Fetal Tissue Research on the Rebound

Last month's National Institutes of Health (NIH) award of a grant for a study of fetal tissue implants to treat Parkinson's disease was the first since the ban against such research was lifted in January 1993, but it won't be the last. Parkinson's research is just the tip of the iceberg. NIH officials expect to allocate as much as $5 million in funds for other fetal tissue projects this year.

Fetal tissue's pliant properties—it lives longer than adult tissue in a graft, has low immunogenicity, and is still differentiating into mature cells—have long made it an attractive subject for research into basic developmental biology, and for use as a possible medical therapy in which fetal cells would be transplanted like organs to restore diseased tissue in adult patients. The 1988 ban "really stymied progress," said Delbert Dayton, chief of developmental biology, genetics, and teratology at the National Institute of Child Health and Human Development (NICHD). "It has not allowed this country to pursue the research that we really needed to pursue."

Some of that pent-up demand can now be met. Most of the money for fetal tissue research is being allocated by NICHD, the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Neurological Disorders and Stroke (NINDS), and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Dozens of research teams are vying for a piece of the multimillion-dollar action, and applications are flooding in, according to extramural program managers like Alan Levine, chief of cellular hematology at NHLBI. In addition to Parkinson's treatments, program managers are considering proposals for using implanted neurological fetal tissue in diseases such as Alzheimer's, trauma, stroke, and spinal cord injury; implanting pancreatic islet cells for insulin-dependent diabetes; and grafting hematopoietic stem cells from fetal livers for a host of inherited illnesses, including sickle cell anemia, thalassemia, Fanconi's anemia, and severe combined immune deficiency.

NHLBI has the biggest pot of money for this work, and has committed $1.5 million to fetal tissue trials in the 1994 fiscal year. NIDDK has added another $500,000 to this, for a series of cosponsored studies with the heart institute. Most of this money will go toward studying the transplantation of hematopoietic stem cells from fetal livers into in utero first-trimester fetuses diagnosed with an inherited or acquired illness. In one such study under consideration, a gene coding for a protein that blocks HIV replication would be inserted into fetal stem cells. Those cells would then be injected into the fetus of an HIV-infected woman in the hopes that the treatment would produce immune system cells that can resist infection by the virus.

Because of the fetal tissue's low immunogenicity, "these procedures can be done without the need for tissue matching, without the need for preparative regimens to destroy the recipient's bone marrow, without the need for immunosuppressive drugs to suppress the recipient's immune system so it will not reject the donor...and without graft-verses-host diseases," says NHLBI's Levine. The heart institute has already received more than 30 grant applications for this type of work, but will only be able to support eight, Levine says. The other institutes have not yet determined how many studies they will support, but say that awards could be announced as early as this spring.

–Larry Thompson

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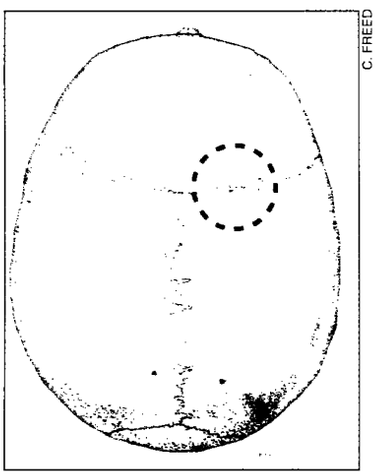
preciate that there are many variables that can influence whether [transplanted] fetal cells survive and whether there is benefit to the patient. Only funding one protocol denies you the opportunity to determine the range of outcomes."

Several researchers have also assailed the ethics of Freed's sham surgeries. "I think that's the most outrageous protocol I've heard of in my life," fumes neurosurgeon Richard Penn of Rush Medical School in Chicago. "We'd all love to do tests like this, but we all do them on our rats." Opening the skull exposes patients to the risks of major surgery but, without the transplants, none of the benefits. France's Marc Peschanski, secretariat of NECTAR, says his country's ethics review boards have expressly forbidden sham surgeries.

Freed counters that the risk of the sham is "vanishingly small" and that the procedure was approved by institutional review boards at all three involved institutions, and it received a green light from NINDS's advisory council. What is more, he emphasizes that the control patients will later be offered transplants through these holes. "No group has thought about these issues more than we have," he says.



C. FREED

Ethical holes. Critics charge the new Parkinson's study involves surgery—through the hole outlined above—with no direct patient benefit.

Ultimately, complaints about Freed's study are being leveled at the peer-review committee at NINDS that evaluated the various proposals. Rush's Penn, speaking for many unfunded researchers who were afraid to criticize this committee publicly, says they were not the group of peers he would have chosen. "As far as I can tell, they didn't have a lot of clinical experience nor were there any eminent neurologists in Parkinson's disease [on the study section that reviewed the grants]," says Penn.

Chicago's Sladek suggests that NINDS's largest failure was that it could have issued a request for applications (RFA) and run a half-dozen different trials simultaneously. "Let's not do this piecemeal," Sladek urges. "Let's do it right. We've been waiting a long time as an academic community and patients have been patient."

But officials at NINDS, as well as Freed himself, don't feel there's much merit to these objections. NINDS's Grady contends that an RFA could have backfired. "We might have limited the responses because an RFA has one response deadline," she says.

And Paul Sheehy, the NINDS scientific review administrator who oversees the study section that evaluated the transplant proposals, flat out rejects complaints about his group's qualifications. Sheehy also emphasizes that, on average, only one in four applications receive NINDS funding. "My impression is that if other investigators can convince their peers that they can dissect out the treatment effect, then their applications would be very well received," he says.

So fetal tissue transplant research, even with the lifting of the ban, remains controversial. But at least now, scientists are framing the debate—and the goal is to benefit patients, not political causes.

–Jon Cohen