NEURAL FETAL TISSUE TRANSPLANTS: OLD AND NEW ISSUES

by Lois Margaret Nora and Mary B. Mahowald

Abstract. Neural fetal tissue transplantation offers promise as a treatment for devasting neurologic conditions such as Parkinson's disease. Two types of issues arise from this procedure: those associated with the use of fetuses, and those associated with the use of neural tissue. The former issues have been examined in many forums; the latter have not. This paper reviews issues and arguments raised by the use of fetal tissue in general, but focuses on the implications of the use of neural tissue for basic concepts of personhood and personal identity.

Keywords: abortion; fetal tissue; individuation; medical ethics; mind/brain; neural fetal tissue; personhood; tissue transplantation.

Although human fetal tissue has been used for research and therapy for many years, transplantation of neural fetal tissue for treatment of neurological disorders is relatively new. The preliminary results of neural fetal tissue transplantation (NFTT) for treatment of certain neurologic conditions are encouraging, but the treatment is still experimental (Kordower et al. 1995; Freed et al. 1992). As uses for neural fetal tissue expand, neuroscentists will be called upon to reconsider the ethical questions raised by fetal tissue transplantation (FTT) for themselves, for the laboratories they direct, and for the patients they treat. In addition, characteristics of certain neural tissues, particularly those of the cerebral cortex, present novel philosophical and ethical questions. Both old and

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[*Zygon*, vol. 31, no. 4 (December 1996).]
 ISSN 0591-2385

new questions deserve careful consideration by those directly involved and by the public-at-large.

This article addresses transplantation of neural fetal tissue from four perspectives. First, we review the scientific and medical reasons for use of fetal tissue, along with the recent history of its use for treatment of neurological disorders. Second, we survey the ethical issues that have surfaced in the debate about NFTT but also are applicable to FTT of all types. Third, we consider how our expanding knowledge of neurodevelopment and the particular characteristics of neural tissue impact the discussion of FTT in general, and NFTT specifically. Finally, we examine some of the basic questions of personhood, identity, and responsibility that arise in the context of neural tissue transplants.

SECTION 1: THE UNIQUE INTEREST IN, AND STRANGE POLITICAL HISTORY OF, FETAL TISSUE TRANSPLANTATION

Tissue and organ transplantation for therapeutic reasons has long been part of the medical armamentarium. Live donor supplies of nonvital, self-replenishing body fluids (e.g., blood, semen) have been available for many years. Corneal transplants harvested from deceased donors were performed in the early 1900s, and the first live-donor kidney transplant was performed in 1954 (Scott 1981, 19). The success of early efforts at transplantation was stymied, however, by several factors. These included concern about the effect of the procedure on the donor, technical factors associated with the surgery, and most significantly, serious medical complications related to incompatability between the donated body part and the recipient. Differing immunologic systems can lead to rejection of transplanted tissue by the recipient. Even worse, the transplanted organ can reject the recipient in a phenomenon known as graft vs. host disease. Attempts to minimize and avoid these complications include careful matching of donor and recipient, and use of immunosuppressive agents. Although new immunosuppressive agents markedly decrease rejection rates, they are generally costly and have significant side effects.

Such difficulties highlight the attractiveness of the use of fetal tissue in transplantation (Crombleholme et al. 1994, 218). Virtually all published positions on the issue of fetal tissue transplantation, as well as state and federal laws, require that the fetus be dead prior to harvesting; being already dead, the fetus experiences no additional risks through harvesting. In addition, the technical aspects of fetal tissue retrieval and handling are less complicated than those faced with solid organ donation from either a living or cadaver donor. The desired fetal tissue is identified microscopically, separated from the remaining fetal body parts, and placed in suspension. Operating suites, large surgical teams, extended

preoperative and postoperative care, and complex modes of handling are unnecessary. Similarly, transplantation of fetal cells into a recipient is less complicated than most organ transplant procedures. Fetal tissue is usually transplanted by injecting the fetal cells into the recipient's host organ, using surgical techniques that are simpler and less risky than those used with whole organ transplantation.

Unlike mature tissue, human fetal tissue is unlikely to be rejected by a recipient or precipitate graft vs. host disease. In general, human tissue is characterized by immunologic markers or proteins on the tissue that are unique to a particular individual. The immunologic markers in donor and recipient tissue account for the rejection phenomenon. Attempts to minimize rejection include matching the immunologic markers of donors and recipients as closely as possible, and using drugs to suppress or modify the ability of either donor or recipient tissue to recognize and attack foreign immunologic markers. Prior to twelve weeks of life, fetal tissue lacks these immunologic markers. Fetal tissue is thus readily accepted by the recipient, and rejection does not occur.

