GENE THERAPY

Should Dying Patients Receive Untested Genetic Methods?

Around Christmastime, when everyone else was opening gifts, National Institutes of Health (NIH) Director Bernadine Healy was opening an ethical can of worms by giving a San Diego doctor permission to try genetic therapy on a 51-year-old woman dying of brain cancer. That would seem to be a generous act, but problems arose because the therapy hadn't previously been tested on humans. And in making her decision, Healy did not consult the Recombinant DNA Advisory Committee (RAC), the NIH board charged with overseeing gene therapy. Her action angered members of the RAC, some of whom expressed outrage over the possibility that it could undermine the existing review process for gene therapies.

To deal with the rumpus created by her decision, Healy called an emergency meeting of the RAC on 14 January. At the meeting, committee members searched for a solution that would allow them to carry out their mandate to review the safety and efficacy of gene therapy experiments without looking like turf-hungry bureaucrats deaf to the pleas of the dying. What they came up with, after a stormy meeting marked by the presence of the dying woman's husband and the physician who is treating her with the untested protocol, is a complex, 10-point recommendation that supports internal NIH review and approval of genetic treatments for dying patients when the RAC cannot meet quickly enough to evaluate them.

The case that started the fracas is that of a San Diego woman with stage four glioblastoma, a uniformly fatal disease. After she underwent a second brain surgery to remove a recurrent tumor in August 1992, oncologist Ivor Royston, president of the San Diego Regional Cancer Center, began growing her tumor cells in the lab. Royston inserted the gene for the immune-stimulating factor interleukin-2 into the cancer cells. Modified in this way, the cells could be injected into the woman's body and used as an anticancer vaccine to trigger an intense attack on the native tumor cells. Several research teams are working on similar approaches, and recent animal evidence from a study at Case Western Reserve University in Cleveland, Ohio (*Science*, 1 January, p. 94), suggests this kind of immune stimulation may cause established tumors to shrink.

The woman received the first treatment with her genetically modified cells on 4 January; her doctors plan to give additional vaccinations every 2 weeks. While Royston reported at the meeting that the woman had experienced no complications from the experimental treatment; her condition, however, has continued to deteriorate.

The case reached Healy's attention partly through the efforts of Senator Tom Harkin, (D–IA), who got involved because the woman originally came from Iowa and her sister had worked on Harkin's campaigns. Harkin asked that a mechanism be established for considering emergency exemptions from the normal review process for dying patients. At the 14 January meeting, Healy insisted her chief consideration was compassion, not politics. "First and foremost," she said, "the decision was a compassionate response to the request of a dying patient. We took action only after we felt assured that there was no significant risk to either the health of the patient or the public." She conceded, however, that not everyone agrees with her point of view: "I realize that one could clearly take issue with a decision to either approve or deny this patient's plea for compassionate use."

RICK KOZAK

Caucus on compassion. Leroy Walters of Georgetown University *(left)*, RAC chairman, and Nelson Wivel presiding over a stormy RAC meeting on compassionate use of gene therapies.

And many of those present at the meeting —both RAC members and others—did take issue with Healy's point of view. Abbey S. Meyers, executive director of the National Organization for Rare Disorders, an organization for patients with uncommon inherited illnesses, and a RAC member, asked, "Are we saying that it is the job of the RAC to turn away and allow these things?" The woman in question, said Meyers, "will not benefit from this experiment. What on earth are we doing?"

Some who are not RAC members and are predisposed to mistrust genetic engineering generally expressed themselves even more strongly. Katherine Matthews, an attorney with the Foundation for Economic Trends, founded by antibiotechnology activist Jeremy Rifkin, said, "The case that brought this [issue of compassionate use] to the RAC is outrageous. Undue political influence is clear." Matthews expressed concern that emergency approvals of treatments for compassionate reasons might be carried out behind closed doors, rather than in the open setting of the RAC; she closed by saying her group would "see the RAC in court" if there were any reduction in public access.

A more moderate position was expressed by RAC member Donald Krogstad, a physician at Tulane University School of Medicine in New Orleans, who agreed that compassionate use of new treaments is an important issue but echoed the concerns expressed by many RAC members that "this protocol has serious scientific shortcomings."

That view was warmly disputed by Royston, who said, "I think this committee is way off track, based on what I am hearing around this table—way off track. Is it right for us to treat this patient? We are absolutely right. The best therapy is experimental therapy, because there is no other therapy." Royston also defended the protocol of the current experiment—a protocol several RAC members said is substantially the same as one Royston submitted to the RAC in 1991 that was rejected for lack of animal data. "I do not want to hear from this committee that I am trying to evade this committee. That is absolutely false," Royston practically shouted. Royston was followed by the woman's husband, who, in an unusual move for a public, government hearing, was allowed to testify without giving his name.

After weighing opinions at both extremes of the spectrum, and in the middle, the usually unanimous RAC approved the 10-point recommendation by a vote of 9 to 3 with a single abstention. Healy says she supports the proposal, but the final outcome has been cast into doubt because of Healy's resignation as NIH director (see story on page 447). If the proposal is eventually accepted, it could open the floodgates to hundreds of requests from dying patients and their physicians to try unproven genetic therapies. According to Nelson Wivel, director of the Office of Recombinant DNA Activities, it probably would take 6 months after acceptance for it to become clear just how large the flood will be.

–Larry Thompson

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