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Carol A. Tauer Ph.D.  
*College of St. Catherine*

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# ***In Vitro* Fertilization: Are There Still Ethical Problems?**

CAROL A. TAUER, Ph.D.\*

**ABSTRACT**—The initial development of the technique of *in vitro* fertilization (IVF) was accompanied by discussion of related ethical questions. Two significant ones were: Did the development of IVF justify the wastage of human embryos which made it possible? Was it justifiable to attempt human embryo transfer without laboratory studies to determine the safety of the technique? Thousands of births as a result of IVF have largely made these two questions moot. But four others remain: Is IVF immoral because it accomplishes procreation in a laboratory rather than through an act of marital union? Is it permissible to maximize the success of IVF through practices which result in the intentional destruction of human embryos or fetuses? Is it ethical to conduct basic scientific research which utilizes laboratory fertilized embryos? Given uneven and often very low success rates for IVF, should public policy act to protect clients or to promote improved IVF practice? While our society is deeply divided as to the resolution of these problems, it is beginning to engage in public debate, particularly on the last two questions.

## **Introduction**

While our nation is still polarized, morally and politically, on the issue of abortion, scientific advances raise new questions about the appropriate treatment of prenatal life. In two areas of scientific research, the questions are particularly pressing and are currently receiving wide attention. The first area concerns a generally accepted treatment for infertility problems, *in vitro* fertilization or IVF. Because this procedure involves fertilization of oocytes by sperm outside the body of a woman, it provides opportunities for studies in reproductive biology which are not otherwise possible. The second area concerns the use of tissue from aborted fetuses for research and transplantation. As this technique begins to offer the prospect of cures for a variety of severe conditions and diseases, the need for significant quantities of fetal tissue could be anticipated.

While these scientific advances offer hope to people who are suffering from infertility or disability, they remind us that our society has not come close to resolving fundamental questions about the status of prenatal human life. The Supreme Court in *Roe v. Wade* (1973) ruled that abortion must be permitted up to the time of fetal viability. This decision was based solely on the pregnant woman's right to

privacy, a right found to be constitutionally protected, that allows her to choose an abortion. The Court made no other statement regarding appropriate treatment of the pre-viable embryo or fetus, and in fact it noted that this matter was beyond its competence. Adding to the ambiguity of the situation, many persons and groups in our society do not accept the ruling of *Roe v. Wade*, and have devoted themselves to overturning its provisions.

Meanwhile, scientists whose work involves the study of prenatal human life wait for funding and regulatory agencies to resolve questions about the ethics of their research. The decisions of these agencies determine whether scientists will be able to carry out the research they believe is essential for progress in biology and medicine. Similarly, individuals and families who are suffering from infertility or disease wait for improved therapies which could enable them to have children or to resume normal, reasonably healthy lives. Our society finds itself torn between two competing values: the pursuit of scientific advances which could significantly improve human life, and respect for deeply held convictions as to the value and sacredness of the prenatal human.

In this review I will concentrate on the specific ethical questions raised by *in vitro* fertilization, leaving the issues related to the use of fetal tissue for further consideration. In the discussion, I will focus particularly on questions about the appropriate treatment of the human embryo and fetus.

## **The Development of *In Vitro* Fertilization**

On July 25, 1978, Louise Brown, the first baby ever conceived in a laboratory, was born in Oldham, England. Her birth was possible only because of many years of laboratory research and numerous clinical attempts to achieve pregnancy with this technique. The physician and the biologist involved with Louise's birth, Patrick Steptoe and Robert Edwards, had themselves worked for over ten years to achieve this goal. As of February 1979, they had attempted the technique with 79 infertile women, of whom only four had become pregnant and only two had given birth (1).

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\*Carol A. Tauer is Professor of Philosophy at the College of St. Catherine. After receiving a Ph.D. in mathematics from the Massachusetts Institute of Technology she served as professor and chair of the Department of Mathematics at the College of St. Catherine. She received a Ph.D. in philosophy from Georgetown University in 1982 through the Kennedy Institute of Ethics, specializing in biomedical ethics. Her dissertation focused on the ethics of research involving prenatal human life, and she has continued to write and lecture on this topic and on new reproductive techniques. Dr. Tauer has recently published a series of articles on the challenge of AIDS for ethics and public policy.

