The Future of the Fetal Tissue Bank

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The fetal tissue bank established by the Presidential Executive Order of May 1992 was canceled in a little noticed clause in the 1993 National Institutes of Health (NIH) Revitalization law (*1*). Should the fetal tissue bank be allowed to slip into obscurity? Or should it be revived? If revived, what goals should it pursue?

The fetal tissue bank was planned to develop in two phases. Feasibility studies would first be conducted to evaluate whether sufficient uninfected, viable, and cytogenetically normal fetal tissue could be retrieved from ectopic pregnancies and spontaneous abortions to meet transplantation research needs. If an adequate amount of material could be made available, a fetal tissue bank would then be established to collect, process, and distribute this tissue through regional centers around the country. The bank would be composed of a coordinated network of retrieval centers, rather than one central collection agency. Five investigators awarded 2-year peer-reviewed grants by the National Institute of Child Health and Human Development (NICHD) carried out the first phase of the project (*2*). However, a decision was made in mid-1993 by the Department of Health and Human Services (HHS) to drop plans for the fetal tissue bank. This decision was reinforced by passage of the NIH Revitalization law.

The main reason given for abandoning the fetal tissue bank was that such a bank is needed only when large quantities of fetal tissue are being used (*3*). As fetal tissue transplantation is still in the experimental stages and requires only small amounts of tissue, it was argued, there is no need to set up a fetal tissue bank at this time. Further, some transplant investigators indicated that they preferred to dissect and process fetal tissue themselves, rather than use tissue retrieved and tested by others (*3*).

No published data are available to indicate the optimal quantity of fetal tissue required to meet transplant research needs each year. Although various estimates form the basis of clinical transplantation protocols, such estimates are often determined by the amount of tissue that is available (*4*). One American investigator who uses fetal brain tissue implants for patients with Parkinson's disease indicated that his work required approximately 200 fetuses a year (*5*). Transplants of fetal pancreas tissue in diabetes research have used tissue from 6 to 18 fetuses of 16 to 20 weeks gestational age per recipient (*6*). If only 10 patients with diabetes per year throughout the United States were to receive transplants of fetal tissue, this research could require as many as 180 fetuses. When the research requirements of other fetal tissue transplant investigators are taken into account, many thousands of sources of fetal tissue could be needed per year. This estimate is confirmed by statements of transplant investigators who objected to the establishment of the fetal tissue bank because it could not supply the several thousand fetuses needed every year for their research (*7*).

The primary reason for establishing a fetal tissue bank, however, is not to facilitate the distribution of large amounts of fetal tissue, but to satisfy ethical concerns. A fetal tissue bank provides a barrier between those who undergo and carry out abortions and those who receive and perform fetal tissue transplants. The presence of this wall of separation lessens the possibility that women who would not otherwise have an abortion will be influenced to do so. It also decreases the chance that conflicts of interest or collusion will occur among those involved in transplant investigations and those carrying out abortions. A fetal tissue bank, in addition, serves as a check on the uniformity, quality, and safety of fetal tissue provided to transplant recipients. Such a bank can develop model standards for quality control and equitable distribution of this tissue.

The Polkinghorne Report, a document developed by a government-appointed committee in the United Kingdom in 1989, recommended the separation of those involved in fetal tissue donation from those who use such tissue. It maintained that this separation is best achieved through the establishment of an intermediary organization (*8*). A fetal tissue bank was therefore established in the United Kingdom, even though the quantity of fetal tissue being used for transplantation research in that country was limited and research was in its early stages (*9*). The British fetal tissue bank undertook to collect and process fetal tissue rapidly, using uniform methods developed in cooperation with investigators (*4*, *9*). For similar reasons of ethics and to ensure an adequate supply of tissue of good quality, we believe that the American fetal tissue bank should not be abandoned.

Ethical Issues

There are good reasons for using fetal tissue from elective abortions in a U.S. fetal tissue bank. This tissue is more plentiful than that from spontaneous abortions and ectopic pregnancies and is less likely to be infected and genetically abnormal. Special ethical concerns, however, have been raised about the use of fetal tissue from elective abortions. The 1988 Panel on Human Fetal Tissue Transplantation Research concluded that it is acceptable public policy to use fetal tissue obtained from elective abortions for medical purposes, provided that certain ethical guidelines are followed (*10*). The recommendations of the Fetal Tissue Panel have the effect of separating the decision about abortion from the decision to donate fetal tissue, thereby alleviating concern voiced by some about direct complicity in abortion by those who use this tissue. They remove incentives for inducing abortion by prohibiting the sale of fetal tissue and directed donation of this tissue to a designated individual. They indicate that the timing and method of abortion should not be influenced by the potential use of fetal tissue and that the consent of the woman who donates fetal tissue must be obtained before the tissue can be used. Although the NIH Revitalization Act specifically dropped the fetal tissue bank, it included certain requirements about fetal tissue use that reflect the recommendations of the 1988 Fetal Tissue Panel.