Additional advantages of fetal tissue are its relative lack of differentiation, pluripotentiality (i.e., ability of tissues to develop into multiple different cell types), and rapid growth rate. These factors contribute to rapid and successful development of the fetal graft in the recipient. The more mature the fetus from whom tissue is obtained, the less likely it is that these characteristics will contribute to the success of the transplant procedure.

The special characteristics of fetal tissue have led to its use for a variety of research and therapeutic purposes over the past two generations. Attempts to transplant human fetal tissue date from the 1920s, and human fetal tissue was used in the development of the polio vaccine in the 1950s (Mahowald 1993a). Grafts of human fetal thymus have been considered standard therapy for the treatment of DiGeorge syndrome since 1968 (Vawter et al. 1990). Conditions for which research on neural fetal tissue therapy is currently pursued include Alzheimer's disease, multiple sclerosis, Huntington's disease, and central nervous system trauma (U.S. Congress, Office of Technology Assessment 1990, 93).

Prior to the 1970s, use of fetal tissue for research and therapy engendered little comment or debate. Following the Roe v. Wade decision of 1973, however, public debate about abortion evoked concerns that fetal tissue used for transplantation might be obtained through elective abortions. Debate surfaced in the 1980s in the context of ongoing basic research in neural fetal tissue transplantation and the first clinical attempts to use neural fetal tissue as therapy for Parkinson's disease (Mahowald et al. 1987, 1307; Mahowald, Silver, and Ratcheson 1987, 9). The controversy surrounding the use of neural fetal tissue initially

centered on abortion, virtually ignoring concerns not previously articulated, namely, those related to the special characteristics of neural tissue and the philosophical implications of its use.

In an attempt to proactively identify issues and provide guidance, a group of ethicists, practitioners, and governmental and public representatives came together in Cleveland in 1986 to examine the topic of neural fetal transplantation and produce a consensus statement (Mahowald et al. 1987, 1307). The following year, a grant application to the National Institutes of Health (NIH) for neural fetal tissue research resulted in the assistant secretary of health issuing a moratorium on federal funding of research involving fetal tissue (U.S. Department of Health and Human Services 1988). At the same time, an NIH advisory panel was convened and charged with examining the ethical issues involved in fetal tissue research and advising the NIH about the possibility of government funding for such research.

In December 1988, the *Report of the Human Fetal Tissue Transplantation Research Panel* was published (Consultants to the Advisory Committee to the Director 1988). This report, approved by an 18–3 majority of panel members, concluded that neural fetal tissue transplantation (NFTT) is an appropriate application of governmental research funds and advised that federal funding of the research be allowed with certain restraints. The majority based its opinion, in part, on the assumption that the issues of elective abortion and fetal tissue transplantation are ethically separable. The minority opinion passionately disagreed with this position.

The Secretary of Health and Human Services rejected the advisory panel's recommendations and indefinitely extended the moratorium on federal funding of fetal tissue transplantation. Despite recommendations by the Cleveland Group and the Stanford University Medical Center ethics committee that were similar to those of the NIH advisory panel, and outcries from some members of the scientific and ethics communities, this position was not changed for several years (Greely et al. 1992). Various legislative maneuvers to reinstate funding were attempted, all without success.

During this federal moratorium, privately funded fetal research and therapy continued both in the United States and elsewhere. A panoply of state laws, most incorporating some variation of the Uniform Anatomical Gift Act (UAGA), allowed fetal tissue donations in some form. Since the moratorium on funding fetal tissue research was rescinded by executive order of the U.S. President, applications to the NIH for fetal tissue research funding have increased. The United States administration has rejected the possibility of embryos being produced solely for the purpose of fetal tissue research (Parens 1995).

SECTION 2. GENERAL ETHICAL ISSUES RELATED TO FETAL TISSUE TRANSPLANTATION

Because many ethical issues that arise in NFTT are the same as those presented by FTT in general, a brief review of these concerns is valuable. The ethical issues related to FTT are of two types: those related to obtaining tissue and those related to subsequent use of the tissue.

Ethical Issues Related to Obtaining Tissue. Much of the ethical debate about FTT stems from its relationship to elective nontherapeutic abortions, i.e., abortions induced for reasons other than the health of the pregnant woman or fetus. Issues raised in this context include consent for the use of fetal tissue, possible complicity in abortion by those involved in FTT, potential incentives for abortion, alterations in abortion timing and methods for nonmedical reasons, and recruitment of the research community into the abortion debate (Mahowald, Silver, and Ratcheson 1987, 9; Strong 1991; Hurd 1992; Post 1991; Burtchaell 1988; Robertson 1990; Shorr 1994).

