Human Embryo Transfer

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Editors

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Don't get hung up on the hard times, the challenges. Tell your story by highlighting the victories. Because it's your victories that will inspire, motivate, encourage other people to live their stories in grander ways.

~Iyanla Vanzant

We have seen amazing progress against cancer thanks to the dedicated work of researchers around the world. Their efforts have led to new and better ways to prevent, detect, diagnose, and treat cancer. As a result, more people are living longer, fuller lives after their cancer diagnosis. We are on the brink of even more life-saving breakthroughs in prevention and treatment. This book is dedicated to these cancer researchers and doctors, who gave us the possibility of living beyond cancer.

Gautam N. Allahbadia and Claudio F. Chillik

Foreword

This monograph, entitled *Human Embryo Transfer*, edited by Dr. Gautam N. Allahbadia and Dr. Claudio F. Chillik, includes in-depth, important, new and useful information about this seemingly simple procedure, the culmination of an in vitro fertilization cycle, and which may determine its final outcome. Transferring the embryos into the uterine cavity is definitely the last and most critical step in IVF. In this monograph, Dr. Allahbadia and Dr. Chillik present their personal and vast experience, together with the work of some of the foremost authorities in the field, in order to summarize the knowledge regarding the queries that revolve around the embryo transfer (ET) procedure.

Many women undergoing in vitro fertilization cycles fail to conceive. Not all the causes can be explained and treated. Failure at the stage of embryo transfer, due to improper preparation or the transfer technique itself, should not be permissible. It has been demonstrated that about 15 % of the transferred embryos are expelled after embryo transfer. Most of these cases are caused due to poor experience of the provider or a faulty embryo transfer technique. In a recent study, it was demonstrated that when embryo transfer was performed by a senior (attending) physician, the pregnancy rate was 29.9 % and only 19.1 % for a resident physician ($p < 0.05$). The importance of a proper embryo transfer method for successful IVF cannot be overstated. Numerous methods including the use of abdominal ultrasound for proper location of the catheter in the uterine cavity, proper application of the speculum on the uterine cervix, correct loading of the ET catheter with culture medium and air bubbles, dealing with a difficult cervical canal caused frequently by an acute anteversion or antelexion of the uterus, anatomical alteration, or using a mock transfer prior to the real one, have been proposed as a means of improving the technique of ET. All these topics have been elegantly discussed here, with the respective chapters providing up-to-date evidence and suggestions.

Proper assessment of the uterine cavity before commencing an IVF cycle is important. This evaluation is accurately described in the first chapter of the monograph. Uterine contractions, as a result of the ET process, is one of the main causes for embryo expulsion, a problem that can be, at least partially, avoided. This issue as well as the interesting and most debatable facts and myths of embryo transfer have nicely been detailed in specific chapters in the book.

In conclusion, the editors have presented new and very practical data on ET, highlighting not just a “simple and routine” process of this last and critical stage of the assisted reproductive technology procedure but one that deserves more care and attention to detail. This valuable and instructive monograph will be a useful tool not only for the learning resident but also for senior physicians, who may experience difficult situations in their daily practice of embryo transfer.

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Dr. Ellenbogen has a special interest in in vitro maturation of oocytes,
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with minimal stimulation and egg donation law in Israel,
and is researching and publishing in these fields.

Received 2012, 2013, and 2014 Star Award of the American Society
of Reproductive Medicine.

Preface

In this book, we have assembled the leaders in their respective fields to update our concepts about the rate-limiting step in assisted reproduction: the embryo transfer. The embryo transfer procedure starts by placing a speculum in the vagina to visualize the cervix, which is cleansed with saline solution or culture medium. A soft transfer catheter is loaded with the embryos and handed to the clinician after confirmation of the patient's identity. The catheter is inserted through the cervical canal and advanced into the uterine cavity. After insertion of the catheter, the contents are expelled and the embryos deposited. Limited evidence suggests avoiding negative pressure from the catheter after expulsion. After withdrawal, the catheter is handed to the embryologist, who inspects it for retained embryos. There is good and consistent evidence of the benefit of ultrasound guidance to ensure correct placement, which is 1–2 cm from the uterine fundus. There is evidence of a significant increase in clinical pregnancy using ultrasound guidance compared with using only “clinical touch.” Having embryos retained in the catheter after embryo transfer is a relatively uncommon and frustrating event. The reported incidence of retained embryos varies between 1 % and 8 %. It can be difficult to explain this unwanted event to patients. Luckily, having to retransfer embryos retained in the transfer catheter does not have any significant effect on clinical pregnancy rates during in vitro fertilization (IVF) treatment cycles.

But, there are still many unanswered questions about a procedure that was first done in 1978 and is still experiencing fine-tuning. In women undergoing IVF and intracytoplasmic sperm injection (ICSI), embryos transferred into the uterine cavity can be expelled due to many factors including uterine peristalsis and contractions, low site of deposition, and negative pressure generated when removing the transfer catheter. Techniques to reduce the risk of embryo loss following embryo transfer (ET) have been discussed in this monograph. There is insufficient evidence to support any specific length of time for women to remain recumbent, if at all, following embryo transfer, nor is there sufficient evidence to recommend the use of fibrin sealants added to the embryo transfer fluid. There is very limited evidence to support the use of mechanical pressure to close the cervical canal following embryo transfer.

Improvements in vitrification now make frozen embryo transfers (FETs) a viable alternative to fresh embryo transfer, with reports from observational studies and randomized controlled trials suggesting that (1) the endometrium in stimulated cycles is not optimally prepared for implantation, (2) pregnancy rates are increased following FET, and (3) perinatal outcomes are less affected

after FET. Laboratory-based studies demonstrate morphological and molecular changes to the endometrium and reduced responsiveness of the endometrium to hCG, resulting from controlled ovarian stimulation. The literature demonstrates reduced endometrial receptivity in controlled ovarian stimulation cycles and supports the clinical observations that FET reduces the risk of ovarian hyperstimulation syndrome and improves outcomes for both the mother and the baby.

Uterine contractile activity plays an important role in the reproduction of mammals, influencing sperm transport in the genital tract and positioning of the implanting embryo within the uterine cavity. In humans, apart from the time of menses, the activity of a nonpregnant uterus is usually not perceived, and it is also not a subject of any routine clinical testing. Major contractile factors in nongravid uteri are oxytocin and prostaglandins, locally produced within the endometrium. Oxytocin synthesis and expression of its receptors gradually increase in the follicular phase, following an increase in estrogen levels, and reach their peaks in the periovulatory period. In stimulated cycles, where supraphysiological estradiol concentrations are present, uterine contractile activity can be elevated. Exaggerated uterine contractions before embryo transfer are observed in one-third of women undergoing controlled ovarian stimulation.

Detection of such patients could enable their qualification for pharmacological treatment. Evaluation of uterine contractions in such cases should be done noninvasively in order to avoid any endometrial trauma. Ultrasound evaluation of the movements of the endometrial interface can be applied, and an entire chapter in this monograph has been devoted to this topic. Pharmacological treatment of elevated uterine contractility before embryo transfer could improve the success rates of fertility treatments. So far, application of beta mimetics or nonsteroid anti-inflammatory drugs has not been associated with any progress. The oxytocin receptor system in the myometrium and the endometrium is a potential target for a new class of medications aiming to improve implantation rates.

We hope that this monograph will help not only the beginners in the field but also the well-established practitioners to update current knowledge and research in the technique and procedure of embryo transfer.

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