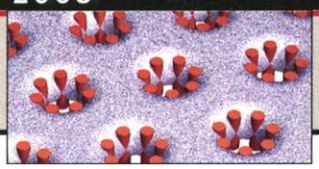
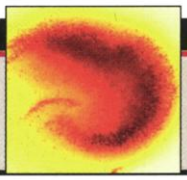


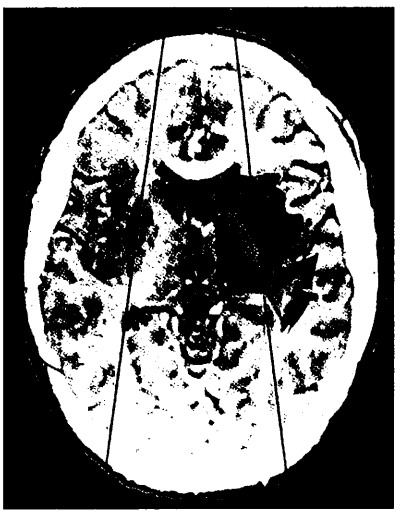


Parkinson's disease is marked by the mysterious death of brain cells that produce a chemical messenger called dopamine, which helps control motor function. The researchers had hoped to replace the lost cells by injecting dopamine-producing neurons from the brains of aborted fetuses into the affected areas of patients' brains. Several studies of this experimental technique had yielded encouraging results, but none included a control group.

The Colorado-Columbia study was the first one the National Institutes of Health (NIH) supported after President Bill Clinton lifted the ban on federal funding for research involving fetal tissue. From the outset, the 1993 award was controversial. Some researchers worried that the decision to fund a trial that used only one of several transplant techniques could harm the field if the results weren't positive (*Science*, 4 February 1994, p. 600; 11 February 1994, p. 737). Those fears seemed prescient last week as newspapers, magazines, and television news programs called the results disappointing and the technique a failure. "It's a bit of a setback," says neuroscientist John Sladek of the Chicago Medical School, one of the early critics of the NIH decision. "But it should not be the end of research on cell therapy for Parkinson's." Indeed, in 1995 NIH funded a second study using slightly different transplant techniques; results are expected early next year.

Freed's team randomly assigned 40 patients to two groups: Half had four holes drilled in their skulls through which fetal cells were injected, while the other half underwent "imitation" surgery, in which the same holes were drilled but no cells injected. (The design itself raised questions because of the risks to those in the control group.) One year later, the patients were asked to evaluate the overall severity of their disease on a scale of –3 to +3. By that measure, the two groups reported no significant difference.

However, on a standardized test in which physicians evaluated patients' symptoms while they were off their medicine, the data were more encouraging. After 12 months, those who had undergone the imitation surgery experienced no significant change, but transplant recipients improved by an average of 15%. After the evaluations, patients were told whether they had received cells, and those in the control group had a chance to receive transplants.



New growth. Dopamine-producing cells (stained brown) survive in a transplant recipient's brain. (Red indicates needle track.)

Three years after the operation, transplant recipients who were under 60 when they underwent surgery had improved by an average of 38% on the standardized test, and older patients by 14%. But by then, some troubling side effects had also appeared: Five recipients began to show jerky movements typical of Parkinson's patients who become oversensitive to dopaminergic drugs. The condition persisted after the patients reduced or stopped taking the drugs. Freed attributes these effects to a possible overgrowth of the transplanted cells or an oversensitization of dopamine-receiving cells in the region.

"Few in the field anticipated that too much dopamine would be an issue," says neurosurgeon Thomas Freeman of the University of South Florida in Tampa, an investigator in the second NIH trial. Instead, he says, most researchers have concentrated on encouraging enough cells to survive to produce sufficient dopamine.

Patients in other ongoing studies in Europe and the United States have experienced similar side effects, although none as severe as those reported by Freed, says neurologist Olle Lindvall of the University of Lund, Sweden. In these studies, he says, researchers transplant fresh tissue rather than cultured cells and use different doses and surgical techniques. Lindvall does not think an overgrowth of dopamine-producing neurons caused the side effects. He notes that autopsy data from two transplant recipients in the Colorado-Columbia study who later died—one in a car accident, the other of a heart attack—found between 45,000 and 63,000 surviving cells per patient. Other studies have suggested that as many as 100,000 surviving cells are required for a functional graft, he says.