Who consents to the use of tissue harvested from an aborted fetus? Our society's emphasis on autonomy leads us to expect that, in general, informed consent is obtained from competent individuals prior to use of their tissues. Accordingly, we have created a panoply of legal mechanisms to mimic consent when tissue is sought from an incompetent individual. The fetus, of course, is incompetent both legally and practically. We may look, then, to the possibility of surrogate decision-making as a mechanism for obtaining consent.

When a surrogate makes a decision on behalf of an incompetent person, he or she is expected to follow a standard of substituted judgment. This means that the surrogate should attempt to ascertain what decision the incompetent individual would have made and articulate that decision. When this standard cannot be followed, the surrogate is expected to act in accordance with what he or she believes is in the best interest of the incompetent individual. Since substituted judgement on the fetus's behalf is impossible, the surrogate decision maker is expected to act in the best interest of the fetus.

Who should be the surrogate decision maker for the fetus? Women who intend to continue their pregnancies generally are considered the most appropriate surrogates to provide consent for or to reject medical interventions on behalf of their fetuses. Some maintain, however, that a woman who chooses abortion demonstrates through that choice that she is not acting in the best interest of the fetus. Through her consent to abortion of the fetus, she may thereby forfeit her right to serve as a surrogate in behalf of the fetus.

The position of the NIH advisory council, as reflected by many

commentators, is that the pregnant woman remains the most appropriate person to give consent in this setting. One argument supporting this position is that fetal remains are tissue from the woman and should be disposed of through the same mode of consent as is applicable to other tissue. An additional supportive argument is that this practice is most in line with societal practice and laws such as the Uniform Anatomical Gift Act.

The issue of complicity received a great deal of heated attention in the debate about FTT and abortion (Strong 1991; Burtchaell 1988; Robertson 1990). Some, for example, have argued that participation in any aspect of FTT implies a degree of responsibility for the elective abortions through which the tissue became available. Two general responses to charges of complicity in abortion by participation in FTT have been articulated. The first response, taken by the NIH advisory panel majority in 1988, rejects the proposition outright. Abortion and tissue retrieval, the panel asserts, are morally separable actions. The analogy that has been offered in support of this view is that the use of organs from someone who has been killed in an accident precipitated by drunk driving does not constitute complicity in the act of drunk driving.

The second response accepts the proposition that some degree of complicity occurs in this setting. On such grounds, it has been argued that practitioners may refuse to participate in FTT and that institutional policies about FTT should allow this refusal. It may concomitantly be the case, however, that the degree of complicity does not justify abandoning potentially lifesaving therapies. In fact, some who accept a degree of complicity maintain that despite its association with the morally questionable or wrong practice of abortion, transplantation of fetal tissue constitutes a good that we may be morally obligated to pursue (Strong 1991).

Regarding the potential of FTT to serve as an abortion incentive, a spectrum of examples is possible. At one end is the woman who conceives in order to provide fetal tissue either for profit or for the benefit of a loved one. At the other end is the woman who agonizes over an abortion decision and is swayed somewhat by the thought that "at least some good would come out of a decision to abort." Between these extremes are many possible scenarios of mixed motives.

Checks, balances, and disincentives have been built into FTT policies in response to these concerns. These include insistence on separation of abortion and retrieval decisions and procedures, prohibition of commercial use of fetal tissue, and preservation of anonymity between donor and recipient. Such restrictions are surely defensible and have been broadly accepted, but they remain challengeable. It is not certain, for example, that abortion and retrieval procedures are empirically separable, and

organ and tissue banks have been functioning legitimately for many years. The basis for challenging the requirement of anonymity arises from its analogy with directed donation of organs from living related as well as deceased donors.

Despite its legality, the moral appropriateness of informed consent for FTT from women who undergo elective nontherapeutic abortions may still be questioned. Nonetheless, beyond the requirements noted above, women considering FTT also should be informed of confidentiality issues, testing procedures, and other aspects of the procedure relevant to their decisions. For example, HIV tests are routinely done on fetal tissue considered for transplantation purposes. An HIV test on fetal tissue is essentially a test of the woman as well because it identifies her HIV status. Informed consent and counseling for the test must be part of the procedure for obtaining fetal tissue.

