POLICY FORUM: BIOMEDICINE

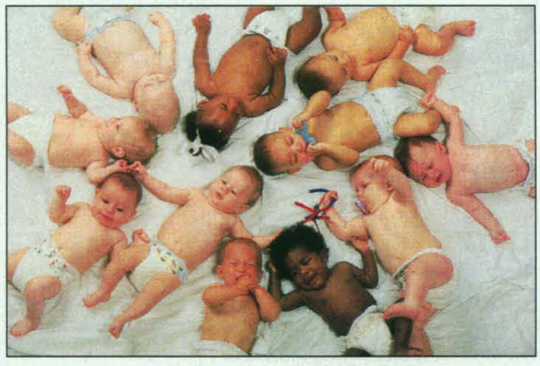
ART into Science: Regulation of Fertility Techniques

ISLAT Working Group

On 25 July 1998, Louise Brown, the first child born through in vitro fertilization, was 20 years old. Since her birth, 300,000 other children have been created worldwide by in vitro fertilization (IVF). Variations of the technology abound, including the use of donor gametes, transfer of the embryo into a surrogate, and preimplantation genetic screening of in vitro embryos. Potential parents now seemingly have greater control over how they bring children into the world. They can even, as did a California couple, choose an egg donor, sperm donor, and surrogate gestational mother, thus creating a child with five or more potential legal parents (*1*).

The assisted reproductive technology (ART) industry, with an annual revenue of $2 billion (*2*), is growing to serve an estimated one of six American couples who are infertile (*3*). Annually, in the United States alone, approximately 60,000 births result from donor insemination (*4*), 15,000 from IVF (*5*), and at least 1000 (*6*) from surrogacy arrangements. In contrast, only about 30,000 healthy infants are available for adoption (*7*). What is striking about this comparison is that every state has an elaborate regulatory mechanism for adoption whereas only two states, Virginia and New Hampshire, have enacted legislation to comprehensively address ARTs.

Despite the fact that many families have been created with ART, the field has not been without problems. These include experimentation without appropriate review, use of embryos without consent, inadequate informed consent, conflicts regarding control over stored gametes and embryos, and failure to routinely screen donors for disease. Currently, the United States has taken a laissez faire approach toward ART. In contrast, other countries combine outright prohibitions of certain procedures, such as sex selection for nonmedical purposes [for example, in Canada (*8*)], and licensing requirements to limit who may perform reproductive technologies [for example, in the United Kingdom (*9*)]. Despite the existence of voluntary guidelines by the American Society of Reproductive Medicine abuses continue to occur. Medical researchers in other fields risk losing federal funds or academic positions if they do not comply with human subjects' protections. Reproductive technologists, many of whom practice in private clinics, do not have such constraints.



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Babies. Why should their safety be better regulated if they were adopted than if they were born through use of assisted reproductive technology?

Regulation of ART

In the United Kingdom a licensing authority was established under the Human Fertilization and Embryology Authority. When such an oversight group was suggested in the United States, reproductive technologists argued that they should not be singled out for regulations that do not apply to other areas of medicine. Yet enhanced regulation is justified in this area because the constraints usually in place in other fields of medicine are lacking here.

For several reasons, reproductive technology has been insulated from regulations that apply to other medical fields. For example, the political undertow from the abortion debate has led every administration from the late 1970s to the present to reject federal funding of embryo and fetal research. As a result, IVF clinics, which do not receive federal research funding, are not required to set up institutional review boards (IRBs) or to review innovative therapies under the human research subject regulations of the Department of Health and Human Services. In fact, IRB review is so rare in this field that it has been viewed as "remarkable" (*10*).

Unlike new drugs and new medical equipment, which are regulated by the Food and Drug Administration, no similar review of innovative ART medical procedures is required (*11*). Consequently, if ART practitioners wanted to undertake an innovative and unproven technique like human cloning, there would be nothing to stop them (other than the legislative bans on human cloning in California and Michigan). In fact, one ART provider has suggested that even though the success rate of cloning is low (1 in 277 in the Dolly experiment), this may not be a barrier because all new reproductive technologies have high failure rates (*12*).

ART also differs from other medical procedures because it is rarely covered by health insurance. For other types of health services, insurers, through managed care outcome studies and evaluation of services, have required proof of efficacy before medical services are reimbursed.

Additionally, medical malpractice litigation, which serves as a quality control mechanism in other areas of health care, does not work as well in the ART field because of the high failure rate (which means that patients do not know whether their lack of success was due to negligence or not). Risks to the children may not be discernible for many years, which may be past the period of time a statute of limitations on a legal suit has run. In "wrongful life" cases, courts have been reluctant to impose liability on medical providers and laboratories for children born with birth defects where the child would not have been born if the negligent act had been avoided (*13*).

