Excellence in assisted reproductive technologies: clinical and laboratory perspectives

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The congress of “Excellence in Assisted Reproductive Technologies (ART): Clinical and Laboratory Perspectives” (<http://www.eia2016.org/en/scientific.php>), was held in Cappadocia, a unique and historic region of Turkey, on April 29–30, 2016. The aim of the congress was to present and discuss the recent advances and current controversies on clinical and laboratory aspects of ART. We were very fortunate to attract as faculty, the leading authorities, international, and national, in their respective fields and held a very successful event that allowed plenty of time for discussion. The congress was attended by just over 400 participants, scientists, physicians, embryologists, and biologists. Below are summaries of some areas of discussion providing the basis for this special issue of JARG dealing with evolving perspectives into the practice of human ARTs.

The receptive endometrium

Since we stand in an “embryo-centric” world, the term “endometrial receptivity” has wrongly posed a passive role to endometrium for years. However, contrary to common mis-

perception, the endometrium actually plays an *active* role in bio-sensing the “correct” embryo to implant and likely selects against “unhealthy” embryos to limit their development [1]. Furthermore, the preimplantation uterine environment is affected by maternal nutritional status and life style and may reprogram or modify embryo development as recently reported by Viella et al. [2]. There appears to be differential expression of secreted maternal microRNAs in the uterine environment during different phases of the human menstrual cycle [2]. When such exosome-associated or free microRNAs are exposed to mouse blastocysts, they have been shown to modulate gene expression of some molecules involved in murine embryonic adhesion [2]. These findings suggest that endometrium not only plays an active role in selection and nourishment but also in programming of the developing embryo.

Individualized controlled ovarian stimulation

Individualized controlled ovarian stimulation (COS) offers each woman the best chance of success with minimal risks in ART. The number of oocytes harvested is a well-accepted surrogate marker of live birth not only in fresh cycles [3] but also for cumulative live birth rates [4]. A recently proposed sub-group, the so-called sub-optimal responders deserves special attention [5] since this subgroup is found in 43 % of the cycles and yields 20–30 % less live birth rates, compared to normal responders from whom 10–15 oocytes are harvested [3]. Although the majority of the available therapeutic options cannot substantially alter the prognosis in poor ovarian responders, and most of the treatment modalities yield equivalent outcomes in normal ovarian responders, the sub-optimal responders could be the only group in which strategies could be tested to enhance clinical outcomes.

Capsule Meeting summary for papers presented in this special issue of JARG.

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Single or sequential culture media

Although there are numerous commercially available culture media for growing embryos to the blastocyst stage, however, it remains a matter of ongoing debate as to whether any one system provides optimal clinical outcomes. In particular, comparative efficacy and safety of the so-called single medium compared with that of the “sequential” system remains to be clarified. In this issue, the systematic review and meta-analysis conducted by Sfontouris et al. [6] concludes that there is insufficient evidence to recommend that either system as superior for culturing embryos to the blastocyst stage.

Preimplantation genetic testing

There is an increasing interest in the utilization of blastocyst biopsy for aneuploidy screening despite the lack of well designed and adequately powered randomized-controlled trials. In this issue, the patient populations benefitting from preimplantation genetic testing (PGT), as well as the level of available evidence is reviewed in the paper of Vaiarelli et al. [7]. Optimum laboratory conditions, including, extended blastocyst culture, vitrification, and blastocyst biopsy, are indispensable adjuncts if one expects to implement a successful PGT program in ART clinics; the best laboratory approaches and management strategies in this context are covered by Capalbo et al. [8].

Controversial aspects of ART

There has been an increasing interest in the frozen embryo replacement (FER) cycles due to a variety of factors. These include the availability of surplus embryos, the adoption of cryo-all cycles to avoid the risk of ovarian hyperstimulation syndrome, PGT, and concerns over the negative impact of controlled ovarian stimulation on endometrial receptivity in a fresh cycle. The available evidence for “cryo-all for all” is limited and is reviewed by Velasco et al. [9]. Moreover, the best individualized approach to prepare endometrium for FER is still a matter of debate and is covered in the systematic review and meta-analysis by Yarali et al. [10].