FTT procedures also raise concerns about the timing and the manner of abortion. A woman might be encouraged to schedule an abortion sooner or later than she would otherwise schedule it to ensure that the desired tissue has reached and not surpassed the level of development optimal for successful transplantation. Similarly, certain abortion techniques may be proposed as preferable to others in order to obtain fetal tissues of a certain type or quality without full explanation of alternative methods of abortion and the various risks and benefits of each. A variety of incentives and disincentives for abortions of certain types and different timing may be provided with little regard to the women involved. As yet, however, no instances in which timing or method of abortion has been altered to facilitate effective transplantation have been reported.

Some critics have raised concerns that FTT creates a publicly funded incentive for the research community to accept and promote abortion. Despite its legality, society is far from consensus on the morality of abortion and related issues. If salaries, tenure, and professional advancement require the continued availability of fetal tissue for research, the biomedical community may enter the debate with reasoning that stems more from personal and financial incentives than from careful analysis of the ethical issues related to the practices. The research community could, in fact, become a tool in the political debate.

A final FTT issue that must be revisited is whether or not sufficient fetal tissue of high enough quality can be retrieved from spontaneous abortions and ectopic pregnancies. The definitive answer to this question is unknown but hotly debated (Garry et al. 1992; Fung and Lo 1990; Branch et al. 1995). As the Stanford Ethics Committee noted, *if* tissue can be obtained in these ways it may be ethically preferable to do so. On the other hand, if tissue obtained through these means is substandard, such use may violate our ethical obligations to the recipients.

To the extent that this question remains unanswered, our current responsibility is to attempt to determine whether or not ectopic pregnancies and spontaneous abortions provide an effective, sufficient source of tissue for research and therapy. If the answer is yes, or if technological advances in fetal tissue culture and cell line development eventually make use of tissue obtained in these less problematic ways possible, we should use this tissue. If the answer is no, the argument in support of retrieval of fetal tissue obtained through elective abortions is thereby strengthened.

Ethical Issues Related to the Use of Fetal Tissue. Clearly the majority of ethical issues related to FTT arise in connection with the harvesting of tissue. Abortion remains the spark that ignites fiery debates on the moral and legal parameters of tissue retrieval. Yet significant issues also surround the use of fetal tissue. (Sanders et al. 1993). Despite progress in research, FTT remains mainly an experimental procedure that as such evokes the same concerns addressed in the development of other therapies.

A basic question is whether or not the use of fetal tissue constitutes therapy or research. In some arenas, such as the use of fetal thymus in DiGeorge's syndrome, FTT is clearly therapeutic because it has proved an effective treatment for many years. On the other hand, fetal tissue grafting in Parkinson's disease is still in the research stage. In general, vulnerable patients should not be research subjects without their consent, and research should not be labeled as therapy prematurely. One advantage of requiring public funding for FTT is the increased rigor to which it is thereby subjected, i.e., by having to meet the ethical requirements of institutional and government review boards.

Beyond concerns about fetuses and recipients, concerns about commodification of women, possible exploitation of poor women, and establishment of a donor class also may be voiced. These become more worrisome to the extent that FTT becomes a profitable as well as a healing enterprise. Many of these concerns are similar to those raised in arguments about surrogate gestation and merit careful attention as the debate continues (Mahowald 1993b, 102–10; Newton 1988).

A final issue to be discussed is the cost of NFTT and its potential benefits. The estimated total costs for a single research protocol patient undergoing transplantation of fetal tissue for Parkinson's disease is over two hundred thousand dollars (personal discussion with C. Goetz). With the moratorium on research funding lifted, increasing amounts of federal dollars will be devoted to this area. In an era of rationing, the costs and benefits to society of this research and therapy must be evaluated, particularly if public dollars are used to fund it.

SECTION 3. NEURODEVELOPMENT OF THE FETUS AND ETHICAL IMPLICATIONS

Although many ethical issues in NFTT are identical with those raised by other forms of FTT, one element is quite unique: the fact that the transplantation involves neural tissue. Neural tissue is critically linked to those abilities and qualities that we value most as human beings. Humans are like other species in that neural tissue controls their automatic bodily functions, senses their external and internal environments, and integrates and responds to information. But unlike other species (as far as we can tell), the neural tissue of human beings also allows us to create, think abstract thoughts, use symbolic language, and modify our environment in multiple complex ways.

Anatomically, the human nervous system is divided into three parts: the central nervous system (CNS), the peripheral nervous system (PNS), and the autonomic nervous system (ANS) (Netter 1983). The central nervous system (CNS) is made up of the brain and spinal cord. The brain includes the cerebral hemispheres and the brain stem. The cerebral hemispheres include cortical tissue, subcortical nuclei, and abundant tracts and connections. The cerebral hemispheres are considered the seat of high-order thinking and provide humans with the ability to engage in abstract thought.