During the development period of *in vitro* fertilization, the literature was filled with discussions of the ethical questions raised. In retrospect, two of these questions seem most significant because, even though they have been resolved in a practical sense, their underlying theoretical issues remain with us. Both of these questions illustrate the tension referred to earlier, and each can be phrased in terms of competing values.

- Does the development of *in vitro* fertilization justify the wastage of human embryos which made it possible?
- Was it justifiable to attempt clinical embryo transfer without laboratory studies to determine whether IVF was safe for the developing embryos?

#### *Wastage of Embryos*

Given the high rate of infertility among couples who wish to have children, estimated at one in six couples in the United States, the development of techniques to assist them is a laudable endeavor. In the process of developing IVF techniques, however, numerous attempts to fertilize human oocytes were made in laboratories throughout the world. The first successful human fertilization was demonstrated by Pierre Soupart of Vanderbilt University in January 1973 (2). "Once fertilization was achieved, embryo transfer to the woman who had provided the oocyte(s) could be attempted. Since at first there was essentially no hope of success, i.e., that the embryos would implant and develop to term, an extended series of experiments was conducted from which the embryos involved could not benefit.

While the goal of relieving infertility was a good one, numerous embryos were created and then expired to support the research needed to develop the *in vitro* technique. According to those who regard these embryos as human beings, literally hundreds of humans gave their lives so infertility treatment could be made available, or so future embryos could be conceived, implanted, and brought to term. Depending on one's view of the moral status of the early embryo, one may hold that the price of success was too high.

#### *Safety of IVF*

The second question raised during the period of initial research involved the safety of the *in vitro* technique. Many scientists wanted evidence that the manipulation of the gametes and embryos in *in vitro* fertilization did not cause birth defects. These scientists advocated laboratory studies on IVF zygotes and cleaving embryos, so that safety would be assured before transfer to a woman was attempted. While prudent, this course of action would clearly require the use of human embryos for laboratory studies, again raising the question of the ethics of such research.

Pierre Soupart in 1978 criticized his British colleagues for omitting human safety studies and moving immediately to embryo transfer. At that time, Soupart had a research proposal under consideration at the National Institutes of Child Health and Human Development (NICHD) in which he proposed to "establish the genetic risk involved in the obtaining of human preimplantation embryos, by tissue culture methods (2). His proposal never received final approval and funding, probably because of its ethically controversial nature. Meanwhile, Steptoe and Edwards achieved their immediate goal, the birth of Louise Brown, and scientists and clinicians throughout the world turned to learning the method and imitating their accomplishment.

## **The Current Situation**

As Louise Brown's birth was followed in rapid succession by hundreds and now thousands of births resulting from IVF, the ethical concerns shifted. These births showed no evidence of increased defect or abnormality resulting from the *in vitro* process. Hence, the question of testing the safety of IVF became moot. The issue of embryo wastage also became less problematic. If an attempt were made to transfer each fertilized egg to a woman, then whatever embryo loss occurred could be accepted, since each embryo had a real chance to develop its potential and come to term.

During the decade beginning in 1978, *in vitro* fertilization was regarded with hope and optimism by most people, from research scientists to the general public. The news media provided extensive coverage of the first IVF baby in a city or state, and infertile couples flocked to the IVF clinics, which sprang up in most major medical centers. As early as December 1978, a Gallup poll showed that 60 percent of the public approved of IVF, while only 27 percent opposed it (3). Public concern seemed to be focused mainly on unusual applications or unexpected problems: the woman in South Africa who gave birth to her daughter's "test-tube" triplets in 1987, and the two fertilized eggs which were left frozen and orphaned in Melbourne when their parents, Mario and Elsa Rios, were killed in 1983.

Ethical questions remain, however. Three of them have nagged us during the entire past decade, while the fourth is an issue that has only recently received publicity. The first three questions are: (1) Is IVF immoral because it accomplishes procreation within a laboratory rather than through an act of marital union? (2) Is it permissible to maximize the success of IVF by using practices that result in the intentional destruction of human embryos or fetuses? (3) Now that human embryos are available in the laboratory setting, is it ethical to conduct the basic scientific research which could be undertaken? The fourth question, raised only recently, is this: Given that the success rates for IVF are vastly uneven and often unacceptably low, should public policy be implemented to protect clients or to promote improvements in the technique?

