



Bringing perspective to the next wave of human ARTs

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Published online: 1 December 2018

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2018 has brought many surprises, some resolutions to high-profile claims, and further prospects at the junction of new technology and human ARTs. Within a year's time, we have seen the publication of reports spanning the old and new when it comes to basic discoveries in mammalian reproduction and their potential applicability to the diagnosis and treatment of human infertility. Moreover, shoe-horning emergent technologies into the everyday practice of human ARTs has become increasingly recognized as a bad idea, broadly speaking, until appropriate and thorough lines of evidence are in hand fully validating safety and efficiency. Such a realization follows the fast-paced dissemination of information through media outlets well in excess, quantitatively and qualitatively, of traditional peer review and its acceptance by the biomedical research community at large.

Among the surprises, this past year has seen the transformation of gene-editing technologies from culture dishes and experimental cell models into the realm of early mammalian development, including the human embryo. Time will tell whether the recent claims from China to have produced twins bearing genetic signatures of CRISPR-based editing will be of the fanciful or factual varieties (www.nytimes.com/2018/11/26/health/gene-editing-babies-china.html). Nevertheless, this year has seen a remarkable increase in the refinement of reagents, recognition of and discourse about the phenomena of off-target hits and their consequences, and the potential corrective and investigational uses this platform has the ability to deliver. Nanosurgical toolkits for gene editing are here to stay and with the power to manipulate genomes large and small, a new level of understanding human development is on the horizon. And with that new knowledge base, the practice of reproductive medicine will be expected to make whatever adjustments are needed to achieve the highest level of patient care.

As rigorous and thorough as current ART practices have strived to be, our field suffered a serious setback with two reports of cryostorage failure in the USA. Not being unmindful of the frailties accompanying our best efforts to assure that such human errors are minimized, close inspection of our practices, protocols, and preferences is bringing improvements in the handling of gametes and embryos to forestall any such incidents in the future. Our issue next month will highlight in detail what ART practitioners need to know moving forward.

Resolving concerns about the prolongation of embryo culture prior to transfer seems to have come to a satisfactory but not immutable conclusion. Such has been the pattern in human ARTs over three decades to extend the *ex vivo* lifespan of the human conceptus, a trend paralleled by the introduction of novel media and culture conditions. And with this trend has come an expanded window of opportunity to judge embryo quality by visual observation—hominid-based or through the lens of time-lapse imaging devices—in conjunction with the necessary add-ons ranging from biopsy at day 3 or day 5, and/or assisted hatching. While the extended culture motif offers new opportunities for embryo assessment and has contributed significantly to the adoption of single embryo transfer (SET), along with this trend in practice comes a growing concern regarding the impact of an ever so brief *ex vivo* existence on the epigenetic status of the embryo and resultant offspring—a subject we are likely to see more of in the future. Opening our sights to the predictable and unpredictable is the key to managing the evolution of human ARTs.

As an example of the instructive value changes in practice provide, this month we offer our readership a special look at the process of twinning. This time, the insights gleaned from the practice of SET cause Sundaram, Ribeiro, and Noel from UCSF to cogitate on matters historically thought to have been resolved (*Multi-chorionic pregnancies following single embryo transfer at the blastocyst stage: a case series and review of the literature*, <https://doi.org/10.1007/s10815-018-1329>). And their fascinating review is followed by a companion commentary by Bos-Mikich (*Monozygotic twinning in the*

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IVF era: is it time to change existing concepts? <https://doi.org/10.1007/s10815-018-1364>).

The final perspective we introduce our followers to in looking towards 2019 is that of the Evolution-Development or EVO-DEVO movement. The importance of the environment within which organisms develop has been recognized with the growth of EVO-DEVO such that most reference now pertains to EVO-DEVO-ENV and will form the basis for adding this important topic area to the purview of JARG. Not since the 1999 groundbreaking treatise by Sarah Blaffer Hrdy (*Mother Nature: Maternal instincts and how they shape the human species*. Ballantine Publishing Group ISBN:0-345-40893-4) has a genuine effort been made to examine the reproductive strategy of humans in the context of evolution. With three decades of new knowledge to build upon, and many more animal model systems for which we have genetic insights into how species achieve successful reproduction, the time seems fitting to revisit problems so central to human ARTs and the matter of aging.

Thus, we bring to our readership two thoughtful accounts on matters EVO-DEVO-ENV. First, Paolo Navarro-Costa from the Gulbenkian Institute in Lisbon takes aim at how environments dictate reproductive strategies in the context of the aging female (*A (micro)-environmental perspective on the evolution of female reproductive aging*, <https://doi.org/10.1007/s10815-018-1355>). Lubinsky then offers a more detailed analysis that gets to the heart of why human ARTs exist given the many factors that must have played into our obvious limitations when it comes to fecundity, at least relative to the other mammals we share this planet with (Evolutionary justifications for human reproductive limitations <https://doi.org/10.1007/s10815-018-1285>).

We hope you find this issue one deserving to share with colleagues and friends during the holiday season. We look forward to sharing the next iteration of JARG with you in 2019, and thank you for your continued support.

Happy Holidays