chapter 9

Quality Assurance in Research and Clinical Care

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Chapter 9

Quality Assurance in Research and Clinical Care

This chapter concentrates on the role that can be played by medical societies, State governments, and the Federal Government to assure high quality in the provision of four particular reproductive techniques: in vitro fertilization (IVF), artificial insemination by donor, embryo transfer, and gamete intrafallopian transfer (GIFT). Surrogate motherhood raises discrete questions related to the relinquishment of parental rights by women who are gestational mothers, and is considered in more depth in chapter 14.

Quality assurance includes protecting individuals from being offered experimental treatments under the guise of therapy and from the inappropriately enthusiastic use of procedures not yet shown to be safe and effective. In addition, some procedures are accepted medical practice for certain indications but not for others. For example, IVF was originally offered only to women with damaged fallopian tubes, but has more recently come to be used for other types of infertility, including male factor infertility. As indications for use expand, it becomes increasingly important for patients to understand the realistic likelihood of success. Differences in success rates among clinics cannot yet be fully explained, and some clinics have yet to achieve a live birth following IVF.

Another concern in this area is that IVF requires the creation of extracorporeal embryos that may then be donated, sold, frozen, or used in research. Restrictions on these dispositions of embryos are not intended to assure high quality medical care per se, but rather are an attempt to limit the abuses that could arise as a corollary to creating extracorporeal embryos.

Finally, the use of donated semen poses the risk of disease transmission. Concern over reports of hepatitis B transmission in the United States and human immunodeficiency virus (HIV) transmission in Australia following donor insemination has led to activity in State legislatures (see ch. 13), the Department of Health and Human Services (DHHS), and various professional societies.

Professional societies influence the research and treatment protocols of medical practitioners. Some, such as the American College of Obstetricians and Gynecologists (ACOG), the American Fertility Society (AFS), and the American Association of Tissue Banks (AATB), have issued reports and guidelines on use of donor eggs and sperm, treatment of extracorporeal embryos, and the general assurance of high-quality medical treatment of infertility.

The American Fertility Society, for example, has set up a voluntary registry of IVF and GIFT programs and a special interest group for those who meet certain minimum criteria for staffing and success in achieving pregnancy. Although membership in the special interest group does not confer accreditation, that term has been used by at least one program to help identify itself as meeting certain standards of practice (see figure 9-1). In addition, all registry members are asked to report on their techniques and success rates, so that the efficacy of various IVF and GIFT protocols can be evaluated.

The first part of this chapter discusses the structure of professional medical societies and their potential for providing practitioner education, for setting a standard of care that protects individuals from experimental procedures offered in the guise of therapeutic treatment, for assuring adequate staffing and laboratory facilities for clinics offering such treatments, and for developing a consensus among researchers and practitioners concerning the handling of extracorporeal embryos and the involvement of third parties in conceiving or bearing a child for another person.

Federal authority can facilitate nonregulatory efforts to assure high quality infertility treatment. Governmental authority can also be brought to bear on these issues with respect to establishing standards of medical practice; approving protocols for research with humans; protecting the extracorporeal human embryo; regulating donor screening and confidentiality; regulating commerce

Figure 9-1.- In Vitro Fertilization Clinic Advertisement
Position Available

IVF Laboratory

New York Medical Center: Immediate opportunities to join the laboratory of established **AFS accredited program involved in In Vitro Fertilization, GIFT, and Gamete Cryopreservation, Previous experience in gamete culture and manipulation, or in tissue culture and genetics would be an advantage. Master's or Bachelor's degree required. Responsibilities would variously include management and clinical service related to the Laboratory, activities such as mouse embryo culture etc., and involvement in research related to the program.**

Interested candidates should forward a resume with references

SOURCE: Biology of *Reproduction,* **April 1987.**

in sperm, eggs, and embryos; and attaching conditions to the delivery of medical services paid for by Government programs or to research financed by Government agencies.

States have actively legislated in areas concerning artificial insemination by donor (see ch. 13), and a number of States have regulations related to fetal research (see app. C). But few have specific statutes on IVF, and no legislation exists on gamete intrafallopian transfer. Since the oversight of medical practice is primarily a State function, regulating these particular technologies will almost always fall primarily to individual States.

The Federal Government has over the last 14 years formed four commissions that have made recommendations on, among other topics, noncoital reproductive techniques: the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; the Ethics Advisory Board of the Department of Health, Education, and Welfare; the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research; and the Congressional Biomedical Ethics Board. The Federal powers to implement the suggestions of these advisory panels are explored near the end of this chapter.

THE ROLE OF PROFESSIONAL SOCIETIES IN ASSURING QUALITY

Membership in a professional medical society is purely voluntary, as is the members' adherence to the organization's medical standards. Physicians are licensed by the State. A medical license not only permits them to practice medicine, but forbids all those without a license from competing by making the practice of medicine without a license a criminal offense. This State license is the only one required to practice medicine or any of its specialties; neither failure to belong to a specialty organization nor failure to maintain such a membership in any way limits a physician's legal ability to practice a medical specialty. Nonetheless, intellectual and economic incentives in the 1930s and 1940s led to the development of certification procedures for specialties, to hospital-based specialty training programs, and finally to the growth in voluntary professional societies of specialists (59).

Professional organizations can set informal standards for clinical care, make their members undergo continuing professional education to maintain active membership status, and require periodic examination and reexamination. A professional organization can also survey its members and gather data on new techniques. Taking part in such studies, however, is purely voluntary on the part of the membership.

In the field of infertility care, one of the most influential medical societies is the American College of obstetricians and Gynecologists. Members, designated as "fellows," must be licensed physicians certified in obstetrics and gynecology, ACOG's first national Constitution and Bylaws, adopted in 1951, listed among its purposes:

- to establish and maintain the highest possible standards for obstetric and gynecologic

education,
- to perpetuate the history and best traditions of obstetrics and gynecology practice and ethics,
- to maintain the dignity and efficiency of obstetric and gynecologic practice in its relationship to public welfare, and
- to promote publications and encourage contributions to medical and scientific literature pertaining to obstetrics and gynecology (46).

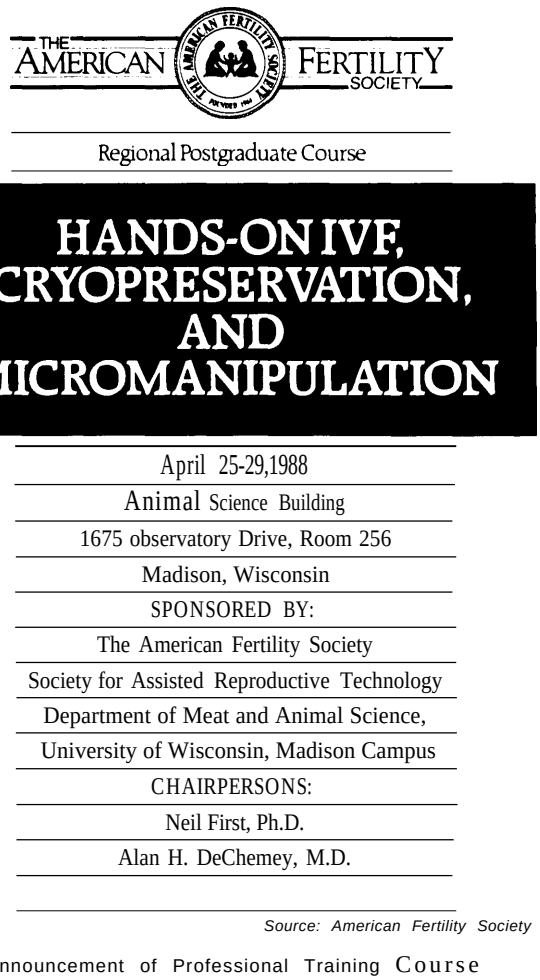
Pursuant to its professional purposes, ACOG has periodically issued statements on the professional and ethical issues raised by use of medically assisted reproduction (3). For example, in 1984 its Committee on Gynecologic Practice classified IVF as a "clinically applicable procedure" (i.e., clinically effective for general or limited use) and then listed personnel and facilities requirements for an IVF program (5). In 1986 its Committee on Ethics issued a statement acknowledging the ethical issues posed by the creation of extracorporeal embryos (4). Statements such as these do not bind a society's members to a particular practice, but do serve to develop some consensus among practitioners.

