Guidelines on number of embryos transferred

The Practice Committee of the American Society for Reproductive Medicine and the Practice Committee of the Society for Assisted Reproductive Technology

American Society for Reproductive Medicine and Society for Assisted Reproductive Technology, Birmingham, Alabama

Based on American Society for Reproductive Medicine (ASRM) and Society for Assisted Reproductive Technology data available in 2007, ASRM’s guidelines for the number of embryos to be transferred in in vitro fertilization (IVF) cycles were revised in an effort to reduce the number of higher-order multiple pregnancies. This version replaces the document of the same name that was published most recently in November 2008. (Fertil Steril® 2009;92:1518–9. ©2009 by American Society for Reproductive Medicine.)

Based on American Society for Reproductive Medicine (ASRM) and Society for Assisted Reproductive Technology (SART) data available in 2007, ASRM’s guidelines for the number of embryos to be transferred in in vitro fertilization (IVF) cycles were revised in an effort to reduce the number of higher-order multiple pregnancies.

High-order multiple pregnancy (three or more implanted embryos) is an undesirable consequence (outcome) of assisted reproductive technologies (ART) (1). Multiple gestations lead to an increased risk of complications in both the fetuses and the mothers (2).

Although multifetal pregnancy reduction can be performed to reduce fetal number, the procedure may result in the loss of all fetuses, does not completely eliminate the risks associated with multiple pregnancy, and may have adverse psychological consequences (3). Moreover, multifetal pregnancy reduction is not an acceptable option for many women.

In an effort to reduce the incidence of high-order multiple gestations, ASRM and SART have developed the following guidelines to assist ART programs and patients in determining the appropriate number of cleavage-stage (usually 2 or 3 days after fertilization) embryos or blastocysts (usually 5 or 6 days after fertilization) to transfer. Strict limitations on the number of embryos transferred, as required by law in some countries, do not allow treatment plans to be individualized after careful consideration of each patient’s own unique circumstances. Accordingly, these guidelines may be modified according to individual clinical conditions, including patient age, embryo quality, the opportunity for cryopreservation, and as clinical experience with newer techniques accumulates.

I. Individual programs are encouraged to generate and use their own data regarding patient characteristics and the number of embryos to be transferred. Accordingly, programs should monitor their results continually and adjust the number of embryos transferred to minimize undesirable outcomes. Programs that have a high-order multiple pregnancy rate that is >2 standard deviations above the mean rate for all SART reporting clinics for 2 consecutive years may be audited by SART.

II. Independent of age, the following characteristics have been associated with a more favorable prognosis: 1) first cycle of IVF; 2) good-quality embryos as judged by morphologic criteria; and 3) excess embryos of sufficient quality to warrant cryopreservation. Patients who have had previous success with IVF also should be regarded as being in a more favorable prognostic category. The number of embryos transferred should be agreed upon by the physician and the treated patient(s), informed consent documents completed, and the information recorded in the clinical record. In the absence of data generated by the individual program, and based on data generated by all clinics providing ART services, the following guidelines are recommended (Table 1):

A. For patients under the age of 35 who have a more favorable prognosis, consideration should be given to transferring only a single embryo (4). No more than two embryos (cleavage stage or blastocyst) should be transferred.

B. For patients between 35 and 37 years of age who have a more favorable prognosis, no more than two cleavage-stage embryos should be transferred. All others in this age group should have no more than three cleavage-stage embryos transferred. If extended culture is performed, no more than two blastocysts should be transferred to women in this age group.

C. For patients between 38 and 40 years of age who have a more favorable prognosis, no more than three cleavage-stage embryos or two blastocysts should be transferred. All others in this age group should have no more than four cleavage-stage embryos or three blastocysts transferred.

D. For patients 41–42 years of age, no more than five cleavage-stage embryos or three blastocysts should be transferred.

E. In each of the above age groups, for patients with two or more previous failed fresh IVF cycles or a less favorable prognosis, one additional embryo...
TABLE 1

<table>
<thead>
<tr>
<th>Prognosis</th>
<th>&lt;35 yrs</th>
<th>35–37 yrs</th>
<th>38–40 yrs</th>
<th>41–42 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleavage-stage embryos&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Favorable&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1–2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Blastocysts&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Favorable&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>All others</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<sup>a</sup> See text for more complete explanations. Justification for transferring one additional embryo more than the recommended limit should be clearly documented in the patient’s medical record.