These recommendations were developed 5 years ago in a rapidly advancing field on the basis of information and capabilities existing at that time. Their purview was limited by the restricted set of questions given the Fetal Tissue Panel by the Secretary of HHS. In our opinion, another panel should be convened to review recent developments in the field and to develop expanded guidelines for fetal tissue use.

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A new fetal tissue panel would need to readdress the scope of the principle of separation. Fetal tissue currently used in transplantation, which is derived from the brain, pancreas, and liver, needs to be removed in a way that renders it identifiable if it is to be usable. A new panel should consider whether changes in the timing and method of abortion that are not significant and that would retain the integrity of the tissue without placing the woman at greater risk would constitute an unacceptable breach of the wall of separation. A new panel should also reconsider the conclusion of the 1988 panel that the consent of the woman to donate fetal tissue is sufficient for the use of that tissue "unless the father objects." There is no legal obligation to obtain the permission of the male partner for a woman's abortion. To open the door to requiring his permission for the donation of fetal tissue after abortion has taken place might place the donor at risk. This recommendation of the panel was changed in the provisions of the NIH Revitalization Act of 1993 pertinent to research on transplantation of fetal tissue. It is important that a new panel elaborate the reasons why this change is ethically sound. Another issue that needs to be addressed is the availability of counseling for women who donate fetal tissue. Both fetal tissue and the women who donate it must be tested to evaluate the risk of infection to the recipient. The results of this testing could have serious implications for the health of the donor. Therefore, appropriate forms of counseling should be made available for donors.

Although a fetal tissue bank in the United States should include tissue from elective abortions, it should not be restricted to this tissue alone. Some investigators and patients, for reasons of conscience, will not participate in research using tissue from this source. In an open, pluralistic society such as ours, their perspective should be accommodated and, if feasible, tissue from spontaneous abortions and ectopic pregnancies should be included in a fetal tissue bank. Potential recipients of fetal tissue implants who have a preference for tissue from sources other than elective abortions should be informed of the advantages and disadvantages of using tissue from all sources and allowed to indicate their preference. If they request tissue from spontaneous abortions or ectopic pregnancies, they should be provided with it if it is available and has been thoroughly screened.

Scientific and Public Policy Issues

Concerns have been raised about the possibility of a major increase in unregulated and undocumented agreements for the acquisition of fetal tissue in the aftermath of the dissolution of the moratorium on the use of fetal tissue from elective abortions (*11, 12*). A large-scale commercial fetal tissue industry could emerge in this country. Yet no guidelines are in place for obtaining, testing, processing, freezing, and storing fetal tissue in the United States. No organized system is being planned to distribute this tissue on a nonprofit and equitable basis. In contrast, the distribution of solid organs for transplantation is coordinated through a national nonprofit network that was initially established with the assistance of federal grants.

Planning should begin now to develop a comparable system for obtaining and processing fetal tissue based on the framework of the originally proposed NIH fetal tissue bank. This would have been composed of a national network of collection, processing, and distribution centers at up to 20 institutions, each with its own network of subsidiary fetal tissue collection affiliates. Trained personnel would have processed fetal tissue, as is the case in the British fetal tissue bank. The original framework would have to be modified to include investigators and centers who respond to a recent request for applications (RFA) inviting proposals for studies of fetal tissue, including that derived from elective abortions (*13*). Centers chosen in the original grant competition should be continued only if their work is favorably evaluated and they fit into a rational framework of regional centers. Such a framework could be established by the NIH, which sets scientific and ethical standards for the rest of the country. A fetal tissue bank established under NIH auspices would carry out a large-scale, systematic comparison of the safety and suitability for transplantation of tissue from all major sources and would develop model standards for uniformity and quality control of fetal tissue that would be adopted around the country.

