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Editorial

After 37 Years What's in Store for IVF? A Look Ahead on the Trends and Developments That Are Shaping the Future of Reproductive Medicine

Zeev Shoham[1]* and Milton Leong[2]

[1]IVF Unit, Kaplan Medical Center, Rehovot, Israel, Affiliated with the Hadassah Medical School, The Hebrew University of Jerusalem, Israel
[2]The Women's Clinic, Hong Kong, SAR, China

The birth of Louise Brown, the world's first test tube baby, in July 1978, marked the beginning of a new era in reproductive medicine. In a world where one in every six couples encounters infertility, IVF technology was considered, at the time, no less than a miracle.

The IVF technique of the late '70s used oocyte retrieval in a natural ovulatory cycle. IVF has since become common practice, no longer regarded as a miraculous phenomenon. So far, more than 5 million babies have been born worldwide through IVF, and great strides have been made in optimizing assisted reproductive technology.

The 80's saw development in embryo culture media and stimulation protocols, as GnRH agonists were introduced. A technology of the 90's aimed to reduce male factor infertility and genetic infertility. Advancements such as preimplantation genetic diagnosis (PGD), genetic screening (PGS) and intra-cytoplasmic sperm injection (ICSI) of both ejaculated and testicular sperm were introduced.

In the early 2000, embryo cryopreservation, assisted hatching and egg donation contributed greatly to the optimal use of surplus embryos.

In the world in which we live today, it is common for women to postpone childbearing well into their fourth or fifth decade. New family types have also emerged. Advanced fertility diagnosis and treatment technologies continue to develop in accordance with these new social realities.

The purpose of this editorial is to discuss recent pivotal developments in the field of IVF that promise higher rates of successful pregnancies and healthy babies.

Trend #1: "Energizing the Egg"

A breakthrough technological development enables clinicians to use oocyte precursor cells to rejuvenate eggs of patients who previously were unable to conceive or who produced consistently poorly formed embryos. This promising technology was developed based on research conducted by Jonathan Tilly, which was published in Nature [1]. Tilly, a researcher at Harvard Medical School and Massachusetts General Hospital, discovered egg precursor cells in the ovaries of adult mice that are capable of generating new eggs. Subsequent research confirmed that these precursor cells also exist in humans and have the ability to mature into fresh young eggs that can be harvested through an ovarian biopsy. In effect, immature egg cells in ovarian tissue could be used either to form new eggs or to rejuvenate women's existing eggs. Such technology can significantly enhance the chances of conception for older women [2].

Based on this and a subsequent studies, Michelle Dipp, MD, Ph.D., Co-founded OvaScience with the vision to turn this new scientific discovery into new fertility treatments for women striving to have their own biologic children. The OvaScience team led the translation of this basic science into a process for use in clinical practice. This treatment enables scientists to obtain autologous mitochondria from these precursor cells and inject the mitochondria into the oocytes at the time of sperm injection.

Massachusetts-based OvaScience received considerable attention at several major scientific congresses during the last year, including ASRM and ESHRE. At the COGI Congress that was held in Frankfurt, Germany in May 2015, we learned that this technology already generated a successful pregnancy and that the first "OvaScience baby" was already born. In addition, in this issue of this journal, there is a paper by Fakih et al. reporting accumulated results from two IVF centers, one in Toronto, Canada, headed by Robert Casper, MD, and the other in Dubai, UAE, headed by Michael Fakih MD. It is worth noting that the Toronto group, in its 34-cycle attempts, using OvaScience's AUGMENT technology, reported an ongoing clinical pregnancy rate of 26% (9/34) and the Fakih IVF center reported 18% (11/60) per cycle initiated. The clinical pregnancy rate per AUGMENT embryo transfer was 46% and 38% respectfully in the two centers.

In summary, 93 patients, from two centers, received 328 IVF treatment cycles before the AUGMENT treatment. Following the treatment, both groups observed marked improvements in pregnancy rates above these historic IVF success rates with a 3- and 6- fold increase in clinical pregnancy rate, and an 11- and 18- fold increase in ongoing clinical pregnancy rates per initiated cycle, respectively. Embryo transfer rates were significantly higher in the AUGMENT treatment group than in the ICSI-only group.

Current OvaScience technology is based on the fact that the cytoplasmic mitochondria are the major energy source for fertilization and early embryo development. It is well known that declining mitochondrial number and function is one of the reasons why women's egg fertilization efficacy decreases, impacting pregnancy rates. Several years ago, Jacques Cohen initiated exchanging the cytoplasm into potentially compromised recipient-patient oocytes in an attempt to add mitochondria to the "older" oocyte, the objective being to improve oocyte reproductive performance [3,4]. This process was questioned by the FDA due to potential safety concerns about the donated cytoplasm/mitochondria containing minute amounts of mitochondrial DNA, and therefore resulted in a three-parent pregnancy (heteroplasmy). Therefore, this practice was abandoned. The advantage of the OvaScience treatment is that it avoids third-party mitochondria by using an autologous source. OvaScience's increased oocyte energy can be obtained clinically by autologous mitochondrial injection derived from an egg precursor cells. It will be very interesting to follow further research on this technology.

