What factors are important for successful embryo transfer after in-vitro fertilization?

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The success rate after treatment by in-vitro fertilization (IVF) depends on the characteristics of the couples being treated, and the performance of the clinic. The former cannot be changed, and embryology laboratories have worked hard to optimize procedures. Numerous studies have been reported on how to improve insemination and culture procedures. The clinicians’ role is confined to stimulation, oocyte collection and embryo transfer. Although each edition of journals on reproductive medicine contains some reports on various stimulation regimens, the physical aspects of oocyte collection and embryo transfer have received limited interest.

We confirmed the efficacy of transvaginal oocyte collection (Kovacs et al., 1990) and reported on the physical effects on the oocyte (Horne et al., 1996). There has been no change in the technique of oocyte collection for the last decade, and most teams are achieving harvest rates of 60–90% of mature follicles.

There has been some discussion in the journals about embryo implantation (Paulson et al., 1990; Meldrum, 1991), but mainly with respect to endometrial receptivity.

The need to revisit embryo transfer technique was highlighted by an embryo transfer workshop held in Sweden during September 1997 (du Plessis and Sjoblom, 1998). A number of conclusions were made at this Scandinavian workshop, and it was decided to compare the opinion amongst highly experienced Australian IVF clinicians. A questionnaire was devised, based on a number of possible critical factors which make up the ‘embryo transfer matrix’ (Appendix I; A. Trounson, personal communication). The findings of this survey are discussed in this paper. It must be stressed the results of the survey are based purely on the opinion of the clinicians and not necessarily on any data.

The director of each IVF Unit in Australia and New Zealand was sent a questionnaire to determine their attitude with respect to each of 12 factors which constitutes the embryo transfer matrix (Appendix I). They were requested to rate each step on a scale of one to ten, where one was irrelevant and ten was very important. The questionnaires were collected, and the information collated on an Excel spread sheet.

Questionnaires were completed by every major IVF Unit in Australia, and four in New Zealand. Some units returned a single questionnaire as the director’s opinion, others returned several, each reflecting the opinions of their individual clinicians. Overall, the cumulative experience of the 50 clinicians who have completed questionnaires, is >500 years of ‘hands on’ IVF practice.

With the 50 questionnaires rating each factor on a scale of 1 to 10, a total score for each parameter was devised out of a maximum of 500. The 12 variables were rated in order of the score they achieved. The mean ± SD for each variable is also summarized in Table I.

IVF and embryo transfer has now been carried out for 20 years. Although many modifications have been made to stimulation, the technique of embryo transfer has changed very little. The Monash team initially used a plastic cannula through which a polyethylene tube containing the embryo in 0.2 ml of culture medium was threaded (de Kretser et al., 1973). Steptoe and Edwards (1976) used a catheter passed through a sleeve in the cervical canal in 0.05 ml of culture medium. A detailed assessment of embryo transfer technique was carried out at Monash in 1980–1981 (Leeton et al., 1982) and the subsequent policy for embryo transfer was then established. As the first choice, an open catheter was used, and if difficulty was experienced then a closed end catheter was then attempted (K-METS: William A. Cook, Australia). Subsequently numerous catheters have been produced. The respondents rated ‘type of catheter’ the third in order of importance out of the 12 options. There is a need for properly designed, prospective, randomized trials to compare the success rates of various catheters.

The factor that got the highest votes was the need to remove hydrosalpinges, which is in line with a recent review (Nackley and Muasher, 1988) which found that the presence of hydrosalpinx has a negative effect on IVF/embryo transfer, the reason being suspected embryotoxicity and possible harmful effects on endometrial receptivity.

The fact that the presence of blood on the catheter or bleeding from the cervix is a negative sign was strongly supported (number two on the list). However, the negative effect of blood is probably the sign of a difficult transfer, and whether the blood per se is a negative factor is not known.

Whether bed rest is necessary, and for how long is still an issue of debate. When IVF first started, patients were rested strictly flat on their backs for 24 h. Subsequently embryo transfer became an outpatient procedure, with most women having only a few minutes rest. The clinicians survey thought that bed rest for 30 min was not important. Supporting evidence for this view comes from a report from Birmingham, UK
to the embryo transfer.

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...has not been repeated by other workers. The role of ‘mock embryo transfer’ was also rated low (tenth) by the clinicians. Some workers advocate performing this in a pre-treatment cycle (Mansour et al., 1990; Knutzen et al., 1992) with significantly better results, others just prior to the embryo transfer.

The use of anti-prostaglandins was universally discarded, but as it is recognized that cannulization of the uterus does cause contractions, and these presumably hinder implantation. Evidence for the potential negative effect on implantation that uterine contractions may cause comes from Fanchin et al. (1998). They carried out 5 min of digital recording of uterine contractions as seen on ultrasound prior to transfer. They found a stepwise decrease in pregnancy rates with lowest to highest uterine contraction frequency.

