and endocrine functions in animal models prompted the rationale that similar transplants of human fetal neurons could improve the clinical symptoms of neurologic disorders such as Parkinson's disease.[18] New approaches to the treatment of this disorder is critical, since the response to currently available drug therapy is reduced as the disease state progresses.

The mechanism by which intracerebral implants exert their effect has been well studied in animal models. Fetal neurons, especially monoamine neurons, express a high degree of neural plasticity and regenerative capacity. These neurons establish extensive efferent synaptic connections with previously denervated or neuron-depleted host brain regions.[2] Thus the grafts partially restore neural circuitry through the development of dendritic processes from the transplant to the host neurons. In the nigrostriatal

dopaminergic systems, grafts of fetal nigral or striatal neurons have restored normal synaptic transmission and have led to partial reconstruction of functional neural transmitter specific patterns of innervation.[2,18]

Several rodent models have been used to study the effectiveness of fetal nerve-cell transplants in restoring or improving neurologic function. One model utilizing rats that are genetically deficient in vasopressin synthesis showed that fetal cells transplanted into the third ventricle of the brain survived and produced a sufficient amount of vasopressin to reverse the state of chronic water imbalance characteristic for this strain. The neural connections established between transplant and recipient neurons demonstrated that the graft cells were specific for the appropriate target cells in the recipient.[18] In a rodent model of Parkinson's disease, the neurotoxin 6-hydroxydopamine is used to damage nigrostriatal dopaminergic pathways selectively. Only fetal dopamine neuronal grafts were able to attenuate the characteristic apomorphine-induced turning behavior observed in these animals. Both light microscopy and electron microscopy have demonstrated that these grafts develop the appropriate "cytoarchitectural" connections with the surrounding neurons.[18]

Although rodent models have provided important information on the potential application of fetal neural tissue to Parkinson's disease, they do not completely model the complex symptomatology observed in the human disease. The MPTP nonhuman primate model is a closer approximation of the human disease. MPTP (l-methyl-4-phenyl-l,2,3,6-tetrahydropyridine) becomes a selective neurotoxin following activation by monoamine oxidase B (MAO-B). MAO-B oxidizes MPTP to a chemical form, MPP+, which becomes ion selectively concentrated in dopamine-producing neurons. Accumulation of MPP+ causes cell death and subsequent behavioral and anatomical alterations in treated monkeys that are almost identical to the pathology and symptomatology seen in the human condition. MPTP-treated African green monkeys show a specific loss of nigrostriatal dopamine neurons and a relatively rapid symptomatic progression from a generalized slowing of movement with slight tremors to akinesia, rigidity, difficulty in initiating movements, and resting tremor. Therefore these monkeys are an excellent model for assessing the effect of fetal neural grafting.

In a study using this MPTP-model,19 three monkeys with neurotoxin-induced parkinsonism received fetal nerve-cell transplants. Two received multiple grafts bilaterally into numerous locations in the striatum. A third received fetal substantia nigral grafts into the cerebral cortex as control and grafts of non-substantia nigral tissue into the striatum. The two monkeys who received grafts of fetal substantia nigra into striatum showed significant improvement in symptoms over a ten-week period following surgery. Immunohistochemical analysis revealed the presence of well-delineated grafts of dopaminergic neurons and fiber systems. Good correlation between cell engraftment and behavioral improvement was observed in both monkeys. The study also indicated that immunologic rejection of the fetal neural graft is not a problem, unlike the previous examples of the use of fetal liver and pancreas.

Based on these promising animal data, fetal implants for Parkinson's, fetal disease have been performed in the People's Republic of China, Mexico, Sweden, Canada, Great Britain, Cuba, and this country.[20] Little information is available on the outcome of the Chinese and Cuban transplants. In the Mexican trial, two patients received human fetal-nerve cell transplants: One patient received fetal adrenal implants while the second received fetal nigral grafts. Initially, both appeared to improve progressively following surgery, but the results achieved have been controversial. The patient receiving fetal nigral transplant appeared to have the greatest improvement in motor skills.

In the two fetal nigral transplants performed in Sweden, suspensions of nigral cells from an embryo less than eight weeks old were injected stereo-taxically into one site in the caudate and two sites in the

putamen. The degree of long-term improvement in motor function with these attempts, as well as with those in the American, Canadian, and English transplants, has not yet been ascertained.

Future Directions

Alternatives to the use of human fetal tissue are available for immunodeficient disorders {e.g., BMT) and diabetes {e.g., adult islet cell transplants). In neural transplants, the use of peripheral neural and paraneural tissues and cell culture .may offer alternatives to fetal tissue. Paraneural cells {e.g., adrenal medulla cells) may be modified into neural-like cells under the influence of nerve growth factor. Adrenal medullary cells from rats, monkeys, and humans develop processes and become neuron-like when treated with growth hormone.[18] Xenografting represents another possible approach. Advances in immunosuppressive therapy may limit rejection of nonhuman fetal substantia nigral implants in Parkinson's patients. An additional research area is modification of human neuroblastoma to become quiescent mitotically and to express a specific neural transmitter to replace, for example, the dopamine that is lost in Parkinson's disease. Finally, it may be possible in the future to genetically engineer cell lines by the inserting of oncogenes to produce cells capable of both proliferating and producing a specific neurotransmitter.