Similarly, the American Association of Tissue Banks issued a statement in 1984 setting forth the qualifications and training needed to serve as director of a tissue bank, including a sperm bank (2). Further, its Reproductive Council listed a variety of conditions that ought to be sufficient to exclude a person from eligibility as a sperm donor, and proposed a series of examinations that ought to be undertaken to detect those conditions.

Another influential group in this field is the American Fertility Society, open not only to obstetricians and gynecologists, but also to urologists, reproductive endocrinologists, researchers, "and others interested. " Its purposes are similar to those of ACOG, and include "extending knowledge of all aspects of fertility and problems of infertility in man and animals."

The AFS Ethics Committee published a report in 1986 that summarized prior AFS efforts with respect to noncoital reproductive techniques (6) and made recommendations for additional action (7). The report noted, for example, the AFS guidelines for minimum staffing, counseling, institutional review, and medical services of an IVF program. These guidelines, and those of ACOG, have been adopted into State law in Louisiana (Act No. 964, 1986), an example of the interaction possible between medical societies and State legislatures. AFS has also initiated a hands-on training program for handling gametes and embryos. Such programs help introduce practitioners to techniques often never seen in medical school or during residency. Of course, short training courses are not equivalent to subspecialty training (12).

AFS recommended in its 1986 Ethics Committee report that IVF clinics develop standard practices for collecting information on pregnancy and live birth rates, for followup on the participants and any resulting children, for genetic screening of gamete donors, and for equipment maintenance. The report stressed the importance of fully



Source: American Fertility Society

Announcement of Professional Training Course

informing potential patients of the success rate and experience of the particular clinic they are visiting, of the availability of alternative therapies or methods to form a family, of the costs they can anticipate, and of the financial or social support they can expect to receive (see box 9-A).

Professional society membership can confuse patients. Numerous 'organizations, such as the American Fertility Society, are open to anyone who expresses an interest in the area; membership does not necessarily indicate special expertise. Patients choosing a doctor should inquire about a physician's past experience with the infertility treatments and certifications in subspecialties, and not rely only on the physician's membership in a society or attendance at a short, continuing medical-education course (12).

Box 9-A.—Questions To Ask Before Beginning IVF Treatment

Before beginning IVF treatment at a particular clinic, patients might want to ask a number of questions, including:

- What is the center's pregnancy rate and how is it calculated? Does the clinic measure success by achieving chemically detectable pregnancies, those confirmed by ultrasound, or live births? What is the most meaningful success rate for this particular IVF attempt, based upon the patient's history of responding to stimulation, transfer, and pregnancy? What is the success rate for patients with similar histories?
- Does the clinic implant all fertilized eggs or only those that appear capable of normal development? Does it limit the number of implanted fertilized eggs to minimize risks associated with multiple births? Can the clinic freeze extra embryos for subsequent attempts? What has been the clinic's rate of loss for those embryos?
- Does the clinic offer psychological counseling or have a regular means of referral for those patients who seek help? Is it coordinated with the medical workup and transfer attempts, to anticipate difficulties or disappointments?
- Is the program community-based or a referral center? Referral centers are beginning to train local physicians to handle preliminary workups and ovulation inductions, so that the patients need travel to the main center fewer times.
- Does the clinic offer assistance in obtaining the highest possible insurance reimbursement for the patient? What has been the reimbursement experience of other patients with similar insurance plans? Does the clinic offer a sliding fee scale for patients with low incomes?

SOURCE: Office of Technology Assessment, 1988.

DISTINGUISHING THERAPEUTIC FROM EXPERIMENTAL TREATMENTS

One difficult problem in assuring high-quality infertility treatment is that of correctly characterizing a new kind of service, such as IVF, as experimental or therapeutic. The classification has implications for whether fees may be charged, for insurance coverage, and for determining the amount of information that must be made available before a person can be considered to have made an informed choice to undergo the procedure. And any classification of IVF as "experimental" further complicates ethical questions concerning the appropriateness of experimenting with human embryos (16).

As noted earlier, ACOG classifies IVF as a "clinically applicable procedure ''—i.e., no longer purely experimental (5). Similarly, a 1986 AFS position paper stated: "IVF is no longer considered to be an experimental procedure" (7). The AFS Ethics Committee, however, did not explicitly find IVF

to be nonexperimental. Although it found the procedure to be ethical medical practice, it concluded that "when a procedure hike IVF] is being done for the first time by a practitioner or for the first time at a particular facility, that procedure should be viewed as experimental," adding "there is merit to the position that charges should be reduced until the clinic has established itself with a reasonable success rate" (7). This line of reasoning could be troublesome, as it is unclear whether it is the number of times a procedure has been done or the success with which it is used that determines its experimental status. Further, even an experienced practitioner might encounter reduced success upon changing laboratories or laboratory personnel.

Some might argue that a procedure is either experimental or it is not, depending on whether it is a deviation from standard medical practice for the purpose of testing a hypothesis or obtaining new knowledge. The fact that a particular person or facility is performing it for the first time does not necessarily change the nature of the procedure itself. The AFS executive board in 1986 passed a resolution calling on insurance companies to reimburse for IVF, as it is no longer an experimental procedure. Institutional Review Boards (IRBs) across the country have also struggled with this issue, some concluding that IVF is research and others that it is innovative or accepted clinical practice.

Federal regulations define "research" (rather than "experimentation") as "a systematic investigation designed to develop or contribute **to** generalizable knowledge" [45 CFR 46.102(e)], thus focusing on the intent of the individual performing the research. In general, before such an activity is conducted on a human subject, there must be successful animal work, a reasonable hypothesis, IRB review, and informed consent from the research subject.

Some commentators have suggested that there is no clear line between experimentation and therapy (as indeed the preceding definitions suggest), and have argued for a continuum that includes a third category of interventions between research and therapy, often designated "innovative therapy." The AFS also suggested new terminology for such categories, proposing '(clinical experiment" for an innovative procedure with little or no historical record of success, and "clinical trial" for the systematic effort to improve the effectiveness of an existing procedure (7).

In a similar vein, the Blue Cross/Blue Shield Association's Technology Evaluation and Coverage (TEC) Program groups procedures, for the purpose of coverage, as experimental (largely confined to animal or laboratory research), investigative (limited human applications but lacking wide recognition as proven safe and effective), and standard (widely accepted as clinically effective, but may need to be qualified as standard only under certain specified conditions) (33).

The Food and Drug Administration (FDA), on the other hand, has not adopted these distinctions, and a drug is either "investigational" (research) or proven "safe and effective" (i.e., therapeutic). IRBs have authority to review and approve all "research" and to decide whether or not a proposed use is '(research. " Rulings by individual medical societies, insurance companies, or governmental agencies are not conclusive. Indeed, such rulings may often be in conflict, as they currently are in the area of heart and liver transplantation and IVF (see, e.g., 45 CFR 46).