Freeman and his colleagues hope their study will answer some of these questions. That double-blind trial, which also uses imitation surgeries, includes 34 patients and tests different doses of cells. Patients are not told whether they received cells for 2 years. Last week's report "has put a huge burden on our trial," Freeman says. "If our trial using different methodologies is negative as well, [continuing the research] certainly will be a bigger uphill battle." –GRETCHEN VOGEL

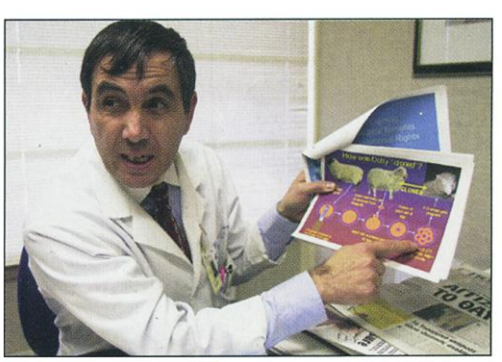
CREDITS: (TOP TO BOTTOM) C. FREED *ET AL.*; *NEW ENGLAND JOURNAL OF MEDICINE* 344 (10), 710 (8 MARCH 2001); JANET WORNE/*LEXINGTON HERALD-LEADER*/AP

HUMAN CLONING

Experts Assail Plan to Help Childless Couples

ROME—A plan to create the first human clone announced here last week is drawing widespread condemnation from the scientific community. Unlike previous such pronouncements, however, experts worry that the three researchers who are intent on treading into this moral and political minefield may have the expertise to carry out their plan—with potentially disastrous consequences for both the mother and her offspring. "They want to use humans as guinea pigs, and this is absolutely preposterous," says Rudolf Jaenisch of the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts.

This is not the first time individuals have threatened to break what has become a taboo in many countries and religions. Three years ago, physicist Richard Seed aired plans to launch a human cloning clinic in Chicago (*Science*, 16 January 1998, p. 315), and has since vowed that he would clone his wife. In addition, a Canadian cult, the Raëlians, laid out its vision of human cloning (*Science*, 25



Cloak of anonymity. Panos Zavos claims his team has animal cloners on board but declined to name names.

June 1999, p. 2083). Few people took either announcement seriously.

The latest pronouncement comes from a trio composed of Severino Antinori, a fertility expert at the Institute of Clinical Obstetrics and Gynaecology in Rome; Panos Zavos, a reproductive physiologist at the Andrology Institute of America in Lexington, Kentucky; and Avi Ben-Abraham, an American-Israeli biotechnologist whose current affiliation was not revealed. Speaking at a workshop at Antinori's institute, Ben-Abraham said that the team has "unlimited funding"—he declined to reveal the source—and plans to carry out the experiments in an undisclosed Mediterranean country. Ben-Abraham hinted that it could be Israel or an Arab nation, claiming that "the climate is more [receptive to human cloning research] within Judaism and Islam."

Fertile-minded. Severino Antinori says cloning could overcome male sterility.

The group wants to use cloning to help childless couples—particularly infertile men—start families. "Cloning may be the last frontier … in our attempts aimed at defeating male sterility," says Antinori, who is no stranger to controversy: In 1994, he used in vitro fertilization to impregnate a 62-year-old woman. The trio would attempt cloning only for childless couples in which the men produce no sperm, Antinori says. He claims to have 600 such couples on a waiting list.

One of the few scientific details of the project revealed at the meeting was that the group plans to follow essentially the same approach that was used to produce the sheep Dolly: Transplant a nucleus from a somatic cell into an enucleated egg and kick-start the process with a jolt of electricity. Zavos claims that the group has many scientists on board, including animal cloning experts; he refused to reveal their names, citing "security" concerns.

