Chapter 8

Ethical Issues

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Chapter 8
Ethical Issues

Neural grafting is a complex subject for ethical discussion because of the scope of the issues it raises. Ethical arguments surrounding neural grafting are part of the continuing debates about the morality of abortion and genetic manipulation, and they rekindle discussions about the treatment of research subjects and the meaning of informed consent. This chapter discusses ethical aspects of the various neural grafting technologies currently being researched.

Some ethical issues raised by neural grafting are not unique to this technology. One such issue is the allocation of scarce Federal resources, since funds committed to neural grafting might be spent on alternative biomedical research or other areas altogether. Questions about funding can be addressed with empirical evidence of the number of individuals affected by diseases, the availability of alternative treatments, and the economic costs that both the diseases and the treatments create for society. Another general ethical concern is the tension between the Federal Government's commitment to promoting the public health and funding biomedical research, and its responsibility to respond to public concern about certain research and its possible applications.

The various grafting materials used also raise ethical issues. Human fetal tissue, in particular, has generated extensive discussion in several forums. A moratorium on federally funded fetal tissue transplantation research was declared in March 1988 by the Secretary of Health and Human Services and was continued indefinitely in November 1989 (see app. A). As a result of this moratorium, a National Institutes of Health (NIH) advisory panel was convened and in 1988 issued a report on the ethics of fetal tissue transplantation (54). The panel's policy recommendations were accepted by a large majority of its members and were accepted unanimously by the NIH Director's Advisory Committee. However, the points on which panel members disagreed were never resolved, and no action was taken on the recommendations by the NIH Director or the Assistant Secretary for Health.

As the technology develops, the use of continuous cell lines as a source of grafting material may also create general concern. Advances in molecular biology suggest it may be possible to develop effective brain and spinal cord grafts by genetically manipulating cells before transplantation. Genetic manipulation of cells has generated considerable controversy since it was first introduced (49), but the somatic cell alterations that would be used for neural grafting are less troublesome than germ cell gene therapy. On the other hand, as cell lines have been developed, questions have been raised about ownership of tissues. Uncertainty about how to determine the rightful ownership of cell lines could complicate the use of this material considerably.

The treatment of patients who receive neural grafts is another area of ethical concern. Issues of protecting patients from undue risk and obtaining adequate informed consent are not unique to neural grafting, but they warrant special attention for this technology. At this stage of research, some persons question whether the risks to research subjects are comparable to the expected benefits. It is also questionable whether requirements for informed consent can be met, given the vulnerability of some persons with neurological disorders.

This chapter describes the ethical concerns that have been raised about neural grafting. It identifies issues and presents the various arguments surrounding them in order to represent the spectrum of attitudes expressed in public debate.

ISSUES RELATED TO RESEARCH FUNDING

Public funding of biomedical technology involves broad analyses of the economic benefits and costs, as well as the social benefits and ethical consequences, a new technology might have. Knowledge of economic consequences is necessary for financial planning but it is also integral to ethical decisionmaking, since the allocation of public funds raises questions about justice and equity. Some persons believe that justice requires the expenditure of funds in areas where they can benefit the greatest proportion of the population rather than a few disadvantaged individuals. If neural grafting techniques are very expensive to study or to provide as medical

Box 8-A—Just Distribution of Resources and the Funding of Heart Transplants

"On February 1, 1980, the 12 lay trustees of the Massachusetts General Hospital announced their decision not to permit heart transplants at that institution 'at the present time. They noted that it was difficult to turn away even one patient in need of a heart transplant, but they underlined the importance of making such decisions 'in terms of the greatest good for the greatest number. ' In June of that same year, Patricia Harris, then secretary of the Department of Health and Human Services, withdrew an earlier tentative authorization for Medicare to pay for heart transplants because of the need to evaluate the technology's 'social consequences,' including its costs. In 1987, legislators in Oregon made an equally dramatic change in the Oregon Medicaid program (the State-Federal program that provides funds to cover medical needs for financially needy citizens in the State). They decided not to pay for most transplants in order to use their limited budget for other purposes, In particular, they noted that the money that would have covered approximately 30 heart, liver, bone marrow, and pancreas transplants would instead be used to provide regular prenatal care for 1,500 pregnant women. The altered allocation was justified by its proponents because it would save more lives. '

The controversy about the funding of heart transplants is an example of the generic ethical issues that may surround an expensive medical therapy. Neural grafting could provoke similar considerations.

SOURCE: T.L. Beauchamp and J.F. Childress, "The Principle of Justice," *Principles of Biomedical Ethics (New York, NY: Oxford* University Press, 1989), pp. 286-287.

therapy, budget restrictions could require that neural grafting activity be limited (see box 8-A).

Questions arise about whether the research and application of technologies such as neural grafting ought to receive Federal support. Some critics consider it unjust to spend a great deal of money to benefit a few persons or to develop a surgical technique for a relatively uncommon condition when the same funds might be used to develop medical treatments that would benefit many more persons. In order to determine whether expenditure of public funds for neural grafting research constitutes just allocation of resources, some background information is required. The following questions are not ethical issues, but answers to them could help the Federal government decide whether to fund neural grafting.

What kinds of diseases might be treated with this technology?

It has been argued that the government ought to fund research that seeks to cure neurological disorders that affect large numbers of U.S. citizens (2). Neural grafting is a possible therapy for Parkinson's disease, Huntington's disease, Alzheimer's disease, spinal cord injury, and other neurological disorders, although whether neural grafting will be successful in any of these remains to be seen (see ch. 5).

What impact do these diseases currently have on society and what threat do they hold for the future?

Neurological disorders exact a high financial toll from society, although measures of their costs and statistics on the number of persons affected vary considerably (see ch. 6). Neural grafting has been suggested as a possible therapy for some age-related diseases, e.g., Parkinson's disease, Alzheimer's disease, and stroke. Should neural grafts prove effective for such diseases and should the prevalence of these diseases increase with an aging society, the demand for neural grafts might increase as well.

What alternative surgical or medical treatments are available?

If neural grafting is more effective and less expensive than alternative treatments for neurological disorders, an ethical argument could be made for Federal support of neural grafting. For most neurological disorders, however, including Parkinson's disease, Huntington's disease, spinal cord injury, and Alzheimer's disease, no cures are available and control of symptoms is inadequate. Symptoms of Parkinson's disease are often treated with L-dopa, but this drug is palliative (it treats only the symptoms of the disease and not the cause), and its benefits diminish as the disease progresses. Some alternative treatments are available or in the process of being developed. For example, a new drug called deprenyl shows promise for slowing the progression of Parkinson's disease (see ch. 6), although it does not stop the progression or affect advanced stages of the disease (45). While neural grafting is a promising

treatment for Parkinson's disease at this time, it, too, may be only palliative (see ch. 5). Fair allocation of health care resources may require that the financial costs of neurological disorders now and in the future be estimated and compared to the costs of neural grafting and alternative treatments. However, fair allocation may also require that resources spent on neurological disorders reflect the impact of these diseases on society.

To what extent does the Federal Government's commitment to funding biomedical research extend to neural grafting research?