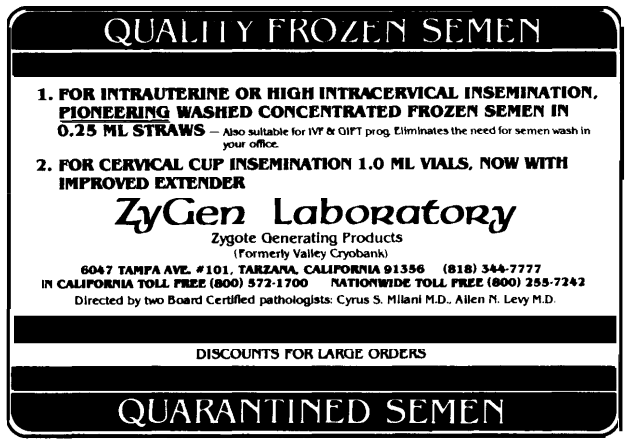
SCREENING DONOR SPERM FOR SEXUALLY TRANSMITTED DISEASE

Professional societies can also continue to work to minimize the risks associated with procedures that have long been accepted as therapeutic. One example can be drawn from the debate over the use of fresh and frozen sperm for artificial insemination by donor. Only by freezing sperm and testing the donor after 3 or more months have passed can sperm be shown to be almost incapable of transmitting the human immunodeficiency virus. This is because current laboratory tests for exposure to the virus areas yet sufficiently crude that they require 3 or more months for the concentration of antibodies to become high enough to be detected. AFS guidelines in place through

1987 did not suggest that physicians abandon the use of fresh sperm, and suggested instead that they carefully screen donors to exclude any whose exposures in the months just prior to the donation might have left them infected. OTA'S national survey found that physician awareness of AFS standards was tantamount to their adoption (63). As long as there was no evidence that this practice had failed to screen out all infected donors, its possible inadequacies were theoretical only, and widespread physician preference for possibly more efficacious fresh sperm was accepted.

Just such evidence came out of Australia, where four of eight women became seropositive after insemination with sperm from a seropositive donor (50). In 1987 there were reports that at least one U.S. sperm bank found that a donor serocon - verted (i.e., tested positive for HIV after having tested negative at the time of donation) during the time that his sperm where quarantined (55, 58)70). Another U.S. sperm bank, despite adherence to the 1987 AFS standards for fresh-sperm donors, subsequently found the donor to be infected and capable of having transmitted the virus at the time of donation (56,70).

In 1988, new AFS standards were developed. They stated that in light of the inability to ensure that sperm are incapable of transmitting HIV without freezing the sperm and retesting the donor, the use of fresh sperm is unwarranted (50). These new AFS standards are identical to those adopted in 1988 by the FDA, in conjunction with the Centers for Disease Control (CDC), and ACOG is expected to follow suit (70).



Source: ZyGen Laboratory

Advertisement by Sperm Vendor

Some physicians express concern that exclusive reliance on frozen sperm, which is widely perceived to be less efficacious (63), will result in a population of women who fail to achieve pregnancy at all when using donor insemination (56, 70). Another concern is that physician education will stress careful screening of donors for HIV, while failing to stress the importance of improving screening practices for more prevalent infectious diseases, such as hepatitis (56), that are also known to have been transmitted by donor insemination in the United States (64). A final concern is that formal regulation by a State or the Federal Government may prevent physicians from returning to the use of fresh sperm should convenient and economical HIV antigen tests become available, making reliable donor screening possible at the time of donation.

NONREGULATORY PROTECTION OF PATIENTS AND RESEARCH SUBJECTS

Short of regulating infertility treatment and research, the Federal Government could work to facilitate greater data collection and self-regulation. This can be done by authorizing additional Federal efforts for epidemiological studies of infertility (see chs. 1 and 3) and by encouraging the use of governmental, professional society, and insurance industry resources to hold consensus conferences and to recommend protocols for high-quality care. For example, consensus conferences could evaluate data on patients and recommend a protocol that lists the best indications for the use of IVF as opposed to GIFT. Conferences and reports could also help define a "successful" program, distinguish experimental from investigative techniques or applications of standard techniques,

and make more uniform the minimum level of staffing for a program.

Concern over costly and possibly premature applications of medical innovations led to the 1977 creation of the National Institutes of Health (NIH) Consensus Development Program (49,62,66). Its purpose is to develop consensus on the clinical significance of new findings and the financial, ethical, and social impacts of a procedure's development and use. To that end, an Office of Medical Applications of Research coordinates consensus conferences and other activities with the NIH Bureaus, Institutes, and Divisions, and guides the appointment of expert advisory panels to review and make recommendations on medical innovations and their applications. Denmark, Israel, the Netherlands, Norway, Sweden, and the United Kingdom have used similar mechanisms to review medical developments (33).

Despite criticisms that the NIH consensus advisory panels have at times been biased, worked from insufficient data, or made unsupported recommendations (1,34,38,48), over 60 consensus conferences have been convened in the last decade, with noticeable effects on the practice of medicine in several areas, including indications for breast cancer screening by mammography, surgical protocols for treatment of breast cancer, and extension of Medicare and private third-party insurance coverage for liver transplantation. Little or no effect has been demonstrated, in contrast, on the practice of cervical cancer screening or rate of cesarean delivery (49), areas that were also the subject of such conferences.

One important consideration in whether an NIH consensus conference is appropriate is whether the questions concerning the medical technology are primarily scientific and clinical, or primarily ethical or economic. The conferences are more effective when they focus on the former. They are also most useful when professional consensus has not yet begun to build.

A 1987 study funded by NIH to assess the effectiveness of its consensus conference program found that all too often the conference lagged behind other professional educational activities, and so was not itself responsible for any demonstrable improvement in clinical practice. The study also demonstrated that simple dissemination of information concerning the best practice of a technique or use of a device would be insufficient unless coupled with an educational program directed at altering physician practice (39).

In addition, one Federal agency is dedicated to technology assessment of clinical medicine—the Office of Health Technology Assessment (OHTA) of the National Center for Health Services Research and Health Care Technology Assessment, under the Office of the Assistant Secretary for Health. Although much of its work is in response to requests from the Health Care Financing Administration for medical guidance prior to decisions concerning Medicare coverage, OHTA can review other technologies as well (48 FR 2444). OHTA reports focus mainly on safety, efficacy, and indications for use, but at times cover cost-benefit analyses too.

Although infertility treatments are of interest to only a small number of Medicare-eligible patients, the Prospective Payment Assessment Commission (ProPAC) could be useful in forging agreement concerning the experimental or clinical status of procedures such as IVF. It was established by the Social Security Amendments of 1983 (public Law 98-21) as an independent, legislative-branch commission to advise and assist Congress and the Secretary of Health and Human Services to maintain and update the Medicare prospective payment system. ProPAC is required to collect and assess information on safety, efficacy, and cost-effectiveness of medical technologies in order to identify medically appropriate patterns of health resources use. Its findings influence the development of the diagnosis-related groups now used as the basis for Medicare reimbursement to hospitals.

Among professional societies, the American Medical Association (AMA) has a diagnostic and therapeutic technology assessment program, under the aegis of the AMA Council on Scientific Affairs. The program uses panels of experts to examine and report on the safety, effectiveness, and indications for emerging or new medical technologies. The American College of Physicians' Clinical Efficacy Assessment Project uses expert opinion and group judgment to provide up-to-date informa-

tion and guidelines for a variety of medical and surgical procedures, with an emphasis on safety, efficacy, and cost. Procedures that have been evaluated by the program include biofeedback for hypertension and ambulatory cardiac catheterization (26).

The University of California—San Francisco is the home of the Institute for Health Policy Studies, a multidisciplinary research institute that studies efficacy and cost-effectiveness of both standard and new medical technologies. Its advice is often requested by Congress and Federal agencies such as the Federal Trade Commission (FTC) and the Department of Health and Human Services. The Institute of Medicine, an organization chartered in 1970 by the National Academy of Sciences, also has an active technology assessment group, and responds to many congressional requests for studies of the efficacy and costs of particular medical and surgical treatments.

