Reproducing the most natural way-the changing face of human ARTs

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This issue of JARG takes a small measure of pride in increasing the awareness of our readership on an important new trend in the practice of human ARTs. Call it returning to a more natural way of reproducing or transitioning away from obtaining the greatest number eggs and embryos for our patients, the adoption of milder forms of ovarian stimulation for egg retrieval is taking center stage around the world. And, the most recent advances in this field are about to be take place on March 22–24, 2013 where the 6th meeting of the International Society for Milder Approaches to Assisted Reproduction(ISMAAR) will be held in Nanjing, China.

In substance, the meeting will encompass several days of talks on topics as wide ranging as biomarkers of gamete quality, fertility preservation, uterine priming and affordable ARTs. Consistent with the theme of milder stimulation, these topics will be integrated by speakers from around the world who share the common imperative to provide safer and more cost effective alternatives to patients who otherwise may have experienced adverse reactions to ovarian hyperstimulation or simply were deterred from obtaining traditional treatments due to the cost. The latter point is both timely and appropriate as efforts are extended to offer ARTs

to prospective families whose economic situation may preclude treatment.

We often measure progress in medicine by the translation of new concepts and technology into the everyday settings of differential diagnosis and therapeutic strategizing. But, every once in a while, old tricks are rediscovered in a contemporary light that afford and inform improved treatment options as a result of the déjà vu experience. Recent testimony to this trend comes from the repurposing of thalidomide for cancer therapy, the expanding the utility of folate for more than the prevention of spina bifida, and the ongoing revisitation of tamoxifen as a breast cancer preventive agent. Perhaps the poster child of such a paradigm is the natural product taxol, which while recognized in the 1950s as a promising chemotherapeutic but discarded then due to toxicity in cancer patients, and now assumes a central role in the management of breast and ovarian cancer in its reincarnated synthetic derivative .

At the heart of any back to nature approach is the conviction that the decisions to proceed in such a direction receive substantiation from the basic biology underlying, in this case, our ability to reproduce. Consider, for example, the seminal work of Professor John D. Biggers, noted mammalian embryologist and demonstrateur of the first mammalian embryo transfer (with his colleague and dear friend the late Anne McLaren). With a firm grasp on the chemical composition of tubal and uterine fluid, and controversy abounding as to why mammalian embryos would not develop in vitro, Biggers set out to formulate a medium that would allow for development of mouse embryos to the blastocyst stage. These embryos would have to withstand the test of time and that of the pertri dish since their transfer into “synchronized” recipients would have to result in the birth of live and normal young.

The approach used to reach this goal was both tedious and ingenious and was not-so casually referred to by Professor Biggers as the “back to nature” experiment.

Capsule The practice of human ARTs has progressed consistently over the past 30 years due to advances in clinical and basic science. This issue features the program, abstracts, and special contributions for the 6th World Congress on Mild Approaches in Assisted Reproduction organized by ISMAAR. The ASRM and editors are not responsible for the comments or content expressed by ISMAAR and publication of these materials does not constitute an endorsement, implied or intended.

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Firmly founded in mathematics and a stickler for statistics, Biggers deployed the Simplex Optimization protocol in arriving at a synthetic approximation of tubal fluid, the physiological environment. After many years of adding back or removing amino acids, sugars and most anything that would be anticipated to have been there in the first place for a “physiological” reason, the result was KSOM. Sound familiar? It should. The result of such heroic efforts rests in the hands of the embryologist on a daily basis in the form of KSOM and other assorted media that have followed the pathway from the bench to the embryology lab of IVF clinics around the world.

So what about returning to nature from the perspective of “controlled” ovarian stimulation (COH)? Take a close look at the cover image this month. Rendered in three dimensional splendor rests a Graafian follicle nurturing the oocyte within its comfy cumulus entourage of granulosa cells and bearing sufficient numbers of mural granulosa and theca cells that we well know form the foundation and future of a pregnancy owing to their remarkable transformation into the corpus luteum. COH, as we know it today, was the

byproduct of the rules of reproductive endocrinology laid down in the 1970s and 1980s—FSH poised on the saddle of the great savior of follicles and capable of rescuing those deemed for atresia and LH, looming in the background for thecal support of androgens, until striking at that champion moment when ovulation would be triggered and consummated. Have the “rules” changed in the 21st century? This provocateur would suggest that they have.

With the basic scientists having chimed in with their advances on how LH really conducts its ovulatory symphony, and the myriad of unanticipated actions of FSH coupled with a bewildering assortment of paracrine signaling factors released from oocytes, granulosa and theca, it would be safe to conclude that our COH protocols are well-deserving of reconsideration and likely revision!

Thus, we enter the world of ISMAAR with a purview that gives pause to an opportunity for human ARTs to change in practice and concept. We sincerely hope you enjoy this issue and the spirit of the meeting as a guide to revisiting human reproduction, the natural way!