

The business of research.

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The report of the Human Embryo Research Panel issued in September, 1994 comes in the aftermath of legislation - the National Institutes of Health (NIH) Revitalization Act of 1993 - that put an end to an eighteen - year de facto moratorium on embryo research in the United States. We are troubled by a number of aspects of the report, especially by (1) the fact that the proposed guidelines apply only to government-sponsored research and leave the for-profit sector unregulated, (2) the misleading impression that all embryo research falling under the guidelines is directed at improving health and not driven by its scientific or commercial potential, and (3) the panel's failure to address germ-line genetic engineering, although the research being regulated clearly points in that direction.

Regulating Human Embryo

Research

The right of legitimate governments to allocate public funds for scientific research has been established in practice and law. With the explosion of publicly funded science after World War II and the experience of unethical human experiments in most industrialized countries, governments were also faced with regulating certain spheres of scientific activity involving hazardous materials, human subjects, animal research, and more recently genetic engineering. The recommendations of the panel would add a new set of guidelines that regulate research with human embryos or ova derived from women or fetuses.

One of the key limitations of this form of regulation is its scope, since any regulations issued by NIH will only apply to federally funded research. NIH has no statutory authority to regulate the emerging IVF industry. So an obvious question is, If regulations are established for federally sponsored research, what will happen to privately funded research? The panel's report states that research on preimplantation embryos is already being carried out in many privately financed laboratories throughout the United States. Is there any reason to believe that federal guidelines will be adopted by private companies? If they are adopted on a voluntary basis, how will compliance be monitored?

An analogy might be drawn with the NIH guidelines for recombinant DNA research. Men those guidelines were first issued in 1976 biotechnology companies were new and few in number, but despite this they were able to lobby

against various congressional bills, which were subsequently defeated. But scores of companies, seeking to gain public confidence in genetic engineering, pledged to abide by the NIH guidelines and with very few reported exceptions, voluntary compliance seemed to work.

This is not a good model for embryo research, however, because the circumstances are different. In the 1970s the biotechnology industry was just getting started and the threat of federal legislation provided a strong incentive for industry compliance with the NIH guidelines. Also, the biotechnology industry was largely made up of molecular geneticists who had appointments at universities and brought the culture of the research universities to the start-up companies. Commercial success was still years away, tempering the profit incentive for circumventing the guidelines. The fact that selected municipalities passed their own standards, which were stricter than the NIH guidelines, also served to keep the industry in check. Furthermore, CEOs were aware that they might be more strictly regulated if many private sector violations were disclosed. Another difference from the present situation is that, at least initially, the NIH guidelines were addressed exclusively to laboratory hazards and did not proscribe experiments on ethical grounds.

In contrast to the conditions surrounding the issuance of the recombinant DNA guidelines, the IVF industry will have been growing for more than a decade before the projected embryo research guidelines are put in place. According to the panel's report, much of the IVF research has been directed by clinicians who lack experience in basic research and developmental biology. In addition, the commercialization of reproductive technologies has resulted in the establishment of profitable enterprises, including sperm banks, IVF centers, and fertility clinics. The issues pertaining to embryo manipulation involve social values and moral judgments, but as the business interests of IVF are to insure that viable eggs can be effectively implanted into a woman's uterus at acceptable cost, commercialization of embryos increases the prospect that there will be no uniformity in the way ethical values and judgments will be interpreted and implemented. No institutional sanctions or incentives currently exist that command uniform compliance across academic and commercial sectors.

The incentive for federally funded researchers to comply with NIH guidelines for embryo research is obvious. First, researchers will not be able to publish results obtained in violation of the guidelines. Second, individuals found violating federal guidelines risk losing their grant support, as was the fate of Martin Cline, who was found to be in

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violation of the NIH guidelines for his 1980 experiments involving the transplantation of genetically engineered cells into the bone marrow of two women. Neither of these incentives obtains in the private sector, however. The manipulation of embryos for profit falls outside the authority of NIH embryo guidelines even though the prospects for doing harm and violating social mores may be even greater in the commercial sector than in institutions subject to the NIH guidelines.

