Ethics Advisory Board Confronts Conception in the Test Tube

In 1972, Pierre Soupart of Vanderbilt University successfully fertilized a human ovum in vitro. His was not the first report but, as he says, "Around 1971 and 1972, there was much skepticism among the scientific community about the various claims published in the literature of having successfully achieved human in vitro fertilization, since no convincing evidence had been submitted." Soupart had unequivocal proof in the form of an electron micrograph of the fertilized ovum, and his success was an important step in research on human reproduction.

Quite naturally, Soupart submitted to the National Institutes of Health (NIH) a grant application seeking funds to continue his work. Specifically, he proposed to take ova during routine gynecological surgery, fertilize them in vitro with donor sperm, and observe the developing embryos for no more than 6 days in culture. Although Soupart had no intention of transferring any of those embryos to a woman, he was well aware that in Britain, Patrick Steptoe and Robert Edwards anticipated doing just that. Soupart, by studying the chromosomal and morphological characteristics of developing embryos, hoped to determine whether in vitro fertilization poses any discernible risk of fetal abnormality, a form of "preventive medicine," at the earliest stages of development, as he calls it.

The NIH received Soupart's grant application in 1973. It had been approved by the experimentation review board at Vanderbilt. In 1974, it was approved by an NIH study section. Then it was endorsed by the appropriate NIH advisory council. On the first of May 1975, Soupart got word his grant would be funded. But to date, Soupart has yet to receive a single cent, yet to fertilize another single egg in vitro.

While Soupart's application was making its way through established channels of grant review, a moratorium was placed on all studies of human in vitro fertilization, and the process of writing a set of new and different guidelines governing the ethical quality of experimentation was begun. The upshot of it all is that the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, a temporary body which has just concluded business after 4 years, decided that certain types of experiments should be reviewed not only by NIH but also by a special board in the office of the Secretary of Health, Education, and Welfare (HEW). And so it is that Pierre Soupart's grant application is the first to come before the newly created Ethics Advisory Board, permanent successor to the commission. The board has before it a statement that says, "The NIH is prepared to fund this application, or any modification thereof. . . ," but NIH can do nothing until the board advises Secretary Joseph A. Califano, Jr., and Califano finally says "yes" or "no."

From the time the Ethics Advisory Board was created last spring, there were plans to bring Soupart's application before it. But the surprise birth in England of Louise Joy Brown, presumably the world's first baby conceived in vitro, put the application at the top of the board's agenda and made its first substantive meeting, held last month under the glare of television lights, the focus of national interest.

In a memo to the board, Califano said research on in vitro fertilization "holds enormous promise" but also "raises questions that reach to our most profound moral and ethical beliefs." Among the questions on the Secretary's mind were these:

> ". . . Can techniques of in vitro fertilization and transplantation of the embryo damage the resulting fetus and lead to abnormal children? Will this research lead to selective breeding, to attempts to control the genetic make-up of offspring or to the use of 'surrogate patents' where, for example, rich women might pay poor women to carry their children? . . . Are any of the participants—such as the research investigator, the clinical practitioner, the hospital or university, the government funding agency—legally liable for defects of a child conceived in the course of such research?"

Having thus instructed the board in the issues it is to address, he also directed the manner in which they proceed. In keeping with the present emphasis on "public participation" in decision-making, Califano told the board to "arrange for public hearings throughout the nation—in every HEW region [there are 10] to stimulate a national debate on this subject. . . ." Whether Califano will require a national consensus before allowing Soupart to proceed is unclear.

Like the National Commission that preceded it, the Ethics Advisory Board is made up of representatives of a variety of disciplines from science to law to ethics and, of course, the public interest.* And like the commission, it began its deliberations with reports from authorities in science and ethics. Among the scientists present, there was a fair amount of debate about the value of conducting extensive animal studies on in vitro fertilization and embryo transfer before moving ahead to human experimentation. Luigi Mastroianni, an infertility expert at the University of Pennsylvania School of Medicine, took the view that more animal work would be useful—he said another two years' worth of data would be "reassuring"—but the majority tended to think that the only way to truly evaluate in vitro fertilization and embryo transfer in the human is to experiment with humans.

A particularly forceful advocate of this position was Harvard physiologist John D. Biggers who argued against extensive (and expensive) animal studies on grounds that no mammal, including primates, is sufficiently like the human in terms of reproductive physiology to constitute a good model. With respect to the question of fetal abnormalities, Biggers again advocated moving directly to human experimentation. To begin with, from what is already known about in vitro fertilization in animals, there is little reason to expect that the procedure leads to an excess number of malformed offspring. Furthermore, among women the natural rate of "fetal loss" or spontaneous abortion is extremely high. Biggers estimates that of every 100 natural conceptions, only 31 babies are actually born. "The human reproductive system is, in a sense, very inefficient," he noted in testimony before the board. And in a paper especially prepared for the occasion he wrote, "It is obvious that the embryos produced by in vitro fertilization will show at least the variability that oc-

*Members: James C. Gaither, a San Francisco attorney, chairman; David A. Hamburg, president, Institute of Medicine, co-chairman. Representing medicine and science: Henry W. Foster, Meharry Medical College; Donald A. Henderson, Johns Hopkins School of Hygiene and Public Health; Robert F. Murray, Howard University College of Medicine; Mitchell W. Spellman, Harvard Medical School; Daniel C. Tosteson, Harvard Medical School; and Eugene M. Zweiback, Omaha, Nebraska. Representing ethics: Sissela Bok, Harvard University; and Richard A. McCormick, Kennedy Institute for the Study of Reproduction and Bioethics. Representing the public interest: Jack T. Conway, United Way of America; Maurice Lazarus, Federated Department Stores, Inc.; and Agnes N. Williams (wife of Califano's former law partner, Edward Bennett Williams).