Among industrial groups, the Blue Cross/Blue Shield Association has two influential programs that affect the degree to which certain medical procedures are recognized as necessary, safe, effective, and covered by insurance. The Medical Necessities Program focuses on identifying procedures that are not effective or not strictly necessary. The Technology Evaluation and Coverage Program develops medical policies for the Association's ***Uniform Medical Policy Manual,*** which is provided to all local plans. Although the manual is largely advisory, its use is required by certain national-account corporate plans that cover residents of the several States. As indicated earlier, TEC is mainly concerned with categorizing medical technologies as experimental, investigative, or standard (33). other private, third-party payer groups with technology assessment programs include Kaiser Permanence, a California-based health maintenance organization with almost 2 million members.

STATE AUTHORITY TO REGULATE INFERTILITY TREATMENT AND RESEARCH

"Police power" is not a term referring to municipal police as much as it is a technical term that has come to refer to all the powers of government to protect the health, safety, and morals of its citizens (17,71). All the traditional powers of government, including police powers, are retained by the States, even if parallel areas of Federal authority have developed. Thus, almost all criminal laws are State laws, almost all public health measures are State measures, all licensing of medical personnel and facilities is based on State law, and almost all tort law is State-based.

Accordingly, the States have the authority to regulate noncoital reproductive techniques directly in a variety of ways. All these are limited by the provisions of the U.S. Constitution regarding the rights of individual citizens, but the State's inherent powers to protect patients, research subjects, and perhaps even embryos are broad and provide many potential avenues for regulation. Those with the most relevance to noncoital reproductive techniques are licensing of health care personnel and facilities, certificate-of-need laws, medical malpractice litigation, restrictions on the sale of embryos, and criminal statutes.

Licensing Health Care Personnel

IVF, embryo transfer, and GIFT are medical procedures requiring the skill of a licensed physician. This means that the State can and does limit the performance of these techniques to licensed physicians, and that any nonphysician performing them is practicing medicine without a license—a crime in all States. Some States have enacted statutes declaring that artificial insemination by donor is the practice of medicine, in order to limit or regularize its use. Others have passed artificial insemination laws designed to ensure the legitimacy of the resulting child (see ch. 13) but that refer only to inseminations performed by a physician, thus creating the possibility that the statutes' terms will not fully apply when artificial insemination by donor is performed without a physician's supervision (see discussion of case of ***Jhordan C.*** in ch. **13).**

The medical justification for restricting performance of donor insemination to physicians is that they are better able to screen donors to ensure that no infectious or genetic disease is passed to the recipient or child. Other justifications include the facilitation of screening for nonmedical conditions, such as welfare dependency, marital status, or sexual orientation. It can be argued, however, that artificial insemination should not necessarily be considered the practice of medicine (36). It is easily performed by a nonphysician, requires no elaborate equipment, and may be used to overcome a social condition—lack of a male partner—rather than a medical condition. Further, physician screening against infectious and genetic disease would not be available for coital reproduction, and thus some might argue is not necessarily an appropriate subject of State law with respect to artificial insemination performed by the recipient herself.

Medical licensing protects both the public, who may be incapable of informed comparison shopping and evaluation of quality, and the profession, which otherwise might suffer from undue or unfair competition. This limitation of services to licensed physicians has at times created considerable controversy in the area of childbirth, notably concerning patients' desires to use midwives, but fewer problems regarding noncoital reproductive techniques. One problem, however, has been the inability of singles and homosexuals to locate physicians who find it ethically acceptable to assist them with IVF or artificial insemination by donor.

ACOG's 1986 Ethics Committee statement acknowledged a trend in the United States to recognize that unmarried persons can provide excellent care for their children, and called on physicians to handle requests for infertility services from these people based on the probable welfare of the child and in such a way as to avoid arbitrariness. It went on to state, however, that physicians ought to be free to acceptor reject patient requests if these considerations are kept in mind (4). To the extent that physicians continue to have qualms about the appropriateness of helping singles or homosexuals to have children, as demonstrated in OTA'S national survey of artificial insemination practice (63), and as long as physicians are the only persons entitled to offer these services, this problem of access will persist among unmarried and homosexual women.

Medical licenses are general licenses—i.e., once an individual graduates from an approved medical school, passes a standard examination, and does an internship or residency, he or she can be licensed to practice medicine. The practice of medicine is broadly defined, and includes diagnosis, treatment, prescription, surgery, and other specific activities as the statute or the State's board of medicine may decree.

Specialty Boards, through which a physician may become board-certified in a specialty following more years of specialty training and passing another exam (e.g., Obstetrics and Gynecology), are private certifying agencies. No State requires that a person be a board-certified obstetrician-gynecologist or a member of a private professional organization in order to provide services related to any noncoital reproductive technique. A State could, however, specify (either by statute or regulation) particular qualifications necessary for providing a specialized service, such as infertility treatment. Thus far, only Louisiana has done this, and only with respect to IVF.

On the other hand, it seems likely that at least some State licensing boards will follow the lead of the Massachusetts Board of Registration in Medicine and require its licensees to follow certain nationally recognized standards in defined specialties, such as anesthesiology. The Louisiana law fits this pattern, as it accepts compliance with the training and staffing guidelines of ACOG or AFS as sufficient to meet State law. The Federation of State Medical Boards of the United States publishes compilations of the activities of State licensing and discipline boards, so that States may compare their provisions with those of others (22).

Licensing also provides State governments with the right to intervene (at the request of a patient, another physician, or any third party) to review an individual physician's practice and to discipline the physician, by sanctions ranging from simple censure to license revocation, for failure to follow proper standards in the delivery or advertisement of medical services (22,27). Physicians who are incompetent or have been negligent on

more than one occasion, for example, could have their licenses revoked (22,27). Although such disciplinary actions have historically been rare, many States are trying to improve the operations of their medical licensing agencies and to strengthen the policing function of these agencies. This mechanism is after the fact, but it might deter some unqualified physicians from claiming to be experts in infertility treatment.

Licensing Health Care Facilities

Following World War II and the passage of the Hill Burton Act of 1946 (which made hospital licensure a prerequisite to receiving Federal funds), States that did not have mandatory licensing for hospitals proceeded to adopt statutes requiring such licensure and setting forth certain minimum standards, mainly for construction (30).

Currently all 50 States and the District of Columbia require that hospitals be licensed, although the scope of the laws varies considerably (71). Traditionally, these statutes have focused on minimum safety standards concerning construction, fire, and equipment, rather than on the quality of services delivered at the facility. Nonetheless, the States do have the authority to regulate service provision. Most, however, rely on a private organization, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). In addition, DHHS has in practical effect delegated to JCAHO much of its own authority to certify facilities for Medicare reimbursement.

About half the States also license medical laboratories, and a majority regulate the qualification of laboratory personnel (53). Clear authority exists to adopt regulations governing medical laboratories. States could, for example, adopt laboratory licensing regulations aimed specifically at infertility clinics or free-standing IVF, artificial insemination, embryo transfer, or GIFT programs. On the other hand, one general exception to laboratory licensure relates to a physician's private office. States do not generally license private doctors' office procedures; they license physicians. Therefore, to the extent that a physician can offer infertility treatment in an office setting, it would be unlikely that facility licensing schemes would apply directly to the activity, although certainly it could influence office practice (23).

Health Planning and Certificate of Need

In the early 1970s, the Federal Government established two separate hospital capital expenditure programs intended to control the cost of medical care: the Section 1122 program authorized under the Social Security Act Amendments of 1972 (Public Law 92-603) and the certificate-of-need (CON) program established by the National Health Planning and Resource Development Act of 1974 (Public Law 93-641). The Section 1122 program provided for voluntary agreements between State governors and the Secretary of HHS, such that any hospital failing to obtain State approval of a capital expenditure would not be eligible for Medicare reimbursement of that capital expenditure. The 1974 legislation created a mandatory national system of State and local health planning agencies to conduct reviews of capital expenditures for construction and major equipment purchases, and to perform other review and monitoring tasks that would help reduce medical costs (57).