#### *Separating Procreation from Marital Union*

*In vitro* fertilization achieves a good result, pregnancy and childbirth for an otherwise infertile couple, through what some conservative thinkers regard as an intrinsically bad means. The foremost critic of IVF on grounds that it is intrinsically wrong is probably the Roman Catholic Church. In its instruction on procreation of February 1987, the Vatican stated that artificial fertilization in the form of IVF is not morally acceptable. The reason given is that IVF separates procreation from the act of intercourse, which is the sign of the spouses' union (4). Thus, it is illicit for the same reason that artificial contraception is illicit.

This view is not uniformly held among Catholic theologians, however. Note, for example, the position of Richard A. McCormick, S.J., who argues that procreation must take place within the context of a loving marital relationship, but that it need not be the fruit of a specific conjugal act (5). As Baruch Brody points out in his fine study of religious perspectives on IVF, a number of religious communities share McCormick's view, while he knows of no others who support the official position of the Roman Catholic Church (6).

### *Taking Chances to Improve One's Chances*

A whole set of ethical issues arises from attempts to optimize the outcome for the couple seeking a child through IVF. Their chances of obtaining a child as the result of a single attempt at fertilization and implantation are very small. Hence various approaches have been devised for increasing the odds. Some of these procedures raise ethical questions at the same time as they further a laudable goal.

In order to maximize the probability of fertilization and pregnancy, the woman is generally given hormonal treatment to cause her to superovulate, or to produce more than one egg in a given cycle. These eggs, usually recovered by laparoscopy, may all become fertilized. If more than one are then transferred to the woman, her chances of achieving a pregnancy will increase proportionately. But the likelihood of a multiple pregnancy will also increase as the number of transferred embryos becomes larger. If three or more of the transferred embryos implant and begin to develop, the woman will be carrying a high risk pregnancy; triplet and higher multiple pregnancies almost certainly will result in premature birth, with consequent morbidity or mortality.

Ought one to maximize the probability of pregnancy by risking such an outcome? Options that have been proposed include the following:

(1) Limit the number of embryos to be fertilized and transferred to three. The probability that all three will implant is very small.

(2) Transfer all fertilized eggs, and if an excessive number implant, use a procedure called selective reduction. In this procedure, a certain number of fetuses are killed, either by a transvaginal technique which aspirates the fluid and fetus from the sac, or transabdominally through injection of potassium chloride into the fetal heart (7).

(3) Fertilize all oocytes recovered, but transfer only two or three. The others may be frozen for future use, donated to another woman, discarded, or used for research.

While the aim may be to increase the probability of an eventual successful outcome, options (2) and (3) raise questions about the ethical treatment of human embryos and fetuses. Selective reduction may be a choice one is almost forced to make after a highly dangerous pregnancy has occurred. Yet the initial decision to risk causing this type of pregnancy was a deliberate one. One cannot shirk responsibility for the consequences of deliberate decisions.

Freezing excess fertilized embryos has generally been regarded as ethically more acceptable than destroying them. However, from one-quarter to one-half of these embryos do not survive the process of freezing and thawing, even in the well-established clinics; and in the absence of better diagnostic techniques, thawed embryos are transferred on the basis of whether they "look good" or "look odd." In a recent article, Andrea Bonnicksen delineates additional ethical problems related to the freezing of embryos, ranging from their legal status to how they are either personalized or depersonalized by the donors or physicians, depending on what they believe the eventual use and outcome will be (8). Freezing, which once seemed like a simple solution to the problem of excess embryos, has now provided a host of new problems.