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curs as the result of natural mating. Thus, we may expect at least 69 percent of the embryos to be defective and unable to develop to term if reimplanted in their mothers." Given these observations, Biggers believes, the "only way you can get data on the risk of human embryo transfer is to do lots of them and monitor the offspring for 20 years."

Getting women to participate in such a bold experiment might not be all that difficult. Although embryo transfer is not a potential solution to all types of sterility, it could theoretically benefit an estimated 560,000 women in the United States who have healthy ovaries (from which to extract eggs) but abnormal fallopian tubes which do not allow the passage of the egg to the uterus. In fact, one such woman was present at the board meeting.

Dianne Grills and her husband, Dennis, came from Tennessee to speak on behalf of Soupart's application. Adopting a "No taxation without representation" theme, the Grills said that they pay taxes and have a right to try to have children. They spoke of the "psychological trauma of infertility" [see box on p. 202] and pleaded that the board "not stop research on the brink of discovery." If the board holds hearings throughout the country, it will hear from lots of couples like the Grillses who are now looking across the Atlantic for a solution to their problem.

Ethics

Assuming that a strong case can be made on scientific grounds for Soupart's rather selective experiment, as well as for proceeding with in vitro fertilization as a treatment for infertility, it is really the ethical concerns about the research that stand in its way. At root, the issue turns on the "status" of the in vitro embryo and the question of abortion.

If you fertilize a human egg with human sperm do you have a human being from the start or, at least through the first stages of cell division, do you have only human tissue? Ethicist LeRoy Walters, director of the Center for Bioethics at the Kennedy Institute, Georgetown University, surveyed the ethical literature for the board, revealing a wide range from conservative to liberal views. Pressed for his own opinion, Walters took what many present considered a reasoned middle position. The "moral status" of a human embryo conceived in vitro, he believes, falls into a "unique category because of its human potential. It is more than a mouse but less than a fetus." Where do you draw the line regarding in vitro experimentation? Walters suggests about 14 days, the time it would take for the completion of implantation in the mother's uterus were the embryo to be transferred.

But theologian Paul Ramsey of Princeton University emphatically disagrees. In a written comment to the board Ramsey declared that "in vitro fertilization and embryo transfer should not be allowed by medical policy or public policy in the United States—not now, but ever." Ramsey's reasons included the need to avoid adding to the trauma of the abortion debate, the possibility of producing a damaged fetus, the "assault this procedure brings against marriage and the family," and the prospect of substituting laboratory generation for human procreation.

Reality

As the Ethics Advisory Board devises what in the end must be a politically acceptable solution, around the world, research in human in vitro fertilization marches on. On a visit to Britain in August to meet with Steptoe, members of the board's staff heard that other embryo transfers have already taken place and that before long Louise Brown will not be the world's only baby conceived in a test tube. It is well known among reproductive physiologists that work along these lines is progressing in Australia, and Biggers reported news of similar research in the Soviet Union and Germany.

Furthermore, enough is known about the procedure to assume that Steptoe and Edwards succeeded because, after many failures, they found the key to transferring the embryo at just the right time, when the uterus is biochemically ready to accept it. The British team has yet to publish its research, but Steptoe told ethics board staff director Charles McCarthy that they plan to do so within 3 months. It could well be that the procedure, while perhaps not suitable for use in what Steptoe calls "any crossroads hospital," will soon be relatively easy to accomplish. That could make the board's deliberations somewhat beside the point if embryo transfer were to become feasible without much further research. In this regard, Walters posed an important question. Is embryo transfer "research," and therefore subject to federal guidelines governing human experimentation? Or is it "innovative therapy," simply progress in medical practice and therefore no more subject to federal guidelines than any other therapy a physician might provide?

Board chairman James C. Gaither told *Science* that he hopes his group can make a recommendation to the Secretary by February or March. However, scheduling a series of public hearings in order to comply with Califano's directive to "assure that all interested parties have an opportunity to make their views known," may mean that their recommendation will come a little later.

—BARBARA J. CULLITON

1971: Steptoe Promises to Protect Test-Tube Baby from Publicity—1978 . . .

Among the ethical questions that surround the birth of Louise Joy Brown is one about the propriety of her birth announcement, made as it was through the exclusive offices of the *Daily Mail*. Did Steptoe and Edwards behave improperly when they encouraged their patients to sell their story to the highest bidder in the press or were they sensibly assuring the baby's financial future? Was it ethical to sell their own part in the story?

In 1971, David R. Zimmerman, a free-lance journalist and author from New York, wrote to Steptoe requesting the exclusive right to report the birth of the first baby conceived in vitro. He promised coverage that "anticipated and answered legitimate questions, while avoiding sensationalism and bad taste." He also promised anonymity for the doctor's patients. In light of recent events, Steptoe's reply, which Zimmerman has shared with *Science*, is worth recording.

Steptoe wrote: "The results of any clinical research work will be published in the proper manner in medical and/or scientific journals, and as such will be immediately available to medical journalists and correspondents and I suppose other reporters. It would be impossible for us to give you a first exclusive journalistic report in the way in which you request.

"I would also point out to you that we consider it our medical ethical duty to protect both our patients and any subsequent offspring from publicity. Their problem is a fully private one and would be solved in a private way. This, of course, does not mean to say that the general principles of management of these couples and their treatment would not be made available, but it will certainly not involve any personal stories at all."

Times change.—B.J.C.