Issues related to human oocyte vitrification: a consideration of the facts

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Dear Editor,

The advent of human oocyte vitrification has resulted in improved oocyte survival and reproductive potential that are equivalent to those of fresh retrieved oocytes. This has led the American Society for Reproductive Medicine (ASRM) in 2013 to change its position and classify oocyte cryopreservation as a non-experimental technique [1]. However, this change in position relied mainly on small-scale trials that came from the most experienced reproductive centers. Indeed, the ASRM had emphasized this fact and questioned whether the results of these trials can be generalized and reproduced in other fertility centers. However, since this change in committee position, there has been an increase in cycles that utilize vitrified oocytes, for the purpose of generating commercial banks of donor oocytes and for fertility preservation [2]. Although limited data is available on the outcomes of these cycles, the recent results show a persistently worse outcomes when using vitrified compared to fresh oocytes [3]. These worrisome results are particularly relevant to women who cryopreserve oocytes for social or medical reasons, for whom, this maybe their only hope to have their biologic offspring. This highlights the need of reproductive centers offering fertility preservation for continuous surveillance of the laboratory techniques to ensure consistent results. The following case can be an example of this issue.

A 36-year-old healthy woman underwent three consecutive fertility preservation cycles which yielded a total of 43 MII

oocytes that were vitrified. The oocytes from the first and second cycles (14 and 12 oocytes respectively) were vitrified by two senior embryologists and the oocytes from the third cycle (17 oocytes) were vitrified by a junior embryologist. Seven years later, at the age of 43, the patient returned for fresh IVF cycle with a partner. The patient opted also for oocytes thawing and fertilization. All the oocytes were thawed on the same day by the same embryologist. There was a significant difference in the oocyte survival rate between the three groups of oocytes: 71.4% (10/14) and 70.5% (12/17) for the first and third cycle, and 16.7% (2/12) for the second cycle ($p = 0.04$). These resulted in the formation of 18 embryos; of these, 8 were found to be euploid when tested by comparative genomic hybridization (CGH). Furthermore, four embryos were obtained from the fresh cycle; however, all were aneuploid when tested by CGH. Two embryos were transferred on day 5; however, pregnancy was not achieved.

Three important points can be drawn from this case. First, as expected, oocyte vitrification for social fertility preservation is a way to obtain euploid embryos for use at an advanced age, when oocyte aneuploidy rate is high. This is not surprising, but has been minimally demonstrated. Secondly, oocytes can be vitrified for long periods (7 years in this case) and yet can survive, fertilize, and result in the formation of euploid embryos. The third point is that slight intra-laboratory variations in vitrification technique can result in different oocyte survival rates, even when performed under the same laboratory protocol.

A recent study that analyzed the outcomes of oocyte donation cycles in the USA showed that between the years 2013 and 2015, there was a 44% increase in the utilization of vitrified oocytes along with a 33% decrease in the use of fresh oocytes [4]. However, cycle cancellation rates in vitrified-thawed oocytes cycles increased from 8.5 to 15% compared to a decrease from 11.7 to 9.1% in cycles that used fresh oocytes between these years. This increase in cycle cancellation among vitrified oocyte cycles is likely related to lower oocyte survival rate and a lack of viable embryos to transfer. Furthermore, the live birth rate per recipient cycle start was

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lower in vitrified compared to that in fresh oocytes cycles (51.1 vs. 39.7%, $p < 0.001$) [4]. These lower results in outcomes despite an increase in the utilization of vitrified oocytes may reflect the spreading of the practice from centers of excellence to the average reproductive centers [5].

In the era of delayed child bearing, it is expected that the utilization of vitrified oocytes will increase further. The worse results in outcomes that are shown in the “real world” practice should urge for optimization of the vitrification and thawing procedures that will ideally be automated with minimal reliance on manual techniques. Initial results of automated systems for oocyte vitrification have shown promising results [6]; however, more studies are needed until these systems can be used in the daily practice. Further, reproductive centers should track laboratory performance to ensure consistent results, and accordingly these results should be incorporated during patient counseling.

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