

## **Autologous Endometrial Coculture**

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July 25<sup>th</sup>, 1978 marked a revolutionary time in reproductive medicine—the birth of the first baby from *in vitro* fertilization. This pioneering work by Drs. Edwards and Steptoe has undergone tremendous refinements since those early days in England. The efficiency of ovarian stimulation has been improved with the use of leuprolide acetate (Lupron) and now both urinary and “genetically” derived injectable gonadotropins. The once big hurdle of fertilization has been largely overcome with the advent of microsurgical fertilization (ICSI-intracytoplasmic sperm injection) in the early 1990s. With these advances an increased number of patients are able to undergo an embryo transfer, but unfortunately the chance that an individual embryo will implant and a pregnancy result is relatively low. The cause for this may be due to the failure of chromosomally incompetent embryos (genetically abnormal) to implant, or that chromosomally competent (normal) embryos are grown in a suboptimal environment resulting in a decreased pregnancy potential. In an effort to improve the *in vitro* culture conditions and “more closely” mimic the *in vivo* environment the use of coculture was adapted to human IVF.

Coculture involves the growth of embryos on top of a layer of cells with the addition of the typical liquid media traditionally used in IVF. Initially research with mice and farm animals demonstrated that embryos grew faster on top of a layer of cells and this translated into higher pregnancy rates. There was hesitation on introducing coculture into human IVF because the cells used were either from another “donor” patient or from an animal source (cow, monkey, rat, etc.). This leads to concerns of the transmission of a viral or bacterial infection into the coculture system. Despite these theoretical concerns, in the late 1980s coculture was adapted to human IVF. Since then numerous articles have been written on the use of these “helper” cells in human IVF, demonstrating, although somewhat controversial, the improvement of embryo quality and enhancement of pregnancy rates. The government’s position on coculture with nonhuman cells changed as of April 2002. The FDA recommends that clinics using nonhuman cells must submit an investigational new drug application with the FDA following the guidelines of xenotransplantation.

In the mid to late 1990’s I was involved in the developing a unique coculture system utilizing the **patient’s own endometrial cells (Autologous Endometrial Coculture)** while at The New York Hospital – Cornell Medical Center. Extensive research and experience with this system resulted in multiple peer reviewed papers that have been presented at international meetings. The results of these studies suggest that patients with repeated failures of IVF have improved outcome with the use of this coculture system. Also, when patients with multiple failed attempts had their embryos split after retrieval and grown on conventional media (standard liquid used in IVF) versus on their own uterine lining cells (coculture), the embryos on the coculture cells were more advanced and less fragmented. We are currently offering Autologous Endometrial Coculture at Abington Reproductive Medicine in conjunction with The Toll Center for Reproductive Sciences at Abington Memorial Hospital. Currently this system is being actively used in only a few other major medical centers worldwide.

### **How does the coculture cycle work?**

Patients who are appropriate candidates for a coculture cycle undergo an endometrial biopsy in a cycle preceding their IVF cycle. This allows the removal of a small piece of uterine lining (~1-2 inches) that will be brought back to our research lab. The tissue sample will then be treated in the lab, purified and frozen until the patient undergoes their IVF cycle.

The patient’s IVF cycle will proceed as a typical IVF cycle. They will be treated with injectable medications that will cause the growth and development of multiple ovarian follicles. The patient will then undergo transvaginal egg retrieval. At this time the patient’s *own endometrial cells* will be thawed and prepared for their embryos. The day after retrieval when fertilization is confirmed, the fertilized eggs (embryos) will be placed on the patient’s *own endometrial cells*. The embryos will then be monitored on a daily basis for growth and development. On day 3 a determination will be made in regards to which embryos to transfer, as well as the possibility of further development on the coculture cells and transfer on day 5 or 6 (blastocyst transfer).

### **What are the risks of coculture?**

The risks of coculture are very minimal. Since the uterine coculture cells are derived from the same patient that will have their embryos placed on them there is no added risk of foreign viral transmission to the embryos or ethical concerns inherent with the use of animal cell lines. This complies with the most recent guidelines set forth from the FDA. The use of this system has been used in over 1000 patients with no reported side effects. Complications of uterine infection or damage occurring from the endometrial biopsy are exceedingly rare.

**What are the benefits of doing coculture?**

It is still controversial whether the use of coculture significantly improves pregnancy rates. The addition of coculture to a standard IVF cycle may enhance the culture environment and lead to improved embryo quality and pregnancy rates.

**Who is an appropriate candidate?**

Patients who have failed multiple attempts at IVF with either good or poor quality embryos. In addition if a patient has poor quality embryos after one failed IVF attempt, coculture should be considered.

**Conclusion**

The above review of **Autologous Endometrial Coculture** is intended to make you aware of a “State of the ART” technology available for IVF patients. All couples need to be evaluated on an individual basis taking into account their unique set of circumstances to arrive at an appropriate treatment plan.