In 1992 a federal law was passed to require ART clinics to report success rates to the Centers for Disease Control (*14*). Implementation was slow—the first report was published in December of 1997. In 1992 there was concern that the federal government did not have the constitutional authority to regulate ART clinics, because medicine is traditionally regulated at the state level. Since then, however, federal court cases have established Congress' ability to regulate medical clinics, whether or not they receive federal funds, if patients travel across state lines to use them, if supplies come from out of state, and if the doctors attend conferences in other states (*15*). All of these factors are present in ARTs.

The consequences of the laissez-faire approach have been documented by the re-

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port of the New York State Task Force on Life and the Law (*16*).They identified various major problems, such as clinics' lack of oversight, variability in success rates, failure to assess risks associated with ovarian hyperstimulation, failure to disclose multiple gestation risks, insufficient follow-up data collection efforts, and inconsistent reporting of risk data for egg donation (*16*). Despite their criticisms, the New York Task Force would impose few new responsibilities on physicians to change practices or curb abuses. In contrast, we recommend a federal law to set a minimum standard requiring IRB approval of new ARTs; data collection, reporting, record keeping, and informed consent. Noncompliance would result in criminal or civil liability.

Data Collection, Reporting, Records

ART should be treated as a science. Currently, ART practitioners experiment on patients in the clinical setting without required peer review of research methods or protocol oversight. With ARTs, experimental techniques have been introduced rapidly in many of the more than 280 ART clinics in the United States without sufficient prior animal experimentation, randomized clinical trials, or the rigorous data collection that would occur in federally funded studies (*17, 18*).

Intracytoplasmic sperm injection (ICSI) has been used since 1993 as a therapy for male factor infertility. Only recently has it been observed that children born after this procedure are twice as likely to have major congenital abnormalities as children conceived naturally (*19*). The newly discovered risks include an unbalanced chromosome complement and male infertility (*20*). Children conceived through ICSI may experience mild or significant developmental delays during their first year more often than children conceived by natural conception or IVF (*21*).

ART procedures may present risks to women as well. ARTs increase pregnancy-related risks to women—higher rates of preeclampsia, diabetes mellitus, bleeding, and anemia (*22*). There is some indication that hormonal stimulation during ART may increase the risk of ovarian cancer (*23*). Yet new techniques are used on women before being adequately researched in animals. IVF itself was applied to women years before it was applied to baboons, chimpanzees, or rhesus monkeys, leading some embryologists to observe that it seemed as if women had served as the model for the nonhuman primates (*24*).

Our analysis of public health implications of ART indicates the need for more consistent record keeping and review. Sperm and egg donation account for more than 60,000 births annually, yet there is no uniform procedure for storing information regarding the donor, the resulting birth, and medical history information. The recent discovery that a California semen donor transmitted polycystic kidney disease to at least one child and possibly many other children (*25*), and the case of Dr. Cecil Jacobson (*26*) who secretly inseminated over 70 of his patients with his own sperm, are striking examples.

Data should also be collected on long-term health risks of treating women with fertility drugs. Studies should be undertaken on ART children to assess the long-term medical and psychological effects of ART procedures, especially cryopreservation. All ART clinics should be required to obtain and maintain updated medical and family information about both donors and ART children, including any reported change in medical status of donors.

Number of Embryos Transferred

Unlike England, where doctors are prohibited from implanting more than three or four embryos, the laws in the United States set no limits on how many embryos a physician may implant. The New York State Task Force deferred to the American Society for Reproductive Medicine's voluntary recommendation that generally only four embryos be transferred, but it is clear that the guidelines are not being followed. In fact, the recently published report by the Center for Disease Control (*5*), examining data collected from 281 ART programs in 1995, shows that in some programs seven or more embryos are being transferred during an IVF cycle. Out of ART births, 37% are multiples as compared with 2% in the general population. Multiple pregnancies present significant risks to the resulting children in terms of increased frequency of death within the first year and long-term disability (*27*). We recommend that a federal law be adopted limiting the number of embryos transferred per cycle to women to four.

Informed Consent and Disclosure

Basic informed consent requires that the patient or patients be told the risks, benefits, and alternatives of a treatment. Clinics should, at minimum, be required by federal law to disclose pregnancy rates; how pregnancy is confirmed; the live birth rate for the clinic; and the risks, benefits, and specific procedures for the technique being considered. Clinics should also disclose the risks associated with fertility drugs. They should disclose the risks of multiple births, including potential medical and psychological problems for the offspring.

The clinic should be required to disclose all embryo disposition options: storage, donation for use by another couple (known or unknown), donation for research, or destruction. Moreover, the clinic should disclose which services it actually offers, including the costs, duration, and location of gamete and embryo storage, and which services it does not offer that other clinics do.

Conclusion

ART involves creating children and building families, a fundamental social value. These minimum scientific standards for the practice of ART were designed to protect the interests of all participants—couples, children, donors, and health care providers.

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