

# Oocyte Cryopreservation Results Have 'Arrived'

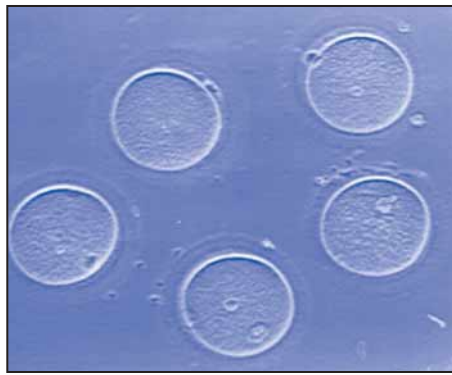
BY KATE JOHNSON  
Montreal Bureau

MONTREAL — Preliminary results from an ongoing study of oocyte cryopreservation show “the highest pregnancy rates so far reported,” making egg freezing “a viable clinical option,” according to Dr. John K. Jain, the principal investigator.

“Egg freezing has turned a corner—it’s arrived,” said Dr. Jain, of USC Fertility, the nonprofit fertility practice of the University of Southern California’s Keck School of Medicine, Los Angeles.

A total of 20 women (mean age 31 years) have been enrolled in the study, which provides them with in vitro fertilization at no charge. To date, five of eight women have become pregnant after having their eggs removed and frozen for 1 month, then thawed and fertilized by intracytoplasmic sperm injection, followed by subsequent embryo transfer.

He reported the findings in a poster at



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Slow-freezing methods are believed to contribute to high pregnancy rates.

the joint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society.

A recent metaanalysis of all published frozen-egg pregnancies (118) suggests a worldwide live birth rate of 21.6% per transfer in women with a mean age of 33 years, reported Dr. Kutluk Oktay in a separate presentation at the meeting (see accompanying story). Unpublished data from the World Congress on Human Oocyte Cryopreservation suggest that the highest U.S. success rate until now has been a 34% pregnancy rate per transfer at Assisted Fertility Services of the Community Health Network in Indianapolis.

Dr. Jain attributes the success of his egg freezing protocol to a combination of culture medium and freezing method. The center uses a slow-freeze protocol in sodium-depleted, choline-substituted medium.

Two of the five women have delivered singletons, with the other pregnancies (including a set of triplets) well into their second or third trimesters, he said.

Each transfer procedure included an average of 3.2 embryos, compared with an average of 2.7 embryos per transfer reported in the egg freezing metaanalysis.

The American Society for Reproductive Medicine currently recommends that in women younger than 35, no more than two embryos should be transferred; it also recommends that consideration be given to single embryo transfer in patients with the best prognosis.

The optimal number of embryos to transfer following oocyte cryopreservation is still undetermined, Dr. Jain said. ■

## In Vitro Fertilization Still Best Bet for Those Considering Future Fertility

MONTREAL — Women who freeze their eggs at age 33 hoping to pause their biological clocks are actually no better off than if they simply underwent a fresh IVF cycle—if necessary—at age 42, according to new research.

The first metaanalysis of oocyte cryopreservation success rates shows the technique is 4-5 times less efficient than standard in vitro fertilization with fresh oocytes, reported Dr. Kutluk Oktay of Cornell University, New York.

A total of 118 babies worldwide have been born from frozen oocytes—97 from the slow-freeze technique and 11 from vitrification techniques, Dr. Oktay said at the joint annual meeting of the American Society for Reproductive Medicine and the Canadian Fertility and Andrology Society. Previous estimates of about 180 frozen-egg births might have been confused by overlapping reports in the literature, he explained.

Dr. Oktay compared data from the 118 frozen-egg pregnancies with data from a control group of 397 fresh intracytoplasmic sperm injection (ICSI) transfer

cycles. Women who had cycles involving frozen eggs had a mean age of 33; those who had ICSI cycles, mean age was 33.6.

Assessment of the number of live births per injected oocyte shows the rates in the frozen-egg cycles were 3.4% (slow freeze) and 4.5% (vitrification), compared with 6.6% in fresh IVF/ICSI and 7.5% with the addition of subsequent frozen-embryo transfers.

There are insufficient data to assess the vitrification method, he said, but compared with slow-freeze oocyte cycles, fresh IVF plus subsequent frozen embryo cycles had an implantation rate per transferred embryo almost four times higher (36.9% vs. 12.8%; odds ratio 3.68).

Similarly, live births per transfer were significantly higher (OR 3.58) in the fresh-IVF/frozen-embryo cycles (50%) compared with slow-freeze oocyte cycles (21.6%).