Because neural grafting techniques are still being studied, the question at this point is whether the government has an obligation to support neural grafting research. Given the government's commitment to support basic scientific research and to further the health of the Nation, it might be expected that basic research which could aid in developing new neural grafting technologies would be funded. This is, in fact, the case: Only research on the implantation of human fetal tissue from induced[1] abortions does not receive Federal funds (53,57). The moratorium on Federal funding for human fetal tissue grafting research was declared because specific ethical issues surrounding this research came into conflict with the government's general commitment to fund basic research. The ethical issues related to fetal tissue grafting will be discussed later in this chapter.

Would funding neural grafting require the government to redirect limited funds from other areas of research?

It has been suggested that, in order to fund neural grafting research, resources might be provided at the expense of other projects that could lead to more effective or less controversial treatments for neurological disorders (38) or increased "understanding of the fundamental biological principles underlying the normal function and dysfunction of the human nervous system" (11). In general, Congress allocates funds for biomedical research to Federal research agencies, but the distribution of those funds to the institutes within the agencies and then to individual investigators falls outside Congress's purview (12). Federal research grants are made on the basis of merit, as determined through peer review of research protocols. Neural grafting research receives Federal funding when grant proposals scientifically warrant that support. Withholding research funds from neural grafting frees resources for other projects, but there is no guarantee that those funds will be put toward other neurological research.

ISSUES RELATED TO TISSUE SOURCE

Questions about the propriety of federally funded neural grafting research are not limited to resource allocation-they also address the propriety of using various graft materials. As discussed in chapter 4, a number of neural grafting materials are used, some of which are more ethically problematic than others. Autografts and allografts using adult tissue are relatively free of ethical controversy: For example, the primary ethical reasons for not doing adrenal medullary autografts to treat Parkinson's disease are likely to be related to protection of the research subject rather than to the source of the grafting material.

Fetal Tissue

Adult human neural tissue is not a suitable material for grafting, so scientists have turned to human fetal neural tissue. Fetal tissue is promising from a scientific point of view, but it is also the most ethically controversial grafting material because it is usually obtained from abortions.

While use of aborted fetal tissue in research is not new, the current ethical arguments surrounding its use and the Federal attitude toward funding such research reflect a different level of concern than has previously been demonstrated. The use of human fetal cells played an important role in the development of vaccines for polio and other childhood diseases (20,48), and research on the transplantation of fetal thymus glands into infants with DiGeorge's syndrome was performed in the United States 20 years ago (7,30). The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (hereafter referred to as the National Commission) scrutinized ethical issues related to the use of fetal tissue in research and

[1]The Department of Health and Human Services referred to "induced abortion" in the fetal tissue transplantation moratorium (57). Where the moratorium or Federal activity surrounding it is discussed in this chapter, "induced abortion" will be used. Where a distinction is made between different types of induced abortion, more specific terminology will be used.

developed the guidelines used to create the 1975 Federal regulations for use of fetal tissue in research (52). The National Commission's report and the regulations that developed from it [45 CFR 46] focused on research performed on living fetuses and paid little attention to fetal cadavers. Both specified only that research on cadaveric fetal tissue should "be conducted in accordance with commonly held convictions about respect for the dead, and in accordance with State and local laws" (10). No moral distinction was made about the means of fetal death. As a result, research using aborted fetal tissue for experimental purposes has been, and continues to be, relatively uncontroversial. The moratorium on Federal funding of research involving transplantation of human fetal tissue obtained from induced abortions into humans is a recent exception (see app. A).

Fetal Research v. Fetal Tissue Transplantation Research

What makes transplantation research different from other research that uses cadaveric fetal tissue? Some persons perceive a significant ethical difference. In fetal research,[2] cadaveric fetal tissue is used to *develop* a treatment; in fetal tissue transplantation research, fetal tissue *is the* treatment (43). These persons question whether fetal tissue should be used to benefit an individual recipient.

On the other hand, some persons perceive no ethical difference between the transplantation of cadaveric adult organs and tissues and those of cadaveric fetuses. Unless the decedent has explicitly refused to donate body parts, adult cadaveric tissues may be donated by the next of kin as a gift and may be removed for transplantation by a coroner or medical examiner. Once these conditions are met, tissues may be used to benefit a single recipient. In this view, cadavers do not have protectable interests, and tissue from dead fetuses is no different than tissue from dead adults.

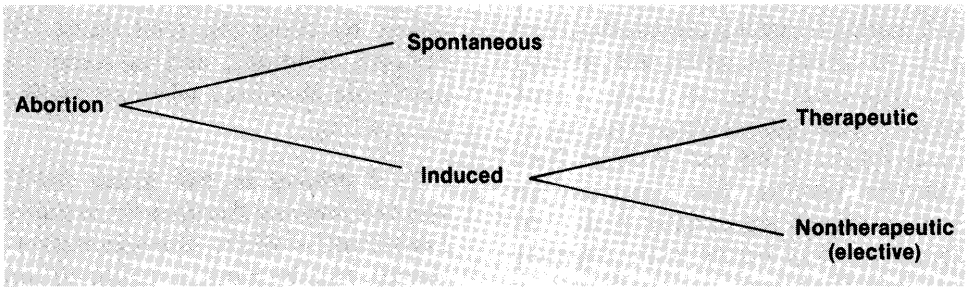
Procurement of Fetal Tissue

Most ethical objections to the use of fetal tissue for neural grafting relate to tissue procured from nontherapeutic induced abortions (to be referred to hereafter as elective abortions) (see figure 8-l). Many persons who object to the use of fetal tissue from elective abortions have suggested that fetal tissue from spontaneous abortions (miscarriages) could be used for transplantation without ethical objection because fetal death is not intended. The first human fetal nervous system grafts used tissue from spontaneous abortions (29), but since spontaneous abortions are seldom anticipated and usually take place outside a hospital, it is difficult to collect the tissue for grafting. Tissue from therapeutic induced abortions for cervical cancer or ectopic pregnancy has also been suggested as an ethically unobjectionable alternative, since protection of the pregnant woman's life, not the termination of pregnancy, is the primary purpose of the abortion. There is some question, however, as to whether a physiological anomaly that caused the pregnancy to be terminated (as evidenced by spontaneous abortion, ectopic pregnancy, or cancer) would make the tissue inappropriate for grafting (10,39). Ectopic pregnancy is more likely to result from a physiological anomaly of the woman than a defect in the fetus (17), but without thorough genetic and physiological testing, the use of tissue from spontaneous and therapeutic induced abortions for neural grafting might be considered unethical because of the risk to the recipient if the graft material is infected with a virus or bacteria or has a genetic anomaly that could affect the recipient (3,10,39). While grafting fetal tissue from spontaneous abortions and therapeutic induced abortions could avoid association of neural grafting with elective abortion, it may not be a practical source of graft material.

Some persons object to the use of electively aborted fetal tissue for grafting because procurement of the neural tissue might cause pain or even death to the fetus. Research has indicated that neural tissue from electively aborted fetuses between 8 and 12 weeks of development is the most clinically appropriate for neural grafting (48). This early stage of development makes it unlikely that a fetus would be viable after an abortion procedure (5). First-trimester abortions are usually performed by vacuum aspiration, a procedure that seldom results in a live, or even intact, fetus (10). Concern has been expressed, however, that elective abortions performed at a later gestational age might allow a fetus to survive the procedure and that the separation of neural tissue for the graft would not only cause great pain but could

[2]The National Commission report and the Federal regulations for fetal research identify several types: activities directed toward fetuses in utero as subjects, activities directed toward viable fetuses ex utero, activities directed toward nonviable fetuses ex utero, and activities involving the dead fetus, fetal material, or the placenta [45 CFR 46].

