

American Scientists Raise Medical and Psychological Issues

By MICHAEL MASON
and LAWRENCE K. ALTMAN

In urgent telephone calls and agonized e-mail messages, American scientists are expressing increasing concerns that the world's first partial face transplant, performed in northern France on Nov. 27, may have been undertaken without adequate medical and ethical preparation.

Some scientists say they fear that if the French effort fails, it could not only threaten the life of the transplant recipient, a 38-year-old Frenchwoman, but jeopardize years of careful planning for a new leap in transplant surgery.

"We've been working on the ethics and the science for some time, going slowly while we figure out immunology and patient selection criteria and indications," said Dr. L. Scott Levin, chief of plastic and reconstructive surgery at Duke University Medical Center. "This flies in the face of everything we've tried to do."

The scientists' worries stem in part from the execution of the surgery, and in part from news reports over the weekend that called into question the patient's emotional state.

Dr. Maria Siemionow, director of plastic surgery research at the Cleveland Clinic, who has been preparing to perform a full face transplant, said that the way the transplant was conducted appeared to conflate two experimental protocols: the transplantation of facial tissue and the infusion of stem cells from the donor bone marrow into the patient in an attempt to prevent rejection of the new face.

The first procedure, although untried until now, has been well studied, and the microsurgical techniques involved are commonplace. But the second has been successful in human subjects only rarely and only recently. While pilot studies do suggest that an infusion of stem cells from the donor can help produce "chimerism" in humans, a state in which foreign tissue is tolerated by the body with comparatively little or no suppression of the immune system, it is far from standard practice in transplantation.

The French team's decision to perform two novel procedures simultaneously means that it may be difficult to determine the cause of success or failure of the transplant, Dr. Siemionow said.

"They should not be doing two experiments on the same patient," she added. "Ethics aside, it will make it difficult to get clean answers — if it works, why does it work, and if it goes wrong, was it the transplant or the stem cells?"

In a telephone interview yesterday, Dr. Jean-Michel Dubernard, the surgeon whose team performed the groundbreaking operation, in which the patient received lips, a chin, and

PIONEER AT STORM'S CENTER

A profile of Dr. Jean-Michel Dubernard, the face transplant surgeon. *Science Times*, Page F1.

a nose from a brain-dead donor, defended the infusion of bone marrow stem cells and denied that the procedure was a step into uncharted territory.

"It is not two experiments at the same time," he said.

But American experts said that the French team's approach diverged in other ways from what had been scientific consensus about how to proceed. The transplant was performed months after the woman's injury, and before any attempt at conventional reconstructive surgery.

The French doctors said traditional surgery could not have salvaged the woman's face. Dr. Benoit Lengele, a Belgian specialist in facial injuries, and other experts had judged that reconstructive surgery would be "very difficult, if not impossible" in

Did the surgery involve two experiments, and was the patient ready?

the patient's case, Dr. Dubernard said.

Yet reconstructive surgeons in the United States and in Europe routinely operate on patients with similar injuries, some missing as much as half their faces. Surgeons like Dr. Siemionow have long argued that the first face transplant should be attempted only on a patient who has tried to live with the alternatives.

The psychological issues are as complex as the surgical ones. Scientists have been concerned about how thoroughly the patient was emotionally prepared for the procedure, concerns that were only heightened when *The Sunday Times* of London reported that she had admitted that she sustained her injuries during a suicide attempt. According to the newspaper, the woman said that she was mauled by her family's Labrador retriever after she took an overdose of sleeping pills and collapsed. She believed the dog was trying to revive her, the newspaper said. The *Times* also reported that the donor had committed suicide.

The reports greatly alarmed experts in the field; the experimental protocols devised at both the Cleveland Clinic and the University of Louisville explicitly preclude emotionally unstable candidates. Patients with a history of depression sometimes do

not comply with the complicated drug regimens necessary to prevent organ rejection.

The news reports, however, were vigorously denied yesterday by Dr. Dubernard, who responded, "No, no and no!" when asked if his patient had tried to take her own life. He said the woman had taken only two sleeping pills for insomnia after a family argument.

Dr. Dubernard said that the woman was approved as a candidate for a face transplant only after a thorough psychological examination by an independent expert and by mental health professionals working with the transplant teams in Amiens, where the operation was performed, and in Lyon, where the woman is now being monitored for rejection reactions.

"These people are not stupid," he said.

The patient, who had difficulty eating before the transplant because of the injuries, ate dinner Sunday night and lunch on Monday, Dr. Dubernard said. Dr. Dubernard said the woman had visited the Edouard Herriot Hospital in Lyon "in October and again in November to meet the transplant team and to ask questions."

Yet longer-term psychological evaluation might have been useful for another reason, experts said. Since this is the first transplant of its kind, and it strikes deeply at questions of personal identity, the French patient's emotional stamina will be sorely tested. Already some news reports in Europe have identified the woman, who requested anonymity, and published pictures of her before and after the surgery.

Scientists planning for the first face transplant knew it would happen. One of the Cleveland Clinic's screening criteria is that a candidate for this procedure must be able to withstand intense public scrutiny — to be able to see pictures of the face's former owner, for example, on tabloid covers at the checkout rack. Resilience is important both for the first patient, say researchers, and for those who would follow.

"Every patient, when you talk to them, their goal is just to get out of the limelight," said Dr. David Young, associate professor of plastic surgery at the University of California, San Francisco, which also has been drawing up plans for a face transplant. "If this works, many potential patients who are on the fence will change their minds. But if this thing crashes and burns, it will damage the field."

For some experts, even the best-case situation has a down side.

"We want for this to go well," said Dr. Siemionow. "But if it does, then I am afraid everyone will forget that the ethics were not proper here. And if it does not, then they will be blaming the transplant procedure but not the ethics behind it."