In conclusion, there is a need to further validate procedures such as type of catheter used, the role of ultrasound controlled transfer, duration of leaving the catheter in utero, the subsequent period of rest, and the use of antispasmodics by randomized, controlled trials. This is where clinicians need to take a lead role. Because of relatively large numbers needed, multicentre studies need to be organized to answer some of these questions. Al-Shawaf et al. (1993) attempted to assess the effect of ultrasound assistance, the use of the Wallace catheter compared with the Frydman catheter and the duration of resting supine, but found no difference. This may have been due to the relatively small numbers (n = 241), or their inability to unbundle the three variables.

We must stress that the findings of our survey are purely the opinions of clinicians. However, there is a relative shortage of good data and we believe that clinical studies together with better understanding of the physiology/biochemistry of implantation, identifying better embryos, and perhaps prolonged culturing in vitro will enable pregnancy rates to improve.

Acknowledgements
I am grateful to Professor Alan Trounson who devised the ‘embryo transfer matrix’ on which the questionnaire was based. I also would like to thank the IVF Directors of all Australian and some New Zealand IVF units who completed the questionnaires, and Vivien Macleaylan for her help with the statistics.

References

Table I. The relative importance of each factor as rated by the total, mean score and SD. The maximum possible score for each variable was 500

<table>
<thead>
<tr>
<th>Priority</th>
<th>Mean score</th>
<th>SD</th>
<th>Total score</th>
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<tr>
<td>1</td>
<td>6.8</td>
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<td>340</td>
</tr>
<tr>
<td>2</td>
<td>6.6</td>
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</tr>
<tr>
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<td>6.1</td>
<td>2.7</td>
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</tr>
<tr>
<td>12</td>
<td>1.9</td>
<td>1.5</td>
<td>93</td>
</tr>
</tbody>
</table>

*Only 42 clinicians responded to this question.*

(Sharif et al., 1988) which, although not a controlled trial, shows favourable pregnancy rates, despite the patients being allowed to get up immediately after the transfer. A study by Botta and Grudzinskas (1997) found that 24 h of bed rest after embryo transfer did not influence the pregnancy rate.

Not touching the fundus was thought to be the third most important factor on the clinicians’ survey. It has actually not been possible to find data on this aspect of embryo transfer. Avoiding attaching a tenaculum was the fourth most popular factor. Similar to bleeding, this probably reflects the difficulty of the transfer.

Whether the mucus should be removed, how much, and how, is still a point of debate. There is little concrete evidence on which to base any firm decisions, and the group rated this factor ‘intermediate’.

Another area which needs further assessment is the role of ultrasound monitoring during transfer. This is technically difficult, as the best way to ultrasonically view the uterine cavity is by transvaginal approach. During embryo transfer it is most difficult to place an ultrasound probe and the speculum and catheter. If abdominal scanning is used, the bladder needs to be filled, and the catheter tip is not easily visualized on the scan. The clinicians rated this number 11 out of 12, but this may reflect a lack of familiarity rather any evidence. A pilot study by our unit (Hurley et al., 1991) did not show significant difference, and the clinicians found it very difficult. Woolcott et al. (1997) found that ultrasound guidance during embryo transfer improved the placement of the catheter tip with respect to the endometrial surface. They found that endometrial movement was a significant positive factor. However, I believe that this area needs further investigation, as it is highly likely that some embryos are misplaced. A novel approach was described in a pilot study by Parsons et al. (1987) who utilized transurethral scanning of embryo transfers. This has not been repeated by other workers.

The role of ‘mock embryo transfer’ was also rated low (tenth) by the clinicians. Some workers advocate performing this in a pre-treatment cycle (Mansour et al., 1990; Knutzen et al., 1992) with significantly better results, others just prior to the embryo transfer.

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Appendix I. Questionnaire used to gauge the opinions of IVF clinicians

EMBRYO TRANSFER

It has been postulated that each of the following factors may affect the success of embryo transfers.

We are interested in your opinion with respect to the importance of each of these steps. Please rate each of the steps on a scale of 1 to 10, with 1 being irrelevant and 10 being very important.

1. A dummy run embryo transfer some time prior to the treatment cycle.
2. Clear details of the uterine cavity shape and length as diagnosed by ultrasound prior to the treatment cycle.
3. The absence of bleeding from the cervix and no blood on the catheter.
4. The use of simultaneous ultrasonic monitoring where the catheter is going using a trans-abdominal probe.
5. Leaving the catheter in place for greater than 1 minute to allow the fluid to disperse.
6. Removal of all mucus from the cervical canal prior to transfer.
7. Not touching the fundus of the uterus.
8. Bed rest for 30 min after transfer.
9. Use of anti-prostaglandins to prevent uterine contractions.
10. The type of catheter used. (Your preference............)
11. To avoid the use of a tenaculum to straighten the cervical canal.
12. Prior to the treatment cycle, remove hydrosalpinges if present.

NAME:..................................................
CLINIC:.................................................