The University of Minnesota established its program for *in vitro* fertilization in early 1983. Initially, all eggs which fertilized were transferred back to the woman, with the exception that "obviously abnormal embryonic cells will be discarded and not used for fertilization (9)." Recently freezing has become an option, and in 1988, a pregnancy was

achieved using a frozen embryo. Dr. George Tagatz, director of the program, reports that they are currently implanting up to four embryos at a time, and that he is aware that a selective reduction has occurred in the course of a triplet pregnancy (10). Within this program, Dr. Tagatz presents the possible options to the couple seeking IVF, explains their risks and benefits, and then allows the couple to choose the option they prefer. He suggests that he is taking a less paternalistic approach than he did at the beginning of the program, a stance in line with a general trend in physician-patient relationships. This approach has much to commend it. When the fate of human embryos and fetuses is involved, however, one may ask whether paternalism toward them would be an appropriate ethical response, which may supersede the exercise of parental autonomy.

### *Using Early Embryos in Research*

A debate which continues to plague the scientific, ethical, and political scene echoes earlier discussions of research involving human embryos that cannot benefit from it. The presence of human zygotes and embryos in the laboratory setting provides scientists with an unusual opportunity to investigate aspects of human reproduction. The process of cell differentiation, the nature of genetic diseases, reasons for miscarriage, new contraceptive methods, as well as investigations of other phenomena such as cancer-causing cells: scientists have envisioned a wide variety of valuable research utilizing laboratory-fertilized embryos (11). Eventually, too, a kind of prenatal therapy might be developed; genetic manipulation through gene "surgery" or replacement could possibly be performed on the undifferentiated embryo.

In the United States, research involving fetuses is governed by federal regulations, which were implemented in 1975. However, these regulations do not cover research involving preimplantation embryos; such research must be approved by an Ethics Advisory Board or EAB (12). The EAB was appointed in 1977, and after careful study, it issued general guidelines to govern federally-funded research involving *in vitro* fertilization. Research could ethically be conducted in order to demonstrate the safety and efficacy of *in vitro* fertilization, provided the gamete donors gave consent, and on condition that the embryos were not sustained in the laboratory beyond 14 days. The board did not approve or disapprove other possible goals of embryo research, but did take a big step in accepting the use of some embryos for purposes beyond the development of their own potential.

While this report might have formed the basis for consideration of a series of research proposals, the EAB only reviewed one proposal (Pierre Soupart's) during its brief lifetime. Its report was tabled by HEW, its charter expired in 1980, and no human IVF research has been considered for federal funding since that time.

Whether embryo research should or should not be facilitated by public policy is highly debatable, but it is an issue worth debating. Because of the demise of the Ethics Advisory Board which was mandated to make recommendations in this area, and because of the generally volatile atmosphere in the U.S. on abortion related issues, there has been a conspicuous absence of American public debate on *in vitro* research during the past decade. In contrast, in Australia, Great Britain, and other countries of the European community, there has been vigorous public discussion for a number of years. In Great Britain, the debate has even reached parliamentary level. Recently an international conference convened in Canada to develop "An International

Ethic for Research with Human Beings (13).” Among other issues, this conference began to explore the ethics of laboratory research with human embryos at the international level.

It is well-known that many persons and a number of religious groups hold that the moment of fertilization marks the beginning of a new human life, and that the zygote and early embryo must be given all the protections due to a human being. What is not as well known is the fact that some conservative ethicists and theologians, even within bodies like the Roman Catholic Church, have come to regard the period immediately following fertilization (variously estimated from 7 to 14 days post-fertilization) as somewhat anomalous (14, 15, 16, 17, 18). During this time, the dividing embryonic cells behave more as a cellular mass than as a unified organism. The cells are totipotent, each one having the ability to develop into any sort of organ or tissue, or in fact, into an entire fetus. If some of the cells are destroyed or damaged, the others can go on to develop normally. Twinning or embryonic cloning, and conversely, the recombining of two or more embryos, are possible during this period. Thus, it might be said that we do not have an individual and integrated human organism until differentiation has begun and the phenomena of twinning and recombination are no longer possible—a time that is generally identified as 14 days after fertilization.

The unusual character and status of the very early embryo, often called the preembryo, have led various advisory bodies to permit research on preembryos up to 14 days gestational age, but not thereafter. Persons who recognize full human status at fertilization could not support such a position; but a broad spectrum of informed ethical opinion seems willing to permit it. In fact, the only public policy body in the U.S. which considered the matter, the Ethics Advisory Board of 1977-78, approved the funding of certain types of embryo research if limited to this 14-day period.