Figure 8-l—Types of Abortion and Morally Relevant Differences Among Them



Without any qualification, the term "abortion" reveals nothing except that a pregnancy has ended. This termination is not usually considered morally bad in itself. Spontaneous abortions may be considered unfortunate but are not usually considered morally blameworthy. The abortions that usually generate ethical controversy are those that are induced.

There are two types of induced abortions: therapeutic and nontherapeutic. Although some persons object to any induced abortion on the grounds that the premature termination of fetal life constitutes murder, others find that moral distinctions may be made, depending on the reason for the abortion. Conditions such as cancer of the cervix or uterus and ectopic pregnancy will usually lead to the death of both the pregnant woman and the fetus if the pregnancy is not aborted. If the life of the woman is endangered by cervical cancer, the Roman Catholic Church teaches that "the treatment is not really an abortion, even though the fetus dies. The intent of the action is the removal of the life threatening rendition, and the death of the fetus is a foreseen but unintentional consequence." Other persons argue that when a fetus's and a woman's rights to life conflict, the woman's life maybe saved at the expense of the fetus's. There are many other points of view on this question. Although there is some disagreement as to whether a pregnancy maybe terminated if bringing the pregnancy to term will result in the death of the woman but the birth of a baby, therapeutic induced abortion is not as controversial as nontherapeutic induced (elective) abortion. Many reasons have been put forth for both the morality and the immorality of nontherapeutic induced abortion.

SOURCES: Adapted from M.B. Mahowald, "Neural Fetal Tissue Transplantation: Should We Do What We Can Do?" *Neurologic Clinics* 7:745-757, 1989; A. Moraczewski, regional director, Pope John XXIII Medical, Moral, Research, and Education Center, Houston, TX, personal communication, April 1990.

actually cause the death of the fetus (27). The use of a living fetus for transplantation is a form of vivisection, which is generally recognized to be unethical and which, moreover, is prohibited by Federal law: As long as the fetus is alive, its tissues may not be removed for any research or therapeutic procedure [45 CFR 46]. The distinction between a live fetus and a dead fetus with living tissue is extremely important in this regard.

Arguments For and Against Human Fetal Tissue Transplantation Research

Arguments for and against using electively aborted fetal tissue for neural grafting address the issues raised by research already under way and the future use of fetal tissue grafting on a large scale. These arguments raise four main questions:

- . Is the means of fetal death ethically relevant to any subsequent use of the tissue?
- . Is it ethical to use electively aborted fetal tissue as therapeutic treatment for another individual?
- . What are the ethical implications of a public policy that supports fetal tissue transplantation research?
- Whose consent, if any, is necessary for the use of aborted fetal tissue for neural grafting?

Is the means of fetal death ethically relevant to any subsequent use of the tissue ?-While disputes over the morality of abortion have complicated and politicized discussions about the use of electively aborted fetal tissue for neural grafting, the ethical *relevance* of an elective abortion to the transplantation of fetal tissue is the true subject of public debate. Both opponents and supporters of elective abortion rights have articulated a number of reasons for supporting fetal tissue transplantation research, and both have also identified reasons for not doing so.

The main argument supporting fetal tissue transplantation states that there is no relevant difference between the transplantation of cadaveric fetal tissue (i.e., tissue from a dead fetus) and any other cadaveric tissue. (This position has been taken by both supporters and opponents of elective abortion.) The argument, which claims that it is not unethical to use tissue from elective abortion, is based on the

premise that by the time the fetus becomes a possible source of transplantation tissue it is already dead and that the reamer of death is irrelevant to any subsequent use. The NIH Human Fetal Tissue Transplantation Research Panel compared the use of tissue from a dead fetus and the use of tissue from accident and murder victims. The persons from whom organs are obtained are already dead, and using the organs in no way harms them, deprives them of respect, objectifies them, or uses them as a means to another's end. Neither does it indicate approval of the death or the manner in which it was brought about. On the contrary, using organs and tissues from these victims is thought to allow some good to come from their death and thus is morally permissible.

Another argument suggests that there is a moral obligation to help others when it is possible to do so and thus it is unethical *not* **to** use tissue from elective abortions. Some persons believe that since the aborted fetus is already dead and its tissue legally may be used for research and medical treatments, and since fetal tissue grafts may benefit others, preventing use of that tissue is ethically reprehensible. They believe that since the dead have no interests to protect, using fetal tissue does not harm the fetus physically or morally. They believe that using cadaveric fetal tissue for grafts that relieve suffering is morally good and thus perceive an ethical imperative to use that tissue to help others.

Other persons disagree with the claim that the means of fetal death is morally irrelevant to the use of the tissue for grafting and perceive a moral obligation ***not*** to use fetal tissue for transplantation. Many of these persons also strongly oppose abortion. One argument is that using electively aborted fetal tissue for neural grafting indicates indifference to the means of fetal death. Another argument says that using aborted fetal tissue for neural grafts constitutes *post facto* complicity in murder (8). Those who hold this position argue that because abortion is murder, the procurement of fetal tissue from abortion clinics requires collaboration with murderers. For example, since surgeons who perform neural grafting must have access to fetal tissue, they must work hand-in-hand with abortionists to obtain the tissue while the cells are still alive. Unlike surgeons who retrieve organs from murder or accident victims, those who retrieve and transplant aborted fetal tissue participate retroactively in the killing by obtaining the consent of the pregnant woman for use of the tissue (in cases where this is done), by collecting fetal tissue from those who perform abortions, and in some cases by killing nonviable abortuses when separating neural tissue for grafting.

Is it ethical to use tissue from an electively aborted fetus as therapeutic treatment for another individual?—While transplantation of cadaveric tissues has become a common practice and is regulated under the Uniform Anatomical Gift Act (UAGA) in all 50 States (see ch. 7), some persons object to the use of fetal tissue for transplantation into individual recipients on the principle that one should not treat the fetus as the means to another's end. They believe the "consideration of any class of human subjects as no more than a commodity to be used for the benefit of others is wrong" (27). They do not believe that the alleviation of suffering justifies the use of aborted tissue. In their belief, no matter how good an outcome might derive from fetal tissue transplantation, it does not justify the moral devaluation of the fetus necessary for that outcome to occur.

Other persons question why the transplantation of cadaveric fetal tissue should be treated differently from the transplantation of any other cadaveric tissue. The use of cadaveric adult organs is rarely regarded as indicative of disrespect, commodification, or devaluation (56). Why, then, should transplantation of cadaveric fetal tissue be considered a moral devaluation? Some persons believe transplantation of cadaveric tissue into individuals is more acceptable than using it for general research, since "it may do more good to heal than simply learn how to heal" (31).

What are the possible consequences of a public policy that supports fetal tissue transplantation research?—Some persons are concerned that Federal funding of fetal tissue transplantation research would lead to an increase in the number of abortions performed in the United States. The Department of Health and Human Services (DHHS) expressed this concern in continuing the human fetal tissue transplantation research moratorium in November 1989. These persons believe women may decide to abort if they believe fetal tissue could help another person and that women who are ambivalent about their pregnancies will consider fetal tissue grafting a justification for having an abortion (35). If fetal tissue grafting research shows promise for Parkin-

son's disease or other disorders, they argue, the supply of fetal tissue will not satisfy the demand. Elective abortion might implicitly or explicitly be encouraged in order to make more fetal tissue available. Some persons believe it would be ethically unacceptable if the ability to donate fetal tissue for grafting influenced even one woman's decision to have an abortion (35).