Consider some of the prohibitions the embryo panel proposes. Its guidelines state that donors of sperm, eggs, or embryos should not receive more than reasonable compensation. But what is "reasonable" when the donation of eggs for research introduces health risks, pain, and discomfort? Women are routinely prescribed drugs to induce superovulation, undergo ultrasonic transvaginal oocyte retrieval or are impregnated by artificial insemination, and are at greater than usual risk of ectopic pregnancy. If, as is likely, the demand for eggs will greatly exceed supply, in the absence of strict federal oversight the price of eggs will be determined by the market. Though the 1984 National Organ Transplant Act prohibits the commercialization of organs, this act may not apply to the sale of gametes and embryos. For this reason some states have enacted legislation restricting the sale of human fetuses.

Another area proscribed by the panel's proposal is sex selection of embryos, except to prevent diseases linked to the X chromosome. However, clinics are in the business to satisfy customers. If customers want to select for sex, what is to prevent private IVF clinics from implanting embryos of the desired sex? Twinning of embryos for gestation is also deemed unacceptable under the proposed standards. But there is nothing to stop private clinics from catering to clients who, for whatever reasons, may desire twins separated in time. If twinning followed by transfer into a woman's uterus is unacceptable in research, then it should be proscribed in IVF clinics. These two examples point to a flaw in the current approach, which restricts certain manipulations of human embryos and sets national standards and procedures for the review of federally funded research, but leaves states to regulate commercial IVF clinics and laboratories.

The Medicalization of Infertility

We also have other questions about the content of the Human Embryo Research Panel's report. The report is intended to allay fears and diminish opposition of religious groups who see human embryo research as an attack on human dignity. The document argues (1) that human embryos do not have "the same moral status as infants and children" and (2) that the permitted research will be of

"significant" human, and clinical, benefit. While we accept the first of these claims, the document offers no evidence to substantiate the second.

We agree that the research will be of scientific interest, which in itself may be a "human benefit," but its clinical benefits are highly questionable. To the extent that the research might increase scientific understanding of the processes of fertilization, early cell division, and implantation, it might improve the success rate of IVF. However, it is debatable at the outset to what extent the "infertility" that IVF tries to "cure" is a health problem rather than a social problem. Much infertility is generated by social circumstances: infections due to poorly constructed IUDs, untreated pelvic inflammatory disease, hormone-induced endometriosis, gonorrhea and other sexually transmitted diseases, etc. At present, infertility is being increasingly medicalized and its social origins go unmentioned, while nontraditional ways to build families are being downplayed or even opposed. It is not clear that the inability to produce a biological child is a health concern for which medical intervention is the best remedy.

Yet, without the medicalization of infertility and the public acceptance of IVF as a proper scientific and medical response, there would be no way to justify the collection of eggs and their fertilization outside a woman's body. Societal acceptance of IVF constitutes the essential port of entry into all forms of human embryo research.

However, the collection of eggs, and hence IVF, involves health risks whose full extent is not known, partly because IVF is largely in commercial hands. As a result, there has been insufficient follow-up of its consequences for both the women undergoing the procedure and the children resulting from it. The NIH document stipulates that women must be informed of the risks of hormonal stimulation of the ovaries, a routine practice permitting physicians to "harvest" more than one ovum as well as to schedule the release of the ova from the ovary. This hyperstimulation of the ovaries is known to increase the risk of developing ovarian cancer, though no one yet knows the full extent of this risk nor whether some women are at greater risk than others. This is a serious issue that has not received sufficient attention from IVF advocates. It is especially serious for women who are not themselves candidates for IVF, but are producing eggs either for someone else or for research. How can physicians "explain" these risks, as the document states they must, when the extent and perhaps even nature of these risks is unknown?

Preimplantation Genetic Diagnosis

One of the benefits cited in the report is the improvement of techniques for preimplantation diagnosis of genetic and

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chromosomal abnormalities associated with severe inherited disorders. Predictive genetic diagnoses are worrisome because they feed the mistaken ideology proclaiming that genes are the chief determinants of human health and well-being. In addition, in most situations, genetic predictions are only statistical. Since most conditions are quite variable, the diagnoses cannot predict individual outcomes.