***Corresponding author:** Zeev Shoham, IVF Unit, Kaplan Medical Center, Rehovot 76200, Israel, Tel: +972-52-253-0370; E-mail: zeev1@mail.huji.ac.il

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Trend #2: Vitrification

Another technology revolutionizing IVF is vitrification, the cutting-edge cell-cryopreservation process. Vitrification technology enables women to freeze oocytes, achieving high survival rates, which were not possible until very recently. During vitrification, eggs are plunged into liquid nitrogen and instantly frozen, ensuring that this largely water-based cell does not form crystals that would expand and disrupt the egg's membrane [5,6].

This fast-freezing technique has improved the chances of frozen embryo survival. Data from a Danish study has shown that babies born from frozen embryos weigh slightly more than other IVF babies, but it is not clear whether this is due to the freezing process itself or the fact that hormones were not needed during the fertilization process.

Oocyte vitrification also allows young women to preserve their eggs, since eggs can be harvested from pre-pubescent females and stored without harm for decades. This technology impacts greatly our ability to assist women who either expect to delay reproduction or need to undergo chemotherapy treatments to fight cancer [6].

Experts predict that within the next four years, 25 percent of all fertility preservation will utilize vitrification. It will be most interesting to follow vitrification research, as we have begun to truly understand the subtle effects of freezing and thawing on embryos. In the future, it may well be that routine to freeze all embryos and transfer them in normal cycles. The key to making this technology routine is standardization, meaning the implementation of standard protocols that provide consistent (blastocyst) vitrification results.

Trend #3: Time-Lapse Technology

A third recent significant development is the time-lapse (incubator) technology, which features cameras for photographing embryos at regular intervals. Time-lapse technology leaves embryos undisturbed between fertilization and transfer, minimizing disruptive events that may harm the embryos [7].

Previously, embryos had to be removed from their incubators daily for microscopic analysis. With time-lapse technology, the embryos are monitored constantly; a computer analyzes development, giving more precise information than ever before. When examined microscopically once a day, embryos may look equally healthy and similar to one another. However, statistically only 25% of them have the potential to develop into successful pregnancies. Using time-lapse technology, we are able to gain a more detailed and continuous insights into embryo development, enabling us to determine which embryos make up the 25% with potential and to select them for implantation. For instance, research has determined that embryos with chromosomal abnormalities take more than 100 hours to reach the blastocyst stage. This means that the timing of embryo development is crucial. The computer is able to identify which embryos have delayed development with higher risk of chromosomal abnormalities [8]. Outcome of properly designed randomized controlled trials examining the role of time-lapse technology in improving IVF outcome is awaited with interest.

Technology: Propelling IVF from Its Infancy into Adulthood

To conclude, future technology trends can solve "egg factor" problems and address the challenges of implanting healthy embryos that have improved chances of generating successful pregnancies. Technology is the greatest change agent of the modern world. The enormous benefits of these new transformative technologies will contribute to the gradual reduction of egg donation as an infertility treatment, allow better monitoring of the developing embryo, enable the selection of the healthiest embryo, and preserve women's fertility capabilities, all to advance the fertility treatment process to deliver a healthy child.

References

1. Johnson J, Canning J, Kaneko T, Pru JK, Tilly JL (2004) Germ line stem cells and follicular renewal in the postnatal mammalian ovary. Nature 428: 145-150.
2. White YA, Woods DC, Takai Y, Ishihara O, Seki H, et al. (2012) Oocyte formation by mitotically active germ cells purified from ovaries of reproductive-age women. Nat Med 18: 413-421.
3. Cohen J, Scott R, Schimmel T, Levron J, Willadsen S (1997) Birth of infant after transfer of anucleate donor oocyte cytoplasm into recipient eggs. Lancet 350: 186–187.
4. Cohen J, Scott R, Alikani M, Schimmel T, Munne S, et al. (1998) Ooplasmic transfer in mature human oocytes. Mol Hum Reprod 4: 269-280.
5. Arav A, Yavin S, Zeron Y, Natan D, Dekel I, et al. (2002) New trends in gamete's cryopreservation. Mol Cell Endocrinol 187: 77-81.
6. Baldwin K, Culley L, Hudson N, Mitchell H, Lavery S (2015) Oocyte cryopreservation for social reasons: demographic profile and disposal intentions of UK users. Reprod Biomed Online DOI: 10.1016/j.rbmo.2015.04.010.
7. Arav A, Aroyo A, Yavin S, Roth Z (2008) Prediction of embryonic developmental competence by time-lapse observation and 'shortest-half' analysis. Reprod Biomed Online 17: 669-675.
8. Liu Y, Chapple V, Feenan K, Roberts P, Matson P (2015) Clinical significance of intercellular contact at the four-cell stage of human embryos, and the use of abnormal cleavage patterns to identify embryos with low implantation potential: A time-lapse study. Fertil Steril 103: 1485-1491.