Many of these manipulative procedures, particularly the development of genetically engineered cells, will not be accomplished in the near future. In the meantime, human fetal tissue transplantation research continues to hold potential clinical benefit to Parkinson's patients and those suffering from other disorders. For example, the continued efforts to purify specific fetal cell populations may improve the application of fetal cell transplantation for immunodeficient disorders and diabetes. The results of future transplant studies will be needed to further assess this procedure.

Legal and Ethical Implications of Fetal Tissue Use

The transplantation of human fetal neural tissue or fetal pancreases and, to a lesser extent, fetal lymphoid cells, is subject to federal regulations protecting human subjects {i.e., recipients of the procedure). Approval of the transplant protocol therefore requires review and approval by an institutional review board {IRB) to ensure that the risks to the patient are minimized. The acquisition of tissue from an aborted nonliving fetus is not governed by federal regulations. Instead, federal regulations leave the disposition of fetal remains to state and local regulation:

Activities involving the dead fetus, macerated fetal material, or cell, tissue or organs excised from a dead fetus shall be conducted only in accordance with any applicable state or local laws regarding such activity. {Title 46 Part 45 of CFR 46.210).

The acquisition and use of tissue obtained from dead fetuses is governed by the Uniform Anatomical Gift Act (UAGA), which has been adopted by all states and the District of Columbia. The UAGA provides the primary legal standard for fetal tissue use, permitting fetal tissue to be donated for research purposes with the consent of either parent and without objection from the other.[21]

Several states have restrictive statutes governing the donation of fetal tissue for research. Massachusetts and Michigan have laws that prohibit abortion if it is conditional on the use of the fetal tissue for research. Arizona law specifically prohibits postmortem use of fetal remains for "any medical experimentation" if the tissue is derived from an induced abortion. Other states (e.g., Ohio, Oklahoma and Indiana) have statutes that restrict research on aborted fetal remains.

The demand for fetal tissue transplantation for neural or pancreatic cell engraftments may be expected to increase if further clinical studies conclusively show that this procedure provides long-term reversal of

neural or endocrine deficits. The ethical issues that fetal cell transplantation has raised are distinct from ethical points addressed during the previous discussions of fetal tissue research.

Prominent among the currently identified ethical concerns is the potential for fetal transplants to influence a woman's decision to have an abortion.[22, 23] These concerns are based, at least in part, on the possibility that some women may wish to become pregnant for the sole purpose of aborting the fetus and either donating the tissue to a relative or selling the tissue for financial gain. Others suggest that a woman who is ambivalent about a decision to have an abortion might be swayed by arguments about the good that could be achieved if she opts to terminate the pregnancy. These concerns demand the prohibition of (a) the donation of fetal tissue to designated recipients; (b) the sale of such tissue; and (c) the request for consent to use the tissue for transplantation before a final decision regarding abortion has been made.

The abortion process may also be influenced inappropriately by the physician. Consequently, measures must be taken to assure that decisions to donate fetal tissue for transplantation do not affect either the techniques used to induce the abortion or the timing of the procedure itself with respect to the gestational age of the fetus. Also, to avoid conflict of interest, physicians and other health care personnel involved in performing abortions should not receive any direct benefit from the research or transplant use of tissues derived from the aborted fetus. The retrieval and preservation of usable tissue cannot become the primary focus of abortion. Therefore, members of the transplant team should not influence or participate in the abortion process.

There is potential commercial gain for those involved in the retrieval, storage, testing, preparation, and delivery of fetal tissues. Providing fetal tissue by nonprofit mechanisms designed to cover costs only would reduce the possibility of direct or indirect influence on a woman to acquire her consent for donation of the aborted fetal remains.

In summary, the use of fetal tissue for transplantation purposes is ethically permissible when:

(1)The Council on Ethical and Judicial Affairs' guidelines on clinical investigation and organ transplantation are followed, as they pertain to the recipient of the fetal tissue transplant (see Appendix).
(2) Fetal tissue is not provided in exchange for financial remuneration above that which is necessary to cover reasonable expenses.
(3) The recipient of the tissue is not designated by the donor.
(4) A final decision regarding abortion is made before initiating a discussion of the transplantation use of fetal tissue.
(5) Decisions regarding the technique used to induce abortion, as well as the timing of the abortion in relation to the gestational age of the fetus, are based on concern for the safety of the pregnant woman.
(6) Health care personnel involved in the termination of a particular pregnancy do not participate in or receive any benefit from the transplantation of tissue from the abortus of the same pregnancy.
(7) Informed consent on behalf of both the donor and the recipient is obtained in accordance with applicable law.

CONCLUSION

At this time, fetal neural grafting is a promising area of clinical investigation that should continue to receive federal funding. The current transplant experiments may be viewed as the initial step in determining the effectiveness of this approach for the treatment of Parkinson's disease, other neurodegenerative conditions, and diabetes. Parkinson's disease remains the most attractive disorder for this procedure because of the relatively localized region of deficit compared to more widespread degeneration observed in such neurologic disorders as Alzheimer's disease.

