As IVF success rates begin to plateau despite ongoing development in embryo culture and selection technologies, more attention is being given to understanding the role of the other participant in human implantation; the endometrium. Since the early days of IVF it has been understood that ovarian stimulation disrupts the luteal phase, and current regimens include hormonal support to sustain the early conceptus, and support implantation. However, only in recent years has the impact of ovarian stimulation on the integrity and function of the endometrium become understood.

Initial reports of advanced development of the endometrium according to Noyes histological criteria indicated that there may be a problem. Clinical studies, showing higher implantation rates when embryos were transferred to oocyte donation recipients, in whom the endometrium has not been exposed to supraphysiological levels of sex steroids, supported these observations. Elegant studies in rodents demonstrated that the duration of the window of implantation is dependent on levels of estrogen administered in the luteal phase (Ma et al 2003). At a molecular level, ovarian stimulation has been shown to impact on integrin and e-selectin expression which are key factors supporting apposition of the embryos prior to implantation. More recently, the focus has switched to the impact of ovarian stimulation on endometrial gene expression, and it has become clear that extensive gene expression dysregulation occurs during the crucial window of implantation (Horecajadas et al, J 2009).

In addition to studies looking at the impact of ovarian stimulation on gene expression, our group has developed a non-invasive means of analyzing the protein content of endometrial secretions at the time of embryo transfer in IVF cycles. Using this technique, we have identified significant effect of ovarian stimulation on the expression of a number of cytokines, chemokines, growth factors and signaling factors in the secretions of the endometrium, with which the embryo begins the molecular dialogue which will ultimately determine whether the embryo will implant successfully or not. (Boomsma et al, 2010)

The evidence for a detrimental effect of ovarian stimulation on endometrial receptivity is now clear, and raises questions as how best to ameliorate this effect. The move towards milder stimulation regimens, increasing use of cryopreservation of embryos and transfer in a natural cycle are addressing this issue. However, adjunctive therapies aimed at improving endometrial receptivity in IVF cycles have as yet not been shown to be beneficial.

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