Egg freezing in women aged 33 has success rates comparable with those achieved using fresh IVF in women aged 41 and 42 years, he concluded.

—Kate Johnson

## DRUGS, PREGNANCY, AND LACTATION

### Inhaled Corticosteroids and Fetal Growth

The widespread prescribing of corticosteroids in medicine includes many clinical situations during pregnancy, which naturally raises concerns about the safety of these drugs in pregnant women. Over the past several years, information on this topic has begun to accumulate, providing stronger evidence about the safety of inhaled corticosteroids in this population.

Most recently, in October, the largest study to date, conducted by the Organization of Teratology Information Services (OTIS), on the use of medications for asthma during pregnancy and their effects on fetal growth was published. The main finding was that treatment of pregnant women with  $\beta_2$ -agonists and inhaled steroids did not have adverse effects on fetal growth and that systemic corticosteroids had a minimal effect on birth weight and length.

The prospective study compared birth size and the incidence of babies born small for gestational age (SGA) in 654 infants whose mothers had taken inhaled or systemic corticosteroids and  $\beta_2$ -agonists for asthma during pregnancy with birth size and incidence of SGA in 303 infants whose mothers did not have asthma. Women from North America were enrolled between 1998 and 2003. There were no significant differences in the incidence of SGA for weight between the groups. There was a small reduction in birth weight among those exposed to systemic steroids: In this group, the mean birth weight, adjusted for other risk factors, was 3,373 g, compared with a mean of 3,540 g among controls, 3,552 g among those exposed to  $\beta_2$ -agonists only, and 3,524 g among those exposed to inhaled steroids.

Mean birth weight and mean birth length, adjusted for risk factors, among infants whose mothers had been treated with inhaled steroids were not significantly different from those of controls or of infants whose mothers had used  $\beta_2$ -agonists only. The adjusted mean birth lengths were 51.3 cm in the inhaled steroid group and 51.5 cm in the  $\beta_2$ -agonist group.

The authors, from the University of California, San Diego and the OTIS Research Group, concluded that these results were “reassuring and support the recommendations of adequate control of severe asthma during pregnancy,” and that “the modest effect of systemic steroids on fetal growth should be weighed against the necessity to achieve adequate control of severe persistent asthma and to prevent hypoxia during pregnancy” (J. Allergy Clin. Immunol. 2005;116:503-9).

While these conclusions are not novel, this study is a major breakthrough

because it combines information from teratology information centers in North America to provide much larger numbers than were available previously.

Women and physicians should be informed there are some risks: In 2000, my colleagues and I published a meta-analysis of all available studies of women who were given high-dose steroids during pregnancy for various reasons. The results clearly indicated that the use of systemic steroids during the first trimester was associated with a

two- to threefold greater risk of oral clefts. This finding was consistent with extensive animal data that have shown the same association.

However, inhaled corticosteroids, commonly used as first-line therapy for asthma, result in an extremely low systemic dose, and none of the available reviews on the use of inhaled steroids during pregnancy have

found any association with a greater risk of oral clefts. The  $\beta_2$ -agonist albuterol is not teratogenic.

There is emerging evidence that repeated weekly corticosteroid injections for fetal lung maturation in cases of premature rupture of the membranes may result in brain damage in some babies. But this is not relevant to the use of inhaled corticosteroids in pregnant women with asthma.

Therefore, based on this recent study and previous data, pregnant women should be encouraged not to neglect their asthma therapy because of concerns about potential effects on the fetus. The risks include higher rates of perinatal complications, mostly prematurity, when asthma is poorly controlled. We are aware of fatal cases of women who stopped much-needed asthma treatment during pregnancy.

The authors of an editorial accompanying the OTIS study state that inhaled steroids “do not seem to significantly impair fetal growth,” but add that “before ruling out with confidence any potential adverse effect” of inhaled steroids on fetal growth, “there is a need for larger studies adequately powered to answer this question” (J. Allergy Clin. Immunol. 2005;116:501-2). While I agree we always need more studies, the risk-benefit ratios should dictate optimal treatment of maternal asthma.

DR. KOREN is professor of pediatrics, pharmacology, pharmacy, medicine, and medical genetics at the University of Toronto. He heads the Research Leadership in Better Pharmacotherapy During Pregnancy and Lactation at the Hospital for Sick Children, Toronto, where he is director of the Motherisk Program, a teratogen information service ([www.motherisk.org](http://www.motherisk.org)).



BY GIDEON KOREN, M.D.