Are commercial egg banks all they are cracked up to be?

The use of donor oocytes has increased markedly in the past 10 years, accounting for approximately 16.5% of transfers performed in the United States in 2018 (Society for Assisted Reproductive Technology [SART] online access). As eloquently predicted by Akin et al. (1) in 2007 with the first reported clinical utilization of a commercial egg bank (CEB), CEBs have now become "part of the landscape of donor egg IVF." Commercial oocyte banks offer increased efficiency of third-party reproduction with reduced recipient wait times, increased donor diversity, and potentially decreased excess embryo wastage and storage.

In the adjoining article, Williams et al. (2) provide an analysis of success rates with donor oocytes that are cryopreserved and shipped to in vitro fertilization (IVF) programs from CEBs compared with donor oocytes from program-generated donors, that is, donors undergoing egg aspiration at individual IVF programs inseminated without previous vitrification (fresh). Their data included the first year the identified source of donor eggs was reported to the SART through the most recent year of finalized data (2016–2018). They report similar live births rates irrespective of oocyte source with the first single embryo transfer cycle (program-generated donor vs. CEB, 55.4% vs. 53.3%, respectively; odds ratio [OR], 0.92; $P=.026$).

We must interpret these data regarding live birth rates with fresh vs. cryopreserved oocytes with caution. As the investigators rightly pointed out, the data field regarding fresh or previously cryopreserved oocytes may have been reported inaccurately. Member clinics reported 30.6% of CEB donor cycles as using "fresh oocytes," which is logistically impossible.

In addition, the covariates such as age and body mass index (BMI) are not reported based on oocyte source (CEB vs. program). A true confounder is a risk factor for outcome and is associated with study exposure, although not a consequence of exposure. They only show results for outcome but not exposure (program vs. commercial). Table 1 lists the number of oocytes retrieved but also does not indicate source as program vs. commercial. The investigators state that the number of oocytes retrieved per stimulation is reported to the SART for both program donor cycles and egg bank cycles, yet CEBs typically do not provide that information to the treating clinic. This makes the comments concerning egg number in the discussion about overstimulation of commercial donors confusing as well as how to interpret higher implantation rates with higher numbers of oocytes (>16), which would occur more often with fresh oocyte retrieval and less so with CEB oocytes.

Interestingly, the online SART data for the years of interest (2016–2018) report approximately a 10% difference in live birth rates with fresh donor oocytes compared with frozen donor oocytes (2016, 50% fresh donor vs. 39.4% cryopreserved donor oocytes; 2017, 49.2% fresh donor vs. 43.1% cryopreserved donor; 2018, 50% fresh donor vs. 39.0% cryopreserved donor). These are unadjusted data but deserve attention. A 2018 publication examining SART data from 2013 through 2015 found that the use of cryopreserved donor oocytes increased by 44% but resulted in significantly lower live birth rates compared with fresh donor oocytes (39.7 vs. 51.1, respectively; $P\leq.0001$) (3). Another analysis of the 2013 SART data also found a decreased likelihood of pregnancy (adjusted relative risk [aRR], 0.88; 95% confidence interval [CI], 0.81–0.95) and live birth (aRR, 0.87; 95% CI, 0.80–0.95) with cryopreserved donor oocytes (4).

This article notes a decline in pregnancy with increasing age and BMI. The investigators adjust the data for a comparison group that is <30, with normal BMI and a blast transfer. Some of the reduction in differences noted from the unadjusted SART data may occur after adjustment of different variables, such as BMI and age. Therefore, after adjustment are the similar pregnancy rates reported by Williams in the 2 groups due primarily to differences in the demographics of the 2 populations, that is, are fresh donor recipients younger and thinner? As noted earlier, these variables are not shown between the 2 groups. Table 2 lists the logistic estimates of the adjusted OR to live birth. The adjusted ORs for fresh and CEB oocytes were 1.24 ($P=.047$, 1.00–1.54) and 0.92 ($P=.026$, 0.85–0.99), respectively. Furthermore, their adjustment was performed by including age and BMI as covariates in the logistic model, which at times can be problematic and hide the true associations particularly because no test of interaction was performed. If age and BMI are true confounders, a more efficient adjustment would have been stratification on those variables.

Why is our commentary leaning toward critical examination? This study raises the following question: will CEBs soon replace program-generated donation and be subject to the same oversight as donor sperm? Currently, quarantine of oocytes is not required by the Food and Drug Administration for nonidentified (anonymous) or directed donation. The American Society for Reproductive Medicine Committee Opinion concludes with "moderate evidence" that the pregnancy rates per transfer between fresh and previously vitrified donor oocytes are not significantly different but advocate for more data regarding cumulative live birth rates with cryopreserved donor oocytes. If outcomes truly do not differ among fresh vs. cryopreserved donor oocytes, are we compelled to manage donor oocytes similarly to that of donor sperm? A decade ago, the American Society for Reproductive Medicine delayed declaring egg cryopreservation as nonexperimental with some of these concerns and as how few IVF laboratories had demonstrated proficiency with egg vitrification, and they instituted programs with the SART and Society of Reproductive Biologists Technologists to address it. Thus, that this data would be used to eliminate the option of fresh oocytes is very concerning, particularly because we are not yet able to support the "noninferiority" of CEBs on the basis of these data by Williams et al. (2).

Additionally, at an estimated mean cost per oocyte of $2,225 and a recommended minimum of 6 oocytes per cycle

(5), is utilization of a CEB cost-effective, as further costs of intracytoplasmic sperm injection, culture, and embryo transfer still must accrue? An appropriate cost analysis remains to be determined. This is mentioned in the article by Williams et al. (2) as often only 6 oocytes are obtained per CEB cycle and multiple rounds of fertilization and culture may occur.

As third-party reproduction and oocyte cryopreservation continue to increase, more data regarding the utilization of CEB s is needed. CEBs offer an additional option for patients undergoing assisted reproductive technique, yet we believe fresh oocyte donation is still the "gold standard" for our patients and should not be eliminated by regulation.

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