If preimplantation diagnosis begins to be used routinely, IVF could become the preferred means of procreation for those who want to avoid using abortion to prevent the birth of a child predicted to be born with a disability. However, only a small minority of women will be able to afford to take that route.

Acceptance of the more or less routine use of preimplantation predictions could result in two possible scenarios, both of them bad. First, prospective parents who can afford it will be made to feel that they owe it to their future children, society, and themselves to test embryos for all possible genetic variants and select only those that measure up to some arbitrary standard. This would funnel personnel and scientific resources to one segment of the population and expand geneticization. In addition, the medical profession would need to set up hierarchies of "acceptable" and "unacceptable" conditions, so that tests would be performed to detect the unacceptable ones. Such distinctions constitute a form of discrimination that would have to be tested in the courts. Why should it be permissible to eliminate embryos (or indeed fetuses) predicted to develop Down syndrome or cystic fibrosis, while forbidding the elimination of those predicted to be female or, for argument's sake, gay? (We doubt that "gayness" is a biological trait that can be predicted.) In either case, we will as a society accept it as our right to decide which of us is or is not fit to live in the world.

There is also a scientific issue. At this point, there is no way to assess the accuracy of health predictions based on preimplantation diagnoses. Animal studies are making clearer day by day that genetic predictions can be way off the mark. In fact, complete deletions of some genes that were thought to be essential for an animal's survival have had no observable effects. Yet, human embryos said to harbor a "bad gene" will be discarded and there will be no way to verify whether and to what extent the predictions may be wrong.

The least that should be done to establish the potential predictive validity of preimplantation diagnoses would be extensive anonymous testing of the general population to ascertain to what extent healthy people carry DNA sequences that preimplantation diagnoses would predict to

be "bad." Without such scientific verification, genetic clairvoyance will lead to invasive, risky, and expensive medical procedures with no health benefits. In evaluating the personal, social, and economic costs of preimplantation diagnosis we must not ignore the fact that an unregulated and largely for-profit IVF industry will be only too eager to expand its market to include this entirely new cohort of candidates for IVF.

Nuclear Transplantation

The report approves of transplanting a nucleus into an enucleated egg and calls for additional review for similar experiments involving transfer of the modified egg into a woman's uterus. The long-term rationale for the research is to circumvent or correct a cytoplasmic defect. A plausible real-life scenario, which is forbidden by the panel, is that a woman has a "defect" in her cytoplasmic DNA, but not in her nuclear DNA. She wants to have a child that inherits her nuclear DNA, without risking that it be born with the condition mediated by DNA in her cytoplasm. She therefore wants to use the fertilized (or otherwise activated) egg of a donor who does not have the condition in question, but she wants to have the nucleus of that donor's egg removed and replaced by the nucleus of one of her own cells. This, of course, is what we mean by cloning and it is forbidden by the report. However, though this experiment is explicitly only permitted for research purposes, the document characterizes the research as aiming "to circumvent or correct an inherited cytoplasmic defect." So once again health concerns get dragged in for justification, even though they surely do not merit consideration. (Can we look forward to future litigation about whether the donor of the egg cytoplasm or the egg nucleus is the "real" mother?)

Germ-Line Genetic Engineering

It is of major concern to us that the panel's report is notably silent on this issue, although everything in the document builds up to it as the next logical step. In fact, investments in research into preimplantation genetic diagnosis and the other extra-uterine manipulations of eggs and embryos only make scientific and economic sense in the context of germ-line modifications. It was extremely important that the panel state its opposition to germ-line genetic manipulation, and it is worrisome that it chose not to do so.

In summary, we believe that the current federal approach to embryo research and development fails to provide oversight for the rapidly growing IVF industry and creates an artificial divide between embryo manipulation for research and embryo manipulation for profit. In addition, justifications for this research on health grounds are

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grossly overstated and mask important questions regarding the social origins of infertility. Our analysis of the report is not based on fears about the "moral status" of the embryo, but on the fact that we consider the use of public funds for embryo research to be largely misdirected and likely to result in harm to women, as well as in legal and moral conflicts that exacerbate inequalities and divisions in our society.

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