The peripheral nervous system (PNS) is made up of the spinal nerves and most cranial nerves, elements that lie anatomically outside the CNS. The PNS includes a variety of sensory receptors, sensory nerves, motor nerves, and interneurons that modulate the functioning of the sensory and motor nerves. The autonomic nervous system (ANS) is housed in both the CNS and PNS. The ANS controls the automatic functions of our bodies, including heartbeat, reflexive sexual responses, and the body's "fight or flight" response to threat.

Human prenatal development is divided into several periods. The first begins at fertilization and continues until the middle of the second week of development. During this time, the developing human organism is called a preimplantation embryo. After implantation of the blastocyst occurs, the embryonic disc is formed and the developing human is called an embryo. (Some writers use the term *embryo* for the preimplantation embryo as well.)

The embryonic period of development extends from the middle of the second week after fertilization until the end of the eighth week. This is a period of remarkable growth and differentiation of tissues. By the end of the embryonic period, the identifiable beginnings of all the organ systems are present. The developing human is then considered a fetus. Fetal development extends from the end of the eighth week following fertilization until birth. This is a period of further differentiation of the

various organ systems and further remarkable growth.

Neural development begins soon after fertilization (Moore and Persaud 1993; Korein 1990). The neural plate, an embryonic structure that first appears at about day eighteen, is the precursor of the neural folds and the neural crest. The neural folds develop into the CNS; the neural crest develops into a number of tissues, including the PNS.

By the fourth week of development, the three primary brain vesicles have formed, and by week five, the five secondary brain vesicles are identifiable. One of these vesicles, the telencephalon, includes those tissues that become the cerebral hemispheres. By the sixth week of development, the beginnings of the major connection between the two hemispheres have appeared. By eight weeks after fertilization, the spinal cord and brain stem are present with functional neurons and synapses (connections).

The telencephalic vesicles are recognizable as the cerebral hemispheres by the end of three months of development. In addition, by this time each hemisphere has further developed into three functionally different parts. One of these, the suprastriatum, is not present at all in the lower vertebrates, but becomes the most prominent portion of the telencephalon in humans. This is the portion of the brain that constitutes the cerebral cortex and its underlying white matter, that is, the portion of the nervous system responsible for the characteristics that human beings seem to value most.

Despite continuing development of neurons and the cerebral hemispheres, no discernible cortical activity is noted until around twenty weeks' gestation. As far as we can tell, the developing embryo or fetus has no capacity for awareness of self, pain, mentation, emotions, learning, or attention, let alone more complex information processing, during this time. Around twenty weeks, however, concurrent with ongoing cortical layering and differentiation, the fetus becomes sentient. The fetus is increasingly capable of experiencing the environment at this time (Anand and Hickey 1987, 1322; Korein 1990). Although this level of functioning is quite primitive compared to the capabilities that develop later, it represents a dramatic shift in fetal capability and arguably increases the obligations of others to the fetus.

Gestation is a time of increasing neural cells and expanding brain function. By the end of the sixth month of fetal life, almost all of the nervous system cells that will ever exist in the individual are present. Although the number of neural cells does not increase after birth, there is continued neural development for many years. For example, dendritic connections between neurons are initiated during fetal development but continue to develop in infancy.

Normal aging is accompanied by variable loss in cerebral functioning

associated with cell death. A variety of pathologic conditions, including stroke, dementia, seizures, and tumor, also may cause neural cell dysfunction or death and associated changes in the unique capacities that separate humans from other species. New evidence suggests that some precursor cells may remain in the brain, capable of differentiating into neurons throughout an individual's lifetime (Kirschenbaum et al. 1994).

What, if anything, does the process of neurodevelopment over a lifetime tell us about fetuses, their capacity to be tissue donors, and our responsibilities to them? What are the implications of this information for definition of life, humanness, personhood, personal identity, and death? And do the answers to these questions have specific implications for our responsibilities to the fetus, whether we do FTT, and whether or not we treat NFTT differently than other forms of FTT?

Although contemporary philosophers still debate the relationship between mind and brain, acknowledgment of the central role of cognition or rationality in defining human beings as such is longstanding. Plato and Aristotle are the obvious classical exemplars of this view, but it threads through medieval and modern philosophy as well. In recent years, there has been an increasing tendency to frame this discussion in terms of those individuals who are human (implying membership in a particular species) and individuals who are persons. Identification as a "person" generally confers a right to life and greater claim on the resources of others. Because cognition and rationality are characteristics that depend upon functioning of certain neural tissues, this debate occurs again in the setting of NFTT.