Other persons disagree that elective abortion would have to be encouraged to make fetal tissue available for grafting. Some claim that the number of elective abortions already being performed in the United States would provide adequate tissue even if neural grafting became standard practice (13). As is the case with kidneys, hearts, and other body tissues that are transplanted, the number of neural grafting procedures performed could be limited to the amount of fetal tissue already available (30). Also, the development of continuous cell lines might make it unnecessary in some cases to procure newly aborted tissue. Fetal tissue might be used to start a cell line without increasing the number of abortions that take place and might not therefore be ethically objectionable to some persons (34). Currently, there is no evidence to support or refute the contention that fetal tissue grafting research would cause an increase in the number of abortions performed, either because of a need for grafting material or because women perceive an altruistic justification for elective abortion.

Women's groups in particular have objected to the claim that the opportunity to donate fetal tissue for transplantation after an elective abortion would affect a woman's decision to terminate a pregnancy, even if she did believe that this use of fetal tissue would do good. Other persons argue that requiring anonymity between tissue donors and graft recipients would make specified donation impossible in the event that a woman wanted to provide neural grafting material for a specific recipient.

Whose consent, if any, is necessary for the use of aborted fetal tissue for neural grafting?--Consent is generally required for participants in research protocols and for donors of tissue. It is not certain, however, what role consent would play in donating fetal tissue for neural grafting research, and there is debate about who should give it.

The donation of adult cadaveric tissue for transplantation, and fetal tissue in some States, is regulated under the UAGA (see ch. 7). As fetal tissue grafting research progresses, the models for obtaining consent may have to be modified to include fetal tissue donation, or a new model may have to be created. Those who believe fetal tissue transplantation is analogous to the transplantation of other cadaveric tissue find it appropriate for the next of kin, in this case the woman who has the abortion, to give consent to use fetal tissue for transplantation. However, some persons challenge the woman's authority to give this consent, since, according to their view, she is also the cause of the fetus's death. Consent for fetal tissue use in neural grafting falls between existing regulations and practices.

Some persons hold that a woman's prerogative to donate fetal tissue stems not from her legal status as next of kin, but from a basic right to control her own body and its products. They believe that seeking consent to examine or use fetal remains is consistent with the treatment accorded any other tissue or organ removed during surgery, thus to deny a woman the opportunity to specify what should happen to aborted fetal tissue would be to deny her autonomy (10). Consent should be obtained out of respect for the interests of the woman, who may want the tissue to be handled a certain way after the abortion procedure. For example, some women may hope to benefit another person by donating aborted fetal tissue for transplantation, while other women may want to dispose of the tissue. Whatever the decision and whatever the reason for it, these persons argue that the decision should be the woman's.

Some persons believe that fetal tissue is not the woman's to donate. They believe that no fetus is property merely because it is sustained by another person's body; more important, they believe that after the abortion has taken place and the fetus is no longer part of the body, a woman's claim to bodily property carries even less weight (8,11). These persons argue that the only reason to obtain the consent of the pregnant woman would be for her to act as proxy for a fetus to be used in research [under the Protection of Human Subjects Act [45 CFR 46]. Proxy decisionmaking assumes the surrogate decisionmaker's commitment to act in the interests of the incompetent. Since the woman clearly does not intend to protect the fetus, they believe it is inappropriate for her to act as the fetus' proxy; she should have no say over what happens to the tissue (8).

The donation of cadaveric tissue need not be seen strictly in terms of property or proxy, however. The donation of adult cadaveric tissues by family members is done in the context of a gift-giving model that neither recognizes property rights on the part of the family nor grants guardianship or proxy. The fact that the woman's consent is obtained does not necessarily mean she acts as proxy for the fetus, since her role would be to consent to tissue donation, not research participation. Some persons believe fetal tissue donation is consistent with the accepted gift-giving model for organ donation and constitutes an altruistic act women are morally free to take. Others, however, believe that electively aborted fetal tissue is an inappropriate gift (10).

It has also been suggested that no consent is needed to use fetal tissue for grafting research. Since electively aborted fetal tissue is normally discarded without any specification on the woman's part, it might be justifiable to consider the abortus abandoned and to use it without consent. This method might avoid the obstacles created by views of competing rights (the woman v. the fetus); however, refusing to acknowledge protectable interests on the part of either the woman or the fetus could be interpreted as exploitation. Although tissues and organs from adult cadavers can be used for transplantation without the consent of family members, some women might prefer that the tissue not be used for transplantation. Using the fetal tissue without the consent of the woman could create more problems than it solves.

If it is decided that it is ethically appropriate or necessary to obtain the woman's consent, the question of when to solicit consent is raised. There is some agreement that consent should be obtained only after the woman has conclusively decided to abort, in order to separate the decision to abort from the decision to donate fetal tissue (1,32,48,54). It may also be possible to obtain consent tier the elective abortion has been performed and the tissue has been identified as suitable for transplantation, especially if the tissue is frozen before transplantation, although this option is not entirely free of ethical problems (see box 4-A).

The protocol used in one privately funded fetal tissue transplantation trial solicited consent from the woman after the abortion had been completed (16). The consent form specified that fetal tissue was being solicited for research purposes, which could include fetal tissue transplantation research. This approach provides the woman an opportunity to prevent the use of the tissue for grafting, while not influencing her decision to maintain or terminate the pregnancy. Other investigators may choose not to request consent immediately after abortion because it could be emotionally stressful for the woman (14), although some persons believe that there is no difference between requesting consent for tissue from a woman who has just aborted a pregnancy and requesting organ donation from the family of a deceased adult.

The consent forms used for other fetal tissue research may not be comprehensive enough to address all aspects of grafting. It is not clear whether the abortion consent forms which allow fetal tissue to be donated for research should include clauses specifying that the tissue might be used for transplantation. A separate consent form for fetal tissue transplantation might be appropriate.

Relationships Among the Questions-Attitudes toward consent for the donation of fetal tissue for transplantation are likely to be consistent with beliefs about the relevance of the means of fetal death to fetal tissue transplantation, the appropriateness of using cadaveric fetal tissue for therapeutic purposes, and the ethical implications of public policy that supports this research. The present discussion delineates issues for the sake of illustrating different aspects of the debate, but the arguments of individuals and groups who discuss the ethics of fetal tissue transplantation research are often more fluid.

For example, some persons who oppose fetal tissue transplantation research because they believe such grafting is complicitous with murder readily link three of the four questions discussed above. They feel that the means of fetal death is relevant to grafting fetal tissue because elective abortion is the unjust killing of innocent human beings. A woman who has an abortion therefore should not serve as its proxy. Public support should not be given to fetal tissue transplantation research because it would constitute public approbation for unjust killing (26).

Similarly, some persons who do not object to fetal tissue grafting research argue that the means of fetal death is irrelevant. They believe that once a fetus is dead, it has no interests to protect and maybe treated in the same reamer as adult cadaveric tissue. Consent for its use should therefore be solicited from

the next of kin, which in this case is likely to be the woman who has the abortion. These persons feel that public support of fetal tissue transplantation research would be consistent with other fetal tissue research and cadaveric organ donation and would have no specific ethical implications.

