Fetal-Cell Transplants Show Few Benefits

More than a year after the first transplants of human fetal tissues into the brains of adults with Parkinson's disease, and only a week after the first such reported operation in the United States, researchers concede that few of the patients show definite clinical improvement. In cases where improvement has been noted, it's difficult to show that the transplants are responsible, according to reports from scientists this week.

Moreover, a flurry of apparently irreconcilable results from researchers performing similar surgeries in animals has sparked renewed uncertainty about how such transplants might work. As basic assumptions about the therapy are called into question, some investigators wonder aloud about the wisdom of pursuing more widespread human trials.

"This is still a procedure that has a high morbidity, a high mortality, and patients that have Parkinson's disease do have access to good treatment by conventional means with which they can live a normal life span," says Donald M. Gash, a pioneer in monkey brain-cell transplants at the University of Rochester (N.Y.). Gash spoke this week in Toronto at the 18th annual meeting of the Society for Neuroscience, where researchers working with both animals and humans presented the most detailed results yet of the experimental therapy (SN: 11/5/88, p.296).

"The results have not been impressive," says Anders Bjorklund of the University of Lund, Sweden, describing two Swedish Parkinson's patients who received human fetal-cell transplants last November and December. "The implantations [in Sweden] have not had any clinical significance."

Scientists have hoped that transplanted cells producing the neurotransmitter dopamine might make up for the dopamine deficits that cause the tremors and rigidity characteristic of Parkinson's. However, Bjorklund reports, sensitive brain scans using positron emission tomography have "not given any evidence of a surviving, dopamine-producing graft" in either patient.

In contrast, significant improvements in a few patients are reported by Ignacio Madrazo, who 14 months ago performed in Mexico the world's first reported transplant of human fetal cells into a patient, and by Juan-Jose Lopez-Lozano, who has performed five human fetal-cell transplants in Spain since late 1987. But others express skepticism about those results, with some scientists' questions verging upon accusations of exaggeration.

In similarly controversial reports, Cuban researchers now describe positive results in 10 patients — but these researchers are using their own measures of improvement rather than standard, accepted measures. Scientists now estimate human fetal-cell transplants total 30 to 40 worldwide.

With no convincing demonstration that cell grafts are really surviving in humans, and no way to rule out non-graft-related mechanisms contributing to patients' recovery, scientists are counting on more animal studies to help them understand neural regeneration in the brain. For example, some intriguing studies now suggest that long-term, intact graft survival may not be required for clinical improvement. Instead, grafts may secrete one or more unidentified "trophic substances" that stimulate the brain's own recovery processes. Once those processes are initiated and new cell growth begins, this research suggests, the graft can die. Such a finding could alter transplantation strategies.

Among other recent findings discussed this week in Toronto:

- University of Colorado researchers in Denver say it will take three to six months before they know if fetal cells transplanted Nov. 9 into the brain of a man with Parkinson's will improve his disease.
- The precise location of a transplant in the brain appears to be more important than researchers had realized.
- Fetal brain cells increasingly appear to have advantages over dopamine-producing cells transplanted from an adult patient's own adrenal glands, perhaps in part because the adrenals in Parkinson's patients are often deficient in dopamine to begin with. — *R. Weiss*

Interleukin-2 fingers Kawasaki's syndrome

Scientists have developed a rapid test for Kawasaki's syndrome, an inflammatory disorder afflicting more than 3,000 U.S. children annually. The test may help pediatricians diagnose and treat children with Kawasaki's within the first week of illness. Standard diagnosis takes much longer, and by the time the disease is recognized, children may already have suffered heart damage, say the researchers who created the test at the Baylor College of Medicine in Houston.

"An elevated level of serum interleukin-2 receptor is a sensitive screening test in Kawasaki's syndrome. One hundred percent of patients in the first week of illness had significantly elevated levels," Karyl S. Barron told scientists this week at the American Heart Association meeting in Washington, D.C.

The Baylor team identified 82 children with Kawasaki's and found high levels of interleukin-2 receptor when they looked at the children's blood serum. During the first week of illness, these patients had receptor levels six times higher than a group of healthy controls. Interleukin-2 helps marshal the body's defense system by triggering white blood cells to attack an invading organism. To do its job, interleukin-2 has to interact with a receptor located on the white blood cell. In patients with Kawasaki's, high numbers of these receptors float freely in the blood, where they bind with interleukin-2, disrupting the immune system.

The relatively rare disorder was named after the Japanese pediatrician who identified it in 1967. Symptoms include a bright red rash, red lips and tongue, swollen hands and feet, a fever and in some cases heart damage. The disorder can be difficult to diagnose because it is often mistaken for measles. It seems much more prevalent in Japan, but public health authorities believe the disease is underdiagnosed in the United States.

The cause of the disease remains unknown, but some scientists believe it is triggered by a retrovirus similar to that causing AIDS (SN: 10/17/87, p.246). "We now hypothesize that the pathologic release of interleukin-2 receptor into the blood may explain many of the immune abnormalities seen in Kawasaki's syndrome," Barron says.

The research team found even higher levels of the receptor in Kawasaki children who later went on to develop coronary artery aneurysm, a weakening of the vessel wall. The test may be used to identify children at risk of aneurysm, enabling physicians to begin early treatment with aspirin and gamma globulin, a protein the body uses to fight infection. Right now, physicians often give aspirin/gamma globulin therapy to all Kawasaki patients even though only 20 percent of them go on to develop an aneurysm if untreated. Those who get an aneurysm run a higher risk of having a fatal heart attack, because the healed aneurysm can leave scar tissue blocking the coronary artery.

In a separate presentation at the same meeting, Barron reported that aspirin and gamma globulin treatment given to Kawasaki patients within seven days of fever onset helps prevent aneurysm formation. The efficacy of such treatment has been reported before, but Barron's study shows that a smaller dose of the expensive gamma globulin acts as effectively as larger amounts. — *K. Fackelmann*