The donation of fetal tissue for transplantation from spontaneous or induced abortions is governed legally by the Uniform Anatomical Gift Act. Many states prohibit experiments on fetal remains, but such statutes may not apply if fetal cell transplantation becomes routine (i.e., nonresearch in nature). The principal ethical concern in the use of human fetal tissue transplants is the degree to which the decision to have an abortion is separated from the decision to donate the postmortem tissue. Safeguards to reduce any motivation, reason, or incentive by the woman to have an abortion can be developed to allow the benefits of this procedure to be made available to those who are in need of improved therapies.

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APPENDIX

Current Opinions of the Council on Ethical and Judicial Affairs
of the American Medical Association, 1986

Clinical Investigation: Replacement of Vital Human Organs (2.07).

The following are guidelines, suggested by the Council, in conducting experimental or clinical investigation, such as with mechanical devices or animal organs, for the replacement of human organs that are no longer functional:

(1) Experimental or clinical investigations should be conducted as part of a systematic program competently designed, under accepted standards of scientific research, to produce data which are scientifically valid and significant.

(2) The physicians conducting clinical investigation should demonstrate the same concern and caution for the welfare, safety, and comfort of the person involved as is required of physicians who are furnishing medical care to patients independent of any clinical investigation.

(3) Voluntary written consent must be obtained from the patient, or from his or her legally authorized representative if the patient lacks capacity to consent, following (a) disclosure that the physician(s) intend to use an investigational or experimental procedure, (b) a reasonable explanation of the nature of the procedure to be used, risks to be expected, and possible therapeutic benefits, (c) an offer to answer any inquiries concerning the procedure, and (d) a disclosure of alternative procedures, if any, that may be available. Physicians should be completely objective in discussing the details of the procedure to be performed, the pain and discomfort that may be anticipated, known risks and possible hazards, the quality of life to be expected, and particularly the alternatives. Especially, physicians should not use persuasion to obtain consents which otherwise might not be forthcoming, nor should expectations be encouraged beyond those which the circumstances reasonably and realistically justify.

(4) In clinical investigation primarily for the accumulation of scientific knowledge, adequate safeguards should be provided for the welfare, safety and comfort of the patient. The medical profession recognizes as fundamental social policy that the advancement of scientific knowledge must always be secondary to primary concern for the individual. The physician must nevery deny the patient the best possible therapeutic modality in favor of an experimental treatment which is less likely to succeed.

(5) With the approval of the patient or the patient's lawful representative, physicians should cooperate with the press and media to ensure that medical news concerning the progress of clinical investigation or the patient's condition is available more promptly and more accurately than would be possible without their assistance. On the other hand, the Council does not approve of practices designed to create fanfare, sensationalism to attract media attention, and unwarranted expressions of optimism because of short term progress, even though longer range prognosis is known from the beginning to be precarious. With the approval of the patient or the patient's family, the Council, however, encourages the objective disclosure to the press and media of pertinent information. The situation should not be used for the commercial ends of participating physicians or the institutions involved.

The Council has not evaluated nor does it have sufficient information upon which to base an evaluation as to the extent to which cases involving the use of animal organs and mechanical hearts conform to the above guidelines. These guidelines are provided to the public, the medical profession, and the scientific community in the belief that they may find them helpful in making their own independent judgments. (I, III, V)

Organ Transplantation Guidelines (2.15). The following statement is offered for guidance of physicians as they seek to maintain the highest level of ethical conduct in the transplanting of human organs.

(1) In all professional relationships between a physician and patient, the physician's primary concern must be the health of the patient. The physician owes the patient primary allegiance. This concern and allegiance must be preserved in all medical procedures, including those which involve the transplantation of an organ from one person to another where r both donor and recipient are patients. Care must, therefore, be taken to protect the rights of both the donor and the recipient, and no physician may assume a responsibility in organ transplantation unless the rights of both donor and recipient are equally protected.

(2) A prospective organ transplant offers no justification for a relaxation of I the usual standard of medical care. The physician should provide the 1 patient, who may be a prospective organ donor, with that care usually given others being treated for a similar injury or disease.

(3) When a vital, single organ is to be transplanted, the death of the donor shall have been determined by at least one physician other than the recipient's physician. Death shall be determined by the clinical judgment of the physician. In making this determination, the ethical physician will use currently accepted and available scientific tests.

(4) Full discussion of the proposed procedure with the donor and the recipient or their responsible relatives or representative is mandatory. The physician should be objective in discussing the procedure, in disclosing known risks and possible hazards, and in advising of the alternative procedures available. The physician should not encourage expectations beyond those which the circumstances justify .The physician' s interest in advancing scientific knowledge must always be secondary to the primary concern for the patient.

(5) Transplant procedures of body organs should be undertaken (a) only by physicians who possess special medical knowledge and technical competence developed through special training, study, and laboratory experience and practice, and (b) in medical institutions with facilities adequate to protect the health and well-being of the parties to the procedure.

(6) Transplantation of body organs should be undertaken only after careful evaluation of the availability and effectiveness of other possible therapy. (I, III, V)