Issues Surrounding Fetal Tissue Transplants as Standard Therapy

The preceding arguments have been presented in public debates about the ethical implications of fetal tissue transplantation research. Some of the potential problems can be illustrated dramatically by describing the consequences should fetal tissue grafting become standard therapy. ("Standard therapy" describes procedures that are no longer regulated as research.)

Some persons have expressed concern that Federal support of fetal tissue transplantation through funding or regulation of the procedure would legitimize and institutionalize elective abortion.[3] Others persons contend that since elective abortion is legal, and since the Federal Government profits from it by taxing abortion clinics (3), it is already both legitimate and institutionalized. They argue that claims that Federal support of neural grafting research would further institutionalize the practice carry no weight. Fetal tissue from elective abortions would be used after the abortion has already taken place and would have no effect on law or policy concerning abortion itself. Still other persons believe that even though elective abortion is legal, it should not be encouraged. If fetal tissue transplantation is accepted as a medical treatment, they believe it maybe impossible to make abortion illegal again. Even some persons who support the freedom to have an abortion do not necessarily consider it a practice they would like to see endorsed by a public policy; i.e., while abortion should be legal, it does not follow that fetal tissue should be used for neural grafting.

Another concern is that the use of electively aborted fetal tissue as standard therapy may lead to commercial exploitation of fetuses. This concern has also been expressed in more extreme terms: Some argue that using aborted fetal tissue for neural grafting may make it a commercially desirable commodity and lead to the establishment of a fetal tissue industry. As in the development of reproductive technologies and the increase of surrogate motherhood, the growing demand for neural grafts might cause the fetus to be increasingly perceived only as a potential source of grafting material. It has been argued that the fetus should neither be endowed with a financial value, as it would be in a commercial exchange, nor be conceived for the sole purpose of using its tissue for transplantation (1,13,48,54). In 1988, the National Organ Transplant Act was amended to prohibit the sale of certain fetal organs and tissues, although neural tissue is not specified [Public Law 100-607].

Precautions against this consequence have been suggested. If it were likely that women could be coerced into conceiving and aborting in order to provide fetal tissue to benefit others, profit restrictions might create a disincentive. Payments to women who abort, including compensation for the cost of the abortion procedure, might be prohibited, as might payments to doctors, clinics, or any other parties involved in the abortion procedure. Tissue banks used to distribute fetal tissue maybe prohibited from profiting from their role. To prevent women from conceiving in order to provide tissue for grafts, specification of tissue recipients, including the woman herself, might also be prohibited (1,32,48,54).

Concern has been expressed that women, as the ''producers' of fetal tissue, could also be commercially exploited in order to obtain tissue in adequate quantities and of useful gestational age. There has been some suggestion that women who are ambivalent about terminating their pregnancies may be vulnerable to coercion by a physician who wants the fetal tissue for research or for another patient. This threat might be removed by requiring absolute separation of the doctors who perform abortions and those who do transplantation. One way to accomplish this might be to establish tissue banks for fetal tissue distribution, as is being done in Great Britain (44).

On the other hand, there have been strong objections to the assumption that women have limited abilities to make their own reproductive choices and that they can be easily coerced. Similar concerns have been raised about women who act as

[3]Legitimation is described by the Center for Biomedical Ethics (10) as the justification of an act or practice "in such a manner that others become more inclined to regard it as acceptable and to engage in it." Institutionalization may be seen to carry legitimation one step further, in that institutions (in this case the U.S. Government), by incorporating a practice, accept and engage in it, and in some cases profit financially from it.

surrogate mothers. The charge that the practice of surrogacy exploits women has been called paternalistic because:

> It questions women's ability to know their own interests and to enter into a contractual arrangement knowingly and competently. There may well be a coercive aspect to commercial surrogacy, since money. . . can serve as a coercive inducement to do something a person might not otherwise do voluntarily. . . . What they are really saying is that those who elect to enter surrogacy arrangements are incompetent to choose and stand in need of protection (28).

Many persons also have rejected the argument that women need to be protected from solicitation of fetal tissue.

The question of whether a woman's medical care might be altered (either with or without her consent) in order to obtain tissue of an appropriate gestational age and in the best possible condition for grafting has also been raised (33). There is general agreement that the means and timing of an abortion should be based on the pregnant woman's medical needs and not on the future use of the fetal tissue (32,48,54). On the other hand, not all variations in medical treatment will cause harm to the woman. Requiring that the woman's medical care always be placed first, that the timing and method of abortion not be altered, that separate doctors perform abortion and neural grafting procedures, and that only first-trimester abortuses be used might ensure that obstetrical care is not compromised for the sake of neural grafting.

Some fear that using electively aborted fetal tissue for grafting would gradually erode respect for human life. This argument can be seen in terms of a slippery slope, and what is perched at the top of the slope is our view of humanity. The concern is that, as society becomes accustomed to a new technology and its social consequences, social effects which now seem extreme or immoral might become acceptable. The increments by which society moves toward policies that are now appalling to some persons may pass unnoticed, and the result might be a society that by current standards is ethically unacceptable. A gradual acceptance of new developments, however, does not necessarily mean that ethical standards erode. Another interpretation of the same evidence might be that society learns from experience and that as current fears are proven unfounded or preventable, they are cast away.

When the practice of retrieving organs from accident and homicide victims first began in the 1960s, many persons held similar fears about whether transplanting those organs was morally acceptable without the prior consent of either the deceased or the deceased's next of kin (21). This concern was alleviated to a large extent as it became clear that cadaveric tissue could be transplanted without violating most ethical standards for treatment of the dead [although some religious traditions continue to oppose the practice (40)]. Each State established standards for the use of cadaveric tissue that respected not only the cadaver, but the families who were asked to make the decision to donate. Although familial consent for cadaveric organs is not a legal necessity in all cases, it is customarily obtained before organs are removed. This practice has alleviated many fears about moral violations against both the deceased and the living. Fetal tissue use might be regulated in a similar manner.

There is some concern that, since there is no distinct time when a procedure stops being research and becomes standard therapy, fetal tissue grafting might be put into widespread use despite ethical objections to it and without ethical norms to guide it (see ch. 7). If such research becomes standard therapy, there may be no way to control or restrict its use, even if ethical reasons are found for doing so. If an experimental therapy, especially one funded with tax dollars, proves successful, it might be extremely difficult to deny that treatment to a demanding public, whatever social and ethical consequences it might have and whatever alternative treatments might be forthcoming. It can also be argued that it is unfair to withhold a treatment from the taxpayers who funded the research that developed it.

It is not necessarily the case, however, that fetal tissue grafting techniques will become standard therapy (41). While it is reasonable to expect that they will, continuing research could reveal information about the etiologies of diseases and the mechanisms of neural repair that suggest better or less controversial alternatives to fetal tissue. Fetal tissue transplantation research may lay the groundwork for other therapies without ever being used widely itself. In that case, present concerns could prove unfounded.

At this stage of scientific research it is difficult to predict accurately what the consequences of widespread fetal tissue grafting are likely to be. By the

time adequate research has been done and a procedure is proven effective, there maybe a more certain factual basis for any ethical discussions. At the same time, Federal standards for the procurement of tissue and regulation of technology transfer might prevent many of the anticipated consequences.