Some States have used their CON programs to control the introduction of expensive new medical technologies, such as heart transplants. The CON mechanism could be used for large clinics or hospitals offering IVF, embryo transfer, or GIFT, in order to ensure adequate laboratory facilities and equipment, and to determine patient need in light of the efficacy of the procedure, before extensive funds are committed. At least two university clinics and one private clinic have had to comply with CON procedures before establishing IVF facilities (7). But CON procedures are generally not applicable to small office practices, although some exception is made if the services are reviewable were they offered by a hospital or if they go beyond those generally offered in a physician's office (7,31). Further, Federal funding for CON and Section 1122 programs dropped to zero in fiscal year 1987, and the 1974 legislation was repealed in January 1987. By late 1987, only 40 States maintained either a CON or a Section 1122 program, and many States do not structure their programs to apply to nonhospital facilities (69). of those that do, many do not review expenditures of less than $1 million, which makes their applicability to even hospital-based IVF programs somewhat doubtful.

Medical Malpractice Litigation

Tort law is a nonregulatory means for social control of risks to health and safety (10). Permitting individuals **to sue** those who have wronged them through negligence serves as a mechanism for financial and emotional compensation, and for quality control. Of these three, the one most relevant **to** noncoital reproductive techniques is quality control. Theoretically, by making people responsible for their actions, individuals have an incentive **to act** responsibly. In practice, medical malpractice litigation suffers from numerous shortcomings, including the fact that it focuses on past errors rather than future improvements. Nevertheless, it has had **a** profound effect on the practice of medicine and infertility treatment. For example, concerns over malpractice liability have altered the way physicians balance the risk of multiple births against the goal of initiating conception when fertility drugs are used to stimulate ovulation.

The medical profession largely sets its own practice standards. Accordingly, to prove medical malpractice by an infertility specialist, another infertility specialist generally must testify that what the practitioner did was not "good and accepted medical care" for the specialty, and thus amounted to a breach of the practitioner's duty to the patient. Otherwise, the plaintiff patient would need to show that the accepted medical practice in this field is itself so poor that it constitutes negligence toward the patient,

The major issue in this context is how such standards of practice are set in the treatment of infertility, particularly when treatment involves noncoital reproduction, The standard of care in medicine is generally defined by "standard medical practice"-i.e., what reasonably prudent physicians customarily do. The problem is that, at least with IVF, embryo transfer, and GIFT, these procedures are so new that no "standard" of practice exists yet, and practices actually vary widely. In addition, negligence litigation **as an** alternative to regulation is probably "unsuitable for deterring systems failure in cases where the system is new and is introduced into the marketplace without the realization that it is having a significant harmful effect on health, safety or the environment" (10).

ACOG and AFS have made an effort to identify good medical practice in the area of noncoital reproduction. As indicated earlier, both organizations develop and publish guidelines for practice, to be used for practicing and teaching their specialties. It is made clear, however, that these guidelines are voluntary. As ACOG states in the introduction to its published standards:

> It is important, particularly **to** those agencies or individuals who may consult **this** manual in preparing codes and regulations governing the delivery of obstetric-gynecologic health care, to recognize that the standards **set** down here are presented **as** recommendations and general guidelines rather than **as a** body of rigid rules. They are intended **to** be adapted **to** many different situations, taking into account the needs and resources particular to the locality, the institution or type of practice. Variation and innovation which demonstrably improve the quality of patient care are to be encouraged rather than restricted (5).

These guidelines can play a central but not determinative role in malpractice litigation. The general rule in medical malpractice litigation is that the physician must demonstrate that his or her practice conformed with that of the "reasonably prudent physician" (or specialist, if the defendant is a specialist) under the same or similar circumstances. Nonconformity is evidence of negligence. Conformity is evidence of due care, but is not an absolute defense to an assertion of negligence. Conformity to professional custom or guidelines is just one circumstance considered when assessing whether an act was negligent.

One reason compliance with such professional guidelines is not determinative is that a court may find that an entire profession or specialty has lagged behind in adopting rules required by the standard of reasonable prudence. Defendants have tried unsuccessfully to use adherence to customary standards as a conclusive defense. Over 50 years ago, Justice Holmes noted:

> In most cases reasonable prudence is in fact common prudence; but strictly it is never its measure; a whole calling may have unduly lagged in the adoption of new and available devices. It never may set its own tests, however persuasive be its usages, Courts must in the end say what is required; there are precautions so imperative that even their universal disregard will not excuse their omission (60).

Even compliance with a Federal or State statute may not be sufficient to defend fully against a claim of negligence:

> While compliance with a statutory standard is evidence of due care, it is not conclusive on the issue. Such a standard is no more than a minimum, and it does not necessarily preclude a finding that the actor was negligent in failing to take additional precautions (52).

Overall, while compliance with professional or Federal guidelines is evidence of due care, physicians must continually improve their own safety practices to be free of all charges of negligent care.

Regulating Research on Embryos

States specifically addressing IVF research, with the exception of Louisiana, have focused on monitoring and recordkeeping, rather than on limiting research. (See ch. 13 and app. C for summary of State IVF statutes.) Some fetal research statutes, however, are sufficiently ambiguous that they might apply to IVF research or at least have some chilling effect on embryo research within the affected State. (See ch. 13, table 13-2, and app. C for discussion of applicability of fetal research statutes to IVF treatment.)

The laws of Arizona, Massachusetts, Michigan, North Dakota, Ohio, and Rhode Island extend to research with "embryos," and in Kentucky, Louisiana, Missouri, Oklahoma, and Pennsylvania they apply by functional definition to any product of conception (7). Furthermore, in Maine, Massachusetts, Michigan, North Dakota, Rhode Island, and Utah the fetal research statutes are not limited to postabortion products of conception or research in connection with abortion.

Even where statutes are restricted to the products of an abortion, it is still somewhat unclear whether ova fertilized in utero by artificial insemination and then flushed from the uterus prior to implantation would be covered, and thus numerous statutes might possibly be applied to research applications.1 The applicability, however, of all these fetal research statutes is in question in light of the 1986 case *Margaret S. v. Edwards,* which struck down for vagueness a Louisiana ban on experimentation with fetuses obtained from induced abortions (see chs. 12 and 13) (42).

Criminal Statutes

States have the authority to declare criminal, within constitutional limitations, activities dangerous to the public health, safety, welfare, or even morals. Some States, as indicated, make it a criminal offense for a nonlicensed person to offer artificial insemination by donor or outlaw certain types of fetal research. The statutes in Florida and Louisiana prohibiting the purchase and sale of human embryos are based on consideration of the fetus or embryo, as well as larger considerations of public morality and respect for the products of human conception, Criminal homicide statutes are grounded in concerns for public safety, however, and rarely apply to the destruction of embryos in vitro. Few States have extended homicide laws to include unborn children without indicating that they are referring to unborn children in utero (9). Further, in at least two States with embryo protection statutes (Massachusetts and Illinois), district attorneys have agreed not to seek to prosecute any physician engaged in IVF, whether therapeutic or research, so long as the physician agrees to attempt to implant all the embryos created by the process (see ch. 13).

*These include statutes in Arizona, Florida, Indiana, Lousiana, Maine, Massachusetts, Michigan, Missouri, Montana, Nebraska, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, Utah, Wyoming. See app. C for summaries of State fetal research statutes' applicability to embryo research.

FEDERAL AUTHORITY TO REGULATE INFERTILITY TREATMENT AND RESEARCH

In theory, the Federal Government can only exercise those powers specifically granted to it in the U.S. Constitution. None of those powers relates directly to medical care or to human reproduction, so all the laws on licensing health care personnel and defining family relationships are State laws, as described in the preceding section.

