Preserving integrity, along with fertility

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Published online: 4 June 2012
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As the northern hemisphere emerges from spring to summer, the outcome measures of yet another successful round of fertility preservation are evidenced all around us—at least for the flora and fauna that flaunt their most recent achievements under the banner of fecundity. Passing along their genetic heritage to yet another generation of germ-line carriers, variously represented by the likes of pollen, larvae, tadpoles, and all those adorable fluffy (or slimy) newborns, springtime brings with it proof-of-principle for the widespread success and utility of fertility preservation (FP) at its finest. Whether your persuasion is hibernation, cryopreservation, dessication, or just a good jolt of “game-changing” hormones to awaken your reproductive tract from a deep sleep, organisms of limitless variety take full advantage of their clever strategies to maintain and preserve their fertility until environmental cues prompt them to do otherwise. No surprise that our species has jumped on the bandwagon. But for what purpose?

The answer to this question is embedded in the drive to offer aspiring parents options for assuring that some fraction of their genetic uniqueness will be passed along to offspring, no matter what time of the year these children would be born. Unlike our multicellular, fecundity-driven companions on this planet, *Homo sapiens* has only recently pursued fertility preservation as a means to the end of reproducing. And somewhat ironically, the indications for moving this field forward derive from challenges imposed as our

reproductive lifespans wax and wane. At one end of the spectrum, salvaging gonadal function in prepubertal girls and boys whose fertility is likely to be compromised by other life-saving medical interventions has catalyzed research and clinical translation. At the other end of the spectrum lies the continuing belief that extending our reproductive lifespan by a decade or two, in order to achieve career goals is fine, as long as the medical community can offer a safe way to store gametes, gonads, or embryos (when possible) in order to evade, avoid and otherwise put asunder the naturally progressive loss of gamete quality that comes along with our farewell to fecundity. Easier said than done—this special issue of JARG casts the status of fertility preservation into a perspective of promise and problems.

It was just 5 months ago that the International Society for Fertility Preservation met in Miami to hold its second international congress. The November 2011 issue of JARG exposed our readership to the meeting abstracts reflecting as it were the “state-of-the-ART” in the rapidly expanded field of fertility preservation. Attendees of that meeting witnessed more than they bargained for, given the pace at which new technologies are being refined and signs of achievements that pertain to managing fertility for much more than the population of cancer survivors (now estimated to be 1/400 adults) that was originally targeted for such treatments. In assembling this focus issue on fertility preservation, we are fortunate to offer a series of papers of original research in this area, spanning acute care options for newly diagnosed cancer patients, network building to link reproductive medicine specialists with oncologists, and a promising 10-year follow-up report of ovarian function in women who received cryopreserved ovarian tissue transplants. With promises of manipulating the gonadal aging process in men and women through these and related technologies now capturing the attention of the public, thanks in

Capsule The rapidly growing field of fertility preservation brings practitioners of assisted reproduction advances in basic and applied science and concurrently, an opportunity to re-examine the ethical underpinnings and moral obligations of a body of work-in-progress.

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large measure to “multiple-medioma,” it is imperative that the medical community meld rigorous ethical standards with sustained deliberation, as this field continues to evolve.

A step in this direction has been taken by the ISFP Board of Directors by their recommendations published in this issue, based upon deliberations held at the ISFP meeting, last December. As a point of departure for physicians eager to adopt the tools of the FP trade, such guidelines provide a welcome beginning. This piece is followed by papers that deal with specific types of cancer patients and will hopefully provide some insight into the differing needs and requirements attendant to patients with hematological malignancies, including lymphomas, and breast cancer. Finally, a glimpse into the future of FP is provided by a series of papers covering a wide range of issues that will likely preoccupy the time and efforts of basic and clinical scientists alike.

Toward this end, our lead article comes from the work of Dr. Kim, focusing on ovarian functionality in a cohort of patients he has treated with heterotopic tissue grafting. Demonstrating a full 7 years of functionality with previously cryopreserved ovarian tissue commands attention from the dual perspective of long-term tissue banking and protracted restoration of cyclicity, an important goal for patients seeking to avert premature menopause. Oktay and colleagues continue to lead the way in designing treatment strategies for FP, compatible with the patient-specific requirements for starting an ovarian stimulation cycle and offer clinical experiences for such “Random Cycle Starts.” Dr. Gracia and her colleagues

share their experience in establishing and effecting ovarian tissue cryobanking through a consortium exemplifying the collaborative interactions required to meet the multidisciplinary dimension of patient care in the context of oncofertility. Were this not enough to digest, additional papers reveal the role that oocyte cryopreservation and *in vitro* maturation as adjunct technologies that, while continuing to evolve, are playing and will continue to play a central role in FP.

Many outstanding questions remain. Have methodologies been optimized to guarantee the genetic and epigenetic integrity of cryopreserved gonadal tissues and gametes? Are geographic and technical parameters at a stage where all patients can reap the benefits of sophisticated advances, independent of social status, financial strain, and medical indications or complications? For cancer survivors in particular, what assurances are there that when tissues are transplanted they bring with them no traces of the original malignancy that prompted seeking such a therapy in the first place? The re-introduction of cancer cells, or their cancer stem-cell progenitors, would be a devastating prospect for any individual thought to have had a new lease on life. And finally, for how long can gametes or gonadal tissues be safely stored? If the answer does turn out to be “forever,” then we may as well formally join the ranks of the endangered species and proclaim the field of fertility preservation as one having assumed the character of “Orwellian,” for better or worse.