Cell Lines

Continuous cell lines (CCLs) promise self-perpetuating cells that can be propagated indefinitely. When the small number of cells used to initiate a cell line are derived from a consenting participant, there are few ethical implications related to the tissue itself, although there may be questions of ownership of the cell lines (50). CCLs derived from fetal tissue may be one of the more scientifically promising neural grafting materials, but ethical issues arise from the fact that cadaveric fetal tissue may be used to start them, and ownership of the tissue will be difficult to determine.

The use of CCLs could either perpetuate or resolve the debate about the use of electively aborted fetal tissue for transplantation, depending on which of the arguments described in the previous section are accepted. Those who believe that elective abortion is immoral and that any subsequent use of the tissue is also immoral are likely to object to fetal tissue CCLs for the same reason they object to fetal tissue transplantation (8).

Objections may be weaker, however, on the part of persons who object to fetal tissue transplantation on the grounds that it might promote abortion (11,34), decrease the value of human life, or use the fetus as the means to another's end. Theoretically, only a few cells from a fetus would be needed for all future fetal tissue grafting. Thus, far less tissue would be needed to start a CCL than would be needed to provide a neural graft. If fetal tissue from spontaneous or therapeutic abortions is thoroughly tested for any genetic anomalies or disease, such tissue might be used for cell lines, ensuring that fetal tissue grafts will not increase the number of elective abortions that take place. Using CCLs might also make it improbable that a woman would conceive in order to provide aid to a specific recipient. Continuous fetal cell lines may make it possible to use fetal tissue for transplantation without leading to anticipated undesirable consequences.

Ownership of Tissue Used in Cell Lines

The question of whether the person whose cells are used to start a cell line has proprietary claim over the line is another new and as yet unresolved issue. A California appellate court ruled in 1988 in *Moore v. Regents of the University of California (37)* that a plaintiff whose tumorous spleen was used to start a commercially profitable CCL without his permission has property claims over his body tissues and any commercial products derived from them. The California Supreme Court reversed this decision in July 1990-the majority, consenting, and dissenting opinions were all based on ethical concerns, although they reached different conclusions (see box 8-B). Until this issue is decided by legislative action or the U.S. Supreme Court, however, there are no clear legal rules for identifying property rights over body parts.

The question of ownership of fetal CCLs adds to the confusion. Claims that women have property rights over fetal tissue have been challenged in debates about abortion and consent for tissue donation, and these claims may be more contentious if bodily property becomes marketable.[4] Because the development of CCLs can be very profitable, questions of ownership of body tissues and cell lines derived from them have become increasingly important.

As previously discussed, it has not been established whether the basis for requiring consent for the use of aborted fetal tissue from the woman who elects the abortion is an acknowledgement of her ownership or her guardianship of fetal tissue, or even whether her consent is seen as appropriate at all. If fetal tissue donation is an act of altruism, the same justification used for other types of fetal tissue research may hold. It is arguable, however, that altruism is not the motivation for a gesture that could be extremely profitable to the person who gives consent. If the consent requirement is based on an assumption of ownership, consent provides a means for the donation of personal property. But should a pregnant woman be considered a partial owner of the cell line, based on proprietary rights? Is it ethical to regard the woman as the owner of fetal tissue that can be used in a commercial undertaking? Is she

4"In the ..... case, the appellate court held that "... even though full property rights are not recognized in a dead body, a limited property interest has been found. . . .[However, w]e are not calledupon, nor are we attempting, to resolve the complex issues relating to the human fetus".

Box 8-B—Moore *v.* Regents of the University of California

The case John Moore brought against the investigators who used his body tissues to start a commercial continuous cell line raises fundamental questions concerning a patient's right to the control of his or her own body and whether the commercial exploitation of a patient's cells by medical care providers, without the patient consent, gives rise to an action for damages.

In 1976, Moore sought medical treatment at the Medical Center of the University of California, Los Angeles, for a condition known as hairy-cell leukemia As a necessary part of the treatment for this disease, Moore's spleen was removed.

Without the patient's knowledge or consent to donate his cells for research, the medical staff examined the excised tissue and determined that Moore's spleen cells had unique qualities. Through genetic engineering, they developed from the spleen cells a cell line that is capable of producing pharmaceutical products of enormous therapeutic and commercial value. The university patented the cell line, along with methods of producing many products from it, The university also entered into a series of commercial agreements for rights to the cell line and its products with two corporations. The commercial value of the products was predicted to be approximately $3 billion by 1990.

Moore sued the university and the corporations on several grounds, one of which was that "had he known what was taking place, he would not have consented to the splenectomy for these research and commercial activities; would have insisted on participating in control of the use of his blood and bodily substances; would not have permitted these materials to be used by defendants solely for their independent research, commercial activity, and economic benefit; would have considered treatment at another medical facility where his wishes would have been carried out; and would have sought participation in the economic benefit.

The first court dismissed the case. The appellate court found that:

> The Protection of Human Subjects in Medical Experimentation Act, adopted m 1978, expresses a strong public policy that medical experimentation on human subjects "shall be undertaken with due respect **to the preciousness** of human life and the ***right of individuals to determine what is done to their own bodies" [Cal.*** Health & Safety Code 24171] [emphasis added]. . . . The essence of a property interest-the ultimate right of control--therefore exists with regard to one's own human body.

The **California** Supreme Court found in July 1990 that:

> Neither the Court of Appeals' opinion, the parties' briefs, nor our research ***discloses*** a case holding that a **person retains** a sufficient interest in excised cells to support a cause of action for conversion. . . . There are three reasons why it is inappropriate to impose liability for conversion based upon the allegations of Moore's complaint. First, a fair balancing of the relevant policy considerations counsels against extending the tort. Second, problems in this area are better suited to legislative resolution. Third, the tort of conversion is not necessary to protect patients' rights.

Rather than deciding on property rights over body tissues, the Supreme Court held:

> . . . that a physician who is seeking a patient's consent for a medical procedure must, in order to satisfy his fiduciary duty and to obtain the patient's informed consent, disclose personal interests unrelated to the patient's health, whether research or economic, that may affect his medical judgment.

This decision applies only to California Without congressional action or a ruling by the U.S. Supreme Court, State courts and legislatures are free to decide for themselves whether an individual who donates body tissue should be thought to own it or be able to profit from its use in the development of cell lines and other biologics.

SOURCES: Moore v. *Regents of tbe University of California,* 202 Cal. App.3d 1230,249 Cal. Rptr. 494 (1988), reh. granted, 252 Cal. Rptr. 816, 763 P.2d 479 (1988); Moore v. *Regents of the University of California, Supreme Court* of the State of California, case No. ***S006987, July 9,*** 1990.

entitled to profit from the fetal cell line, or would that constitute exploitation of the fetus?

It might be possible to prevent women who donate fetal tissue from profiting from cell line development, but what about allowing investigators to profit from the cell line? This, too, could be perceived as exploitation of the fetus. Also, denying the woman any profit from products of her own body but allowing others to-profit may be exploitative of and discriminatory against those women.

Waiving the consent requirement might be one way of avoiding these pitfalls. This would indicate that a woman does not have proprietary rights to the fetus and that a proxy donation is inappropriate in

this case. It might ensure that fetal tissue is not donated purely for personal profit and eliminate competition for women to donate their fetuses in order to profit. On the other hand, if consent is not obtained from women, this omission could be seen as denial of autonomy or exploitation. The recent *Moore* decision could make patients more reluctant to donate tissues and organs for research.