Jaenisch and others have denounced the effort. "What these guys are suggesting is ridiculous," he says, warning that the rare cloned mammals that survive from hundreds of fertilized eggs often suffer severe health problems. "Many die very soon after or have serious problems, such as kidney and brain abnormalities or no immune system," he says. There's no reason, Jaenisch adds, to think that such problems—seen in all five mammalian species cloned so far—won't affect human clones. Dolly's creator, Ian Wilmut of the Roslin Institute in Edinburgh, U.K., adds: "We had a lamb born recently which looked perfectly formed, but it couldn't stop hyperventilating; in the end we decided it was kinder to kill it. It turned out that the muscles and arteries leading to its lungs were malformed. I would like to know what they propose to do with a human in a situation like this."

The mother of a human clone might also be at risk. Mammalian clones are often extra-large, and pregnant mothers become dangerously swollen and frequently miscarry. Antinori's team claims that problems with embryo culture medium could be the cause of this syndrome, and that altering the medium's ingredients could avoid the complication. Wilmut acknowledges that's a possibility but says that until this problem is resolved, human surrogate mothers would be put at great risk. Jaenisch says epigenetic factors may affect a clone's health and account for the high rate of failure in bringing cloned embryos to term. "They cannot screen for epigenetic abnormalities in the same way they can screen for chromosomal aberrations," he says.

Undaunted, Antinori revealed that the trio would meet in October in Monte Carlo, Monaco, to fine-tune its plan; the researchers hope to start implanting embryos within 2 years. Said Zavos, "The genie is out of the bottle." –JOHN PICKRELL

GENDER EQUITY

NSF Program Targets Institutional Change

Huddled around a campfire in the Colorado Rockies last fall, 30 women engineers plotted how to improve conditions for their academic colleagues. Out of that meeting, part of a 3-day workshop, came the idea for a Women in Engineering Leadership Institute (WELI). The campers' timing couldn't have been better: Last month, the National Science Foundation (NSF) unveiled plans for a new $20-million-a-year program aimed at improving career prospects for women scientists and engineers in academia, and organizers of the nascent institute are already working on a grant proposal.

The competition may be fierce. WELI will be competing for one of five to 10 "institutional transformation" awards that NSF hopes to make by this fall as part of its new program, called ADVANCE. The program, which replaces NSF's earlier efforts to tackle the chronic problem of women being underrepresented in science, will also fund fellowships for women just starting or return-

ScienceScope

Purchasing Paralysis Rules meant to improve purchasing practices across the French government are stifling research, according to an Internet petition signed by more than 3200 French scientists. The guidelines, adopted over the last 2 years (*Science*, 12 March 1999, p. 1613), require all government-funded institutions to use only approved suppliers for purchases above $570; competitions are held at the beginning of each fiscal year.

The rules have put many researchers in a bind. Last month, for example, the autoclave in a microbiology lab at the University of Paris's Orsay campus broke down. But the only model that would fit through the lab's doors is made by a manufacturer that is not on the approved list.

Some help is on the way. The finance ministry earlier this month announced that, starting in September, it will triple the amount, now $43,000, that is exempt from the rules. (The Orsay lab had already reached that level.) But the lab would still have to wait 6 months to replace its autoclave. Such "paralysis of research activities is unacceptable," says Orsay microbiologist Betty Felenbok, a leader of the petition campaign (http://193.55.31.113). The petitioners want the bar for individual purchases raised from $570 to $2800 and no limit on purchases under that amount from unapproved suppliers.

Harvard's Catch Science advocates have a new and influential ally on the university scene. He's economist Larry Summers, named this week as the new president of Harvard University.

Summers, 46, who served as Treasury secretary in the Clinton Administration, became the university's youngest tenured professor at the age of 28. As part of the Clinton team, "he was an early and constant supporter of the need to keep the engine of intellectual capital going," says John Podesta, former White House chief of staff and now a professor at Georgetown University law school in Washington, D.C. Podesta says Summers pushed a number of research-related initiatives, from climate change to precollege education, during his stint in Washington.

Summers beat out University of Michigan chief Lee Bollinger and Harvard Provost Harvey Fineberg in the race to succeed Neil Rudenstine. He will take over on 1 July.

CREDITS: (TOP TO BOTTOM) MASSIMO SAMBUCETTI/AP; LAWRENCE JACKSON/AP