Revised minimum standards for in vitro fertilization, gamete intrafallopian transfer, and related procedures

A PRACTICE COMMITTEE REPORT
Guidelines and Minimum Standards

I.

Introduction

Treatment of the infertile couple is evolving rapidly. Perhaps no area in this specialty better exemplifies the advances of technology than assisted reproductive technology (ART). Periodically, the ASRM reviews and publishes updated guidelines in the form of minimum standards for ART programs and guidelines for human embryology and andrology laboratories. This latest ``Revised Minimum Standards for In Vitro Fertilization, Gamete Intrafallopian Transfer, and Related Procedures'' represents a document which is designed to assist ART programs in establishing and maintaining a successful clinical practice. It replaces ``Revised Minimum Standards for In Vitro Fertilization, Gamete Intrafallopian Transfer, and Related Procedures (February 1990) and the guidelines for embryology laboratories found in ``Guidelines for Human Embryology and Andrology Laboratories'' (October 1992). The document is not designed to cover all clinical situations or practices, but rather should be reviewed by ART program and laboratory directors to be certain that their programs' practice reflects current recommendations. It includes new sections on ethical and experimental procedures, record keeping, and informed consent, all of which are areas of increased importance in contemporary ART practice. This document is intended to enhance the already high standards practiced by ART programs.

II.

Personnel

A. An ART program must include, as a minimum, personnel with the following expertise. A single individual may fulfill the requirement for expertise in one or more areas. There should be a backup system in place for all personnel essential to a program.

1. Each program must have a designated overall practice director, medical director, and laboratory director. One individual may fulfill more than one of these positions; however the medical director must be a licensed physician.
2. An individual with training and experience in reproductive endocrinology, particularly in the use of ovulation-inducing agents and the hormonal control of the menstrual cycle. An individual who has completed an American Board of Obstetricians and Gynecologists (ABOG)-approved fellowship in reproductive endocrinology and infertility fulfills this requirement
3. An individual with expertise in pelvic reparative (infertility) surgery as well as experience in laparoscopic and ultrasound-guided oocyte retrieval techniques.
4. An ultrasonographer with specialized training and experience in gynecologic sonography who provides the monitoring of follicular development.

5. An individual experienced in male reproduction (andrology) with special competence in semenology. If this individual is not a urologist, then there also should be an available consultant urologist with expertise in reproductive surgery.
6. Each practice must have an embryology laboratory director. This laboratory director must have personal experience in the organization and maintenance of a basic or clinical embryology laboratory as well as in tissue culture techniques.
7. If gamete and/or embryo cryopreservation is offered, there should be an individual with specialized training and experience in gamete and embryo cryopreservation techniques.
8. If oocyte microoperative techniques are offered, there should be an individual with specialized training in gamete biology and experience in microoperative techniques.
9. Rapid assays of all the necessary reproductive hormones (including estradiol and progesterone) should be available as required. A program may utilize outside laboratories which demonstrate adequate competence, quality control, and service.

B. Specialized Training and Experience

1. It is recommended that an individual board certified in reproductive endocrinology and infertility direct the follicular recruitment phase of the ART cycle. Although individuals with equivalent training and experience are acceptable in established clinics, new practices are encouraged to have a trained reproductive endocrinologist supervising the follicular recruitment.
2. Each physician performing oocyte retrievals should have performed at least 20 follicular aspirations under direct supervision within a practice that meets these standards. Satisfactory completion of this training should be documented by a signed letter from the practice director. Each physician should continue performing a minimum of 20 aspirations or transfers per year. It is recommended that the physicians involved in the supervision of the follicular recruitment and oocyte retrieval procedures be responsible for the ultrasound monitoring of follicular development and that an ultrasound scanner be available in the clinical area for this purpose.
3. The embryo laboratory director should be an individual with demonstrated knowledge of all laboratory aspects of ART. To be acceptable as an embryo laboratory director, an applicant should fulfill both of the following requirements:

a. Hold an earned doctorate degree (Ph.D.) from an accredited institution in a chemical, physical, or biological science as the major subject or a medical degree (M.D. or D.O.) from an accredited institution or have qualified as a laboratory director or supervisor prior to January 1992. It is recommended that all embryology Ph.D. lab directors become board certified in embryology. The laboratory director should have the expertise and/or special training in biochemistry, cell biology, and physiology of reproduction with experience in experimental design, statistics, and problem solving/troubleshooting. The laboratory director should be responsible for formulating laboratory policies and protocols and should communicate regularly with the medical director regarding patient progress and protocols as they affect the laboratory aspects of treatment.
b. Have 2 years of documented pertinent experience in a program performing IVF-related procedures. This experience should include:

(1) Familiarity with laboratory quality control, inspection, and accreditation procedures.
(2) Detailed knowledge of cell culture, ART, and andrology procedures performed in mammalian systems.