Yet the Federal Government is not powerless in this area. With respect to health care in gen-

era], and to noncoital reproductive techniques **in particular, Congress can influence the development of medical techniques forcefully in areas where it has indirect authority to get involved. First, it can encourage nonregulatory efforts by governmental agencies, professional societies, research institutes, and industrial groups, in order to influence the clinical practice of new infertility therapies, a topic discussed at the end of this chapter. Second, the Federal Government has extensive regulatory powers over health care under its taxing and spending power and under the interstate commerce clause.**

Taxing and Spending Authority

Article I, Section 8 of the U.S. Constitution states that "Congress shall have Power to lay and collect Taxes." This is a direct authority, and Congress may tax individuals whom it may not otherwise regulate independently. This same section also provides that Congress may spend money "for the **common Defense and general Welfare of the United States." It is through the use of conditional appropriations —i.e., attaching strings to grants of money—that Congress derives its power to regulate through spending (61).**

One question is whether the '(general welfare" clause grants Congress authority to do whatever is **in the "general welfare" of the country, or whether it is restricted to spending money. Attempts to limit the use of Federal funds to noncoercive purchases have proved ineffective, and it is generally recognized that Congress itself can decide how to spend Federal monies, limited only by the Bill of Rights and the Constitution's implicit protections of State sovereignty (29,61). There is no longer any question that:**

> . . . the Federal Government, unless barred by some controlling constitutional prohibition, may impose the terms and conditions upon which its money allotments to the states shall be disbursed, and that any state law or regulation inconsistent with such Federal terms and conditions is to that extent invalid (37).

The State **must, of course, comply with the Federal conditions only if it wants to receive the Federal funds (28).**

Research on Human Subjects

The most important area **in which Congress has used its spending power to adopt regulations related to noncoital reproductive techniques has been in the area of research on human subjects.**

Current Federal regulations on research with human subjects have evolved from a combination of circumstances involving the military, the executive branch, and Congress. The key document in this brief history is the Nuremberg Code, developed by U.S. judges sitting in judgment of Nazi physicians under U.S. military authority following World War 11 (20). That document sets forth basic rules still in use today. It was adopted by the United Nations and the U.S. Army, but not formally used to help determine DHHS policy until the mid-1960s, when the Department's first regulations on research with humans were promulgated.

Following a series of public scandals involving unethical research, including the Tuskegee syphilis study (65) and the Jewish Chronic Disease Hospital case (32), Congress passed the National Research Award Act of 1974 (Public Law 93-348), establishing the National Commission for the Protection of Human Subjects of Biomedical *and Be*havioral Research to study medical research settings and to recommend regulatory standards. The Commission was established within the Depart**ment of Health, Education, and Welfare (now** DHHS). The Commission's activities led to the adop**tion of a number of regulations concerning federally funded research with human subjects.**

The regulations provide that institutions receiving Federal funds (the only ones bound by the regulations) can voluntarily agree to have all of the research done on their premises or by their employees and faculty members subject to the Federal guidelines. Most institutions have agreed to be bound by Federal regulations, and have evidenced this agreement in the form of a "general assurance" given to DHHS (40).

The regulations provide that all federally funded research, except that which is specifically exempted, shall be reviewed by a local review group called an Institutional Review Board to ensure that risks to subjects are minimized, that risks are reasonable in relation to anticipated benefits, that selec -

tion of subjects is equitable, and that informed consent is obtained and properly documented.

During the National Commission's 4-year tenure it issued a number of reports, which led to DHHS adoption of a series of specific regulations applying to research "involving fetuses, pregnant women, and in vitro fertilization" (45 CFR 46.201-46.211). The National Commission limited its definition of '(fetus" to a product of conception from the time of implantation, so research on extracorporeal embryos was not covered.

Because research on embryos and fetuses was seen as so difficult and divisive, the Commission recommended the establishment of an Ethics Advisory Board (EAB) within DHHS to continue to examine this area, render advice to the Secretary, and review specific proposals to fund IVF research. These recommendations were all adopted as regulations.

One commentator proposed that DHHS promulgate guidelines for the EAB to follow in considering proposals. These guidelines would contain minimum qualifications for IVF experimenters, standardize the laboratory conditions that must exist, develop safety standards for conducting human IVF experimentation, and establish when an IVF conceptus may be destroyed (8). The American Medical Association suggested establishing international and interprofessional groups to study the ethical, medical, and legal issues associated with IVF (35). The Ethics Advisory Board concluded that IVF and embryo transfer research could be acceptable from an ethical standpoint if certain stringent criteria were met (44 FR 35033) (67).

The provision that had the most profound effect on keeping the Federal Government out of funding, and thereby reviewing, IVF research was:

> No application or proposal involving human in vitro fertilization may be funded by the Department or any component thereof until the application or proposal has been reviewed by the Ethical Advisory Board and the Board has rendered advice as to its acceptability from an ethical standpoint [45 CFR 46.204 (D)].

In 1974, a researcher was told that his request for a $375,ooo grant from the National Institutes of Health would be reviewed by the EAB. The grant application proposed to remove approximately 450 eggs from women undergoing surgery; the eggs would then be fertilized, with subsequent microbiopsy of the fertilized eggs. Thus, the embryos were not intended to mature to a live birth. The EAB approved the project provided that the fertilized eggs not be sustained beyond the stage normally associated with the completion of implantation, or no more than 2 weeks after fertilization. The application was never approved by the Secretary of Health, Education, and Welfare (41), however, and in 1980 the Ethics Advisory Board ceased to exist. Although the Secretary of HHS has the authority to waive the criteria for ethically acceptable IVF research, in part by reconvening the EAB to approve the waiver, this has never been done. Nor has a new EAB ever been appointed. The result has been an unofficial moratorium on all Federal funding and oversight of IVF research.

In 1980, pursuant to Public Law 95-622, a new Federal commission was created for 3 years by Congress—the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. It endorsed the conclusions of the EAB on IVF, but completed no further analysis on noncoital reproductive techniques (51).

The regulations on research with human subjects have also been adopted, with a few modifications, by the FDA (51 FR 20203-20208), and will likely soon be adopted by other Federal agencies involved with such research. These regulations could be important for the responsible development and early use of noncoital reproductive techniques, since they provide a principled framework within which to assess their risk/benefit ratio, to protect participants, and to ensure informed consent.

Although these regulations were employed in the initial tests of GIFT in Texas and of embryo transfer in California (13), they have generally not been used recently for IVF, on the basis that IVF is not a clinical experiment but rather a clinical practice, albeit with a developing procedure. However, no uniform protocol for IVF exists. Further, the technique never went through a formal or

regulatory research stage in the United States to demonstrate either safety or efficacy, in large part due to the lack of Federal direction and Federal funding.

In 1985 Congress authorized a 12-member, bipartisan Biomedical Ethics Board consisting of six senators and six representatives (Public Law 99-158). Pursuant to the statute, the Board was named in 1986, and in 1987 began appointing a 14-member Advisory Committee composed of citizens with interest or expertise in biomedical ethics. The Board is directed to conduct studies in the area of ethics and health care, including studies on two specific topics:

- the nature, advisability, and biomedical and ethical implications of exercising any waiver of the standard of risk that is applied to all human research subjects, as defined in 45 CFR 46. 102(g), when considering the conduct or support of research involving human fetuses (to be completed no later than May 20, 1988); and
- research and developments in human genetic engineering (to be completed no later than 18 months after the appointment of the Advisory Committee).

To date, the Board and its Advisory Committee have not begun to function,

During the 36 months allotted for study of fetal research protocols, the 1985 legislation repeals the Secretary of HHS'S prior authority to call for a waiver of the CFR regulations governing the degree of risk to which a fetus may be subject in the course of research. Although this has been perceived by some researchers as a formalization of the moratorium on funding for IVF research, in fact it has little effect on embryo research. The CFR regulations set forth limits on the risks to which a fetus may be subjected during research, but "fetus" is carefully defined to mean "the product of conception from the time of implantation ... until ... expulsion or extraction" [45 CFR 46.203(b)]. This definition would exclude eggs fertilized either in vitro or in vivo if they are never implanted in a uterus.