An initial issue to be considered is the administration of a fetal tissue bank. The Central Laboratory for Human Embryology at the University of Washington and the National Disease Research Interchange in Philadelphia, centers with a history of providing fetal tissue for medical research, have established criteria that could provide the starting point for developing administrative procedures for collecting, processing, and distributing fetal tissue. Other grantees and transplant investigators also could bring their experience and expertise to the development of methods for organizing the retrieval, distribution, and tracking of fetal tissue. Ultimately, a centrally coordinated national network of regional centers, along with transplant surgeons and other consultants, could develop administrative standards for equitable distribution of fetal tissue.

Secondly, the safety and suitability of the tissue to be used in transplantation must be carefully monitored. Tissue derived from spontaneous abortions is often infected and bears a small risk of transmitting human immunodeficiency virus (HIV) and other potentially fatal viral infections (*14*). Tissue from elective abortions may be infected by vaginal flora or intrauterine transmission of maternal infections such as syphilis, herpes simplex, toxoplasma, chlamydia, cytomegalovirus, rubella, hepatitis B virus, and HIV (*4, 14–18*). Published reports from several American transplantation teams indicate that they are attempting to counter many of these risks. For example, tissue from elective abortions is rejected at the University of Colorado if either the donor or her sexual partner has a history of venereal disease, hepatitis, infection with HIV, or intravenous drug abuse (*19*). At Yale University, fetal brain tissue is screened for bacterial, fungal, viral, and mycoplasma contamination, and donor serum is tested for HIV and hepatitis B (*20*).

More extensive information has been published about procedures used to evaluate and reduce the risk of infection from fetal tissue at the central fetal tissue bank in London (*4*). Fetal tissue from donors for whom an abortion was performed because of infection such as rubella virus, cytomegalovirus, HIV, hepatitis B, and toxoplasmosis is not used. Fetal tissue from donors who are known carriers of certain diseases, such as hepatitis B or HIV, also is avoided. The blood of donors and fetal tissue are tested for evidence of infection from syphilis, hepatitis B, and HIV. If the tissue is cryopreserved, the HIV-negative donor is retested after at least 90 days, and the tissue is used only if the donor is seronegative. Fetal tissue is washed in sterile solutions, and in antibiotics and antifungal solutions prior to transplantation. As a way to reduce the risk of transplanting genetically abnormal tissue, tissue from spontaneous abortions is not used if karyotypic or DNA analyses cannot be performed or if the fetus shows obvious anatomical abnormality. Because of the variability of tests currently performed at different laboratories, it would be advisable to develop some universal codification of testing procedures for fetal tissue, as is done in blood banking, to reduce infective and genetic risk.

A third matter to be addressed is the cost of such a bank. This depends not only on the amount of tissue needed, but also on the nature and scope of the screening performed. One rough estimate from A. Fantel, the director of the only laboratory in the United States with long-term experi-

ence at grading, separating, and analyzing fetal tissue, is that it would cost from $1000 to $2000 per specimen per year (*21*). This would cover donor interview and medical record examination; specimen procurement; grading, staging, and teratological examination; donor serologic screening for HIV and hepatitis viruses; specimen screening for mycoplasma and chlamydia; bacteriology; cytogenetic examination; histopathology; and the data compilation and review required to produce and deliver a complete report on each specimen. These costs include significant input from epidemiologic personnel as well as experimentation with tissue growth and cryopreservation. On the basis of this estimate, it can be concluded that to perform appropriate tests on the several thousand tissue specimens currently used for transplantation research per year would cost approximately $6 million.

Costs for administration and distribution would also need to be added to this estimate. The initial costs of establishing a national network of regional centers for fetal tissue banking should be borne, in part, by the federal government, in the way that the network of solid organ banks was established. The idea of profit from the sale of the human fetus or fetal tissue is incompatible with their special ethical significance (*22*). Therefore, regional centers should develop standards for nonprofit processing and distribution of fetal tissue.

Conclusion

There are good ethical and scientific reasons to retain a centrally coordinated fetal tissue bank system and to open this system to include tissue derived from elective abortions. Since fetal tissue transplantation promises to increase rapidly, this is the time to develop a set of ethical and scientific guidelines for such research in the United States. The fetal tissue bank, a once notorious political football, can become a primary source of standards for collecting and processing fetal tissue for transplantation. Moreover, it can provide a locus for developing equitable criteria for the distribution of this material. If this is to be accomplished, the scope and goals of the fetal tissue bank set out in the Executive Order of 1992 must be expanded, large-scale research must be carried out on tissue derived from elective abortions, and the bank must be adequately funded.

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