If the medical director is also the laboratory director, there should be a qualified, designated laboratory supervisor. The embryo laboratory supervisor should have a Bachelor's or Master's degree in a chemical, physical, or biological science as a major subject.

The embryology laboratory director or supervisor should have had a period of training of at least 6 months and completed at least 60 ART procedures in a program that performs at least 100 IVF procedures per year with a minimum annual 10% IVF live birth rate per retrieval cycle.

A procedure is defined as a combination of the examination of follicular aspirates, insemination, documentation of fertilization, and preparation for embryo transfer. Satisfactory completion of this period of training should be documented by a signed letter from the laboratory director of the training practice. In lieu of formalized training, a similar experience within the director's own practice is sufficient, provided the practice has performed at least 100 total retrievals and has had at least an annual 10% live birth rate per retrieval cycle.
The embryo laboratory technologists should have an earned Bachelor's Degree from an accredited institution with a chemical, physical, or biological science as the major subject. The technologists should have documented pertinent experience in cell culture and sterile technique with evidence of completion of 30 complete IVF procedures under continuous supervision of the laboratory director or supervisor. Experience and documented training in cell culture, sperm-egg interaction, or related areas of animal reproduction are desirable. The embryology laboratory technologist works under the supervision of a laboratory director or supervisor. Programs for the appropriate training of embryo laboratory technologists should be in place for each program with documentation of completion for each employee.

Each staff embryologist (including the embryology laboratory director or supervisor) should perform at least 20 ART procedures a year.

Among the embryology laboratory staff there should be one or more persons with knowledge and experience in the following fields: (1) preimplantation embryology, (2) andrology, and (3) prefertilization and postfertilization events.
III.

GIFT and Related Procedures

The American Society for Reproductive Medicine has issued a list of minimum standards for GIFT (1). Because technical considerations at the time of oocyte recovery may prevent tubal transfer and/or oocytes in excess of those recommended for tubal transfer may be obtained, it is recommended that GIFT only be performed in a facility that is prepared to carry out IVF, as an alternative or in addition, in the event that the GIFT procedure turns out not to be feasible and/or excess oocytes are recovered. Accordingly, a GIFT program must have an embryo laboratory and personnel capable of performing IVF. In addition the program should be capable of

fertilizing nontransferred oocytes and freezing the resulting embryos if they are of good quality. That is not to say that GIFT is not an appropriate treatment choice for certain patients, but only that the embryo laboratory equipment, procedures, quality control, and personnel must be proven by successfully performing IVF.

IV.

Embryo Laboratory

A. Quality Assurance

The quality of the embryo laboratory is recognized as one of the most important components of a successful ART program. However, there are inherent difficulties involved in evaluating the ``quality'' of any laboratory system. It is therefore necessary to allow flexibility in the interpretation of any standards of quality to accommodate different methods of maintaining laboratory quality.

The following quality control procedures should be considered as guidelines, subject to reasonable amendment:

1. Laboratory ``contact materials'' are defined as those items (disposable or recycled) that come into direct physical contact with gametes, embryos, or their supporting culture media.
2. Assays need to be applied to cell culture media and contact materials to rule out toxins, inappropriate ionic concentration, microbial contamination, or other potential hazards to human gametes or embryos.
3. Each laboratory should design its individual quality control procedures. Laboratories should include among quality assurance assays bioassays such as mouse IVF, one-cell or two-cell mouse embryo development in vitro, or human sperm survival assays.
4. All media used for ART procedures should have the following information available for each batch: Lot # of media, date prepared, bioassays, osmolarity, pH, method of sterilization, and expiration date.
5. It is recommended that the laboratory undergo certification by the CAP/ASRM Accreditation Program or a similar mechamism.

B. Laboratory Facilities

Embryo laboratories should have the standard features of a ``clean room'' including controlled temperature and humidity and filtered air with an appropriate number of air changes per hour. Walls and floors should be composed of materials easily washed and disinfected and the use of carpeting should be avoided. Aerosols and toxic pest control substances should not be used in the embryo laboratory.