The question of ownership of fetal tissue used for CCLs will have to be addressed by State or Federal legislatures at some point. The fact that cell line development may be financially profitable complicates fetal tissue donation for scientific purposes. If a woman who undergoes an abortion donates fetal tissue for cell line development and profits from the cell line, it could be perceived as exploitation of the fetus. If she does not receive any payment from a commercially profitable cell line, but other persons do profit from it, it could be perceived as exploitation of both her and the fetus. If consent is not obtained from the woman, it may constitute a denial of her autonomy. Finally, if one believes that the individual from whom cells are obtained to start a CCL is the only one who should consent to this use, then consent should only be obtained from the fetus. Should fetal tissue cell lines be prohibited? Should the scientists who develop cell lines be denied the opportunity to profit financially from them? Are there justifications for using fetal tissue to start CCLs that make it unnecessary to decide whether fetal tissue ought to be considered property? These questions are only beginning to be addressed.

Genetic Manipulation of Cells Used for Grafting

Genetically modified cells have been used for neural grafting in animal experiments. The possibility of using them in humans raises the question of whether it is ethical to manipulate genes that would be passed on to future generations. As this debate has developed, it has become clear that somatic cell gene therapy (which modifies the DNA of certain differentiated cells in the body that cannot be passed to offspring) is relatively uncontroversial; it is germ cell gene therapy (which modifies undifferentiated cells that may later become gametes and thus may be passed to offspring) that creates concern (49). Genetic manipulation of CCLs for neural grafting would constitute somatic cell gene therapy and thus remove any possibility of inheritance.

Many of the fears expressed about genetic manipulation have to do with possible eugenic misuses—namely, the use of gene therapy to promote or exaggerate desired qualities in individuals rather than to correct anomalies that lead to illness. At this time it is difficult to see how gene therapy could be performed on cells for enhancement purposes: Not enough is known about the brain to design grafts that would improve particular physical or intellectual abilities. Instead, gene therapy might be used to design grafts that could alleviate specific neurological disorders in a host—by producing neurotrophic factors or neurotransmitters, for example. Grafts could be engineered to compensate for specific deficiencies in the recipient.

ISSUES RELATED TO GRAFT RECIPIENTS

Neural grafting also presents ethical issues related to the graft recipients. These ethical questions exist for any new procedure, but they may be especially pertinent to clinical (human) trials of neural grafting.

Federal law dictates that federally funded protocols must be sent to an Institutional Review Board (IRB) for approval of the legal and ethical features of protocol design [45 CFR 46], particularly features relating to treatment of research subjects. Of the seven criteria for IRB approval of research, two may pose problems for neural grafting research. These are the requirements that risks to subjects be reasonably comparable to the expected benefits and that the investigator obtain the subject's informed consent to participate in research.

Risks to Research Subjects

Risks **to** subjects are always difficult to determine at the beginning of clinical trials; it has been suggested that the lack of knowledge about how grafts work may make the risks associated with neural grafting particularly difficult to determine (27). The question that arises when anew therapy is presented for experimentation on human subjects is whether there is evidence that it promises significant benefit to the patient and does not present undue risk. This risk-benefit analysis is performed by several parties involved with the research protocol: the investigator, the IRB, and the prospective research subjects and their families.

Considerable debate surrounds the experimental use of fetal and adrenal tissue grafts to treat persons with Parkinson's disease (see ch. 5). In fact, some persons believe investigators had not gathered

enough data from animal studies to warrant progressing to clinical trials (22,36) and, therefore, may have been unable to meet their responsibilities to vulnerable human research subjects. Some persons claim that it is impossible for investigators or subjects involved in neural grafting research to balance risks and benefits unless they can estimate realistically what those benefits and risks will be. That claim, however, may be made of all clinical research (25). Some persons have argued that the patient undergoing neural grafting for the treatment of Parkinson's disease may be risking more than is justified if the graft is unsuccessful, if it is affected by the same neurodegenerative processes that made the graft necessary in the first place (19,27) [although it has been pointed out that the original degeneration in Parkinson's disease takes place over the course of several decades (5)], or if there is a delayed immunological response to the graft that proves more harmful than the disease.

Information should be obtained from the least possible amount of research conducted during the shortest possible period of time (9). The number of trials performed is another important consideration in protecting research subjects from unnecessary risks. Some observers suggest that controlled studies and pooled results from different locations may be the most efficient means of deriving data. This suggests single-protocol research pursued at multiple centers, formation of a comprehensive database, constant monitoring and interpreting of data, as well as constant updating of information given to subjects for informed consent (18). On the other hand, if neural grafting research on a particular disease is deemed an important public health priority, it might proceed more quickly and in accordance with diverse research protocols. In order for the transition to be made from clinical trials to therapeutic use in this case, many more patients will have to be enlisted as subjects; the human costs, as well as the medical and research costs, may be very high (18).

Informed Consent

One important ethical question is whether neural grafting protocols conform to standards of protection for research subjects. Since informed consent requires "[a] description of any reasonably foreseeable risks or discomforts to the subject [and] a description of any benefits to the subject or to others which may reasonably be expected from the research' [45 CFR 46.116], each patient must conduct a risk-benefit analysis of his or her own. This entails two kinds of information, the scientific and the personal (15). The first is made up of the objective data about the disease, alternative treatments, and social support systems and agencies; the second encompasses the subjective data related to the patient's experience.

The objective data for this analysis must be provided by the researcher. It should include the prognosis if the disease runs its course, the availability of alternative treatments, the fact that the procedure is experimental, the extent of uncertainty involved in the surgery, the intended and possible long-term outcomes of surgery, the availability of social support systems and agencies to aid recovery, and a thorough description of what the surgery will involve, including the pain and suffering likely to accompany the procedure and the immediate recovery from it, as well as risks of complications. The hard data will vary depending on the disease, the age of the patient, and the type of graft used.

The subjective data needed for a risk-benefit analysis can only come from the patient, for they involve the patient's perception of his or her quality of life. Quality of life is a concept that describes the experience of the individual, what kind of life is possible given the person's condition, and whether that condition will allow the individual to have a life that he or she views as worth living (23). There may be differences, however, between how a person perceives the quality of his or her own life, how an observer *assumes* he or she perceives the quality of his or her life, and how an observer *evaluates the* quality of that person's life (51). The severe physical and emotional suffering associated with neurological disease and injury are frequently thought to create poor quality of life, but it is important that patients have the freedom and medical information necessary to make their own quality of life evaluations.

The same conditions that depreciate the quality of life of individuals with neurological diseases and spinal cord injuries may make these persons especially susceptible to coercion. While the possibility of undue influence exists in any research situation, patients with neurological disorders may be especially vulnerable to judgments about their quality of life made by researchers or family members. One reason is that patients who have an apparently permanent injury or an incurable disease may be

tempted to try anything that might be of help. In many cases, there are few or no alternative treatments or support services for neurological disorders, and what treatments there are may have limited efficacy. For some patients, this lack of alternatives constitutes sufficient reason to participate in neural grafting research. A necessary condition for all research subjects, however, is that they be free to make uncoerced, informed choices.