Testing for congenital and acquired thrombophilia is common in females undergoing ART worldwide [11]. However, current evidence does not support routine screening or treatment in the setting of ART even in patients with recurrent implantation failure and is covered in this issue by Ata et al. [12].

Despite efforts to personalize an ART cycle, luteal phase has been one of the most ignored topics. Nevertheless, new personalized, innovative strategies have recently been introduced particularly in patients triggered with GnRH-agonists

for final oocyte maturation as is covered by Andersen et al. [13]. And finally, this meeting addressed the subject of male factor as is reviewed in the article on state-of-the-art assessment of male factor infertility before ART by Esteves et al. [14].

References

1. Teklenburg G, Salker M, Molokhia M, Lavery S, Trew G, Aojanepong T, et al. Natural selection of human embryos: decidualizing endometrial stromal cells serve as sensors of embryo quality upon implantation. *PLoS One*. 2010;5(4):e10258. doi:10.1371/journal.pone.0010258.
2. Vilella F, Moreno-Moya JM, Balaguer N, Grasso A, Herrero M, Martinez S, et al. Hsa-miR-30d, secreted by the human endometrium, is taken up by the pre-implantation embryo and might modify its transcriptome. *Development*. 2015;142(18):3210–21. doi:10.1242/dev.124289.
3. Sunkara SK, Rittenberg V, Raine-Fenning N, Bhattacharya S, Zamora J, Coomarasamy A. Association between the number of eggs and live birth in IVF treatment: an analysis of 400 135 treatment cycles. *Hum Reprod*. 2011;26(7):1768–74. doi:10.1093/humrep/der106.
4. Drakopoulos P, Blockeel C, Stoop D, Camus M, de Vos M, Tournaye H, et al. Conventional ovarian stimulation and single embryo transfer for IVF/ICSI. How many oocytes do we need to maximize cumulative live birth rates after utilization of all fresh and frozen embryos? *Hum Reprod*. 2016;31(2):370–6. doi:10.1093/humrep/dev316.
5. Polyzos NP, Sunkara SK. Sub-optimal responders following controlled ovarian stimulation: an overlooked group? *Hum Reprod*. 2015;30(9):2005–8. doi:10.1093/humrep/dev149.
6. Sfontouris IA, Martins WP, Nastri CO, Viana IGR, Navarro PA, Raine-Fenning N, et al. Blastocyst culture using single versus sequential media in clinical IVF: a systematic review and meta-analysis of randomized controlled trials. *J Assist Reprod Genet*. 2016;33(9).
7. Vaiarelli A, Cimadomo D, Capalbo A, Orlando G, Sapienza F, Colamaria S, et al. Pre-implantation genetic testing in ART: who will benefit and what is the evidence? *J Assist Reprod Genet*. 2016;33(9).
8. Capalbo A, Romanelli V, Cimadomo D, Girardi L, Stoppa M, Dovere L, et al. Implementing PGD/PGD-A in IVF clinics: considerations for the best laboratory approach and management. *J Assist Reprod Genet*. 2016;33(9).
9. Garcia Velasco J. *J Assist Reprod Genet*. 2016;33(9).
10. Yarali H, Polat M, Mumusoglu S, Yarali I, Bozdag G. Preparation of endometrium for frozen embryo replacement cycles: a systematic review and meta-analysis. *J Assist Reprod Genet*. 2016;33(9).
11. Kwak-Kim J, Han AR, Gilman-Sachs A, Fishel S, Leong M, Shoham Z. Current trends of reproductive immunology practices in in vitro fertilization (IVF)—a first world survey using IVF-worldwide.com. *Am J Reprod Immunol*. 2013;69(1):12–20. doi:10.1111/j.1600-0897.2012.01183.x.
12. Ata B, Urman B. Thrombophilia and assisted reproduction technology—any detrimental impact or unnecessary overuse? *J Assist Reprod Genet*. 2016;33(9).
13. Andersen CY. *J Assist Reprod Genet*. 2016;33(9).
14. Esteves SE. Novel concepts in male factor infertility: clinical and laboratory perspectives. *J Assist Reprod Genet*. 2016;33(9).