Thus, the 1985 law does not affect the ability of the Secretary to waive the limitations on IVF research, limitations that were recommended by the EAB although never adopted into regulation. EAB approval is still required for DHHS funding of IVF research. Only a request by the Secretary of HHS to waive EAB review, coupled with a reconstitution of the EAB so that it might agree to waive its right to review, can permit funding of IVF research without Ethics Advisory Board review.

The effect of this moratorium on Federal funding of IVF research has been to eliminate the most direct line of authority by which the Federal Government can influence the development of both embryo research and infertility treatment so as to avoid unacceptable practices or inappropriate uses. It has also dramatically affected the financial ability of American researchers to pursue improvements in IVF and the development of new infertility treatments, possibly affecting in turn the development of new contraceptives based on improved understanding of the process of fertilization.

Models of Financing

Other countries that offer IVF seem to have done better at monitoring it than the United States has, probably because IVF is covered by their nationally financed health insurance plans. Through this financing power, the services are generally restricted to State-licensed clinics, and uniform guidelines for their provision can be developed and enforced. Although it seems unlikely that the United States will soon directly fund infertility services that include artificial insemination by donor, IVF, embryo transfer, and GIFT, it is useful to consider the range of regulatory authority that such funding would permit.

Direct funding would give the Federal Government the authority to determine a wide variety of requirements for the delivery of a safe and high-quality service. One model of this is DHHS'S 1987 "Medicare Program Criteria for Medicare Coverage of Heart Transplants" (52 FR 10935). Among other things, it provides that to be eligible for Medicare reimbursement for heart transplantation, the facility must develop adequate patient selection criteria and patient management plans and protocols, and must have a sufficient commitment of resources, sufficient clinical expertise in related

areas, adequate data maintenance, and reasonable laboratory facilities.

Most innovative, however, is the requirement that the facility have a demonstrated experience and survival rate before any procedures will be reimbursed, Tying reimbursement to actual performance could have a powerful influence on the quality of services made available to the public. Specifically, proposed regulations would require a facility to have performed a minimum number of heart transplants, with specified actuarial survival rates (52 FR 10935).

The use of appropriate success standards in IVF (standards that, of course, private insurance companies could adopt) would reduce the number of facilities eligible for reimbursement under any scheme, since some of the estimated 169 IVF and GIFT programs in this country have yet to record a birth. It should be noted, however, that such a scheme might affect the willingness of clinics to accept patients of advanced age or who have a particularly difficult prognosis, as their less successful outcomes might affect possibilities for reimbursement despite the fact that the medical care was of acceptable quality.

Aside from direct Federal funding, five States have mandated that private insurance companies cover IVF (see ch. 8). Private insurance companies are free to set their own reimbursement or coverage policies by contract. Most cover generally accepted medical procedures, but not experimental procedures. Since there is no universal definition of "experimental," coverage often varies. When a new procedure is moving from the experimental to the realm of the generally accepted practice, there is likely to be a timelag during which individual insurance companies will be making the coverage decision (47).

Indirect Financing

The Federal Government also has the power to condition the receipt of Federal funds by a State (instead of by a health care provider) on the State's taking a specific regulatory action, such as in regard to noncoital reproductive techniques. This is true even when the connection between the State program and infertility is quite attenuated. For example, when Congress enacted the Child Abuse Amendments of 1984 (Public Law 98-457) in partial response to the controversy over medical care for severely or terminally ill newborns, it specifically required States accepting funds under this act to adopt certain regulations and procedures on child abuse and neglect.

Congress could equally mandate that States receiving such funds develop specific policies with regard to monitoring noncoital reproductive techniques, under the theory that these techniques require more monitoring than others because they are designed to produce children, and that the best interests of these children require that such services be of the highest quality. This would be true even without any inference that children conceived or born by use of reproductive techniques such as IVF or surrogate motherhood are at all harmed.

Similarly, the Federal Government has the authority to condition funding of Aid to Families with Dependent Children programs or family planning agencies on adoption of stated standards relating to infertility services if these were also offered by such agencies. An analogous example is the Federal requirement regarding consent to sterilization.

Authority Over Interstate *Commerce*

The second major area over which Congress has wide authority to regulate noncoital reproductive techniques is through the commerce clause of Article I, Section 8, which provides the authority "To regulate Commerce with foreign Nations, and among the several States, and with the Indian Tribes ."

Congressional authority to pass laws relating in any reasonable manner to interstate commerce is "such broad power that judicial review of the affirmative authorization for congressional action is largely a formality" (61). Most judicial review focuses instead on the intent of Congress to interpret the reach and scope of the legislation. For example, "unless Congress conveys its purpose clearly, it will not be deemed to have significantly changed the Federal-State balance" (68).

Monitoring the Use of Noncoital Reproductive Techniques

The Centers for Disease Control (CDC) may ask State departments of health to monitor artificial insemination by donor or other uses of third-party gametes for the presence of human immunodeficiency virus or antibodies, or for the presence of other communicable diseases. CDC is not a regulatory agency and has no direct authority to regulate individual physicians or State health departments. It is under the authority of the Secretary of HHS and acts under the Secretary's general statutory authority. For example, under the Public Health Services Act (42 U.S.C. 201 et seq.), the Secretary has general authority to enact regulations to prevent the spread of diseases across State or national borders. The Secretary has used this authority to limit the travel and transportation of individuals with specific communicable diseases.

In 1988, the CDC used its authority to issue guidelines for donor insemination, so that the risk of HIV transmission could be reduced (64). While not mandatory, these guidelines do set an unofficial standard of the minimum quality of care expected from physicians. The CDC may also ask for cooperation from local health departments (which do have direct "police power" regulatory authority to demand cooperation) for assistance in collecting data relevant to communicable diseases, and this request is likely to be complied with if it is reasonable (43).

Antitrust and Information Disclosure

In response to the "trusts" developed by the railroads in the late 19th century, Congress passed the Sherman Antitrust Act in 1890 (which forbade "conspiracy in restraint of trade or commerce, " and made the exercise of monopoly power a felony) and, in 1914, the Clayton Act and the Federal Trade Commission Act. The Clayton Act declared illegal four specific practices (price discrimination, tying or exclusive dealings contracts, corporate mergers among competitors, and interlocking directorates among competitors). The Federal Trade Commission Act created an independent Federal administrative agency with the power to study (and later to take enforcement action against) '(unfair methods of competition" and '(unfair or deceptive acts" (21).

The antitrust laws have only recently been used against medical practitioners (11). Some groups, for example, charged that obstetricians in a certain area had conspired to fix prices for abortions and other services to try to eliminate these services from the marketplace (24). It is unlikely that the Antitrust Division of the Justice Department (or private individuals or corporations) will find any occasion to attack concerted action in infertility services, since these are generally run as small businesses rather than as large-scale operations. Yet the Federal Trade Commission could become involved in examining potential "unfair practices."

One of the practices FTC has found unfair is a seller's refusal to disclose information about various aspects of products (18). Examples include the failure to disclose the efficiency rating (('R value") of home insulation, the octane level in gasoline, or the drop-out and placement rates of vocational schools (18).