<sup>b</sup> Favorable = first cycle of IVF, good embryo quality, excess embryos available for cryopreservation, or previous successful IVF cycle.


Fertility and Sterility®

may be transferred according to individual circumstances. The patient must be counseled regarding the risks of multifetal pregnancy. Both the counseling and the justification for exceeding the recommended limits must be documented in the patient’s permanent medical record.

F. In women ≥43 years of age, there are insufficient data to recommend a limit on the number of embryos to transfer.

G. In donor egg cycles, the age of the donor should be used to determine the appropriate number of embryos to transfer.

H. In frozen embryo transfer cycles, the number of good-quality thawed embryos transferred should not exceed the recommended limit on the number of fresh embryos transferred for each age group.

III. Because not all oocytes may fertilize when gamete intrafallopian transfer is performed, one more oocyte than embryo may be transferred for each prognostic category (5).

Acknowledgments: This report was developed under the direction of the Practice Committee of the Society for Assisted Reproductive Technology and the Practice Committee of the American Society for Reproductive Medicine as a service to their members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations. This report has been approved by the Executive Council of the Society for Assisted Reproductive Technology and by the Board of Directors of the American Society for Reproductive Medicine.

The members of the ASRM Practice Committee have the following potential conflicts of interest: Marc A. Fritz, M.D., Nothing to disclose; Steven J. Orvy, M.D., IntegraMed: ownership/stock, contract; Kurt T. Barnhart, M.D., M.S.C.E., Xanodyne Pharmaceuticals, Inc.: investigator, clinical trial; Third Wave Technologies, Inc.: investigator, clinical trial; Wyeth: investigator, clinical trial; William H. Catherino, M.D., Ph.D., EMD Serono, Inc.: grant/research; Ferring Pharmaceuticals: grant/research; Tokai Pharmaceuticals, Inc.: grant/research. Marcelle I. Cedars, M.D., Nothing to disclose. John Collins, M.D., Nothing to disclose. Jeffrey M. Goldberg, M.D., Nothing to disclose. Clarisa Gracia, M.D., Pfizer Inc.: grant/research. Mark Licht, M.D., Nothing to disclose. James H. Liu, M.D., Ferring Pharmaceuticals: grant/research, consultant; Wyeth: grant/research. Boehringer Ingelheim GmbH: grant/research. Teva Pharmaceutical USA Inc.: grant/research, consultant. Solvay Pharmaceuticals Inc.: consultant. Catherine Racowsky, Ph.D., MedicAll: advisory board; Schering-Plough: speaker’s bureau. Glenn Schatman, M.D., EMD Serono, Inc.: speaker’s bureau; Schering-Plough: speaker’s bureau; Ferring Pharmaceuticals: speaker’s bureau; Theraplex, LLC: consultant, ownership/stock, advisory board; Femisys Inc.: consultant, ownership/stock. Michael A. Thomas, M.D., Watson Pharmaceuticals, Inc.: consultant, BAYER HealthCare: consultant; Ausio Pharmaceuticals, LLC.: consultant; Wyeth: speaker’s bureau. Robert W. Rebar, M.D., Nothing to disclose. Andra R. La Barbera, Ph.D., Nothing to disclose.

The members of the SART Practice Committee have the following potential conflicts of interest: Glenn Schatman, M.D., EMD Serono, Inc.: speaker’s bureau; Schering-Plough: speaker’s bureau; Ferring Pharmaceuticals: speaker’s bureau; Theraplex, LLC: consultant, ownership/stock, advisory board; Femisys Inc.: consultant, ownership/stock. David Battaglia, Ph.D., Nothing to disclose. Thomas “Rusty” Pool, Ph.D., Irvine Scientific, Inc.: ownership/stock. Incept Biosystems, Inc.: consultant. Anthony Pospisil, M.D., Ferring Pharmaceuticals: consultant. Michael Reed, Ph.D., Nothing to disclose. Denny Sakas, Ph.D., Molecular Biometrics, Inc.: ownership/stock. Fady Sharara, Ph.D., EMD Serono, Inc.: grant/research; Ferring Pharmaceuticals: speaker’s bureau; Schering-Plough: speaker’s bureau. Michael Vernon, Ph.D., Nothing to disclose. Eric Widra, M.D., Nothing to disclose.

REFERENCES