#### *Providing IVF as Effective Therapy*

Recently an additional ethical issue related to *in vitro* fertilization has been given prominent attention. Critics noted that, after a decade of clinical application of IVF, the success rates for the procedure were still low, and in many clinics, unacceptably low. On the one hand, there was fear that the public, and more importantly, infertile couples, were being misled by distorted claims for the success of IVF. On the other hand, there was concern that the efficacy of the procedure could not be improved unless IVF research was encouraged and funded.

Currently, it is difficult to obtain accurate and reliable statistical data on the success rate for IVF. Clinics are not required to report to any registry or regulatory body. Published statistics usually represent a group of clinics, so that figures from an individual center cannot be distinguished. In addition, a “success” may be counted in a variety of ways: fertilization and transfer, a biochemical pregnancy (rising  $\beta$ -hCG level), a clinical pregnancy (sac with discernible fetus and positive heartbeat), or an actually delivered infant (premature or full-term). Since the rate of spontaneous abortions among IVF clinical pregnancies is high, about 50 percent (10), counting clinical pregnancies as successes will obviously skew the data. An infertile couple wants a baby, not just a pregnancy.

Individual clinics differ greatly in the information they provide to prospective clients, often misleading them (whether intentionally or not) as to their actual chances of

success (19). In providing data to central registries, however, most clinics now report the success rate as the number of live births compared with the number of oocyte retrieval cycles. Arthur Caplan, Director of the University of Minnesota Center for Biomedical Ethics, cites two reports on the efficacy of IVF that use this method of calculating (20). The first report, combining 30 centers in the United Kingdom in 1985, shows a success rate of 8.9 percent. The second, grouping data voluntarily reported from 41 American clinics in 1986, shows a rate of 6.4 percent. While these percentages are low, the least efficient centers may not even be included in the published data. A survey by the American Fertility Society indicates that about half of the clinics that offer *in vitro* fertilization in the United States have not yet produced a baby.

Experts estimate that about half of the 3000 births resulting from IVF in the United States have occurred at just three centers (19). While the University of Minnesota program is smaller than these three, its success rates are relatively high. Out of 56 oocyte retrievals in an 18-month period from July 1985 through 1986, 14 percent resulted in live births. Out of 52 retrievals in 1987, 17 percent produced babies (10).

Because of the desperate need experienced by many infertile couples, they are easy targets for exploitation. Infertility treatments carry a heavy emotional and psychological cost; couples describe themselves as being on an emotional roller coaster. The financial cost is also high, generally between \$4500 and \$6500 for each attempt, besides expenses for travel, relocation, and lost work time. A subcommittee of the House Committee on Small Business has recently conducted hearings to determine whether the IVF “business” is taking unfair advantage of the plight of these couples. Currently, this subcommittee is conducting a survey of the 169 U.S. clinics that offer IVF; the survey will help the subcommittee decide whether federal regulation and/or a national registry should be instituted.

The medical profession ordinarily regulates itself, but the potential for abuse in the uncharted territory of new reproductive techniques may call for supplementary measures. Two simple requirements would address many of the problems that have been noted. The first step is to require each clinic to provide unambiguous, easily understandable data about its record of past successes, using a standard method of calculating. Besides sharing this information with clients, the clinic should be required to report it to a national registry, so that a database for assessment and planning can be developed. The second step is to set minimum requirements for practice in this field, leading to licensure of centers that qualify. A center that did not meet the licensure standards would not be eligible for payment by private insurers or public funds. (Five states currently require insurance companies to cover infertility treatment: Arkansas, Hawaii, Maryland, Massachusetts, and Texas.)

These two measures, which Congress has begun to consider, are straightforward means of handling already-identified problems. They are relatively uncontroversial, since their aim is to prevent exploitation, deceptive practices, and the exercise of professional incompetence. Thus they operate within the framework of consumer protection, a legitimate function of government.

A third possible step is more controversial. In assessing the statistical data available, Arthur Caplan comments that the overall rate of success, well below one in ten, appears very low for a medical procedure that is described as a therapy. Ordinarily, one expects a better chance of success from a

therapeutic procedure. How can this rate actually be improved, not just in the best centers, but for a broad range of competent ones?