Criteria for personhood in the developing human organism have been proposed and defended by authors whose views are both minimally and maximally demanding. These views create a spectrum of possibilities of when personhood should be recognized. One example of the minimalist approach is offered by John Noonan (Noonan 1970, 51). Noonan argues that a right to life begins at fertilization through conception by human parents. He says that genetic identity and species membership as human confers personhood. He does not distinguish between persons and humans. Noonan says that being human confers the same status and protection as that of a person, either because persons and humans are the same thing or because potential persons merit the same protection as actual persons.

Less minimalist than Noonan, Norman Ford regards individuation rather than genetic distinctness as essential to personhood (Ford 1988, 75–79). For about two weeks after fertilization, fertilized ova may split into several genetically identical embryos (which then develop into twins, triplets, or another grouping of individuals), and genetically identical but separate cells may fuse into one. For Ford, personhood does

not begin until this possibility of division or recombination is settled, i.e., when the number of new individuals who will continue to develop has been determined. A similar approach has been used by the NIH Human Embryo Research Panel, which recently recommended approval of research on preimplanted human embryos before the fourteenth day after fertilization (Parens 1995, 36). The panel offered the absence of developmental individuation as a reason why the moral status of these embryos should be considered less compelling than that of infants.

Noonan and Ford do not require brain activity or, in fact, neural activity of any sort as a prerequisite for embryonic or fetal personhood. However, brain activity is essential to others' definitions of the point at which personhood begins. J. Korein describes brain life as beginning when the cerebral-reticular system attains its fundamental structural functional complexity in its most incipient form (Korein 1990). The cerebral-reticular complex is constructed during the tenth through twentieth weeks of fetal gestation, and further refinement occurs between the twentieth and thirtieth weeks. Korein uses this information to identify twenty weeks as the minimal age at which brain life has its start in human beings.

Hans-Martin Sass argues for a two-phase definition of "brain birth" (Sass 1989). The first phase occurs when there is clear biological development of the brain as a distinct organ. This corresponds to the eighteenth day after fertilization, when the neural plate has formed. The second phase of brain birth occurs at about the seventieth day after fertilization, when synapses allowing neuronal cross-talk between cortical tissues are formed. Sass places fetal "personhood" between the two dates at about the fifty-fourth day after fertilization, when postmitotic stationary neurons begin to form at the cortical plate.

Both Korein and Sass propose identifying brain life with human life, and the onset of brain functioning (albeit different levels of brain functioning) as the onset of our societal responsibilities to fetuses as persons. The fetus may, they would argue, be a *human* before this, but not a person. Until it reaches this point of development, the fetus is not entitled to the same considerations that a person would receive.

Further along on the minimalist-maximalist spectrum are a variety of opinions that demand increasing levels of capability prior to recognizing the personhood of an individual. Those who articulate the most demanding criteria include Fletcher, Warren, and Tooley (Fletcher 1979, 7–18; Warren 1984, 102–19; Tooley 1984, 120–34). None of these commentators would confer a right to life on a human entity until significant cortical functioning occurs. In fact, their criteria include an awareness of self and ability to relate to others, which are only observable sometime after birth. An anencephalic infant would never meet their

criteria for personhood. Some severely autistic and retarded individuals might similarly never attain personhood under these criteria.

In a related approach, Peter Singer defines the onset of responsibility *to other living beings* (defined more broadly to include nonhuman beings as well as humans) as when sentience is achieved by the developing organism (Singer 1994, 58). The capacity to experience pain, as we have seen, occurs sometime during the last half of fetal development. Singer's proposed responsibilities do not necessarily grant a right to life to the sentient organism but rather a responsibility on the part of moral agents not to inflict pain.

What implications do these approaches have for fetal tissue transplantation? All of the positions described, with the exception of Noonan's, could be used to permit abortion at some point in fetal development based on lack of personhood. It should be noted that the application of minimalist criteria for personhood does not necessarily preclude a conclusion that abortion is justified. For example, one who defines an embryo or fetus as a person might still recognize a woman's right to make abortion decisions.

Any approach that distinguishes between humanhood and personhood and then denies personhood prior to a specific stage of neural development is unlikely to disallow NFTT prior to that stage. Until personhood is attained, there is nothing unique about neural tissue compared to other tissues that make it more or less accessible, from a moral or philosophical perspective, for harvesting.