Analogously, FTC could find it an unfair practice for infertility clinics not to disclose their pregnancy or live-birth rates, or any other piece of information that consumers need to decide whether to attempt a pregnancy by noncoital reproduction, or whether to make the attempt at a particular clinic. Misleading advertisement of success rates could also be subject to FTC scrutiny and regulation (54). The difficulty of choosing a single method by which to calculate and advertise success rates for IVF (19)44)45), however, points up how hard it is to determine that a particular figure is misleading (see box 9-B),

Regulation of Products

The commerce power, of course, also provides specific authority to regulate articles of commerce that pass between two or more States. This authority has been used most specifically in the health care field by the establishment of FDA, which is authorized to regulate drugs and medical devices and to prohibit trade of such products in interstate commerce until they have been demonstrated safe and effective. Although this authority is extremely broad, it is of limited value with respect to noncoital reproductive techniques, since they generally do not involve the use of new drugs or medical devices, but rather of new (or

Box 9-B.—How IVF Success Rates Can Be Reported

The reporting of IVF data is limited only by one's imagination in contriving some new yardstick of performance, short of a normal liveborn child (44).

In early 1988,41 U.S. IVF clinics reported, as a group, their success rates for 1985 and 1986 (45). These clinics represent about one-fourth of all IVF programs active in the United States and are generally the most successful. This first combined report of IVF clinics characterized the average 1986 IVF success rate as 16.9 percent (clinical pregnancy per embryo transfer cycle). ("Clinical pregnancy" denotes positive fetal heart documented by ultrasound.) This figure is one of several ways to calculate IVF success rates and may be misleadingly optimistic for some patients. It may also be inadequate to reflect success rates for procedures using frozen embryos obtained in earlier stimulation cycles.

It is important to note that regardless of how averages are expressed, they can be misleading for an individual patient. Patients who are older, who have a history of repeated miscarriages, or who have other special risk factors have smaller chances for success. Conversely, some candidates for IVF are much more likely than average to have a successful pregnancy.

Assuming an IVF candidate has passed a battery of tests determining her general appropriateness for the procedure, she's ready to start her first ovarian stimulation cycle. On average, 6 of 10 women are successful at stimulation and fertilization, leading to an embryo-transfer attempt. Following embryo transfer, the chance of becoming clinically pregnant is about 1 in 6 (16.9 percent), the figure highlighted in the report of the success rate of the 41 clinics. However, a woman still faces the risk—about a l-in-3 chance—that her pregnancy is ectopic, or that it will end in a miscarriage or stillbirth. Therefore, her chance of walking out with a baby after one embryo transfer cycle is about 1 in 9 (l0.7 percent). Calculated per stimulation cycle, a woman's chance of taking home a baby is about 1 in 16 (6.3 percent). She also has a 1 in 1,000 chance of winding up in the hospital due to hyperstimulation from the drugs.

On average, each patient **at the 41** IVF clinics undertook 1.6 stimulation cycles, so the 1 in 16 chance of taking home a baby following one stimulation cycle can also be quoted as an overall 1 in 10 (10 percent) chance of taking home a baby after undertaking an average course of IVF treatment.

Every couple is unique, and the chances of success may vary from the averages quoted here or by an IVF clinic. A particular patient's or clinic's past success with stimulation, egg retrieval, and fertilization may make one or another type of reported success rate more useful. Couples undertaking medically assisted conception should keep in mind that miscarriage rates are high for all pregnancies, IVF-induced or not, and that they may have to undergo many attempts before a successful pregnancy is achieved. With IVF, the odds per stimulation cycle, and even per embryo transfer, of taking home a baby are low.

Percentages mean nothing. I know, like ***every*** woman who waits ***in an IVF clinic, that anything less than 100% is a failure (19).***

SOURCE: Office of Technology Assessment, 1988.

old) physical manipulations or surgical procedures. Unlike drugs and devices, surgical procedures and medical manipulations are not regulated by any governmental agency. Physicians are simply held to the standard of the "reasonably prudent physician" in developing and using such techniques.

The Federal Government has also used the commerce authority to require licensing of medical laboratories engaged in interstate commerce (42 U.S.C. 263). It could require Federal licensure of infertility clinics that solicit patients from out of State, although this would be more like regulating medical practice than regulating laboratory quality. On the other hand, tissue banks and other suppliers of screened gametes or even of embryos could probably be regulated in the same fashion as that used for medical laboratories or blood banks. Federal regulation to assure the safety of

semen sold by sperm banks was viewed as unreasonable by only a minority of sperm banks and individual physicians surveyed in 1987 (63).

Patenting Power

The Constitution also gives Congress the explicit authority **to set** up a system of patents and copyrights. Historically, while drugs and medical devices have been routinely patented, it is exceedingly rare for physicians to attempt to patent surgical or medical procedures. Examples of when they have done so include a "method and apparatus for direct electrical injection of gold ions into tissue such as bone, " "cranial insertion of surgical needle utilizing computer-assisted tomography," a "method for maintaining the reduction of a sliding esophageal hiatal hernia)" and a "surgical method of fixation of artificial eye lenses. "

Nevertheless, one venture capital corporation interested in providing embryo lavage and transfer services nationwide did apply for a patent on the process of lavage and fertilized ovum retrieval. That application is pending, along with four other related patent requests for the devices used (25). Although interest in the procedure has waned due to its low success rate relative to alternative procedures (14,15), the company has nonetheless begun to open offices around the United States and in Italy (25).

The U.S. Patent Office can no doubt issue process patents if it so chooses. The real debate over the embryo lavage and transfer patent is whether it should have been applied for in the first place, and, if it is granted, how it could be enforced. One argument in favor of allowing the patent is that its holder can enforce high medical standards by training and monitoring those who purchase licenses to use the patented procedure. Balanced against this is the tendency of a patent holder to keep unfavorable results secret, so that unbiased groups may not have an opportunity to confirm or deny claims made for the process; the inhibition by the patent of the generalized training of medical professionals; and the general inhibition against sharing scientific knowledge. Human reproduction also does not easily lend itself to patent infringement enforcement methods, and patenting new reproductive technologies remains problematic (7).

SUMMARY AND CONCLUSIONS

Professional societies such as the American Association of Tissue Banks, the American College of obstetricians and Gynecologists, and the American Fertility Society have made efforts to regularize the practice of medically assisted conception by offering guidelines on gamete and participant screening, physician training, and clinic staffing. The Federal Government, too, has been active with regard to donor insemination. These efforts, however, may be insufficient. First, as compliance is entirely voluntary, public health hazards—e.g., human immunodeficiency virus transmission by fresh semen—may persist in medical practice, with only the threat of malpractice litigation to act as a check. Perhaps more important, many of the questions surrounding noncoital reproduction, such as recordkeeping or screening of participants who intend to raise the child or contribute to its conception, are really questions of public policy as much as of medical practice. As such, the influence of infertile couples, potential gamete donors or surrogates, social workers, attorneys, business people, and government officials on the development of regulations is appropriate.

The regulation of noncoital reproductive techniques has traditionally been primarily a matter for individual States. Just as they have regulated adoption, custody, marriage, medical licensing, and medical practice, States will bear the responsibility for regulating the noncoital reproductive techniques insofar as they are medical procedures performed by physicians. In this regard, regulations in the area of quality control and monitoring, safety, recordkeeping, inspection and licensing, consent, and requirements for donor screening are all well within traditional State activities and regulation, In extreme cases, such as banning the sale of human embryos or experimenting with human embryos, statutes would have to be carefully

drawn to avoid being struck down for vagueness, as well as based on a reasonable State policy designed to protect the common good.

Federal activity in noncoital reproductive techniques, on the other hand, has been largely restricted to setting up and financing national commissions and groups of various kinds to study the scientific, legal, and ethical issues involved and to make recommendations on the actions of private and governmental organizations. The Federal Government could, however, become involved in other areas it traditionally enters, such as regulating interstate commerce, forbidding the sale of human organs, regulating false and deceptive advertising, and promulgating special rules for publicly supported human research. It could also facilitate nonregulatory efforts to establish more uniform protocols for selecting patients, choosing therapies, and defining successful outcomes. Finally, it could continue its efforts to minimize the risks associated with even the most standard therapies.

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