At present, scientific and technical aspects of IVF are explored largely through a trial and error process. Many factors can be varied, from the dosage levels of the hormones which produce superovulation, to the environmental circumstances surrounding the transfer of embryos. Clinicians and scientists may discover empirically that one approach works better than another, but they know little about *why* it does. Because there has been essentially no basic research on IVF in the United States since 1975, clinical advances are not supported by advances in the scientific knowledge base. As Caplan notes, "More than 160 IVF centers exist but almost no American scientists are trying to understand how IVF works (20)."

Thus, we are again confronted with the question of whether research on *in vitro* fertilization, which necessarily involves research with early human embryos, is morally permissible. In response to growing concern about this matter, Dr. Otis Bowen, Secretary of Health and Human Services, announced on July 14, 1988 that the first steps were being taken toward formation of a new Ethics Advisory Board. The charter for this board was published in the *Federal Register* of September 12, 1988, and public comment has been received. Whether the board will actually be chartered depends on the appointments of the Bush administration to Health and Human Services.

If the board is established, applications from scientists who propose to do fertility research involving preembryos can again be considered for federal funding. The board's establishment would mark the beginning of a new era in the history of IVF: the problems discussed in this review would not then be solved, but they would be debated in the forum of our public life and public policy.

## References

1. Russell, C. 1979. Doctor tells how 'test-tube' babies were achieved. *Minneapolis Tribune* Feb. 11: 26F.
2. Soupart, P. 1978. Cytogenetics of human preimplantation embryos. Research proposal 1-RO1-HD-08837-01 as presented to Ethics Advisory Board, DHEW, Sept. 15.
3. Gallup, G. 1978. Most approve U.S. research on test-tube baby procedure. *Minneapolis Tribune* Dec. 14: 3B.
4. Congregation for the Doctrine of the Faith 1987. Instruction on respect for human life in its origin and on the dignity of procreation. Reprinted in *New York Times* Mar. 11: 10-13.
5. McCormick, R. 1987. Document is unpersuasive. *Health Progress* July-August: 53-55.
6. Brody, B. 1989. Current religious perspectives on the new reproductive techniques. In D. Bartels and A. Caplan (eds.), *Beyond Baby M*. Clifton, NJ: Humana Press, forthcoming.
7. Berkowitz, R. et al. 1988. Selective reduction of multifetal pregnancies in the first trimester. *New England Journal of Medicine* 318 (16): 1043-1047.
8. Bonnicksen, A.L. 1988. Embryo freezing: ethical issues in the clinical setting. *Hastings Center Report* 18 (6): 26-30.
9. University of Minnesota Hospitals 1983. Consent form-*In vitro* fertilization and embryo transfer.
10. Interview with Dr. George Tagatz, M.D., Department of Obstetrics-Gynecology, University of Minnesota, Dec. 21, 1988.
11. Soupart, P. 1979. *In vitro* fertilization and embryo transfer, part I. *Current Problems in Obstetrics and Gynecology* 3 (3): 5-45.
12. 45 CFR 46.204.
13. Miller, J. 1988. Towards an international ethic for research with human beings. *IRB* 10 (6): 9-10.
14. Dedek, J.F. 1972. *Human Life: Some Moral Issues*. New York: Sheed and Ward.
15. Dilanni, A. 1974. Is the fetus a person? *American Ecclesiastical Review* 168: 309-326.
16. Diamond J.J. 1975. Abortion, animation, and biological hominization *Theological Studies* 36: 305-324.
17. Häring, B. 1976. New dimensions of responsible parenthood. *Theological Studies* 37: 120-132.
18. Tauer, C.A. 1984. The tradition of probabilism and the moral status of the early embryo. *Theological Studies* 45: 3-33.
19. New York Times 1988. Pressure to regulate *in vitro* fertilization grows as demand rises. *New York Times* July 28: B7.
20. Caplan, A. 1989. Arguing with success: the moral challenge of *in vitro* fertilization. In D. Bartels and A. Caplan (eds.), *Beyond Baby M*. Clifton, NJ: Humana Press, forthcoming.