Perhaps more important, those who apply maximalist approaches to defining personhood might allow tissue harvesting from living fetuses. If the fetus is a nonperson, it is unlikely that it merits consideration greater than one would grant to another living organism. Certain approaches may include proscriptions against causing pain to sentient fetuses and damaging a fetus in any way that would injure the later-born infant. As noted above, donation from living fetuses is not currently contemplated in any of the consensus statements or positions articulated on this topic. Nonetheless, definitions of personhood may be critical to the next stage of the debate.

Other concerns arise about the implications of definitions of personhood that require higher levels of brain development and cortical activity as well as increasing degrees of social activity. By such criteria, some living human beings never attain the status of person because of anencephaly, congenital abnormalities, and even birth injury. Viewed as nonpersons, these individuals might be viewed as ready sources of organs and other spare parts or even as experimental subjects. To put the issue in Kantian terms, such human beings would then be treated as means rather than ends.

Similar implications apply to persons who lose the capacities that define personhood. Patients with severe dementia or those in persistent vegetative state serve as examples. An individual in a vegetative state has no awareness of self or the environment and no ability to interact with his or her environment. In many instances this state becomes permanent, which means that there is essentially no hope for recovery of cognitive function or awareness. Maximal definitions of personhood would diminish responsibility to such humans. In addition, because of their potential for neural development, it may be argued that human fetuses have a more compelling claim to scarce resources than those whose cognitive and interactive capacities are not recoverable.

SECTION 4. IMPLICATIONS OF NEURAL FETAL TISSUE TRANSPLANTATION FOR TISSUE RECIPIENTS

If an individual's personhood is defined by his or her neural development and functioning, concerns about personhood in the NFTT context extend far beyond issues of whether and how the procedure is done. Speculation about personal identity and changes in personal identity related to tissue and organ transplantation have been the stuff of novels (e.g., *Frankenstein*) and movies (e.g., *The Hand*) for years. While fictional imagery is entertaining, documented instances of changed perceptions, behaviors, and personalities accompanying transplant surgery (of neural as well as nonneural tissue) are more convincing (Warren 1964; Lewin 1988, 879). Yet reported instances of altered pain thresholds, delusions, and frank hallucinosis are poorly understood, and ignorance in this regard tends to impede our understanding of personal identity.

Personal identity seems to be driven by factors both internal and external to the individual, and the importance of external or social factors should not be minimized. For example, public acceptance of biomedical technology involving transplantation from living or deceased human donors is currently widespread. This has not always been the case. When heart transplants were first proposed, some viewed the prospect with alarm because the heart symbolizes the affective lives of persons. This social response impacted how heart transplant recipients viewed themselves and were viewed by others. In time, society recognized that, despite its metaphorical uses, the human heart is functionally equivalent to a pump, sustaining life without influencing affectivity or individual identity.

Most neural tissues do not raise concerns about the personal identity of either the donor or recipient. This is because the tissues themselves have no real role, or even a socially recognized metaphorical role, in establishing or maintaining personal identity. For example, the spinal

cord is for practical purposes a superhighway for the nervous system, and the brain stem controls a variety of involuntary physiologic functions. As important as both the spinal cord and the brain stem are to human functioning, they do not raise issues of personal identity in any way different from other critical organs or tissues such as kidney, heart, or bone marrow.

In comparison with other organs, the brain—particularly the cortex—is unique because it is not simply perceived as, but, in fact, is essential to abstract thought and other cognitive activities that define humans as distinct from other species and from one another. In a very practical sense, NFTT could affect personal behavior of the individual in much the same way as other organ transplants or medical therapies do. For example, in the case of a successful transplant, the patient who otherwise might have been immobile, uncommunicative, and unable to participate in his or her community may be transformed into an individual who fully participates and contributes, whether positively, negatively, or both. Even in the case of a failed attempt at transplant therapy, the patient has been changed by the experience.

Given the particular characteristics of neural tissue and specifically cortical tissue, we must ask ourselves whether there are changes not only in behavior and experience but in one's fundamental identity as a person. Do grafts of neural tissue have the potential to thus radically alter the recipient? Do neural grafts involve the possibility that a critical part of a unique fetus may live and develop into personhood? Do the answers to these questions differ depending upon how much tissue is transplanted, from where in the nervous system it is taken, from how many fetuses it is taken, where in the recipient it is placed, and how much of the recipient's original nervous system remains unaffected?

One can imagine a number of scenarios in which concerns of personal identity might arise with neural transplantation. Consider the following possibilities:

1. Tissue is harvested from the cortex or another part of the brain involved in cognition and self awareness
2. Neural tissue is transplanted into the cortex or area of the brain that is involved in the recipient's cognition or self-awareness
3. The amount or type of neural tissue transplanted will be more than, or the effect of transplanted neural tissue will overcome the effect of, the recipient's own remaining neural tissue

Combinations of these scenarios also may occur.