Some patients with neurological injuries or disease may be incapable of performing the ethical cost-benefit analyses necessary for truly informed consent (6). In these cases, a patient may have to rely instead on the judgment of a family member or legal guardian. The proxy decisionmaker should attempt to evaluate the quality of the patient's life on the same basis the patient would have used. Open communication about what investigators and patients (or their proxies) perceive as the relevant factors in the decision to participate in research is necessary if a patient is to do a risk-benefit analysis without coercion. Given adequate scientific data by the researcher, the patient or proxy can predict more realistically what benefits the patient is likely to gain by undergoing neural grafting surgery.

Three factors make it difficult for investigators to give accurate information about the probable risks and benefits of neural grafting procedures. First, it is uncertain at this early stage of research what the risks and benefits of neural grafting are likely to be. Second, it maybe tempting for investigators to paint a more positive picture than is warranted because of their own high expectations. Finally, researchers may filter empirical evidence through their interpretations of the patient's current or future quality of life, rather than allowing patients to draw their own conclusions (18). These factors apply to all clinical research, but sensitivity to limitations may be especially important for neural grafting research. The solicitation of informed consent from neurological patients or their families must be done with their vulnerability in mind, making clear to the patient or family the degree of uncertainty for the experimental procedure. Although it is impossible in any research setting for a patient to be totally informed of risks and benefits, in the case of neural grafting it may be extremely important for patients to be aware of the scientific limitations at this time.

There may be reasons besides possible changes in quality of life for an individual to turn down the opportunity to receive a neural graft. For some subjects, neural grafting presents a chance for medical science to overcome disease; but for others, neural grafting may present a threat to personal identity and sense of self, aspects of the human mind that are, to some persons, the very essence of humanity (18). The ability to do neural grafting raises questions about whether the mind can be explained in terms of the brain. It is difficult to know what physical functions of the brain define a person's existence as a unique individual or are essential to the retention of his or her personal identity across time. Consequently, some would argue, there is no way to predict the extent to which neural grafting in the brain will or will not interfere with the functions of the mind that determine individuality, personhood, or a sense of self. These are metaphysical questions rather than ethical ones, but they are important considerations for persons in a position to receive neural grafts.

SUMMARY AND CONCLUSIONS

Neural grafting includes a variety of materials and surgical procedures used to investigate and treat a number of neurological disorders. As the grafting materials and techniques viny, so do the ethical issues surrounding them. Whether the Federal Government becomes involved in funding or regulating fetal tissue grafting or not, research in fetal tissue transplantation continues.

Some of the ethical issues surrounding neural grafting are common to any new area of biomedical research or treatment. They include whether to use public funds to support neural grafting research or neural grafting as a standard medical treatment. They also include economic questions about how to establish health-care priorities and how to allocate resources for research.

There are currently few alternative treatments for neurological disorders. Some persons feel that, because neural grafting is an exciting and possibly profitable area of research, it may get more support than alternatives and reduce the impetus to find less expensive, less risky, and less controversial treatments for neurological disorders (38). Decreased support for neural grafting research, however, does not necessarily make funds available for research into other treatments for neurological disease and injury (12). In order to resolve some of the questions about fair distribution of resources, it might be

helpful to evaluate neural grafting in relation to treatments for other diseases and other treatments for neurological disorders, keeping in mind the priorities set and the amount of research funded. In order to make decisions about funding neural grafting research, it will be necessary to estimate the efficacy of the technology, the number of people now affected by neurological disorders, and the number of people likely to be affected in the future.

Ethical issues arising from the surgical procedures and the materials used in the neural grafting process also demand attention. Some of these issues are analogous to issues that have been dealt with already and are reflected in Federal regulations; e.g., informed consent and the protection of research subjects were addressed in the 1970s. Existing regulations, however, may not adequately protect neural graft recipients from the risks unique to brain implantation surgery. The possibility of doing a sufficient risk-benefit analysis has been challenged on the grounds that not enough animal research has been done to know what the benefits of neural grafting are likely to be. Obtaining informed consent from persons with neurological disease may be difficult, both because the risks and benefits cannot be realistically estimated at this time and because of the possible cognitive limitations of persons with some neurological disorders.

On the other hand, there are several reasons why the Federal Government should not involve itself in surgical development. Research risks to the subject are almost always unknown in early clinical trials (24). Furthermore, much surgical innovation, including neural grafting, is therapeutic as well as experimental (25) and, therefore, may be more likely to hold the promise of benefit for the subject [although some commentators have called "therapeutic research" an oxymoron (46)]. Neural grafting investigators should conduct research in a noncoercive manner consistent with the treatment of other research subjects. While it is important for persons developing new surgical techniques to be aware of moral considerations, ethical and practical arguments may be made for allowing, even encouraging, such innovation.

Thus far, the greatest ethical controversy surrounds the use of fetal tissue from elective abortions for neural grafting. Positions taken on the morality of fetal tissue grafting, however, do not depend strictly on a person's beliefs about the morality of elective abortion. Both supporters and opponents of abortion have articulated reasons for denying funding for fetal tissue grafting research, and both have identified reasons for providing it. Tissue from spontaneous abortions, ectopic pregnancies (42), and fetal tissue cell lines have been suggested as ethically acceptable alternatives.

Many different positions are taken regarding the ethics of using fetal tissue obtained from elective abortions for neural grafting. Some of these considerations include the implications of a public policy that either supports or restricts the use of aborted fetal tissue for grafting and the possible consequences of such a policy. It has been suggested that using electively aborted fetal tissue for neural grafting will both harm individual fetuses and deny fetuses respect. It has also been suggested that groups besides fetuses-e. g., women and society at large-may be adversely affected by a policy that endorses fetal tissue transplantation. A number of the arguments against fetal tissue transplantation are based on predictions about its future social effects. While it is important to anticipate potential problems, it is impossible to know at this time whether the consequences predicted will come to pass.

Some persons believe that once a fetus is dead, it no longer has interests to protect and that it is inappropriate for the Federal Government to withhold funding for research that may benefit many sufferers of neurological disorders. A number of groups in the United States and abroad have proposed safeguards for protecting social values and vulnerable groups, while allowing biomedical science to move forward (32,48,54,55) (see app. A, box A-2). It has been suggested that these protections would be most effective with Federal involvement in the research process (4,47). Despite the similarities of the safeguards recognized by the various study groups and the fact that both existing DHHS regulations and Federal laws already implement many of the suggested guidelines (58), some persons remain skeptical about the feasibility of implementing these measures.

The solicitation of consent for the use of tissue from cadaveric fetuses presents another ethical question. Controversy exists about whether the woman who elects the abortion is the appropriate person to give consent and when consent should be solicited. Both the regulations for the protection of research subjects and those for the donation of

cadaveric body parts can help in determiningg the appropriate donor of electively aborted fetal tissue, but these regulations do not explicitly cover the donation of fetal tissue for transplantation research.

The use of fetal tissue to start continuous cell lines further complicates the issue of consent, because questions are raised about whether the donor of tissue used to start a CCL may profit financially from it. Although it maybe deemed appropriate for a woman who aborts to give her consent to use of fetal tissue, it may not be considered appropriate for her to profit financially. While questions regarding the ownership of tissues used for commercially profitable cell lines are being addressed by the courts, discussion has been limited to the ownership of adult tissues. Questions pertaining to the proper treatment of fetal tissue remain unanswered.

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