The embryo laboratory should be located in proximity to the oocyte collection/procedure room. The presence of a general access hallway between the embryo laboratory and the procedure room is not recommended. As an alternative, oocyte identification and isolation can be performed in the procedure room using a self-contained, temperature-controlled and environmental-controlled microscope/incubator unit. Oocytes can then be transported within this unit (or in a portable incubator) to the embryo laboratory at the conclusion of the procedure. Subsequent handling of gametes and embryos should be performed in a specified clean area or in the portable microscope/incubator unit described above.

C. Equipment and Maintenance

All major equipment items should be adequately maintained and have a written schedule of preventative maintenance and/or certification services. Large laboratory items (e.g., laminar flow hoods) should be certified by on- site inspection on a regular (6-12 months) basis with appropriate record keeping. Equipment such as balances, pipettes, thermometers, pH meters, centrifuges, and refrigerators should be calibrated on a regular basis with appropriate records kept of these services.

Routine quality assurance of equipment should include daily checks of refrigerator, freezer, and incubator temperatures; incubator humidity levels; external verification of the gaseous environment in the incubators; level of liquid nitrogen in any embryo or gamete storage container; and the status of gas cylinders and/or liquid nitrogen reservoir supplies. Written records of these checks should be maintained. There should be a regular preventative maintenance schedule for complete cleaning and decontamination of incubators, laminar flow hoods, and related items.

D. Embryo Cryopreservation

Because human embryos cannot be replaced, programs should have freezing equipment with internal power failure backup as well as a second freezing and thawing unit in case of equipment malfunction. Embryo freezers should be calibrated against an external thermometer or thermocouple.

Duplicate records on frozen embryos including, as a minimum, the developmental stage at which frozen, freezing protocol used, recommended thawing procedures, and the physical location of each embryo within the storage container should be kept in the laboratory and with the practice director. Embryo containers should be labeled with the patient's name, identification number, and the date of cryopreservation.

E. Safety

Embryologists are advised to wear nontoxic (nonpowdered) gloves while handling gametes and embryos, in addition to other safety measures as appropriate. These precautions are recommended for both the protection of the embryologist as well as to maintain optimal quality of the culture conditions.

Written procedures should be established for the double-checking and verification of patient identity and the identification of gametes and embryo samples. These procedures should be performed before insemination, embryo thawing, or embryo transfer procedures.

V.

Ethical and Experimental Procedures

It is recognized that ART treatments are rapidly evolving. Because of the ethical concerns involved in treatments which involve the laboratory handling and manipulation of human gametes and embryos, the American Society for Reproductive Medicine's Ethics Committee has issued a report on the ethical considerations of ART procedures (2). It is presumed that all ART procedures will be performed in accordance with the recommendations contained in that report as well as any future reports from the Ethics Committee.

Procedures considered experimental must be conducted under the supervision of an Institutional Review Board (IRB) or equivalent committee.

From time to time, the Board of Directors of the American Society for Reproductive Medicine will issue statements indicating that certain procedures previously considered experimental will henceforth be considered clinically proven treatments.

VI.

Record Keeping

In view of the continuing controversy about the success rate of IVF, it is recommended that all practices performing IVF, GIFT, and related procedures participate in The Society for Assisted Reproductive Technologies (SART) Registry data collection. Furthermore, it is required that each practice release (or permit the release from the Registry) of identifiable, clinic-specific success rates in order that patients and physicians may make appropriate choices among programs. Practices must adhere to ASRM, SART, and Federal Trade Commission guidelines relating to advertising and the use of SART statistics.

In addition, documentation of the proper identification, outcome, and disposition of all oocytes and embryos is important. The documentation should identify all clinic and laboratory personnel who have handled gametes and embryos during each procedure.

VII.

Informed Consent

As with all medical procedures and treatments, the patients must make the final decision as to what is appropriate and acceptable treatment in their particular situation. To comply with this requirement, it is necessary that each prospective patient couple be provided with full written informed consent. Consent forms should indicate that data concerning the patient's IVF cycle is required by law to be released for external auditing. This data reporting may include identifying data. ART programs should conform to the ASRM/SART guidelines concerning informed consent.

It is also important that couples be provided full information concerning alternative procedures available to circumvent their specific infertility problem, including procedures that are not performed by the treating center as well as nonmedical options such as adoption and nontreatment.

References

1. The American Fertility Society. Minimal standards for gamete intrafallopian transfer (GIFT). Fertil Steril 1988;50:20.

2. The Ethics Committee of The American Fertility Society. Ethical Considerations of assisted reproductive technologies. Fertil Steril 1994;62:1-125.

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