Green and Wikler claim that whole brain transplantation involving no alteration or destruction of brain processes would preserve the donor's personal identity within the recipient, thus transforming or

replacing the recipient's previous identity (Green and Wikler 1980). In fact, this seems to us unlikely. Personal identity surely is the result of multiple factors, including genetic makeup, psychological history, memories, environment, and experiences. The exact contribution of each element no doubt differs among individuals. In addition, our self-image is linked to others' perception of, and responses to, the individual. If the brain, with its associated personal identity, of a black male urban teen were to be transplanted into the body of a suburban white middle-aged matron, the previous personal identity of the donor, upon awakening from surgery, would be seriously threatened and compromised. Looking in a mirror, going to the bathroom, hugging an old friend, and hundreds of other events of ordinary daily life would challenge one's previous identity and sense of self. A variety of physical, social, and biochemical factors would require a rapid readjustment and rethinking of who the person is. If the individual were to survive psychologically, personal identity would, at the very least, need to change dramatically and quickly.

Herein lies one of the major differences between brain transplants and donations of other organs. Our brains—particularly cortical elements—are not only the metaphorical seat of the personhood of the human, but they are, to the best of our current understanding, the physiologic seat of the personhood of the human as well. While an appropriately matched heart is an appropriately matched heart is an appropriately matched heart, the same cannot be said for the brain. The function of the heart is that of a pump, and as critical as this pump may be to our physiologic and psychologic health, it is just a pump. Although the pump must work for the person to be alive, it is not the pump that makes the person either *a* person or *this* person. The brain (particularly the cortex), however, affords each individual those capacities that, we believe, make the person *a* person and *this* person. Perhaps it is for this reason that guidelines adopted by the Swedish Society of Medicine specifically disallow transplantation of an entire fetal brain (Mullen and Lowy 1993, 244).

Total brain transplantation is light-years away from the current state of neural grafting technology. Neural fetal brain grafts used for experimental treatment of Parkinson's disease have involved very small amounts of tissue obtained from the substantia nigra and ventral mesencephalon, areas of the brain not felt to impact cognitive functioning significantly. Donated fetal tissue, to date, has come from fetuses that have not achieved the stage of development felt necessary for the fetus to experience its environment or have any sense of self, let alone transfer that sense to a tissue recipient. Typically, NFTT requires tissue taken from multiple fetuses in order to have an adequate quantity for successful transplantation. But even if an entire fetal brain were transplanted, it

is unlikely that significant changes in personal identity would occur in the recipient because of the relatively small amount of tissue transplanted, the early timing of the tissue acquisition, and the lack of experience of the fetus.

In the spectrum of neural tissue transplantation, the transplantation of a small amount of homogenized fetal peripheral nerve anchors the one end of a spectrum, while the Green-Wikler model of transplant of a total adult brain anchors the other side. Multiple cases, including the current state of NFTT, lie between. However, the later in fetal (or postnatal) development the tissue is harvested, the greater the amount of brain tissue transplanted, the higher the percentage of cortical tissue transplanted, and the more affected the recipient is by the graft, the greater the theoretical possibility that personal identity of the recipient would be altered. We may puzzle over whether these same factors would lead to instances in which an aborted fetus's personhood develops in a surrogate body after the termination of its own.

Even if personal identity were totally transformed through neural grafts, ethical arguments could be used to support the procedure. For example, after weighing the burdens and benefits of possible loss or change of identity with a transplant against loss of life or serious morbidity without a transplant, a person might opt for transplant as more beneficial than burdensome. Of course, he or she would be choosing to be a different person, and this does not, in fact, constitute survival of the same person.

As we move forward in this area, more provocative ethical, legal, and religious questions are bound to arise. Who is responsible for the actions of an individual after transplantion of brain tissue? If an individual commits a crime on Monday and has a transplant of significant amounts of cortical tissue on Tuesday, whom do we point to on Wednesday as responsible for Monday's act? If tissue is taken from a fetus, and we find out years later that a genetic marker carried by that fetus predisposes to fits of rage, does it impact our view of the recipient's behavior?

What implications would NFTT have for our view of death? We currently feel comfortable talking about an individual as dead, even if her heart is beating in one person and her kidneys are making urine in two others. This is because the organ that made the person uniquely that person is no longer functioning. Would our moral or psychological comfort level change if memories, behaviors, and other cortically mediated aspects of a person find a new home? As complicated as the medical and technical questions are, the religious, ethical, and philosophical questions are even more challenging.

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